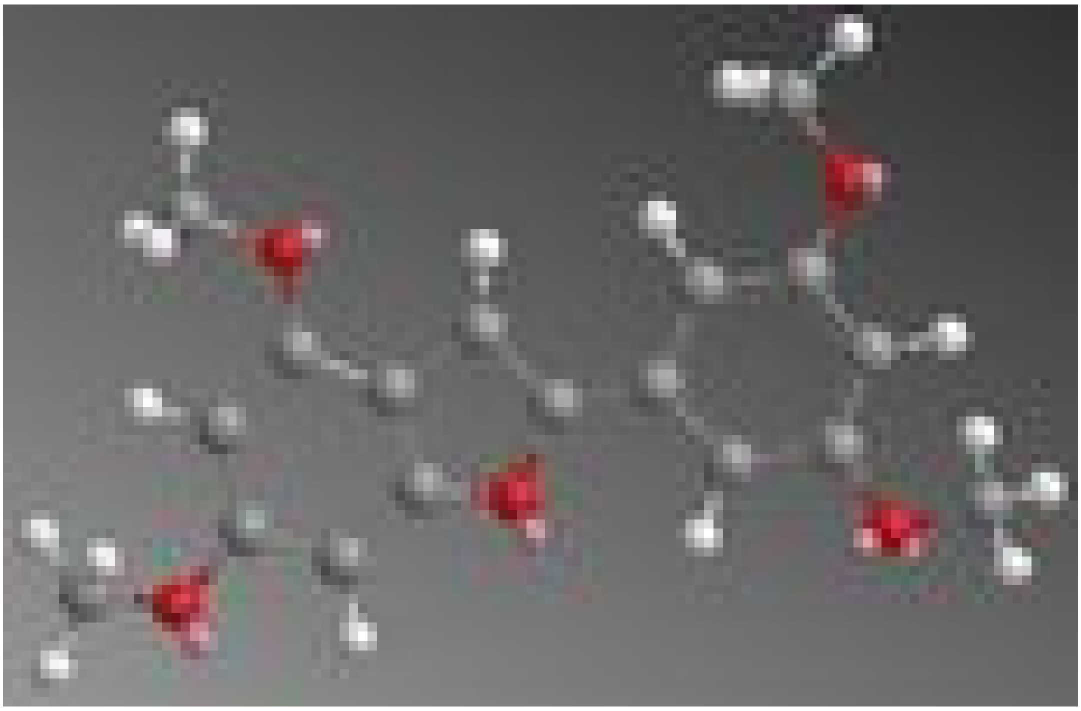
ζ ȷ ū ȷ Λζ ȷ ŦΆƗ ȼ ĦŦ ¢ Ɇ
ŦɃũ ʔ ɋ ɆĿj Ɇ Ŧȷ Łĵ ¢ ζ ΆĿj Ɇ ū ƗɆĦŦ ɋ ʔ
ŨΛɃĦɃ ʔ ȼ ɋ ʔ
ɋĦΆƗ Ū Ɨ ʔ ȼ ¢ Ɇ: Ŧȷ Ū¢ ũ¢ ȼ ¢ Ɇ ɆŦȷ ȿ ȼ ɆɃƗ ʔ ¢ Ɇ ȷ ȿ Άʔ ĦɃɆ-
ȿ Άȷ ʔ ɋΛɃɆ

Ɇĵ ΆɋĿȷ Ɇζ ɃɆ, ɆƗ ʔ ŪΆɆ¢ Ŧȷ ŁđĦɃȿ ɃũĦŦ¢ ȷ ʔĦɃȿ Ƀũ¢ Ɇ¢
ȷ ʔȷ ȿ Ƀũɋ ʔ 2-ȷ ΛƗ ȿ ɃđΆʔ ȻɃū ɃƗ Λȷ ʔĿɋ ʔ



ζ Άȼ ȷ Ũȼ Ɨ ĵ Łȷ ŦɃ ɋĦŨȿ ɋ ζ ȷ ΆĿɋĦŦΆƗ Ɇ¢ Ɇ

Ɇȷ Ũū ɋ ɋ¢ ζ ¢ ȼ Λȷ ŦɃƗ ɋ¢
ū ȷ Λζ ȷ ŦɃŨɃĦɃɆ
ȷ Ū¢ ʔȷ 2011

Ȼ Ⱦȷ Ƚɉ ¢ ȥ ȺȽȷ Ɇ ū Ʉ ɆȽȾ q ʔ ɄɅȻȻʔ ɇ q ʔ ȷ ɄȻȥ Ȼ ʔ q Ɇ¢ -ȷ ʔ ȷ Ʉɇ Ʉ ɂ ¢ -Ʉȷ Ʌȷ ũq ũ¢ Ⱦȷ ȽȺȿ Ⱥũɉ ȻɆ ȡȽȻ qɅȷ Ɇɇ ȽȾ q ʔ ū Ʉ ɆȽȾ q ʔ ɄɅȻȻʔ ɇ q ʔ

ɇ Ƚɇ ȿ ȻɆ ȥ Ⱥɇ ȷ Ʉɇ Ʉ ɉ Ƚȷ ȾȻ Ʉ qȽɄȿ q ȥ ȷ ɇ ȻɆ ȺȽqȽȾ ȺɄ Ɇ¢ Ɇ:

Ɇɉ ȺqȽȷ Ɇȥ ȻɆ, ɆɄ ʔ Ū ȺɆ¢ Ⱦȷ ȽȡȽȻȿ Ȼũ ȽȾ¢ ȷ ɂ ȽȻȿ Ȼũ ¢ Ɇ¢
ȷ ʔ ȷ ȿ Ȼũq ʔ 2-ȷ ɅɄ ȿ ȻȡȺʔ ȻȻ ū ȻɄ Ʌȷ ʔ Ƚq ʔ

Ɇȷ Ʉ ū q q¢ ȥ ¢ ɇ Ʌȷ ȾȻɄ q¢

ȷ .ȥ . 2802-12

ū ȷ Ʌȥ ȷ ȾȻɄȻȽȻɆ

ȷ Ū¢ ʔ ȷ 2011

Ⱥ´ ɘɓəɏ´ ɤ ɜ Ⱦ Ŭɗɖɔɖ Ű ɐ ɠ: Ⱥ´ ɷɞɡɟ ɞɠ Ⱦ Ŭɗɖɔɖ Ű ɐ ɠ ȷ əɖɔɘƳɜɜɖɠ ʔ Ůə ŰƳɟ ɘɜɠ **ɇ ɟ ɶ Ůəɐ ɠ Ů ɘŰɟ ɞ´ ɐ** : Ⱦ Ŭɗɖɔɖ Ű ɐ ɠ ə. ȷ əɏɜɘɜɠ-ȿ ɏŬɜŭɟ ɞɠ Ɇə Ŭə Ű ůɞɨ ɜɖɠ, Ⱦ Ŭɗɖɔɖ Ű ɐ ɠ ə. ȡ Ű ůɷə Ůɜɠ Ʌɞɨ ůůɖɠ, Ⱥ´ ɷɞɡɟ ɞɠ Ⱦ Ŭɗɖɔɖ Ű ɐ ɠ ȷ əɖɔɘƳɜɜɖɠ ʔ Ůə ŰƳɟ ɘɜɠ.

ΛΒȿ ȸûȸɆ

ζ dŬ ΄ɞǝɨ Ůȝŭɘ Ŭűɏɉ ɞgůŬ ɞɛŸűŬ ɞgůɘ ȝ, ɔȝɤ ůŰɐ ɤɠ űgŰɞɞůŲɞɔɧȝŬ, ɏɢŮɘ Ŭȝɕȝ ŮgŰŰɑ ůŮŬ űgŰŸ ΄ɞg Ŭȝɐǝɞgȝ ǝgɉ ɑɠ ůŰɖȝ ɞɘɞɔɏȝŮȝŬ Leguminosae. ɉ gŰɏɠ ɞɘ Ůȝɩ ůŮɠ Ůɛ űŬȝɑɞgȝ ɛŮȝŸǝɖ ůgɔɔɏȝŮȝŬ ůɨȝŭŬůɖɠ Űɞgɠ ɛŮ Űɞgɠ ɞɘůŲɞɔɞȝɘɞɨɠ g΄ɞŭɞɢŮɠ, ɛɛɞɨɛŮȝŮɠ ůŮ ǝŸɞɘgɠ ɘůŰɞɨɠ Űɖȝ ŭɉŸůɖ Űɤȝ ɞɘůŲɞɔɧȝɤȝ (ůgȝŬɤȝɘůŰɘɐ ŭɉŸůɖ) ǝŬɘ ůŮ Ÿǝǝɞggɠ ŬȝŰŰɤȝɘɛɧɛŮȝŮɠ Űɖ ŭɉŸůɖ Ŭgű ȝ (ŬȝŰŰɤȝɘůŰɘɐ ŭɉŸůɖ). ŎȝŬɠ ůɖɛŬȝŰɘɧɠ Ųɉɘɖɛɧɠ 2-Ųɉgǝɞɓ Ůȝɛɞűɞgɉ Ŭȝɑ ȝ Ŭȝɐǝɘ ůŮŬgŰɐ ǝŬŰɖɔɞɉdŬ Ůȝɩ ůŰɤ ȝ.

ɇŬ ŰɘŮgŰŰdŬ ɢɉɧȝɘŬ ǝŬŰŰɓŸǝǝŮŰŰɘ Ŭɧ Űɞ ŲɔŬŭŰɐɉɛ ɛŬɠ ůgůŰɖɛŬŰɘɐ ΄ɉɞů΄ ŸdŮɘŬ ůŰɖ ɛŮɏŰɖ Űɤ ȝ űgŰɞɞůŲɞɔɧȝɤȝ ǝŬɘ ɏɢŮɘ Ŭ ɞǝŰɖɖŮɑ ɛŮȝŸǝɖ Ůɛ΄ ŲɉdŬ ůŰɖȝ ɢɖɛŮŬŬŰɤ ȝ 2-Ųɉgǝɞɓ Ůȝɛɞűɞgɉ Ŭȝɑ ȝ ǝŬůgɔǝŮɉ ɛɏȝŬŰɤ ȝ Ůɛ΄ ȝűɞgɉ Ŭȝɑ ȝ. ¢ ɛŮɏŰɖ Űɖɠ ɓɛǝɞɔɞɘɐɠ ŭɉŸůɖɠ ɛdŬɠ ůŮɉŸɠ ȝɏɤ ȝ ɛɞɉɑ ȝ Űɖɠ ǝŬŰɖɔɞɉdŬɠ Űɤ ȝ Ůɛ΄ ȝűɞgɉ Ŭȝɑ ȝ, ŰŬ ɞ΄ɞdŬ ɏɢɞgȝ Ŭ ɞɛɞȝɤ dŮɑ ǝŬŰŸ Űɖȝ űgŰɞɢɖɛɘɐ ɛŮɏŰɖ Űɞg *Onobrychis ebenoides* Boiss & Spruner Űɖɠ ɞɘɞɔɏȝŮŬɠ Leguminosae, ɏɢŮɘ ŭŮůɘ ΄ɤɠ ŭɘŬdɏŰɞgȝ ɘɢgɉɐ ɘŮɧŰɖŰŰ ůɨȝŭŬůɖɠ ɛŮ Űɞȝ ɞɘůŲɞɔɞȝɘɧ g΄ɞŭɞɏŬ ǝŮ ɏŰɘɘ ŭɘŮɞǝɞɔɖɛȝŬɏɢɞgȝ ǝŬŰŰŰŮɢdŮɑ ůŰɖȝ ǝŬŰɖɔɞɉdŬ Űɤ ȝ űgŰɞɞůŲɞɔɧȝɤ ȝ. ¢ ɔȝɩ ůɖ ΄ɞg Ŭ ɞǝŰɐɖɖǝŮ΄Ÿȝɤ ůŮ ŬgŰɐ Űɖȝ ǝŬŰɖɔɞɉdŬ Ůȝɩ ůŰɤ ȝ Ŭǝǝ Ÿ ǝŬ Űɞ ɘŭɘŬŭŰŲɖɠ ůɖɛŬŭŬɠ ɓɛǝɞɔɘɐ Űɞgɠ ΄ɉɞűɑ, ɛŬɠ ɞŭɐɔɖůŮŮɞ ȝŬŰŭɢɞǝɖɖɨɛŮɛŮŰŰ ΄ ŲɉŸɖɤ ɔŬ Ŭgű.

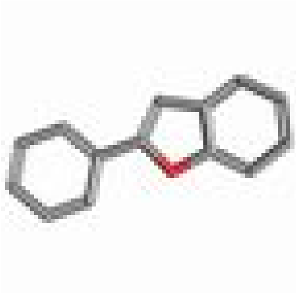
¢ ΄Ųɉɞɨ ůŬɛŮŰŰ ŰɞɢɘŬɐ ŲɔŬŭŬŬɏɢŮɘɨɞ ůŰɧɞgɠ:

1. ɇɖ ůɨȝɖŬŭɖ ɛdŬɠ ůŮɉŸɠ 2-Ųɉgǝɞɓ Ůȝɛɞűɞgɉ Ŭȝɑ ȝ, Űɖ ɓɛǝɞɔɘɐ Űɞgɠ ŬȝŰɘɢɔɞɖůɖ ǝŬ Űɖȝ ŬȝŸ Űɧȝɖ ůɢɏůȝɤ ȝ ŭɞɛɐɠ - ŭɉŸůɖɠ
2. ɇɖ ůgȝɖŰŰɘɐ ΄ŲɉŬŭǝŮɐ Űɤ ȝ űgůɘȝ ȝ Ůɛ΄ ȝűɞgɉ Ŭȝɑ ȝ Ⱶ ǝŬ ⱧⱧ ůŮ ΄ɞůɖŰɖŰŰ ɘŬɐ ɔŬ ȝŬ ǝŬŰŰůŰŰɑ ŮɘɘŮɐ ɖ Ŭȝɘɢǝɖůɐ Űɞgɠ ůŮ *in vivo* ΄ŲɉŬɛŬŰŰɘŸɛɞȝŰɏǝŬ.

Ť Ůíŷə Ůɜɛ 1ɛ

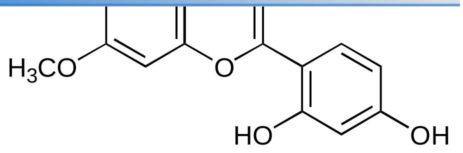
ŪÆq Λ¢ ɇ ŦŤ Ƀ ɀ ÆΛɃƁÉ

[illegible] (Aslam et al., 2006). [illegible] (Luca et al., 2008). [illegible]

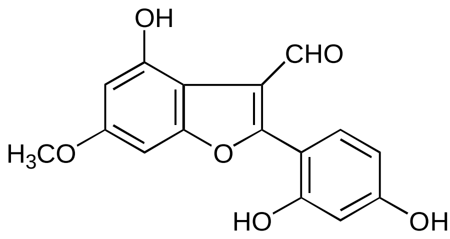


[illegible] 2-[illegible] (Halabalaki et al., 2008). [illegible] 2-[illegible] (SERM) (Papoutsi et al., 2004).

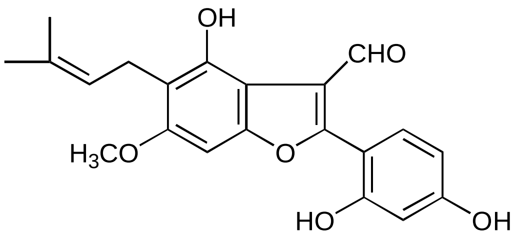
Ʉɞǝǝ Ŭ ǝɏɠ Ů ʂűɖɛɜǝɞɔɜɏɠ ɛŮǝɏŰŰɠ , ɛŮǝɏŰŰɠ ůŮ ´Ůɟ ŬɛŬŰɦɛɤ Ŭ ǝŬǝ ůŮ ʂůŰɞǝŬǝǝɘɟɔŮŰɠ, ɏűŮɞŬǝ ɧŰǝ ŰŬ űɡŰɞʂůŰɟ ɞɔɧɜŬ ɏɞɞɡɜ ŬɞŬɓɞǝɘɏɠ Ů ʂűɟ ŸůŮɠ ůŰŬ ɞůŰŸ ǝŬǝ ɑůɤ ɠ ɛ´ɞɟɞɨɜ ɜŬ ´ɟɞűɡǝŸůůɞɡɜ Ŭ ɧ ǝŬɟǝɑɞ Űɞɡ ůŰɟɖɞɡɠ ǝŬǝ Űɞɡ ´ɟɞůŰŸŰɖ. Ά´ɘ´ǝɏɞɜ, ŮɞŬǝ ´ɘŬɞɧɜ ɜŬ ɏɞɞɡɜ ŰɡŰɔŬŰŰɟɐ Ů ɑɟŬůɖ ůŰɟɠ ǝŮɘŰɞɡɟɔɖɠ Űɞɡ Ůɞűɞɖɖǝɑɞɡ, ůŰɖɜ ŬɞŰɛŰŰɨ ´ʂůɖ Űɤ ɜ ɛŰŰŰɛɛɖɜ´Ŭɡůɘǝɩ ɜ ůɡɛ´Űɤ ɛŸŰɤ ɜ ǝŬŰɖɜ ǝŬŰŸɖǝɘɣɖ. ɄɟɧůűŬŰŰ, ɏɞɞɡɜ Űɟ ɞɑůŬɜ ɜ ɖŰɤ ɟ ɞɨ ɜŰŰǝ ɤ ɠ ɞɘ ñűɡůɘɞɕ ŮǝǝŬŰǝɞɑ ɟɡɖɛʂŰɟɠ Űɞɡ ɞʂŰɟɞɔɜɘɞɨ ɡ´ɞűɞɞɏŬ (SERMs) ǝŬǝ ɏŰɘ ɑůɤ ɠ ɛ´ɞɟɞɨɜ ɜŬ ŬɞŬŰŰŰůŰɖůɞɜ ŬɞŬǝǝŬŰɘŸŰɖɜ ɞʂŰɟɞɔɜɘɞɤ ɖŰ Ŭ ɖŬ(Papoutsi et al., 2004). ɆŮ ɛɖŬ űɡŰɞɖɛɘɞ ɛŮǝɏŰɖ Űɞɡ űɡŰɞɨ *Onobrychis ebenoides* Boiss & Spruner Űɖɠ ɞɘɞɔɏɜŬɠ Leguminosae, Ŭ ɞɛɛɜɩ ɖɖǝŬ Űɖ Ŭ ɜɏŬ 2-űŬɜɡǝɞɓŮɜɞűɞɡɟŸɜǝŬ (ebenfurans I, II, III) (Halabalaki et al., 2000).



ebenfuran I



ebenfuran II



ebenfuran III

¢ ůgůůı ɟ Ǖgůd ´ əd ɟ ɕűɕɟ ɘ ɜ ´ ɕg Ǖɜűɕɨ ɕgɜ Ǖďɜ g´ ɧdǗűd ɧǕɘ ǗǕ űgǕɕɕůǕɟ ɕɔɧɜǓ ´ɟ ɕůǗǗǗɨ ɕgɜ Ǔ ɧ ´ əddı ɟ Ǔ ŭɘǓǗǗɟ Ǔɕı ɜ, ɧ´ ɤ ɠ d ɕůǗǕ´ ɧɟ ɤ ůd, ɕ əǕɟ əɶɕɠ Ǖɕg ůǕɐdɕgɠ əǕɘ ɕɘ əǕɟ ŭɘǓɘɔǕɘǓɘɣɠ ´Ǔdɐ ůǕɠ, ǗǓ ɣɕɕgɜ űɣɟ Ǖɘ ůǕɕ Ů ɶ Ǖɟ ɕ Ǖɕg Ǖɟ Ǖgɜ dǕɘɕɨ Ǖɜŭɘ Ǖűɣɟ ɕɜǕɕɠ. ӯ´ ɤ ɠ ɣǕɘ ɐüd ǓɜǕűǕɟ dǕɑ űgůɘǗ ɓǕɜɕɕűɕgɟ Ǘɜɘ Ǔ əǕɘ ɓǕɜɕɕ´ gɟ Ǘɜɘ Ǔ ɣɕɕgɜ ɘůɕgɟ ɐ ůgɜŭǕǕɘɐ ɘǕɜɧǕdǗǗ ɛ ǓǕɕgɠ ɕɘůǕɟ ɕɔɕɜɘɕɨ ɠ g´ ɕŭɕɕǕɠ əǕɘ ɤ ɠ Ǖɘ Ǖɕɨ Ǖɕg důɤ ɠ ůgɛ´ Ǖɟ ɘűɣɟ ɕɜǗǕɘ ɤ ɠ űgǕɕɕůǕɟ ɕɔɧɜǓ (Halabalaki et al., 2000).

ɟ ɟ ɕɘǗ ǗǓ Ǖɛ´ Ǖɜűɕgɟ Ǘɜɘ Ǔ ɛ ǕɘǗǕɐ ddəǕɜ ɤ ɠ ´ ɟ ɕɠ Ǖd ůgɔɔɣɜǕɘǗ Ǖɕgɠ ɛ Ů Ǖɕɜ ɕɘůǕɟ ɕɔɕɜɘɧ g´ ɕŭɕɕɣǓ əǕɘ ɓɟ ɣddəŮ ɧǕɘ d ůɕǕɘɐ ůgɔɔɣɜǕɘǓ ůɨ ɜŭǕɐdɠ (relative binding affinity-RBA) ɔɘǓǕ Ǖɛ´ Ǖɜűɕgɟ Ǘɜɘ I ɐǗǕɜ 0.29 əǕɘɔɘǓǕ Ǖɛ´ Ǖɜűɕgɟ Ǘɜɘ II 0.28, Ǖɜı Ǖ Ǖɛ´ Ǖɜűɕgɟ Ǘɜɘ III ŭǕɜ ɣŭǕɘŮəǗ ɕɘǓ ůdɛǕɜǕɘɐ ůgɔɔɣɜǕɘǓ ůɨ ɜŭǕɐdɠ. ɟ ɜɘůdɛǕɑ Ǖ ǕɘǕɘ Ǖ ɔǕɘɕɜɧɠ ɧǕɘ Ǖ RBA Ǖdɠ ǗǕɛɕɜɘűǓɜdɠ, d ɕ´ ɕdǓ ɕɟ dǕɘɛɕ´ ɕɘddəǕůǕ ´ Ǖɟ Ǖɛ Ǔ ɤ ɠ ɕgůdǓ ǓɜǓűɕɟ Ǘɠ, ɐǗǕɜ 0.69.

ɆǕd ůgɜɣɕǕɘǓ, ǗǓ ɜɣǓ ǓgǕǗ űgůɘǗ ´ ɟ ɕɧɜǗǓ, ǓɜɘɘəɕɔɐddəǕɜ ɤ ɠ ´ ɟ ɕɠ Ǖdɜ ɘǓɜɧǕdǕǗ Ǖɕgɠ ɜǓ ŭɟ ɕɨ ɜ ɤ ɠ SERMs. ɆgɔɘǕɟ ɛɣɜǓ, ɣɔɘǕɜ *in vitro* ´ Ǖɟ Ǘɛ ǓǗǓ ɔɘǓ Ǖdɜ ɕɘůǕɟ ɕɔɕɜɘɐ / ǓɜǕɕɘůǕɟ ɕɔɕɜɘɐ ŭɟ Ǘůd Ǖɕgɠ ůŮ əǕɟ əɘɘǗ əɨ ǗǗɟ Ǔ ůǕɐdɕgɠ, ǓűǓɜɕəǕɟ əɘɘǗ əɨ ǗǗɟ Ǔ Ǖɕg Ǖɟ Ǔɕɐəɕg əǕɘůŮɕůǗǕɜɓəǗůǗɠ. Ƀɘɛ ǕɘɣǗǗɠ ɣŭǕɘǕɜ, ɧǕɘ Ǖɜ Ǖɛ´ Ǖɜűɕgɟ Ǘɜɘ II ´ Ǖɟ ɕgůɘǗɕǕɘ ůdɛǕɜǕɘɧ ɓǓdɛ ɧ ǓɜǕɕɘůǕɟ ɕɔɕɜɘɐɠ ŭɟ Ǘůdɠ ůŮ

ebenfuran II

in vitro

SERMs

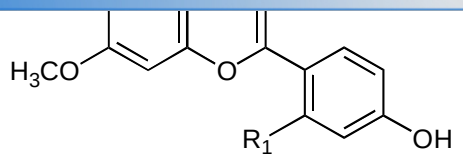
MCF-7

III

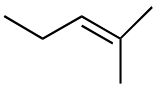
ebenfuran III

IV

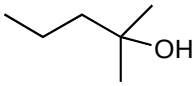
5-



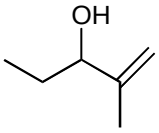
ebenfuran IV R_1= OMe, R_2=

ebenfuran III R_1=OH, R_2= 

ebenfuran V R_1= OH, R_2=

ebenfuran VI R_1=OMe, R_2= 

ebenfuran VII R_1= OH, R_2=

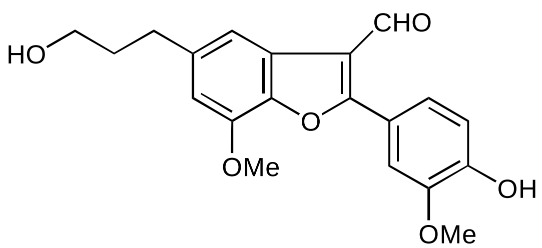
ebenfuran VIII R_1=OMe, R_2= 

? 2- J ΛɈ ş ȻđÅ? ȻȻū ȻɈ Λɉ ? Ħɋ ? ɆĻ ȻÃĦȻ Ɉɉ Ł ¢ đĦȻş ȻũĦɈ¢ ȼȻɈɆ Ɇ¢ ʐ ɉ ɆĦɉ

ɉ ɜŸɛ ŮűŮ ůŰǵ ɓɞɚɐɔɘŸŮɜŲ ɔɣǵ ŰŰŲ ɐɚɡɚɞɘɣǵ Ůɜɩ ůŮǵ ´ɐɡ Ů ŮɜŰ ɜŰŰɘůŰɋ űɨ ůɋ, ŰŰ ɓŮɛɕűɐɡɟ Ÿɜɘ Ů ɚŮɘ ɘűɘŮɋŰŲ Ů ŰŰ 2-Ÿɟ ɡɚɞ- ´Ųɟ ŸɔɤɔŸ Űɡɡǵ ɚŰŰɢɞɡɜ ŮɣɢɐɡůŮ ɋɣůɋ. űɘŮ ɜŮ Ů ɘɩɋɛŮɜɋŮɑ ɋ ů´ɐɡűŮɧŰɋŰŰ Ůɡű ɜ Űɤɜ Ůɩ ůŰɤɜ ɚŮɘ Űɛ Ů ɟɐɡǵ Űɤɜ ɓɞɚɐɔɘɩ ɜ Űɡɡǵ ɘűɞŰɨŰɤ ɜ, ´Ųɟ Űɋɣ Űɡɛ Ů ɛɘŮ ůŮɧ Ÿ Ů ɐɛɐɜɤ ɛɣɜɤ ɜ ɓɞɚɐɔɘŸ ŮɜŲ ɔɩ ɜ 2-Ů ɟ ɡɚɞɓŮɛɕűɐɡɟ Ůɜɞɤ ɜ.

- **XH-14**

2-(3-ʐ Ůɋɐɜɡ-4-ɡŭɟ ɐɜɡ-űŮɞɡɚ)-5-(3-ɡŭɟ ɐɜɡ´ɟɐ´ɡɚɐ)-7-ɛ Ůɋɐɜɡ ɓŮɛɕűɐɡɟ Ůɜɐ-3-ɚŲɟ ɓɐɜŮɚűŮɓűɋ

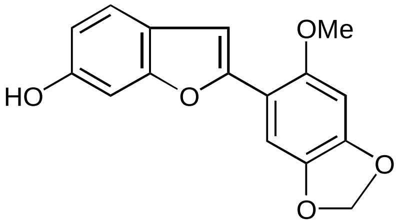


ȼɐ űɡůɘɧ Ůɡű ɓŮɛɕűɐɡɟ Ÿɜɞ Ů ɐɛɐɜɩ ɋɋɚŮŮ ɐ Ű űɡű *Salvia miltiorrhiza Bunge* Űɋǵ ɐɞɐɔɣɜŮŮǵ Lamiaceae, Űɡ ɐ´ɐɞɡ Ű ɡŭŮŰɘɧ Ůɐɨ ɚɩůɛŮ ɣɢŮ ɢɟ ɋůɕɐ´ɐɋɋŮ ůɟ ɣɤ ǵ ůŰɋɜ ȾɞŮ ɔɘŮ Űɋ ɋŲ Ů ŮŮ ɚŲ űɞŮɔŰɘŮɩ ɜ ŰůɋŮɜŮ ɜ, ɧ´ɤ ǵ Űɛ ɐɜɨ ɣɛűɟ Ůɚ ɛŮŰɡ ɛɡɐɚŲ ŭɐɡ ɚŮɚɋ ůŰɋŸɔɢɋ (Yang et al., 1991). ¢ ɣɜɤ ůɋ Ůɡű ŮɞŮɚɋ ´ɟɩ Űɋ ɔɜɤ ůŰ ɣɜɤ ůɋ ɢɤɟ ɐɋ ´Ųɐɡůɘ Ůɐɩ Űɡ ´ɐɡ ůɡɜŭɣŰŰɘ ůŰɜ ɡ´ɐŭɐɢŮ Ůűɜɐůɐɋǵ ɚŮɘ ɣɢŮ Ű ´ɚŮɜɣɚŰɋɛŮ ůɢŰɘŸ ɛŮŸɚɋǵ űɘŮɚɡűɧŰɋŰŰǵ ůŰ ɜŲɧ. ŪŮɟ ŮŰŰɘ ɘűɢɟ ɧǵ ŮɔɤɜɘůŰǵ Űɋǵ ɉ ₁ ŰűŮɐůɞɋǵ (Scammells et al., 1998). Ā´ɘ ɚɣɐɜ ɛŮɣŰŰǵ ɣɢɐɜ űŮɞŮ ´ɤ ǵ ɣɢŮ ɚŮɚ ŮɜŰűŰŰŮŰɘɛ űɟ Ÿůɋ ɣɜŮŰ Űɋǵ ŮŸ Űɡɜɋǵ Űɤɜ ɚŲ ɚɜɞɘ ɜ ɚɡŰŰŸɟ ɤ ɜ, Ůɜ Ů ŸɔŮ Űɋɜ Ů ɧ´Űɤ ůɋ Űɤɜ Ůɜɋɟ ɩ ´ɞɤ ɜ ɚŲ ɚɜɞɘ ɜ ɚɡŰŰŸɟ ɤ ɜ (Chang et al., 2004). ȼɐ ɉ ¢-14 ɣɢŮ ůɡɜŰŰɋŮɢɋɛɘŸ ɛŮɛɘŮ´ɐɟ ŮŮ Ůɜɣ Ů

[illegible] Sonogashira, [illegible]
[illegible], 2009).

- **Cicerfuran**

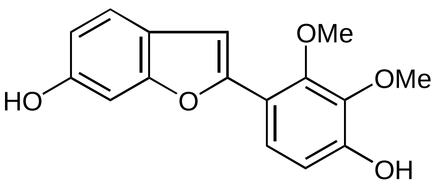
6-[illegible]-2-[6-[illegible](1,3)[illegible]-5-[illegible]][illegible]



[illegible] cicerfuran [illegible] *Cicer bijugum*, [illegible] Fabaceae. [illegible] *Fusarium wilt* ([illegible]) [illegible]. [illegible] cicerfuran, [illegible] (Aslam et al., 2006).

- **Isopterofuran**

2-(2,3-[illegible]-4-[illegible])-6-[illegible]

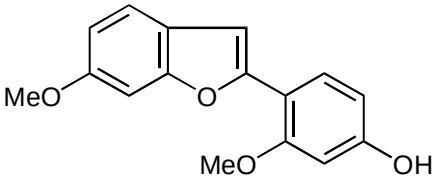


[illegible] isopterofuran, [illegible] *Coronilla emerus*, [illegible] Fabaceae, [illegible]

ůi ɜdŮůd Ű£g ɣGŮɔ ŬɜŰíŮʃdŮı ɦŮɔ ɔœŮŰŬɔ ɛɣůʏ ɛŮ ɣɜŬ ŬɔŮŰĝəœűɜœ Ű£g gŬɔəɕi (Scannell and Stevenson, 1982).

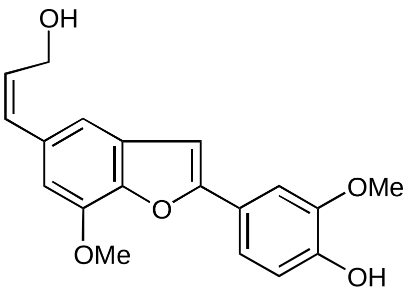
- **Vignafuran**

6-ʐ Ůűɕɜg-2-[(2-ɛ Ůűɕɜg-4-gŭʃ ɕɜg)ű Ŭɜœgəɕ]ɓŮɜɕœűɕggʃ Ɣɜɜœ



¢ɕ vignafuran ɣGŮɔŬ ɕɛɕɜʏ dŮıŬ ɦ ŰŰűi əəŬ Ű£g *Vigna unguiculata (L.) Walp.*, Ůdʃ ɕɜəɕɔɣɜŮɔŰʃ Fabaceae, ´ɕg ɣGɕgɜ ɛɕəgɜdŮıŬ ɦ Ű£ *Colletotrichum lindemuthianum* əŬɔɣGŮɔ Ůɛűŭɜœı Ůɔ ɜůɕggʃ ɐ ŬɜŰ£gədŰɔŰůɜəɐ ŭʃ Ɣůd. ¢ ɕəɜəɐ ůi ɜdŮůd Ű£g vignafuran ɣGŮɔ Ů ɜŰŰĝɕdŮı ɛɣůʏ əŬŰŬəgŰəɕi ůɕdɛŰŰůɛɕi (Sonogashira coupling) Ű£g ɓŮɜɕœűɕggʃ ŬɜəɕiŭŬɔĝəœg, gʃ důɛɕ´ɕɜ ɜŰŰʃ ʏʃ Ŭʃɕgəɐ i əd Ű£ɜ 4-ɓʃʏɛɕ-ʃ Ůɕʃ əɜɦəd (Hiroya et al., 2000).

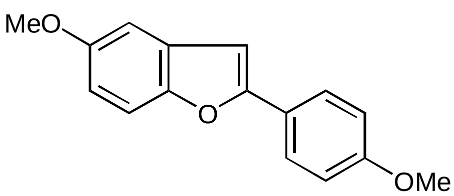
(Z)-2-(3-ҁ Ủďєзŋ-4-ŋŭӈєзŋűŬɞŋэє)-5-(3-ŋŭӈєзŋ´ӈє´-1-Ủɜ-1-ŋэє)-7-ɛ Ủďєзŋϭ Ủɜєє-űєŋӈ Ÿзѳ



ɇ є зỦɜэээзŸѳ ´єŋ Ŭ єŰỦэỦďŰŬэ Ŭ ђ ủэỦэŬŰђ 2-Ŭӈ ŋэєϭỦɜєєűєŋӈ Ŭɜєŋ, ӳєỦэ Ŭ єɛєзɤ ďỦɑŬ ђ Űɜ űŋŰђ *Ȼanthoxylum ailanthoides*. Ѧэєɨ эủɛŬ Ŭ ђ Űɜ űээђ эŬэŰŬ űɨ ээŬ Űɜŋ ŭӳзŰӈ єŋ ŬŋŰɜɨ , ӳєєŋз єӈ ďủɛє´єɖďỦɑủŰɖ эŬɐɐ ďŰӈ Ŭ ŬŋŰэɐ. ¢ ủɨ зďŰủɖ Űɜŋ ɛєӈєɜŋ ŬŋŰɜɨ ӳєỦэ ´ӈ Ŭэɛ ŬŰɜ´єɖďỦɑ ɛӳủɤ Űɖɠ ủŋɛ´ɨ эзɤ ủɖɠ Sonogashira (Lütjens and Scammells, 1998), (Koca et al., 2005).

- **Corsifuran C**

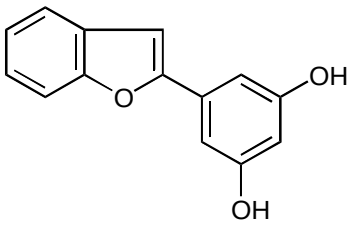
5-ҁ Ủďєзŋ-2-(4-ɛ Ủďєзŋű Ŭɞŋэє)ϭ Ủɜєєűєŋӈ Ÿзѳ



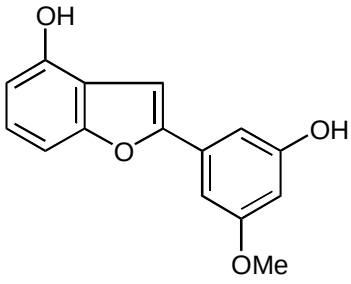
[illegible] *Corsinia* niaceae (Reuß and König, 2004). ¢ [illegible] Suzuki (Geary and Hultin, 2009).

- **Stemofurans**

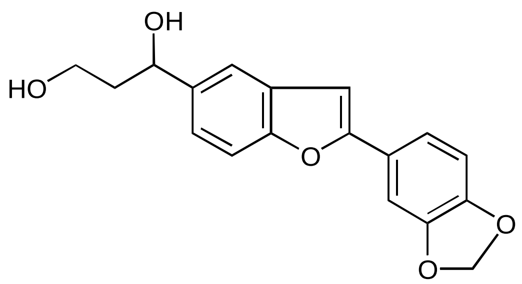
Õ[illegible] 2-[illegible] stemofurans A-K, [illegible] *Stemona collinsae*, [illegible] Stemonaceae. [illegible] stemofuran B [illegible] (Pacher et al., 2002). ¢ [illegible] Stemofuran A, [illegible] [3,3]-[illegible] ?-[illegible] (Takeda et al., 2007).



stemofuran A



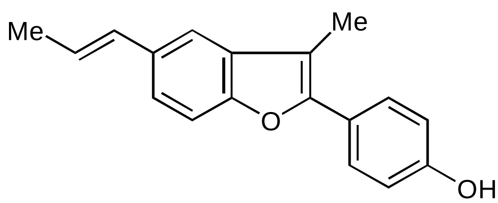
stemofuran B



ɇɐ 2-ŰɟgəəɓǚɛɕűɕgɟŸɜɞ machicendiol Ǔɕǚǚǚ ´ɟɕɥɜ Ǔɕɛɧɜɤůďɠ Ǔɧ Ǘɞ Ǘɢɨ əǚůɛǓǗɞg *Machilus glaucescens* Ǘďɠɕəɕɔɏɜǚǚɠ Lauraceae, ´ɕg ɢɟďůɐɕ´ɕǚǚǚ ůǗď dǙɟǓ ǙǓǗɞg Ÿůdɛ Ǘɞg, Ǘɤɜɟ Ǚgɛ Ǘǚůɛɩ ɜ əǓǗɞg ɏəɕgg (Kundu et al., 1997).

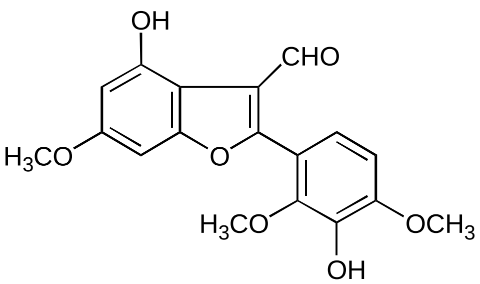
- **Eupomatenoid 6**

(Ǻ)-3-ɛǙdgəɕ-5-(´ɟɕ´-1-Ǚɜ-1-gə)-2-(4-gǚɟɕɜg)ɓǚɛɕűɕgɟŸɜɞ



ŌɢǙ Ǔɕɛɕɜɤ dǗ Ǔɧ Ǘɞ űgǗɧ *Piper decurrens* Ǘďɠ ɕəɕɔɏɜǚǚɠ Piperaceae. ŌɢǙ ǓɕǚǚǚůǚůgɜdǗǚɧ ůǗɧɕɕ əǓǗ ɠɏɢǚǚǚǚǚ ǙɜǗɛgəďǗǚůəɏɠ, ǙǗɜɜǚǚɤ Ǘəɏɠ əǚ ǙǗɛɕəǗɧɜǗɠ ǚɧǗďǗɠ (Chauret et al., 1996). ¢ ůgɜdǗǚɐ ´ɕɟǙǓ Ǚɕəɕgdǚ Ǘɜ ɛďɢǓɜǚɛɧ Ǘďɠ [3,3]-ůəɛǓǗɕ´əɐɠǙǓǚŸǗǚďɠ (Takeda et al., 2007).

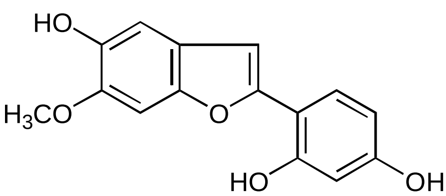
2-(2,4-ɖɪæ Ůďɞɜg-3-gŭɟ ɞɜgűŬɞgɚɞ)-6-ɛ Ůďɞɜg-4-gŭɟ ɞɜgɓŮɜɕűɞgɟ Ŭɜɞ-3-ɘŬɟ ɓɞɜŬɚŭŬɓŭɖ



ɇɞ 2-Ŭɟ gɚɞɓŮɜɕűɞgɟ Ÿɜɞ andinermal A, ɏɢŮɔ Ŭ ɞɛɞɜɤ ɖŮɑ Ŭ ɧ Ůɞ űgŬɧ *Andira inermis* Űɖɠ ɞɘɞɔɏɜŮŬɠ Fabaceae ɘŬɔɏɢŮɔ ŭŬɒɔŮɔ Ŭɜ Űɠ ɚŮɛɤ ŭɘɐ ŭɟ Ÿůɖ (Kraft et al., 2001).

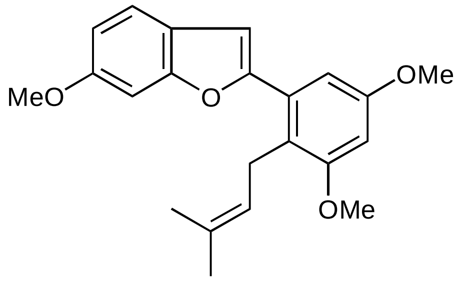
- **ebenfuran I**

2-(2,4-ɖɪɦŭɟ ɞɜg)űŬɞgɚɞ-6-ɛ Ůďɞɜg-5-gŭɟ ɞɜgɓŮɜɕűɞgɟ Ÿɜɞ



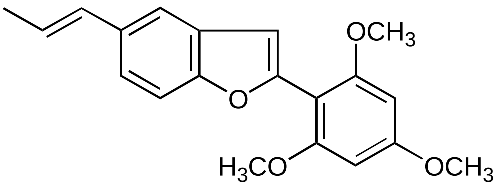
ɇɞ Ůɛ´ Ůɜűɞgɟ Ÿɜɞ I ůŬɞ ɞ´ɞɶ ɏɢɞgɛŮɐŭɖ ŬɜŬŭŬɟ ɖŮɑ ɏɢŮɔ Ŭ ɞɛɞɜɤ ɖŮɑ Ŭ ɧ Ůɞ űgŬɧ *Onobrychis ebenoides*, Űɖɠ ɞɘɞɔɏɜŮŬɠ Leguminosae (Halabalaki et al., 2008). ¢ ůɨ ɜɖŮŭɖ Ůɞg ɏɢŮɔ ´ɟ ŬɔɛŬŬɞ´ɞɖɖŮɑ ɛɏůɤ Űɖɠ ŬɜŬŭɟ Űůɖɠ Witting, ɛŮŬŬɜɨ ɛɖŬɠ ɓŮɜɕgɚɞɜg-g´ɞɘŬŬůŬɖɛɏɜɖɠ ůŬɔɘgɚŬɚŭŬɓŭɖɠ ɘŬɔ Ůɜɧɠ ɓŮɜɕgɚűɤůűɞɜɘɞɨ ɢɚɤ ɟ ɕŭɶg (Duan and Duan, 2010).

2-[3,5-ɋɐɛ Ůɗɕɜɡ-2-(3-ɛ Ůɗɡəɕ ɓɕɡǗ2-Ǜɜ-1-ɡəɕ)ǘ Ǖɜɡəɕ]-6-ɛ Ůɗɕɜɡ ɓǛɜɕǘɕɡɟ Ŷɜɐɛ



¢ ǚɐɛ Ůɗɡəɕɛɕɟ Ǖəɑɖ ɯɕǛə Ǖ ɕɛɕɜɤ ɗǙɑ Ǖ ђ Ǘɛ ǘɡǗђ *Broussonetia papyrifera* Ǘɖɠ ɕɘɕɔɯɜǙǓɠ Moraceae əǙə Ǖ ɕǗǙəǗɑ ǙɜǗǘǗɛəɯǕ Ǘɖɠ Ǘɟ ɤ ɛ ǕǗŶǘɖɠ (Lee et al., 2001). ¢ ǘɨ ɜɗǗɪɐ Ǘɕɡ ɯɕǙə ´ɟ Ǖəɛ Ǘɛ´ ɕɘɖɗǙɑɛ Ůəɡəɕ´ ɕɑǘɖ ɛɯǘɤ ɕɜǙɐɤ Ǘəɐɠ əǗŶəɡǘɖɠ ɛ Ů ɯɜǕ ɐǘɕɡɟ ђ ɕɜɨ (Amberlyst 15) (De Luca et al., 2009).

- **(*A*)-5-(´ɟ ɕ´ -1-Ǜɜ-ɡə)-2-(2,4,6-Ǘɟ ɐɛ Ůɗɕɜɡǘ Ǖɜɡəɕ)ɓǛɜɕǘɕɡɟ Ŷɜɐɛ**



ɇɕ ɜɕɟ -ɜǗɜəɘɜǕɜɑɡ (*A*)-5-(´ɟ ɕ´ -1-Ǜɜ-ɡə)-2-(2,4,6-Ǘɟ ɐɛ Ůɗɕɜɡǘ Ǖɜɡəɕ)-ɓǛɜɕǘɕɡɟ Ŷɜɐɛ, ɯɕǛə Ǖ ɕɛɕɜɤ ɗǙɑ Ǖ ђ Ǘɛ ǘɡǗђ *Krameria ramosissima*, Ǘɖɠ ɕɘɕɔɯɜǙǓɠ Krameriaceae əǙə ɯɕǛə ǚǙəǙə Ǖ ɕǗǙəǙɛ ǕǗəђǗɖǕ ɯɜǕǗə ǘǙǚəŶɟ ɕɘǕ əǙə ´ɡɟ Ǘђ. ¢ ǘɨ ɜɗǗɪɐ Ǘɕɡ ɯɕǛə ´ɟ ɕəɨ ɣǙə ɛɯǘɤ C- Ǘɟ ɡəɑ ǘɖɠ Ǘɖɠ 3-ɓǛɜɕǘɕɡɟ Ǖɜђɜɖɠ (Donnelly et al., 1991).

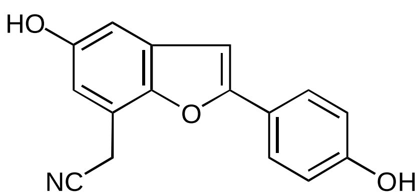
J 2-Ŭɻ gəɛbŮɜɛɛűɛgɻ Ŭɜɑɤ ɜ:

¢ɻ ɦ´ ɛɘ ůɨ ɜdŮůdɖƒəŬɔ bɤəəɔɔəɐ ŭɻ Ɏůɖ

[illegible] 2-[illegible]

[illegible] (Luca et al., 2008). [illegible] 2-[illegible]

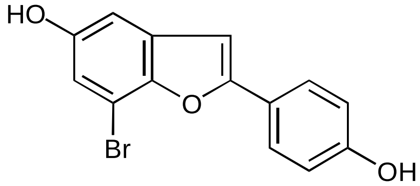
- **2-(5-[illegible]-2-(4-[illegible])[illegible]-7-[illegible])[illegible]**



[illegible] 5-[illegible]-2-(4-[illegible])[illegible] 7-[illegible] ER[illegible]. [illegible] 2-(5-[illegible]-2-(4-[illegible])[illegible]-7-[illegible]) [illegible] (Collini et al., 2004). [illegible]

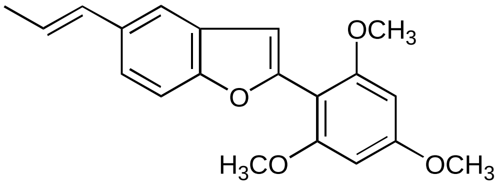
´ ɟɞţђɜŰǿʛ Ŭgŵɨ, ɞ ůəŬ̊Űŷʛ Űɞg 2-
ůŰqəŮɛɏůɤ ůgɛ´ɨəɜɤůqʛ Ŭɜђʛ ɚůɞ´ŬɟŬɿɔɞg
(2-ɚŭɞ-4-ůŬɚgəɚђʛ ɛŮqgəŮŰŶɟŬg) əŬ Ŭɜђʛ ŬŰŰgəŬɞg (4-
ɛŮqɞɜgűŬɞgəŬŰŰgəɏɜɞ), Ŭɞəɞgqɩ ɜŰʛ Űɞ ɛqɢŬɜůɛђ Űqʛ ŬŰɟŬqʛ
Sonogashira (De Luca et al., 2009).

- **7-ɖɟ ɤ ɛ ɞ-5-gŭɟ ɞɜg-2-(4-gŭɟ ɞɜgűŬɞgəɞ)ɓŮɜɕɞűɞgɟ Ŷɜɚɞ**



Ŧɟ ђůqŮŰʛ ɛŮŰŰɟ ɞ´ɏʛ ůŰq 4-ɖɏůq əŬ ůŰqɜ 3õ-ɖɏůq Űqʛ 2-űŬɞgəɞɛŶŬʛ Űɞg 2-
(5-ɟ ŭɟ ɞɜg-2-(4-gŭɟ ɞɜgűŬɞgəɞ)ɓŮɜɕɞűɞgɟ Ŭɜ-7-gə)ŬŰɞɜɚŰɟ ɚɞg ´Ŭɟ Űqɟ qŰɨ-
əŮ´ɤʛ ŬgɜŶɜɞgɜ Űqɜ Ŭ̊əŬŰђŰqŰ ůŰɜ ɞɜůŰɟ ɞɔɞɜɚђ g´ɞŭɞɢɏŬ ERɓ. ŎŰůɞ,
´Ŭɟ ŰůəŬgŶůŰqəŮŰɞ 7-ɓɟ ɤ ɛ ɞ-5-gŭɟ ɞɜg-2-(4-gŭɟ ɞɜgűŬɞgəɞ)ɓŮɜɕɞűɞgɟ Ŷɜɚɞ
ɛɏůɤ ŬɜŰŭɟ ŬůqʛFriedel-Craft ɛŮŰŬɨ ɛqŬʛ Ŭɜɚůђəqʛ əŬ Űɞg 2-(3-ɓɟ ɤ ɛ ɞ-2,5-
ŭɚɛŮqɞɜgűŬɞgə)Ŭɏ Űgəɞ ɢəɤ ɟ ɚŭɞg ɛŮ ´ɟ ɞůqɨəq AlCl$_3$ əŬ ɛŮ ´ŬɟŬŰŷɟ ɤ
Ŭ ɞ´ɟ ɞůŰŰůqŬɛŮPy·HCl (Collini et al., 2004).

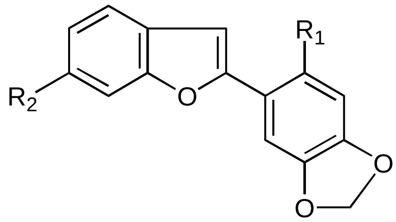
- **(*A*)-5-(´ɟ ɞ´-1-Ŭ̊gə)-2-(2,4,6-Űɟ ɚɛŮqɞɜgűŬɞgəɞ)ɓŮɜɕɞűɞgɟ Ŷɜɚɞ**



¢ ůɨɜqŰůq Űɞg ɜɞɟ-ɜŰɞəɚɜŬɞg (*A*)-5-(´ɟ ɞ´-1-Ŭ̊-gə)-2-(2,4,6-
Űɟ ɚɛŮqɞɜgűŬɞgəɞ)ɓŮɜɕɞűɞgɟ Ŷɜɚɞ (*Krameria ramosissima*), Űɞ ɞ´ɞɞ ɏɢŬ ŭŰɞŬ

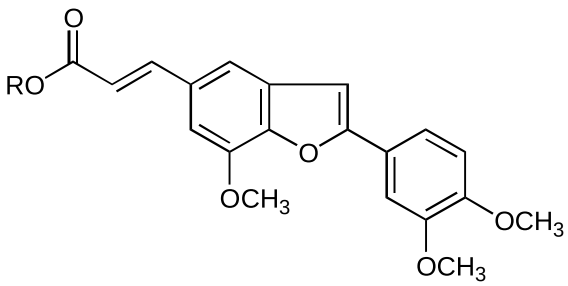
Ů ŭэŸŋ ɟ ɕэŬ əŬэ ´ gɟ ŰŰђ, ɏɢŮэ ´ɟɕəɨ ɣŮэ ɛɏůɤ C-
ɜɖʃ (Donnelly et al., 1991).

- **ɉ ɜŸэɕɔŬ Űɤ ɜ cicerfurans**



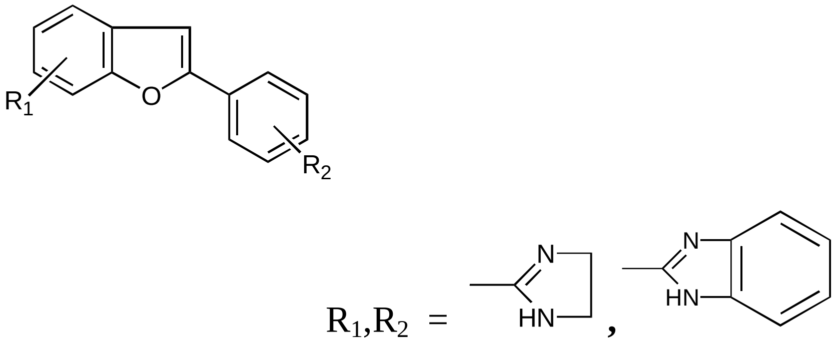
ɇ Ŭ Ŭɜ Ÿэɕɔ Ŭ Űɤ ɜ cicerfurans ɏɢɕgɜ ɛŮэŰŰɖɖŮɑ əŬэ ɏɢɕgɜ ŭŮɒŮэ ŬɜŰɛ gəɖŰŬůɘɐ əŬэ ŬɜŰɓŬэŰɖɟ ɘɐ ŭɟ Ÿůɖ. ¢ ůɨ ɜɖŰůɐ Űɛgʃ ɏɢŮэ Ů эŰgɢɖŮɑ ɛɏůɤ Ů ɕɜŬŭɤ ůɖʃ əŬэ əgəɕ´ ɕɑůɖʃ 2ō-gŭɟ ɕɜgůŰɓŮɜɑ ɜ (Aslam et al., 2006).

- **ɆŬɟ Ÿɔɤ ɔŬ 2-Ŭɟ gə-5-Ŭэə gəɕ-7-ɛ Ůɖɕɜgɓ Ůɜɛɕű ɕgɟ Ŭɜɑ ɜ**



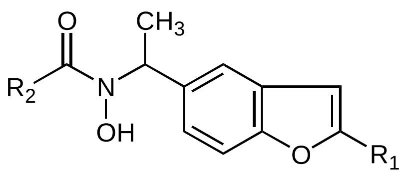
ɀ ɖŬ ůŬэ Ÿ ´ Ŭɟ Ŭɩ ɔɤ ɜ 2-Ŭɟ gə-5-Ŭэəgəɕ-7-ɛ Ůɖɕɜgɓ Ůɜɛɕűɕgɟ Ŭɜɑ ɜ, ɏɢŮэ ůgɜŰŰɖŮɑ ɛɏůɤ ŬɜŰŭɟ Ŭůɖʃ ůgɛ´ɨ əɜɤ ůɖʃ Ůɜђʃ ɓɟ ɤ ɛɕ´ Ŭɟ Ŭɩ ɔɕg ɛŮ űŬɜgəŬэŰŋəɑɘ Űɛg ɢŬэɕɨ (ɉ ɜŰŭɟ Ŭůɖ Castro). Ōɜ Ŭ Ŭ ђ ŬgŰŸ Ű´ Ŭɟ Ÿɔɤ ɔŬ (R=o-methoxyphenyl) ɏɢŮэ ŭŮɒŮэ əgŰŰŬɕŰɜɘɐ ŭɟ Ÿůɖ ŮɜŸɜŰɘŬ ůŰɛ ŬŭŮɜɕəŬɟ əɑɤ ɛŬ Ŭɜɖɟ ɩ ´ɘɕg ´ɜŮ ɛɕɜŬ (Yang and Kong, 2007).

Ůǝɛɞűɞǥɟ Ƴǝǝ Ŭ



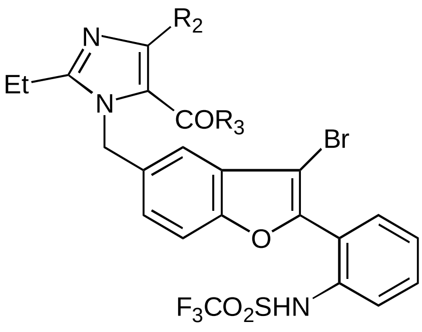
ɀ ďŬ ůŮǥ Ƴ Ŭ ɧ ǝŬŰɜɜɞ Ƴ ǥ´ɞǝŬŰŰůŰɖɛɏɜŬ 2-űŬǥǝɞɓŮǝɛɞűɞǥɟ Ƴǝǝ Ŭ ɏɢŮ ůǥɜŰŰɖŰɑ ɛŮůǝɞ´ɧ Űɖɜ *in vitro* ɛŮɏŰɖ Ű ɜ ŬɜŰ ɟ ɤ Űɞɤ ǝɿ ɜ Űɞǥɖ ǝɞŰŰ ɜ, ǝŬɖɩ ɖǝŬ Űɖɖ ǝǥŰŰɟ ɞŰɜǝɛɖ ǔɟ Ƴůɖɖ ŮƳɜŰŬ ůŮǝɨ ŰŰɟ Ŭ Űɞǥ ɛŬůŰɞɨ Ŭɏɜ Ŭ ɇ Ŭ Ŭ ɞŰŮɏůɛŬŰ ŬǥŰɛɖ Űɖɖ ɛŮɏŰɖ ɛŰɜ ǝɜŬɖŰɟ Ŭ Ůɖɟɟ ǥɜŰǝ Ƴ. ȼ ůɨ ɜɖŰɛ Űɞǥɖ´ɟ ŬɛŰɞ´ɞɛɖɖǝŮ ɛɏůɤ ɛďɖ Űɞ´ɞ´ɞɖɛɏɜɖɖ ŬɜŰǔɟ Ŭůɖɖ Castro, ɛŰŰŬɨ ɛďɖ ɞ-Ŭǝɔɞɜɤ ɛɏɜɖɖ űŬɞɧǝɖɖ ǝŬ Ůɜɧɖ ŬŰǥǝŮɜɞɨ ´Ǜ Ŭɩ ɔɞǥ ɛŮŰɖ ǝŬŰǝǥŰɞ ǔɟ Ƴůɖ Űɞǥ Cu_2O ǝŬ Űɖɖ´ǥɟ ǝɞɖɖ (Bakunov et al., 2008).

- **2-Ɉ´ɞǝŬŰŰůŰɖɛɏɜŬ-5-ɓŮǝɛɞűɞǥɟ Ŭɜǥǝɞɦǔɟ ɞɜŬɛǝ Ƴ ɞɜɏŬ**



ȺŬɟ Ƴɔɤ ɔŬ ŬǥŰɞɖ Űɖɖ ǝŬŰɖɔɞɟ ďɖ ɏɢɞǥɜ ůǥɜŰŰɖŰɑ ɛɏůɤ ůǥɛ´ɨ ǝɜɤ ůɖɖ ɛŮɓƳůɖ Űɖɜ ŬɜŰǔɟ Ŭůɖ Sonogashira ǝŬ ɨ ůŰɟ Ŭ Ŭ ɧ ɛŮɏŰɖ ɏǔŬɞŬɜ ŬɜŬůŰŰǝŰɞ ǔɟ Ƴůɖ Űɖɖ 5-ǝɘ ɞɜǥɔŮɜ Ƴůɖɖ (Ohemeng et al., 1994).

…ɛűɢgɟ Ŷɜɘɛ

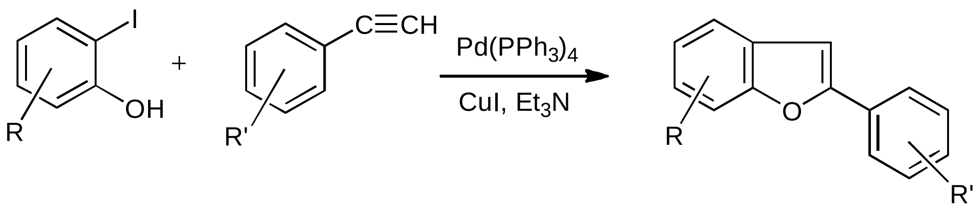


ɇɢ ´Ǔɟ Ŷɔɤ ɔɞ Ǔgǖɧ Ǔ ɢǕǕɚǕɑ ɘůɢgɟ ɧ ǕɜǕǕɒɤ ɜɘůǕɐ ǕɖgƒǕɒɔǕɞǕǕɜůɑɗɖƒ Ŧ. ǑɢǕɘ ůgɜǕǕɖǕɑɛɥůɤ ůgɛ´ɨ ɘɜɤ ůɖɖƒɛǕ´Ǖɘɘ Ŷǖɞ ɤ ƒ ɘǕǕǕɚɨ Ǖɖ, Ǖɧgƒ ɓɘɟ ɢɜɘɞɨ ɢɜɥɢƒ ɛǕ2-ɓɟ ɤ ɛɢ-ɓǕɜɛɜɥɧ ɛǕɖgɚǕɨǕɟ Ǖ(Judd et al., 1994).

1.4.2. ɇɟ ɧ´ ɢɘ ůɨ ɜɖǕůɖƒ 2-Ǔɟ gɚɓǕɜɛűɢgɟ Ǖɜɑɤ ɜ

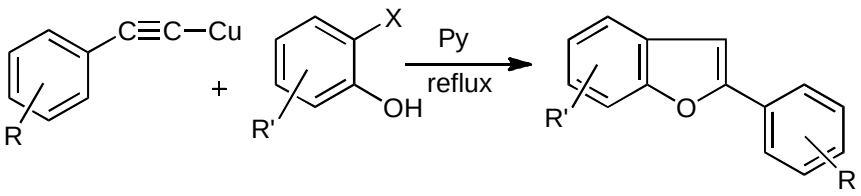
ɟ ɜǕɘǕǕǕɚǕɜ ɜɢɜǕǕǕ, ɖǓ ´Ǔɟ Ǖɖɥůɢgɛ Ǖ ´Ǔɟ ǕɘŶǕɤ ɛǕɟ ɘɢɨ ƒ Ǔ ɧ Ǖɢgƒ ´ɞ ůɖɛǕɜǕɘɢɨ ƒ ǕɧǕɢgƒ ůɨ ɜɖǕůɖƒ 2-Ǔɟ gɚɓǕɜɛűɢgɟ Ǖɜɑɤ ɜ ´ɢg ǕɜǕǕɥɟ ɢɜǕǕɘ ůǕɖ ɓɘɓɚɞɔɟ ǕǕɖǕ.

- **Ʈ ǕǕǕɚgǕɚɐ ǕɜǕɑɥ Ǖůɖ ɘgɘɚ´ɢɑůɖƒ Sonogashira (**Bang et al., 2009), (Jiang et al., 2009).

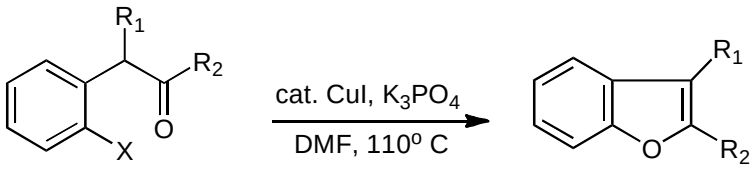


Ŭɟ gə›Ŭə›ŭɑɤ ɜ ɛŮ Ŭə ŮŰgə›ɑŭ›ŬɔŬəəɛi (Castro-

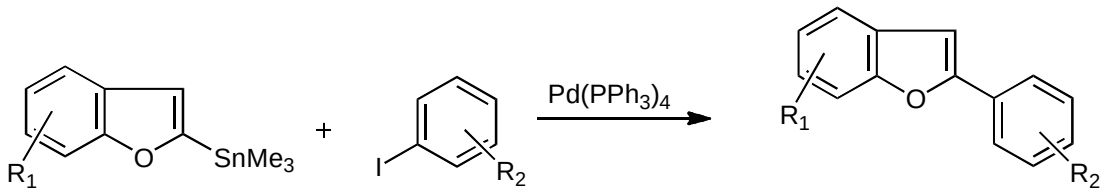
ells et al., 1998), **(**Yang and Kong, 2007).



- **Ť gə›ɛ´ ɛɑʠůɑ Ŭə›ɛɔɛɜɤ ɛɣɜɑʠƒ ƀŮɜɛgə›ɛə ŮŰɲɜɑʠƒ** (Chen and Dormer, 2005).

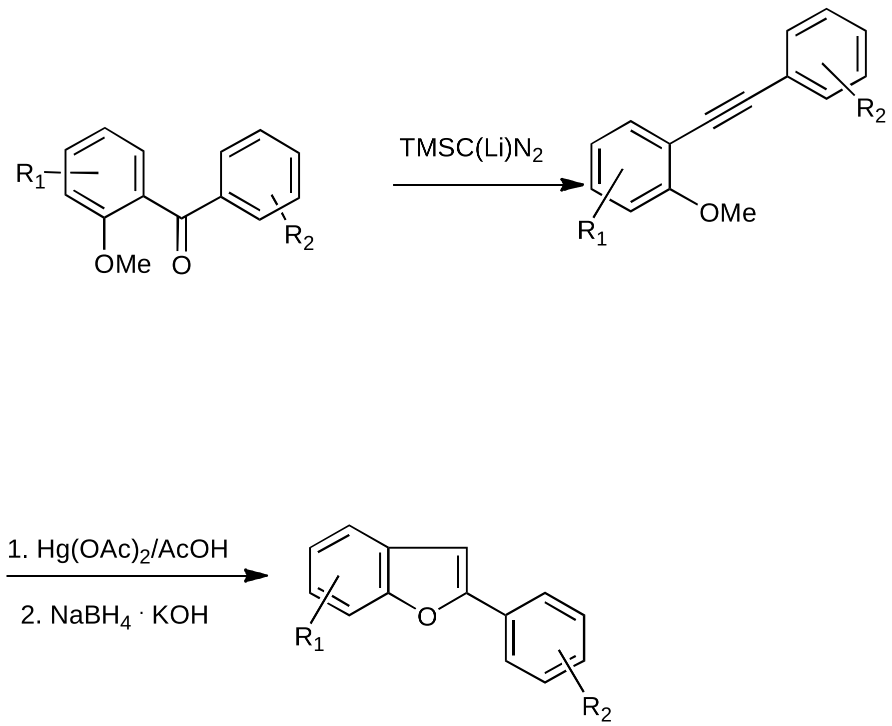


- **Ɇɛɑʠɛ ŮŰ›ůɛ ɦƒ ŭŮůɛ ɛi C-C ɛ ŮŰŬɜi ƀŮɜɛɛűɛgɲ Ŭɜɑɛg ə Ŭə g´ ɛə ŮŰŮůŰʠɛɣɜɛg Ŭɟ gə›Ŭə›ŭɑɛg** (Mann and Widdowson, 1991).

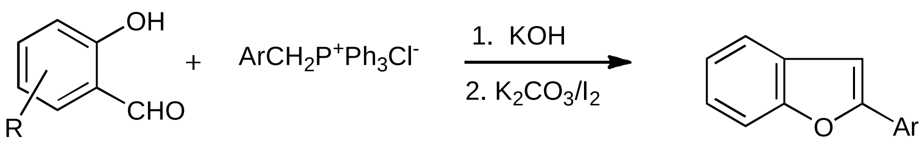


Ǖűȝɜɖɠ ɛŮ ŶəǕǕ əɘɗœɡ Űɛɡ ǗɈ ɘɛ Ǖɗɡəɞůɘəɡəɞ-

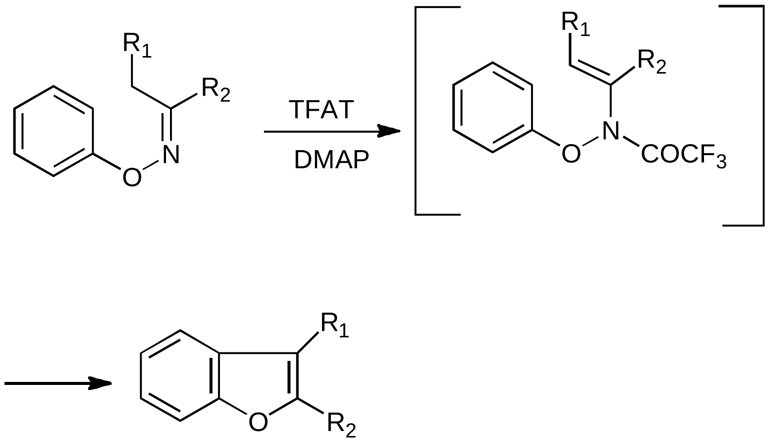
...ıern, 2001).



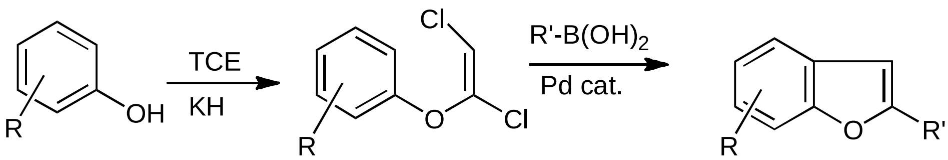
- **Ʌɜŭɕɛ ɕɟ ɘǓəɐ ǓɜǕǔɟ Ǔůɖ Wittig** (Duan and Duan, 2010).



ůиэŸŰǓзɖ ʔ -Ǔɟ ঌǘɖɞɟ ɛǓэ ŰǓɡэ-Ǔзɡǔɟ ɞзɡэ-Ǔɛ ঌзι з



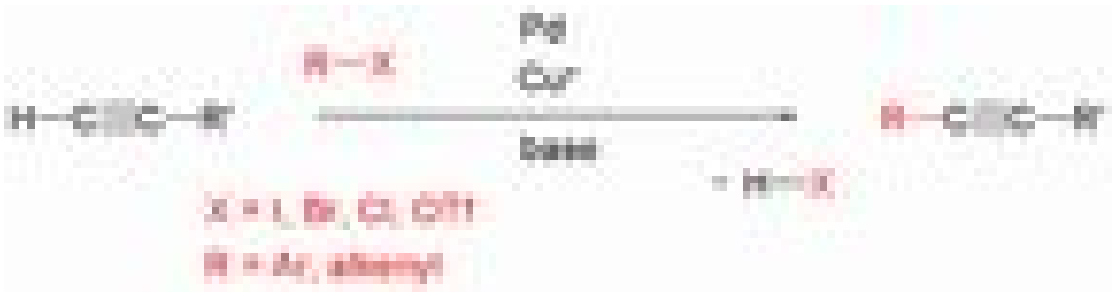
- ɟ зŰǔɟ Ǔůɖ **Suzuki** (Geary and Hultin, 2009).



ɟ ɟэŮŰɟɡ Ǔ ɧ Ǔɡ ´ɟɞǓзŰǔǓɟ ɧɛǓзǓɡ ɛǓɗɧǔɞɡɡ ůɨ зɗŰůɖɡ Ǔɤ з 2-Ǔɟ ɡэɞбǓзɞǘɞɡɟ Ǔзɑ з ´Ǔɟ ɞɡůэŸɞɡз ɛǓзǓэǓɛŰŰ, ɧ´ɤ ɡǓзǓэɖ ɣэ-ǓɣɖŰ´ɟɞůэǓ з ´ɟι Ǔɤ з ɡэ з, ɞэ Ǔэɟ ɞɑ эŰŰǓɨ Ǔɡ, ɞэ ůɢŰǓэŸ ঌɞɡɟ ɣɡ ůɡзɗэǓɡ ǓзŰǔɟ ŸůǓɤ з (ɧзǓɡ / бŰůэɣɡ) эǓэ Ű ´ɞээŸ ůŰŸǘэǓ ɛŮ ɢǓɛɖэɣɡ Ǔ ɞǘɧůǓɡ. ɟ ´ɧ ǓɡŰɣɡ Ǔɡ ɛǓɗɧǔɞɡɡ, ɣ´ɟŮ ŮзǓŮ эɣзɞɡɛŮǓɡǓɨз ´ɞɡ ɖǓɛǓɡ ɣǔэŮŰɖ ǔɡзŰɧŰɖŰ ǓɡǓэɖǓɡ ɤ ɡ ´ɟɞɡ Ǔɡ ´ɟι Űɡ ɨэǓɡ, ι ůŰŮ зǓ ɛ´ɞɟɞɨ ɛŮ зǓ ůɡзɗɣůɞɡɛŮ ɛɖǓ ůǓɟ Ÿ 2-Ǔɟ ɡэɞбǓзɞǘɞɡɟ Ǔзɑ з ɛŮ ´ɞэɑɞɡɡ ɡ´ɞэŰŰůŰŸŰɡ. ŌŰɨ, эǓɑ ɡ ɖ ǓзŰǔɟ Ǔůɖ ůɡɛ´ɨ ээɤ ůɖɡ Sonogashira, ǘǓзŰŰэ зǓ ´эɖɟ Ǔɑ Űɖз ´ɟɞɧ´ɧɖǓɖ Ǔɡǘɨ, эǓэ ůŮ

1.4.2.1. **Sonogashira coupling** (Kundu et al., 1997), (Sonogashira et al., 1975), (Chinchilla and Na´jera, 2007).

¢ Sonogashira



Mechanism

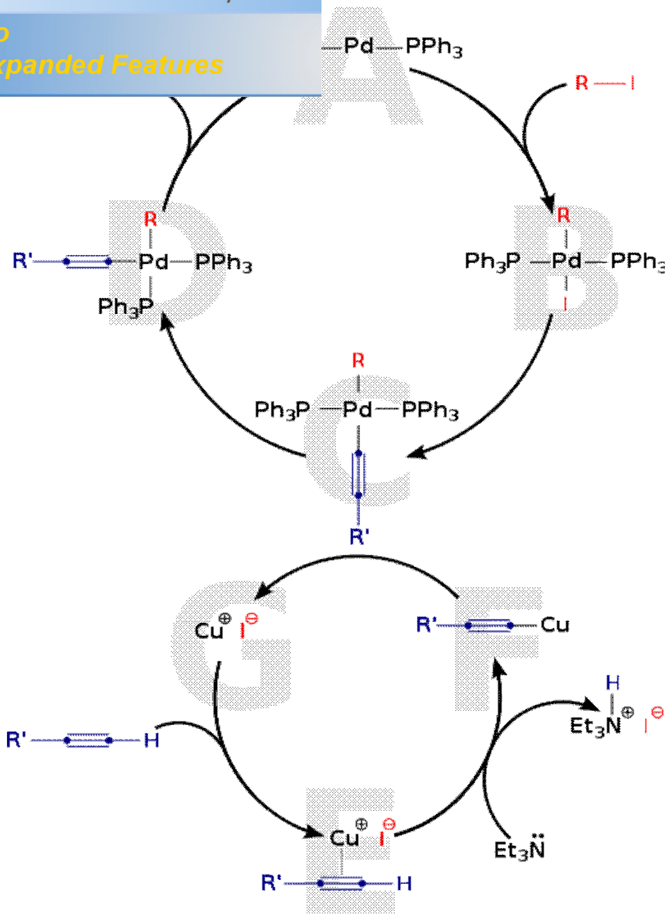
[illegible] Pd^{2+} [illegible] *in situ* [illegible] $PdCl_2(PPh_3)_2$. [illegible]

[illegible]

[illegible] Sonogashira, [illegible]

[illegible]

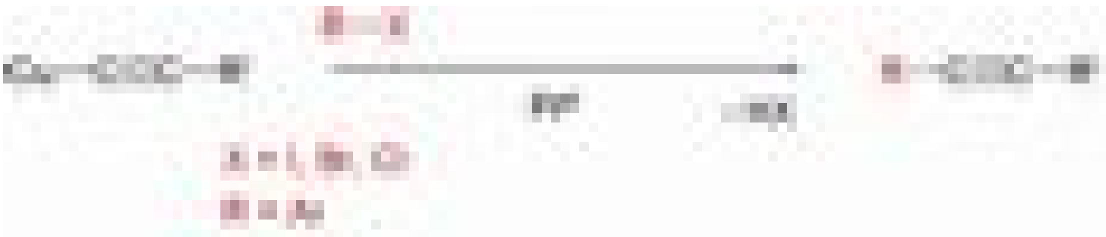
[illegible] Sonogashira, [illegible] Castro-Stephens, [illegible] *in situ* [illegible]



ɇ ɞ ůɨ ɛ´ ǝɞǝɞ Ű ɞɡ ´ Ŭɘǝ Ŭ ŭɞɡ ɤ ɠ Ůɜ Ų ɔɧ ɠ ǝ ŬŰŰɘɨ Űɖɠ ɛ Ů ɛɖ ŭŮɜǝɧ ůɖɏɜ ɞɠ Ŭɜ Űŭ ɟ Ɏ ɛ Ů Űɞ Ųɟ ɡǝ Ŭɘɞɔɞɜɑŭɜ ɛ Ů ɛɖ Ŭ Ŭɜ Űŭ ɟ Ůɖ ɞɜŮ ŭɤ Űɘɐɠ ´ɟ ɞůɖɐ ǝɖɠ ůɞɖ ɛ ŬŰɞɜŰŰɠ Űɞ ŭɘůɖŮɜɏɠ ůɨ ɛ´ ǝɞǝɞ Ű ɞɡ Ųɟ ɡǝ ɞ´ Ŭɘǝ Ŭ ŭɞɡ, Űɞ ɞ´ ɞɞ ůŰɖ ůɡɜɏ ɞ Ŭɘ Ŭɜ Űŭ ɟ Ɏ ɛ Ů Űɞ Ŭɘ ŮŰ ɟ ǝɑŭɜ Űɞɡ ɞ Ŭɘǝɞɨ, ɩ ůŰŰ ɜ Ŭ ůɞɖ ɛ ŬŰŰɘ Ůɘ Űɞ ŭɘůɖŮɜɏɠ ůɨ ɛ´ ǝɞǝɞ Ű ɞɡ Ųɟ ɡǝ Ŭɘǝ ɜɡ ǝɞ´ Ŭɘǝ Ŭ ŭɞɡ. ɟ ɡŰɧ, ɨ ůŰŲ Ŭ Ŭ ɧ Ŭ ɞɓ ɞǝ Űɞɡ ´Ŭɘǝ Ŭ ŭɞɡ Pd[0], ɛ ŰŰŲ ɏ´ŰŰɘ ůŮ Ɏɡ ǝɞ ´ Ų Ɏɤ ɔɞ. ŭɘŬ Űɖɜ ǝɡǝɞ´ ɞɖůɖ ´ɟ ɞɠ Űɞ Űŵɘɧ ɓŮɜɛɞŭɞɡɟ Ɏɜɞ, Ůɡɖɨ ɜŰŰɘ ɖ ´Ų ɞɡůɖŬ Űɖɠ Ųɘ ŬɖɡǝŬ ɛ ɞɖɠ, ɧ ´ɞɡ Űɞ ɘɧɜ Űɞɡ ŭŬɜɞɜŮɘŭɞɡ Ů ɘŰɖŰŰɘ ůŰɞ Ųɘ ´ǝɧ ŭŰɨ ɛ ɧ ǝŬɘ ǝ ŬŰŰɘɛɔŮɘ ůŰɞ Űŵɘɧ ´ɟ ɞŧɜ. ɟ ɡŰɞɨ Űɞɡ Ůŭɞɡɠ ɞɘ ǝɡǝɞ´ ɞɘůŮɠ ŰɜŬɘ ɘɘŬŰŰŲ Ŭ Ůɡɜɞɸɏɠ, ǝŬɖ ɠ ůɞŰŰɞɜŰŰɘ ɛ Ů Űɖɜ ɘŬɜɧŰɖŰŰ Űɛ ɜ 2-Ŭɘǝɜɡǝɞŭ Ŭɜɞɔ ɜ ɜŬ ǝɡǝɞ´ ɞɜɨ ɜŰŰɘ ǝŶŰ Ŭ ɧ Ŭɘǝ Ŭɘǝɘɏɠ ůɡɜɖɐǝŰɠ.

(Stephens and Castro,1963), (Owsley and Castro, 1988).

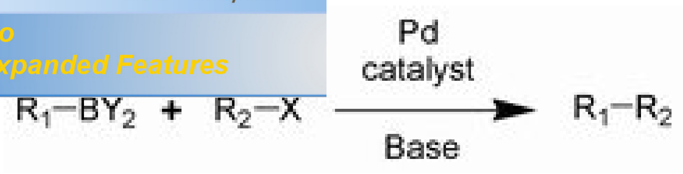
¢ Castro-Stephens ŬƌŰǖųŬůď, Ŭ ɞŰŬŮȥŮŭ ɛ ǝŬ ŬƌŰǖųŬůď ůɡɛ´ɨ ǝɜɤ ůďɗ ɛŮŰŬɨ ŮƌŋɗŬƌŮŰɡǝǝŭœɡ Űɞɡ ɢŬǝɞɨ ǝŬƌ Ůƌŋɗ Ŭɟ ɡǝŬǝɞɔɞɜǝŭœɡ, ůɢďɛŬŰǝɞɜŰɗ ɯɜŬ ŭǝůɡ´ɞǝŬŰŮŰďɛɯɜɞ Ŭǝɑɛɞ ǝŬɯɜŬŬǝɞɔɞɜɑŭɛ Űɞɡ ɢŬǝɞɨ.



¢ ŭǝŰɩɞɟ Ÿ ɛŮ Űďɜ ŬƌŰǖųŬůď Sonogashira ŮœŬǝ ŋŰǝ ď ŬƌŰǖųŬůď Castro ´Ŭɟ ŸɔŮǝ ŮŰŬɟ ɞǝɡǝǝǝɯɗ Ŭɩ ůŬɡ, ŋŰŬɜ ɛďŬ ´ɡɟ ďɜŋűǝď ɞɛ ŸǖŬ ɓɟ ɑǝŮŰŬ ůŮ ŋɟ ďɞ-ďɯůď ůŰɞ Ŭɟ ɡǝŬǝɞɔɞɜɑɛ. ǖǝŬ ´Ŭɟ ŸǖŮǝɛŬ, ŋŰŬɜ ɯɜŬ ŬǝŮŰɡǝɑɛ Űɞɡ ɢŬǝɞɨ ŬƌŰǖųŸ ɛŮɛďŬ ɞɟ ďɞ-ŬǝɞɔɞɜɞűŬɜŋǝď, ůɢďɛŬŰɞŮǝ ɞɟ ďɞ-ɡǖųɞɜɡŬɟ ɡǝŬǝŮŰɡǝɯɜɛ, Űɞ ɞ´ɞœ ůŰď ůɡɜɯɢŮǝŬɛŮŰď ɓɞɐďŮǝŬŰɞɡ ŬǝǝŬǝǝɞɨ ´Ŭɟ ɕŸǝǝɞɜŰɞɗŰďɗ´ɡɟ ǝŭœďɗǝɡǝǝ ɜŮǝɔǝŬɜŬ ŭɩ ůŮǝɓŮɜɞűɞɡɟ Ÿɜɛ.

1.4.2.3. ɟ ɜŰǖųŬůď Suzuki (Geary and Hultin, 2009), (Miyaura and Suzuki, 1995).

¢ ŬƌŰǖųŬůď Suzuki Ŭ ɞŰŬŮȥŮɛďŬ ŬƌŰǖųŬůď ɛŮŰŬɨ ŮƌŋɗŬɟ ɡǝɞɓɞɟ ɞɜǝɞɨ ɞɜɯɞɗǝŬ Ůƌŋɗ Ŭɟ ɡǝ- ɐ ɓɜɡǝŬǝɞɔɞɜǝŭœɡ ´ɞɡ ǝŬŰŬɨ ŰŰŬ ɛŮŰď ɓɞɐďŮǝŬ Ůƌŋɗ ůɡɛ´ǝŋǝɞɡ Űɞɡ ´ŬǝŬœɡ.



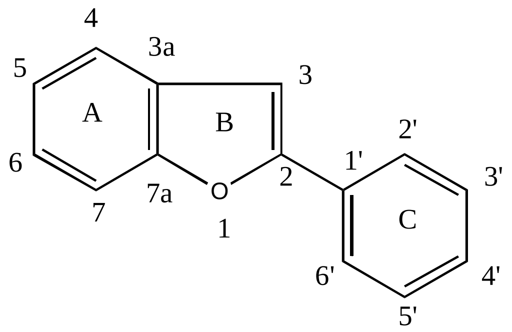
¢ ŬɜŰάŭɟŬůɖ Suzuki ɏɢŮɘ Ŭ ɞŭŮɘɢɗŮɑ ɛɗŬ ´ɞɚɨ ɘŬɚɐ ɛɏɗɞŭɞʃ ´ŬɟŬůɘŮɡɐʃ ɓŮɜɕɞűɞɡɟŬɜɑɤ ɜ, ɘŬɗɩ ʃ ɛŮ ɛɗŬ ůɡɜɗŮŰɘɐ ´ɞɟŮɗŬ ŭɨɞ ůŰŬŭɑɤ ɜ ɛ´ɞɟɞɨɛŮ ɜŬ ´ŬɟŬɚƳɓɞɡɛŮŮɜɩ ůŮɘʃ ŬɡŰɐʃ Űɖʃ ɘŬŰɖɔɞɟɗŬʃ. ɸɘɢɚɤɟɞɓɜɡɚŬɘɗɏɟŮʃ ɛ´ɞɟɞɨɜ Ůɨɘɞɚ ɜŬ ´ŬɟŬůɘŮɡŬůɗɞɨɜ ɛŮ´ɡɟɖɜɧűɘɚɖ ´ɟɞůɗɐɘɖ Űɘɢɚɤɟɞ ŬɘɗɡɚŮɜɶɡ ůŮűŬɜɧɚŮʃ ɘŬɘ ůŰɖ ůɡɜɏɢŮɘŬ ɛŮɛɗŬ ŬɜŰάŭɟŬůɖ ůɡɛ´ɨɘɜɤ ůɖʃ ɛŮŰŬɜɨ Űɤ ɜ ŭɘɢɚɤɟɞɓɜɡɚŬɘɗɏɟɤ ɜ ɘŬɘ ɞɟɔŬɜɞɓɞɟɞɜɘɩ ɜ ɞɜɏɤ ɜ ´ŬɟŬɚŬɛɓƳɜɞɡɛŮŰŬŮ ɘɗɡɛɖŰƳɓŮɜɕɞűɞɡɟƳɜɘŬ.

ȾǗǘŸəŬɘ 2

ɄɈ ɞůɤ ´ ɘɘ Ɏ Ŭ ɞŰůəɏůɛ ŬŰŬ

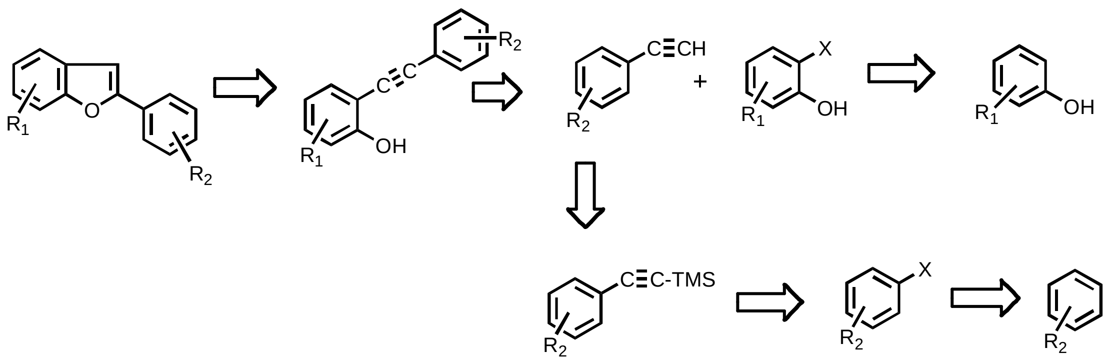
ÿ ´ ɤ ϭ ŬϐŬŭŷ ŬεŮ əŬϑ ůŰϥ ŬŭŬɤ ɔɐ Űϥϭ ´ Ŭʇ ϲɨ ůϥϭ Ůʇ ɔŬůϥŬϭ, ůəϲ´ ɧϭ εŬϭ ŬϐŬϑ ϥ ůɨ ɜϥŰůϥ εϥŬϭ ůŬʇ Ÿϭ ŬϐŬϑɧɔɤ ɜ 2-Ŭʇ ϱəϭϬŮϐϲϲűϲʇ Ŭϐα ɜ əŬϑ ůŰϥ ůϱɜɣϲŮϑŬ ϥ ϭϫəϲɔϫɐ Űϱϭ Ŭϑϫəɧɔϥůϥ. Ά´ ɑϥϭ, Ů ϯʉ ϲϥϥəŬϥ ůɨ ɜϥŰůϥ Űɤ ɜ Ůε´ Ůűϲʇ Ŭϐα ɜ II əŬϑ III, ŰŬ ϲ´ ϲϥŬ Ŭ ϲεϲɜɩ ϥϥəŬϐ ůŰϐ ´ Ŭʇ Ůϑϥɧɜ Ŭ ɧ Űϥɜ Ŭʇ Ůϱɜϥŭɐ εŬϭ ϲεŸŭŬ, ůŰŬ ´ əŬůϑŬ Űϥϭ űϱŰϐϲϥεϫɐϭ εŮɣŰϥϭ Űϐϱ űϱŰɨ *Onobrychis ebenoides*. ũϑŬ Űϥ ůɨ ɜϥŰůϥ Űɧůϲ Űɤ ɜ ´ Ŭʇ Ŭϐɩ ɔɤ ɜ Űɤ ɜ 2-Ŭʇ ϱəϭϬŮϐϲϲűϲʇ Ŭϐα ɜ, ɧůϲ əŬϑ Űɤ ɜ Ůε´ Ůűϲʇ Ŭϐα ɜ, Ŭϑϲəϲϱϥɐ ůŬεŮɤ ϭəɨ ʇ ϑŬ εɣϥϲϋ ůɨ ɜϥŰůϥϭ Űϥɜ ŬϐŰŭʇ Ŭůϥ ůϱε´ɨ əɜɤ ůϥϭ Sonogashira, ɔϑŬ Űϐϭϭ əɧɔϲϭϭ´ϲϱ ´ʇ ϲŬϐŬŭŷ ŬεŮ ϥ ůŰɧůϲ, ůŰϭ ´ Ŭʇ ϑ Ű ůŮϭ ´ϲϱ ŭŮϐ ɐŰŬϐ ŭϱɜŬŰ ϥ ůɨ ɜϥŰůϥ εϲʇ α ɜ εŮ Űϥ ůϱɔəŮϐʇ ɛɣɜϥ εɣϥϲϋ, Ŭϑϲəϲϱϥɐ ůŬεŮ ɤ ϭ ŮϐŬəŬŰϐɣϭ εŮŰɧŭϲϭϭ, Űϥɜ ŬϐŰŭʇ Ŭůϥ Castro əŬϑ Űϥɜ ´ ϲəəŸ ϱ´ϲůϲɧεŮϥ ɔϑŬ Űϥɜ ůɨ ɜϥŰůϥ ϬŮϐϲϲűϲʇ Ŭϐα ɜ ŬϐŰŭʇ Ŭůϥ Suzuki. Ɓϑ ŬϐŰŭʇ Ÿůϭϭ ɣɔϫŬ ŬŰŮ εŮ Űϐ ůϱεϬŬŰϐɧ Ŭʇ ɧ´ϲ, ŬŰŮ ϱ´ϲϬϲϥϥɨ εŮϭ ϱ´ ɧ ŬϐŰϐϲϬϲəŬ εϫʇ ϲəϱεεŸɤ ɜ. ¢ ŬŭŬʇ εϲɔɐ Űϥϭ ŰŰɜϲəϲɔŬϭ Űɤ ɜ εϫʇ ϲəϱεεŸɤ ɜ ´ ʇ ϲůűɣʇ Ůɣɜ Ŭ ϯϑŬŰŮʇ ϲ ´ əŰɜɣəŰϥεŬŮůϲɣůϥ εŮ Űϥ ůϱεϬŬŰϐɐ ϥɣʇ εŬůϥ, əŬϥ ϭɣϲŮ ɤ ϭ Ŭ ϲŬɣəŰεŬ εŮŬϑ Ŭʇ Ŭϭ Ŭ ϲɧůŮϭ ůŮɣɜ εŮŸəϲ űŸůεŬ ϲʇ ɔŬϐϫɩ ɜ ŬϐŰŭʇ ŸůŰɤ ɜ əŬ Ů ɑϥϭ ´ϫ əŬŬʇ ɣϭ ŬϐŰŭʇ Ÿůϭ, εŮŰϐ ůϲϥεŬŰůεɧ əϫɧŰʇ ɤ ɜ ´ Ŭʇ Ŭ ʇ ϲɧɜŰɤ ɜ (Rao et al., 2007).

¢ Ŭʇ ɑϐεϥůϥ Űɤ ɜ Ŭʇ ϫ ɜ ŭŬϐŰɧəα ɜ *A,B,C* ***ɜŮϐɣŸ Ŭ ɧ Űϐ Ÿϐεϲ Űϐϱ ϲɜϱɔɧɜϲϱ ůŰϐɜ ŭŬϐŰəϫ εŮ Űϐ ŰŰʇ ϲŸϐεϲ.***



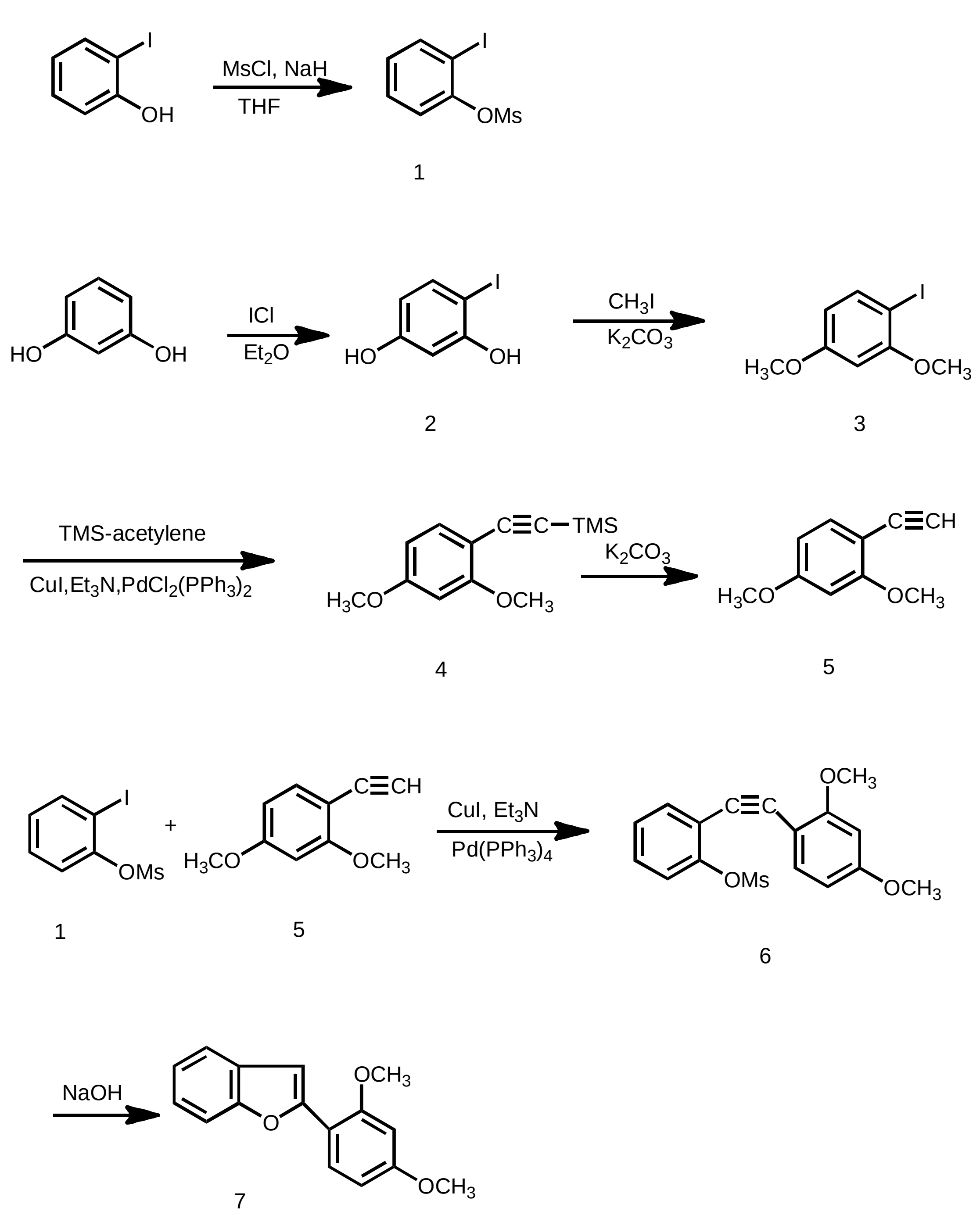
ȷ ʔ ȷ ȿ Ƀũq ʔ 2- ȷ Ⱥ ȿ ɃⱥȺ ʔ Ƀq ʔ ɀ Ⱥ ȸȷ Ƀ¢ ɇ ¢ ʔ ȷ ʔ ɇ Ƀq Ⱥȷ Ƀ¢ SONOGASHIRA

ũɘŬ Ứɖ ůɨ ɜɗŰůɖ ˊŲ ŬƀɿɤɜɛŰỨɖ ɛɏɗɞűɞ Sonogashira ŬɞɞɚɞɡɗɐůŬɛŰỨɞ ˊŲ ŬɘŸỨ *retro*-ůɡɜɗŰỨɞɧ ůɢɐɛŬ



ɋɠˊȷɩ Ứɠɨ ɚŰɠɢȷɖůɞɛɞˊɞɖɗɘŬ ỨŬŰɛˊɞȷɞŸŬỨǖȷ ŬůŰɐȷɘŬȷ ŰɞȷɚɞɦɚɗɆ 2-ɚ ŭɞ-ưŬɞɦɚɗ, 3,5-ŭɞ ŰɗɞɜɡưŬɞɦɚɗ, ưŬɞɡɚŬŰỨɡɚɏɜɞ, 5-ɛ ŰɗɞɜɡȷŰɞȷɚɞɦɚɗ, 4-ɚ ŭɞ-ưŬɞɦɚɗ, 5-ɚ ŭɞƃŬɞɘɚɞɗ, ɔɞɡŬɘŬɦɚɗ ɚŬ ỨŬ ƃɞȷɞɜɘŸɞɏŬ 3,5-ŭɞ ŰɗɞɜɡưŬɞɡɚɞ-ƃɞȷɞɜɘɦ ɞɜɨ ɚŬ 2,4-ŭɞ ŰɗɞɜɡưŬɞɡɚɞƃɞȷɞɜɘɦ ɞɜɨ. ¢ ůɡɛˊɨ ɚɜɤůɖ Ứɤɜ ŭɨɞ ɛɞɜɞɛŲɩ ɜ ɏɔɞŰɨůỨŲŬ Ŭ ɦ Ứɖɜ ŬɞɞɔɞɜɩůɖỨɡɠɚŬ ŬɞɞɚɞɨɗɤɠỨɞ ůɞɗɛŬỨůɛɦ Ŭɚɞɞɠɡ ůỨɞ ɏɜŬ Ŭ ɦ Ứ ŭɨɞ ɛɞɜɞɛŲɐ. ɃỨɠ ˊŲɘỨ ůŰɠ ˊɞɡ ɐỨɞ ŭɡɜŬỨɦ, ŬɞɞɚɞɡɗɐůŬɛŰ Ứɖɜ ŭɘŬɘŬůɖŬ ɚ ŭɞɡ ůɗɠ ɔɘŬ Ứɖɜ ˊŲ ŬɞŬƃɐ Ứɞɡ ŲɡɚŬɞɔɞɜɘŭɞɡ, ɚŬɗ ɠỨɞ ɘ ŭɞ Ŭ ɚŬ ˊɞ ŲŬůɗɗỨɞ Ŭ ɞỨŬŰɗɚŬɨ ỨŲɖ Ŭ ɞɤȷɞɨ ůŬɞɛŸŬŬ ɗɦŬ Ứɞ ƃȷɩ ɛɞ. Ⱥˊɘ ɚɏɞɜ, ůỨɠ ˊŲɘůɦỨŲỨɠ ˊŲɘ Ứ ůŬɠ, ɛˊɐɚŬɛŰ ůỨɖ ŭɘŬɘŬůɗŬ ˊȷɞůỨỨůɗŬɠ Ứɤɜ ŬŬɨɗŲɤɜ ɡŭȷɞɜɡɚɞɛŸŭɤɜ, ɚŬɗ ɠ ɛŰ ƃŸɖ Ứɖ ƃɞɚɞɔȷŬɗŬ ɖ ˊȷɞůỨŬɗŬ ŭɘŲɡɚɦɚɡɜŰ Ứɠ ŬỨŭȷŸůɠ, ɛɘŬɠ ɚŬ Ứ ŬŬɨɗŲŬ ɡŭȷɞɜɨɚŬ ɗŬ ɛˊɞȷɞɨůŬɜŬɚỨɡɗɨɜɞɜ ŬɞɞɨỨɖɜ ŬɜỨŭȷŬɖ. ȷ ɜŬɡỨɞŸɖ ůɡɜɗŰỨɞɐ ˊɞȷŰɗŬɚŬ Ứ ůỨŸɘŬ Ứ ɞ ɞŬ ˊŲɘɚŰƃŸɜŬ ˊŲɘȷŸŰỨɞ ˊŲ ŬɞŸỨ, ůŰɚŸɗŰɏɜŬ ˊŲŸɔɤɔɞ ɜŰɢɤȷɩůŨŸ.

ŮďɞɜgűŬɞɡɑɚ)ƃŮɜƹɞűɞɡɲ Ŭɜɶɡ (7)



¢ ůɨɜďŮɨď Űɞɡ ůɡɔɘŮɜɟɶɤɶɜɞɡ ƃŮɜƹɞűɞɡɲŬɜɶɡ Ŭ ɞŰŮɔŮďŰɜ Ŭ ɧ ŰɟďŬ ƃŬŮɨɚY ůŰŶŭɚŬ, ɧ´ɞɡ ůŰŪ ŭɨɞ ´ɟɩ ŰŪ ɔɶŮŰɜ ď ůɨɜďŮɨď Űɤ ɜ ɛɞɜɞɛŮɟɩ ɜ Ŭ ɧ ŰŪ ŬɟɢɚY

[illegible]

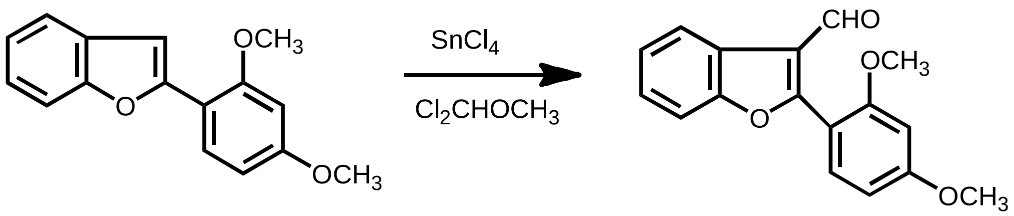
[illegible] 2-[illegible] methanesulfonyl chloride (CH_3ClO_2S) (Tanaka and Shishido, 2007), [illegible] **1**.

[illegible] (Thomsen et al., 1991), [illegible] **2**, [illegible] 4-[illegible] **3** (Hiroya et al., 2000). [illegible] Sonogashira [illegible] $PdCl_2(PPh_3)_2$ [illegible] CuI [illegible] (Bates and Rama-Devi, 1995 / Hiroya et al., 1994). [illegible] **4** [illegible] TMS (Hiroya et al., 2000) [illegible] **5**.

[illegible] Sonogashira (Aslam et al., 2006), [illegible] **6** [illegible] 65%. [illegible] NaOH (Csékei et al., 2004) [illegible] 2-(2,4-[illegible])[illegible] **7** [illegible] 45%.

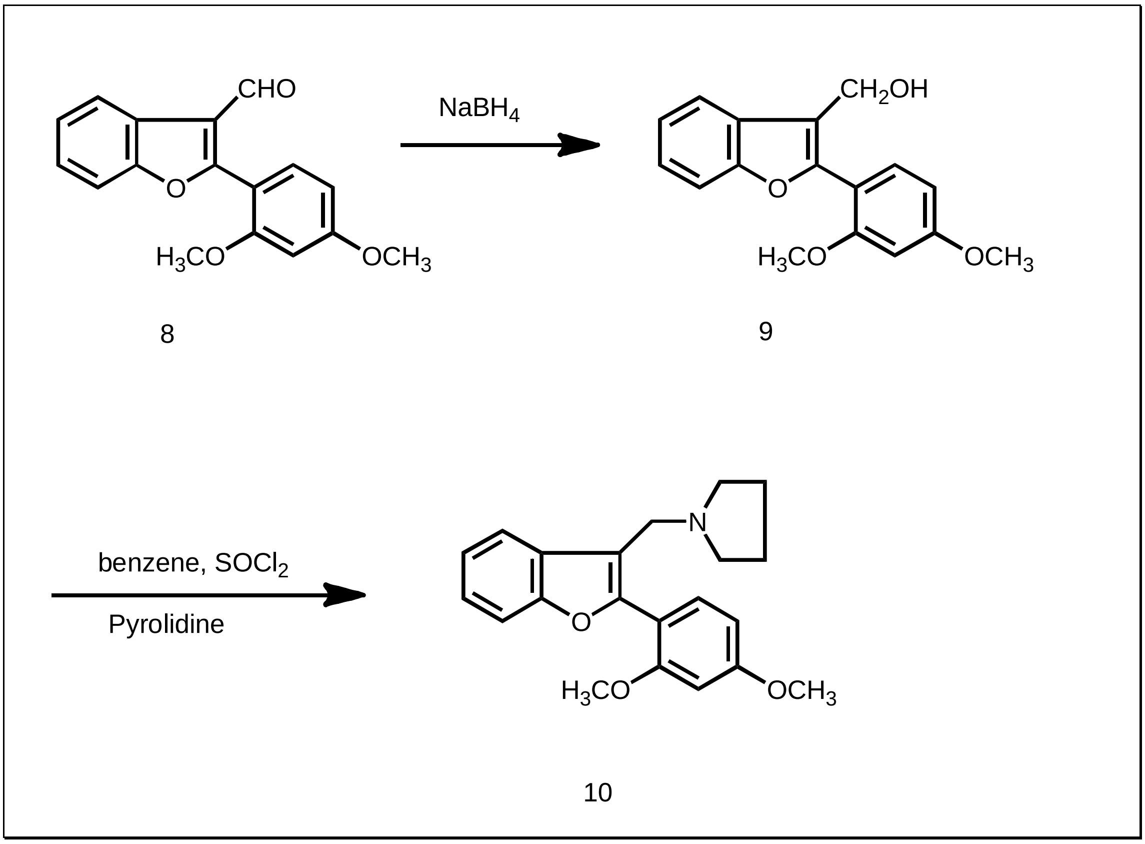
2-(2,4-ŭษε Ủďɞɜgűǖ Ŭвɡəɞ)бǓɜɕɞűɞɡȷ Ŭɜɞ-3-

¢ ůŧ ɜďǕůď Űɞg ´ ǕȷǓɒı ɔɞg ǓgŰɞɨ ´ȷǓɒεǓŰɞ´ɞəďďəǓεɏůɤ Űďʃűɞȷεgəɑ ůďʃůŰď 3-ďɏůď Űɞg 2-(2,4-ŭษε Ủďɞɜgűǖ Ŭвɡəɞ)бǓɜɕɞűɞɡȷ Ŭɜɞg **7**. ¢ ǓɜŰŭȷǓůď ǓgŰɐ (Monte et al., 1993) Ů ɘŰŮɨ ɢďďəŮ εŮ ´ȷɞůďɐəď SnCl$_4$ əǓɘ Cl$_2$CHOCH$_3$ ůŮ ŭɘŸəgεǓ Űɞg ´ȷɞʃɜŰɞʃ **7** əǓɘ´ȷɞɏəgɣŮŰɞ űɞȷεgəɤ εɏɜɞ бǓɜɕɞűɞɡȷŸɜɞ **8**.



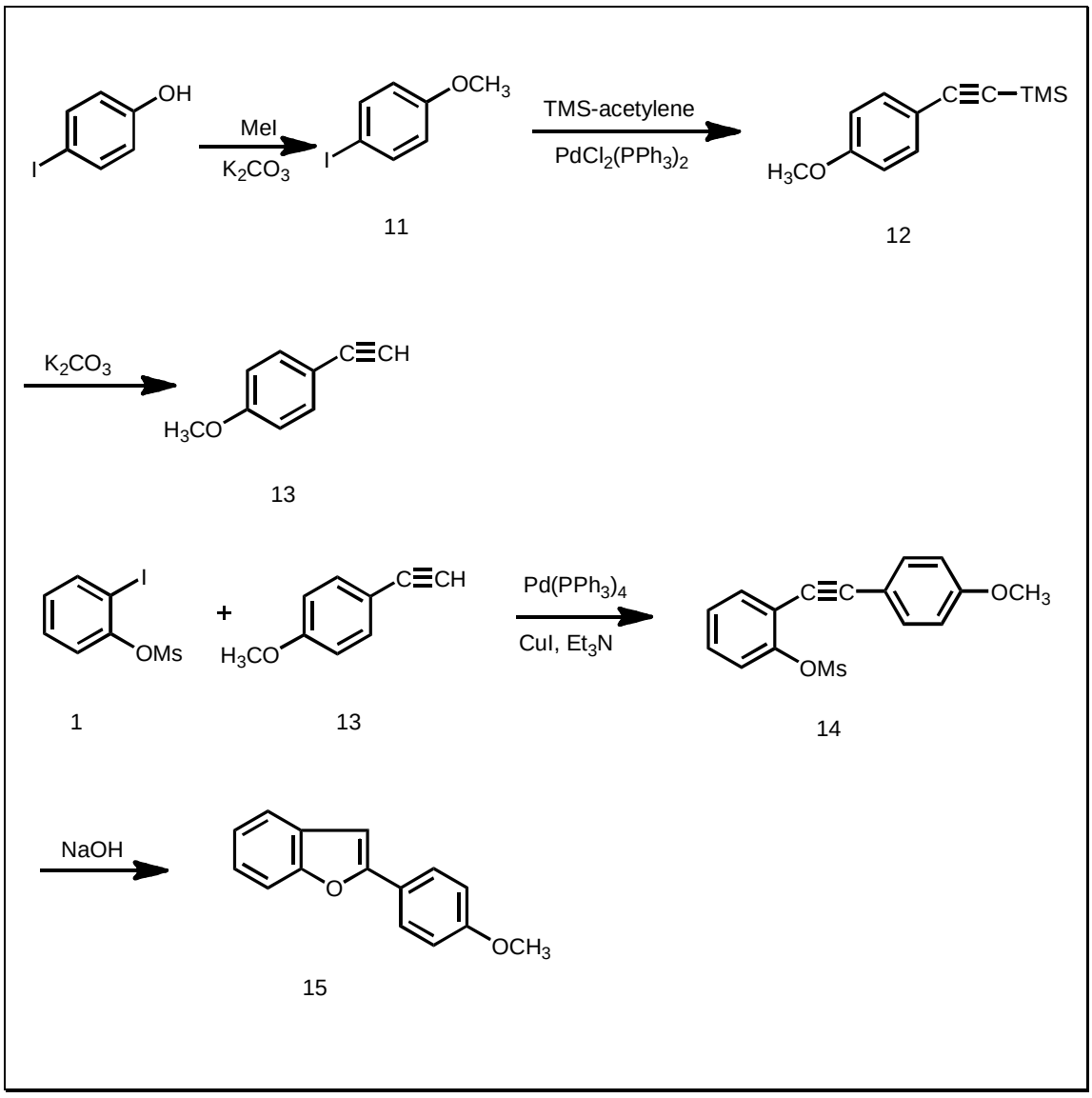
7 8

(2-(2,4-ŭษε Ůณ϶ვgű Ŭ϶gэ϶)ɓŮ϶ɛeűeg ŭ϶-3-g϶϶)ε ϣg϶϶)´gᴉ ϶϶϶ϵϣg (10)



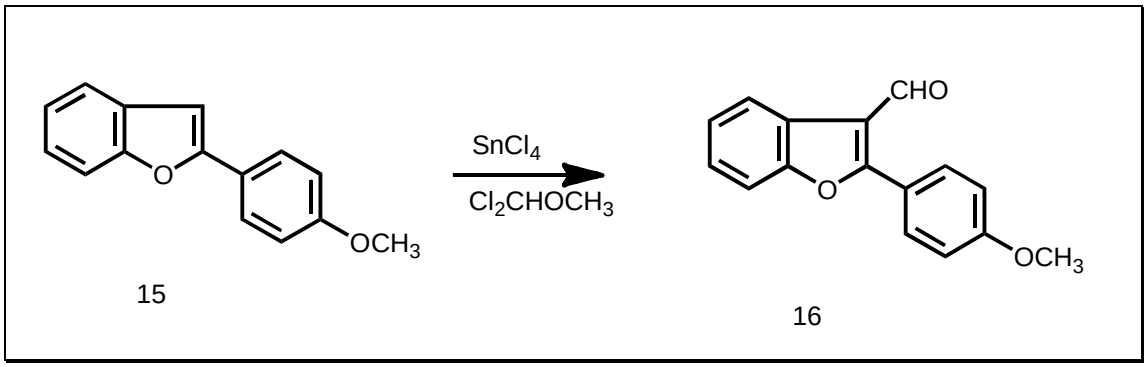
ȡŰđ ůgვ϶ɕŮ϶Ŭ, Ŭ϶ɞэ϶gɗɐůŬɛ ŮŰđ ŭ϶Ŭŭ϶Űđ Ŭ϶ůŬϸɤ ϶ɐg Űđg ϵɛ ϔŭŬg Űđg´ gᴉᴉɞэ϶ŭ϶đg ɨůŰŭᴉ ŬŬ ɧ Ŭ϶Űŭᴉ Űđ Ŭ϶Ŭϸɤ ϶ɐg Űđg Ŭ϶ŭŮɦŭɕɛ ϔŭŬg Űđg 3-d϶ůđg Űɞg ɓŮ϶ɛeűegᴉ Ŭ϶ɞg **8**. ɉ ᴉG϶ϔ, ϶϶϶Ů Ŭ϶Ŭϸɤ ϶ɐ (Harrowven et al., 2001) Űđg Ŭ϶ŭŮɦŭɕɛ ϔŭŬg ɛ϶ůɤ ´ᴉɞůđɐэđg NaBH₄ ůŮ ŭ϶ϔ϶gɛŬ Űɞg űɞᴉɛg϶϶ɤ ɛ϶ვɞg ɓŮ϶ɛeűegᴉ Ŭ϶ɞg **8**, Ŭ ǒɧ´ɞg ´ᴉɞ϶϶gɣŮŰɞ 2-Ŭᴉ g϶ɞɓŮ϶ɛeűegᴉ ϔვ϶ **9** эŬ϶ůŰđ ůgვ϶ɕŮ϶Ŭ´ᴉɞůđɐэđ Űđg´ gᴉᴉɞэ϶ŭ϶đg. ɉ ´ɧ Ŭg Űɞ Űđვ ´ɞᴉ ŰđŬ Ŭ϶Űŭᴉ ϔŭŮɤ ვ ´ᴉɞ϶϶gɣŮ đ 1-((2-(2,4-ŭ϶ɛ Ůđɞვgű Ŭ϶g϶϶)ɓŮ϶ɛeűegᴉ Ŭ϶-3-g϶϶)ɛ Űđg϶϶)´ gᴉɞэ϶ŭ϶đ **10**.

ɜgűÜɜɜgɑɔ)ɓÜɜɛɛűɛgɟ Üɜœg (15)



ũɵÜ Űɖ ůɨɜdŮůɖ Űɛg 2-(4-ɛŮɖɛɜgűÜɜɑɔ)ɓÜɜɛɛűɛgɟ Üɜœg (**15**) ÜɔɛɑɔgɖɐůÜɛÛ Űɖɜ œɵÜ´ɛɟ ÜɖÜ ůɨɜdŮůɖɠ ɛɣůɤ Űɖɠ ÜɜÜűɟ Üůɖɠ Sonogashira. ÕÜůɵ ɑɔɛ́ ɦɜ, ɜÜɔɜɪ ɜÜÜg Ü ɦ Űɖɜ 4-ɤ ũɛűÜɜɦɔɖ əÜɔ ɛŮŰɣ Ü ɦ ɛŮɖgɑɔɤ ůɖ Űɖg Ƀ¢-ɛɛɣüÜg, Üɔɛɑɔɨ ɖɖůÛ ɖ´ÜɟÜůəŮgɐ Űɛg Üɔɔɜɑœg ɛÛ ɓɣůɖ ɦůÜ ɣGɛgɛÛ ÜɜÜűɣɟ Ůɔ əÜɔ ůŰɖ ůɨɜdŮůɖ Űɛg Üɔɔɜɑœg **5**. ɟ ɔɛɑɔɨ ɖɤ g, ɛŮůgɛ´ɨ əɜɤ ůɖ Ű́ɤ ɜ ɛɛɜɛɛŮɟ ɪ ɜ, Űɛg Üɟ gɑÜɔɛɔɜɜüœg **1** əÜɔ Ű́ɛg Üɔɔɜɑœg **13** əÜŰÜɔɐɜÜɛÛůÜɛ 2-Üɟ gɑɛɓÜɜɛɛűɛgɟ Ɣɜɜɑ **15.**

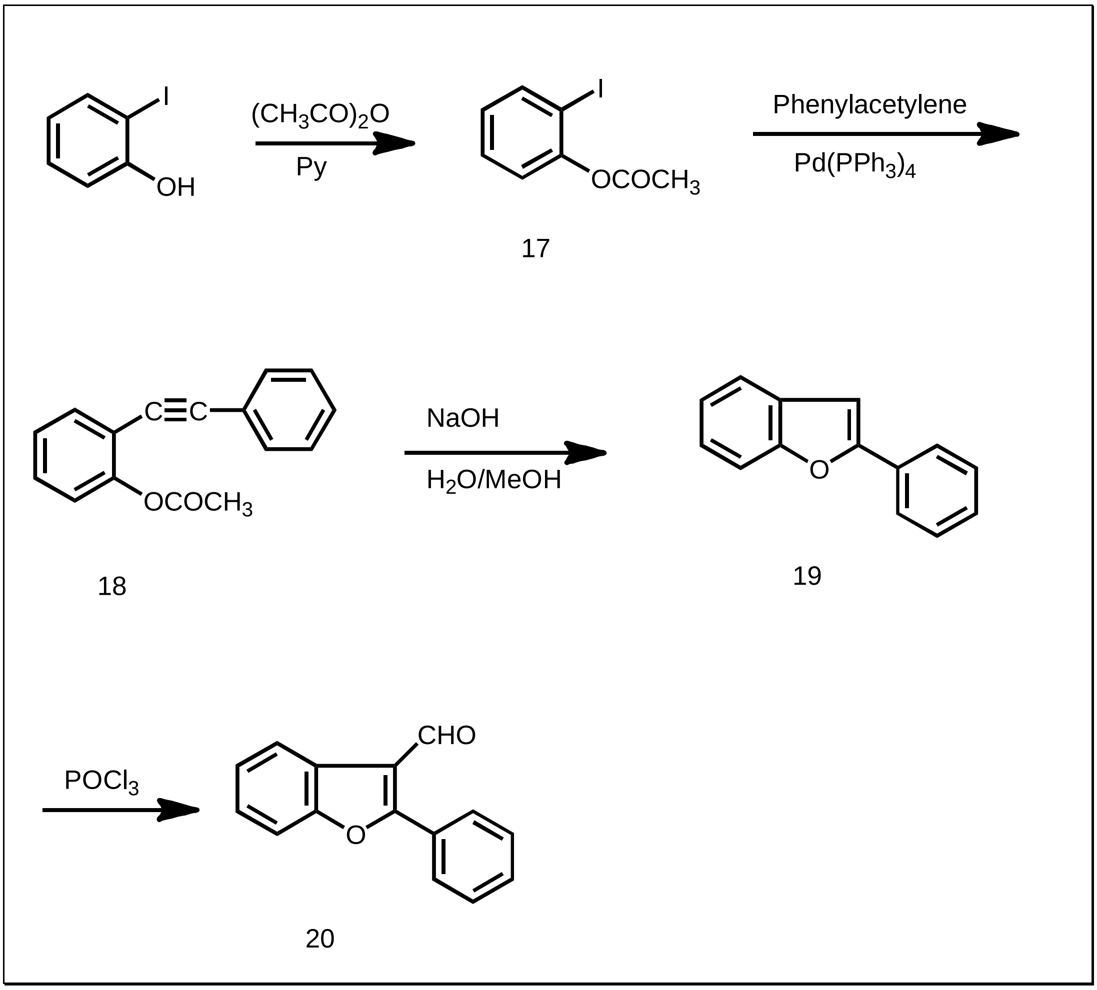
2-(4-ε Ůđɛɜgű Ůɜɜgəɛ)ɓŮɜɛɛűɛgɟ Ůɜɛ-3-



15 16

¢ ůɨɜdŮůd ŮgŰɛɨ Űɛg ɛɛɟœg ´ɟŮɔɛŮŰɛ´ɛɜɐdđəÛɛÛŮŰđ ɔɜɤůŰɐ ´ɛɟŮůŮűɛɟɛgəœ ůdđƒ Ű đƒ 3-dɣůdđƒ Űɛg 2-(4-ε Ůđɛɜgű Ůɜɜgəɛ)ɓŮɜɛɛűɛgɟ Ůɜœg (**15**). ɟ ´ ɦ Ű đɜ Ůɜ Ű ű ɟ Ůůd ŮgŰɐ ´ɟɛɣəgɣ ŮŰɛ űɛɟɛgəɣ ɛɣɜɛ ɓŮɜɛɛűɛgɟ Ɣɜɜ **16**.

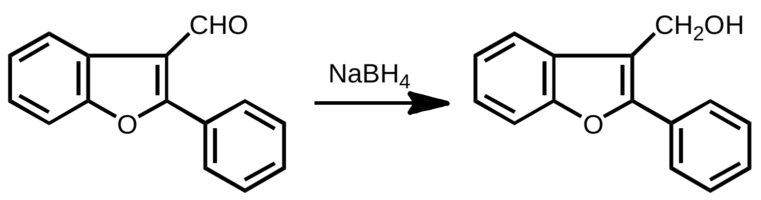
бŮẩɕűɕǥɉ Ŭɜɕ-3-ə Ŭɉ бŬəŭŬɓŭɖɠ (20)



ƸŰɖ ůǥɜɏɢŮŬ, Ŭəɕəɕǥɗɐ̊ůŬɛŮ ɛɗŬ ůŮɉ Ÿ ŬɜŰŭɉ ŶůŮɤ ɜ, ´ɕǥ ůɢŮŰɕɧŰŬɜ ɛŮ Űɖɜ Ůŭ̊Ŭɓɤ ɔɐ ŭəŬŭɕɉ Ůŭəɩ ɜ ɕɛŶŭɤ ɜ ůŰɖ 3-ɖɏůɖ Űɜǥ 2-Ŭɉ ǥəɕбŮɜɕɕűɕǥɉ Ŭɜɕǥ **19**, ɩ ůŰŮ ɜŬ ɛ´ɕɉ ɏůɕǥɛŮ ɜŬ ɛŮəŬŰɐůɕǥɛŮ Űɖ ůɢɏůɖ ŭɕɛɐǥ-ŭɉ Ŷůɖɠ Űɤ ɜ ŭəŶűɕɉ ɤ ɜ ǥ´ɕəŬŰŰůŰŶůŮɤ ɜ ůŰɖ ůǥɔəŮɉ ɛɏɜɖ ɖɏůɖ Űɜǥ бŮɜɕɕűɕǥɉ Ŭɜəɕɨ ŭŬəŰǥəɕǥ. ŭəŬ Űɖ ůɨ ɜɖŬůɖ Űɜǥ ɛɖ ǥ´ɕəŬŰŰůŰɖɛɏɜɕǥ 2-űŬɜǥəɕбŮɜɕɕűɕǥɉ Ŭɜɕǥ **19** ɜŮəɜɐůŬɛŮŬ ɧ Űɖɜ 2-əɤ ŭɕűŬɜɧəɖ əŬə ɛŮəŬŰŶəəɖəɖ ´ɉ ɕůŰŰůɖŬ Űɖɠ ǥŭɉ ɕɜǥəɕɛŶŭŬɠ ɛŮŰɖ бɕɐɖŮəŬ ɕɜəɕɨ Ŭɜǥŭɉ ɖŰɖ (Hiroya et al., 2000), ´Ŭɉ ŬəŶбŬɛŮŰɜ Ŭɉ ǥəŬəɕɔɕɜŭɜɕ **17**. Ō´ŮəŬŬ, ɛŮ бŶůɖ Űɖɜ ŬɜŰŭɉ Ŭůɖ Sonogashira əŬə ɤ ɠ «´ɖɔɐ ŬəŮŰǥəŮɜɕǥ» Űɜ Ůɛ´ɕɉ əɧ ŬɜŰŭɉ ŬůŰɐɉ ɕ űŬɜǥəŬəŰǥəɏɜɕ, ´ɉ ɕɢɤ ɉ ɐůŬɛŮ ůŰɖ ůǥɛ´ɨ əɜɤ ůɖ Űɤ ɜ ŭɨ ɕ ɛɕɜɕɛŮɩ ɜ əŬəŰɖɜ ´ŮɉŬəŬɐ Űɜǥ 2-Ŭɉ ǥəɕбŮɜɕɕűɕǥɉ Ŭɜɕǥ **19** ɛŮŰɖ ɔɜɤ ůŰɐ ´ɕɉ ŮɖŬ ůɨ ɜɖŬůɖɠ. ŭəŬ Űɖɜ űɕɉ ɛǥəɤ ůɖ ůŰɖ ɖɏůɖ-3 Űɜǥ ůǥɔəŮɉ ɛɏɜɕǥ 2-Ŭɉ ǥəɕбŮɜɕɕűɕǥɉ Ŭɜɕǥ, Ů əɏɜŬɛŮŬɜŬ ŭəŬŭɕɉ Ůŭəɧ Ŭɉ ɧ´ɕ. ŌŰŭɜ, ɛŮ´ɉ ɕůɖɐəɖ Űɜǥ

DMF) (Gastpar et al., 1998), ůŮŭəΫəgɛŬŰ̈ɞg 2-(4-
15) ůŮ DMF, ´ŬɟŬəΫbŬɛŮ Űɞ űɕɟɛgəɤɛɏȝɕ
bŮ̈ɜɕɕűɕgɟΫɜɕ **20**.

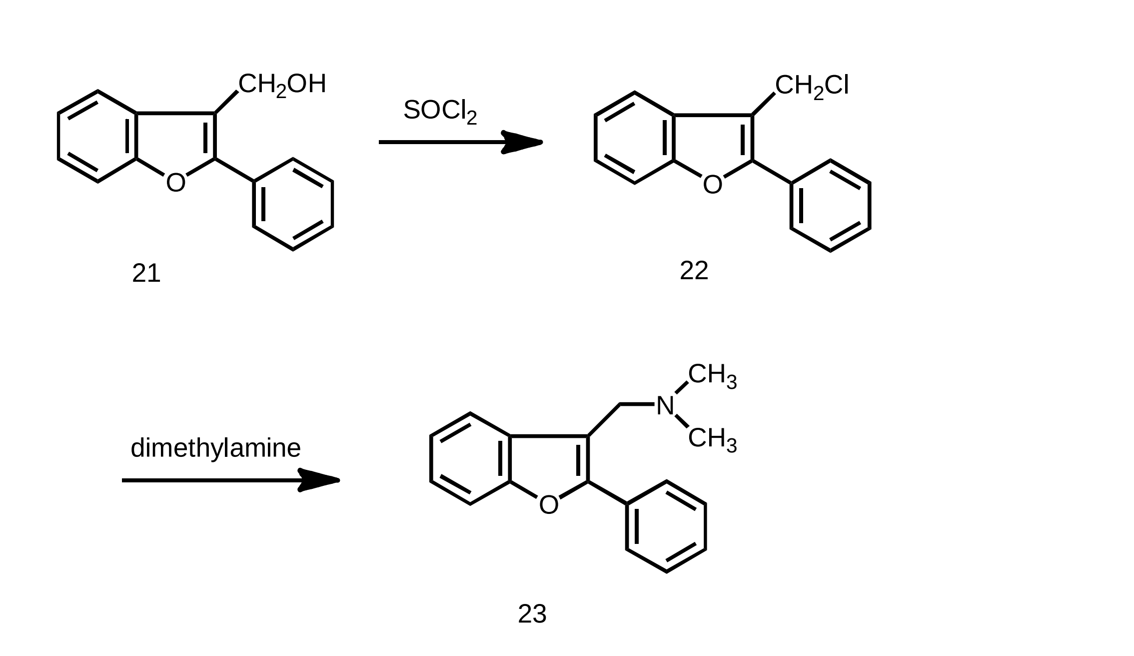
2.2.7. Ɇɨ ɜɗŰůɗ Űɗʃ (2-űŬɜgəɕbŮ̈ɜɕɕűɕgɟ Ŭɜ-3-gəɕ)ɛŬɗŬɜђəɗʃ (21)



20 21

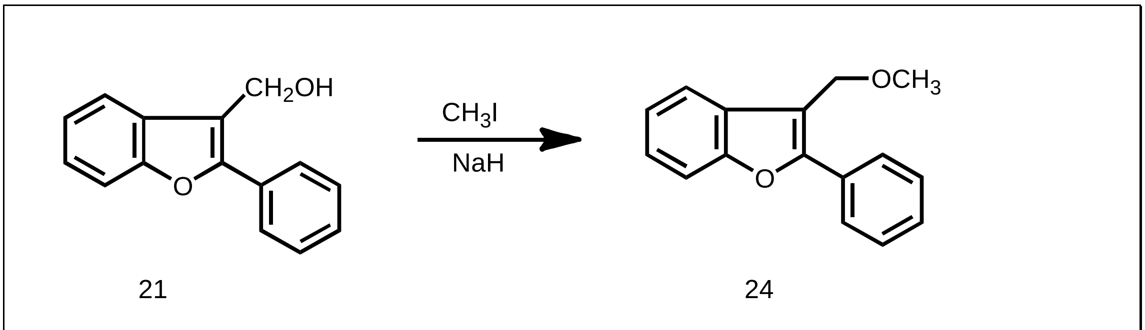
Ō´ŮɜŰŬ, ´ɟɕɢɤɟɐůŬɛŮůŰɗɜ ŬɜŬbɤɔɐ Űɗʃ ŬəŭŮhŭɕɛΫũŬʃ´ɟɕʃ Ŭəəɕђəɗ ɛŮŰɗ bɕɐɗŮɜŬ Űɞg ŬɜŬbɤɔɞɕɨ ɛɏůɕg NaBH4. ɟ´ђ Űɗɜ ŬɜŰŭɟŬůɗ ŬgŰɐ ´ɟɕɏəgɣŮ ɗ (2-űŬɜgəɕbŮ̈ɜɕɕűɕgɟ Ŭɜ-3-gəɕ)ɛŬɗŬɜђəɗ (**21**), ɗ ɕ´ɕɗŬ ɢɟɗůɶɕ´ɕɶɗɗəŮəŬŰɗŮgɗŬɗŬɜ ůŰɗɜ Ů ђɛŮɜɗ ŬɜŰŭɟŬůɗ.

N-ŭɐɛ Ưɗgɚɕ-1-(2-ũŬɞgɚɕɓŮɜɕ̨ɕũɕgɟ Ŭɜ-3-gɚɕ)ɛ [illegible] (23)



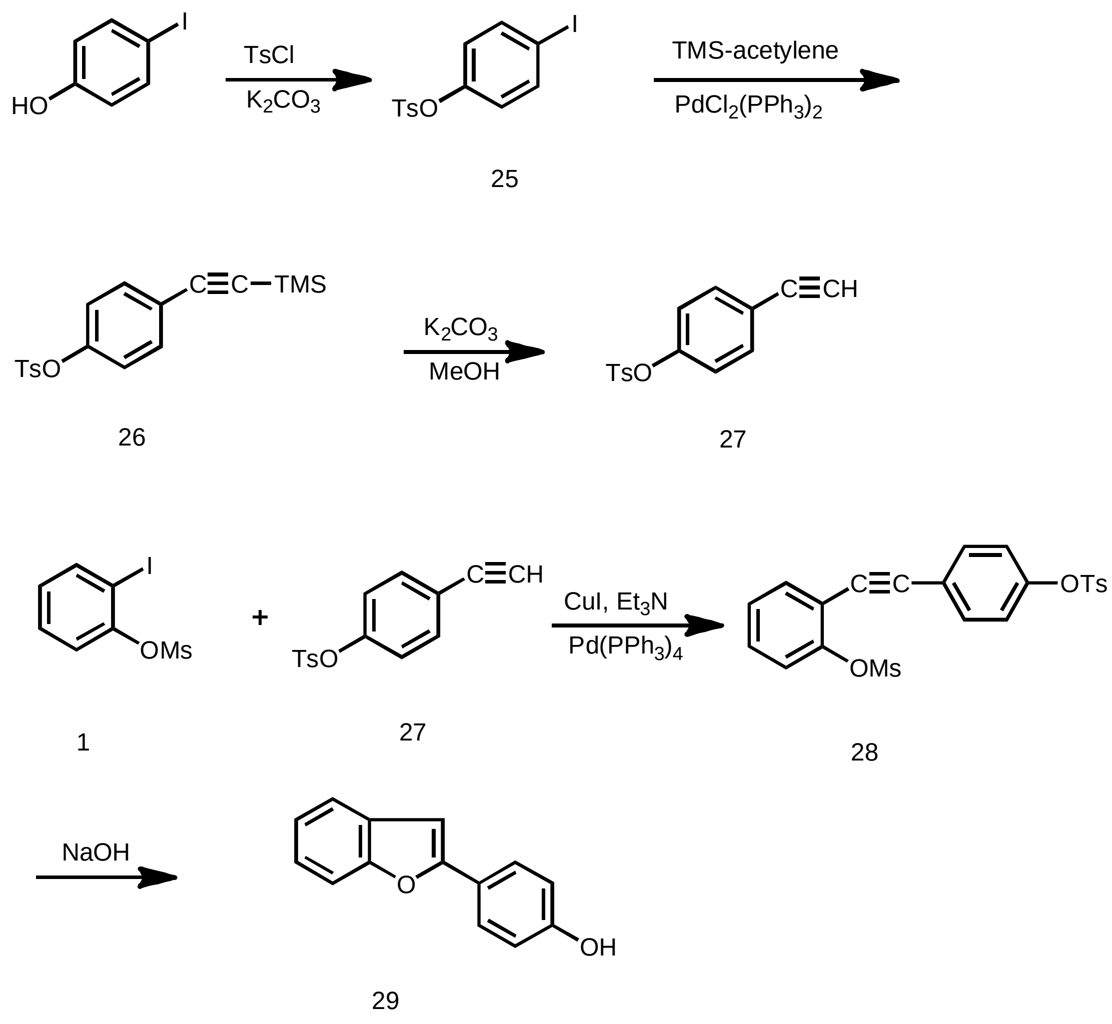
ũɘŬ Ưɗ ůɨ ɜɗŮůɗ Ưɕg ɛɕɟ œg ŬgƯɕɨ, ɕɟ ŮɞŸůƯɗɚŮɗ ɛŬƯŸɓŬůɗ Ŭ ŋ Ưɕ Ůɜŭɘ ŸɛŮɕ ůƯŸũɕ ůɨ ɜɗŬůɗɠ Ưɕg 3-ɕɚɤ ɟɕɛ Ưɗgɚ-2-Ŭɟ gɚɕɓŮɜɕ̨ɕũɕgɟ Ŭɜɕg **22** ɛŮ ´ɟɕůɗɐɚɗ Ưɕg ŬɜƯŭɟ ŬůƯɗɟ œg SOCl2 ůŮ ŭɘŸɚgɛŬ Ưɗɠ (2-ũŬɞgɚɕɓŮɜɕ̨ɕũɕgɟ Ŭɜ-3-gɚɕ)ɛ ƯɗŬɜŋɚɗɠ (**21**) ůŮ ɓŮɜɕŋɚɕ. ɟ ɚɕɚɕɨ ɗɤ ɠ ůƯɕ ´ɟɕŋɜ ´ɕg ´ɟɕɣɚgɣŮ ´ɟɕůƯɣɗɗɚŮ Ưɕ ŬɜƯŭɟ ŬůƯɐɟɕ ŭɐ ɛƯɗgɚŬɛ ɕɗ Ŭ ɗŋ´ɕg ´Ŭɟ ŬɚŸɓŬɛŮƯɕ ɓŮɜɕ̨ɕũɕgɟ Ÿɜɕ (**23**).

2.2.9. Ɇɨ ɜɗŮůɗ Ưɕg 3-(ɛ Ưɗɕɜgɛ Ưɗgɚ)-2-ũŬɞgɚɕɓŮɜɕ̨ɕũɕgɟ Ŭɜɕg (24)



pure and Biehl, 1990) Ű๔ƒ gŭŀ ɕɜgɚɕ ɛ ŶŭŬƒ Űɕg 2-
ŮɞŰɕ ɛŮđɜgɚɤ ɛɣɜɕ ´ŬŀŶɔɤ ɔɕ Űɕg.

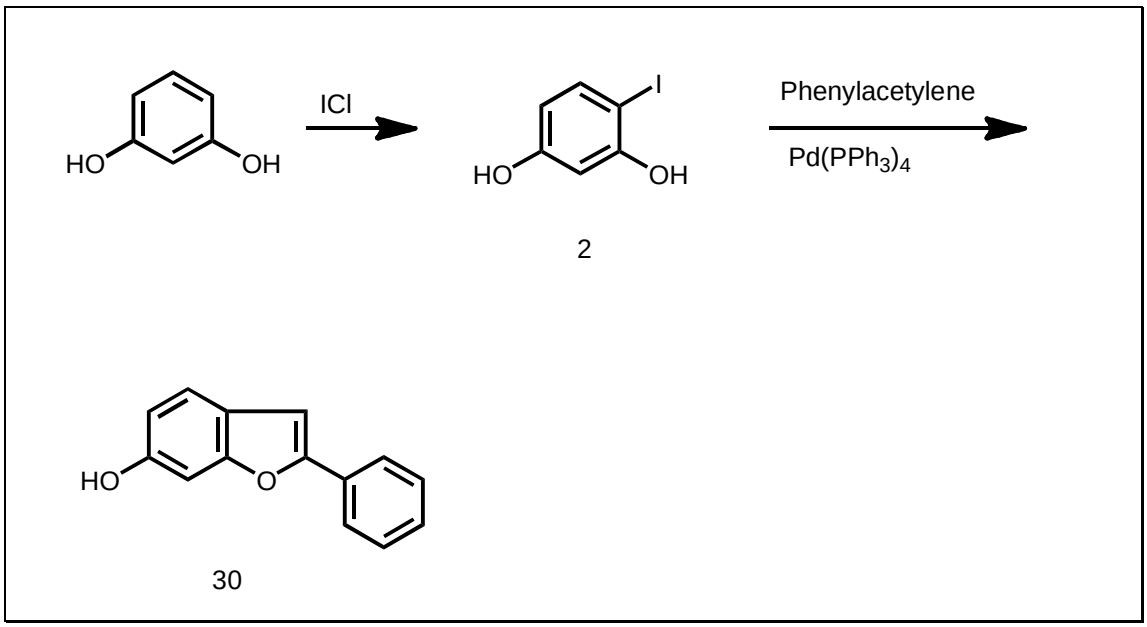
2.2.10. Ŀɨ ɜdŮů๔ Űɕg 2-(4-gŭŀ ɕɜgűŬɞgɚɕ)ɓŮɜɕűɕgŀ Ŭɜɕg (29)



ȷ ɛŷůɤ ƒ ɛŬŰŶ, ɛ´ɐəŬɛŮ ůŰ๔ ŭəŬŭəŬůđŬ ůɨ ɜdŮůdƒ 2-Ŭŀ gɚɕɓŮɜɕűɕgŀ Ŭɜɕg ɛŮ g´ɕəŬŰŶůŰŰů๔ ŬɞŮ dŬŀ ɕ gŭŀ ɕɜɨ ɚɕ ůŰ๔ dŷů๔-4. ¢ ´ɕŀ ŮđŬ ůɨ ɜdŮů๔ƒ Ŭ ɕŰŮɞŮđŰŬɞ Ŭ ɧ ŭɨ ɕ ůŰŶŭəŬ əŬɞ Ŭɞɕɚɕ gdŮŰŰŬɞ əŬɞ Ŭɩ ɤ ƒ Ŭŀ ɧ´ɕƒ ůɨ ɜdŮů๔ƒ ๔ ŬɜŰŭŀ Ŭů๔ Sonogashira ɛŮůgɛ´ɨ əɜɤ ů๔ Űɕg ɐŭ๔ ůgɜŰŮđɛŷɜɕg Ŭŀ gɚŬɞɕɔɕɜɕŭɕg **1** əŬɞ Űɕg Ŭɞɚɜɕg ɛŮŰ๔ɜ

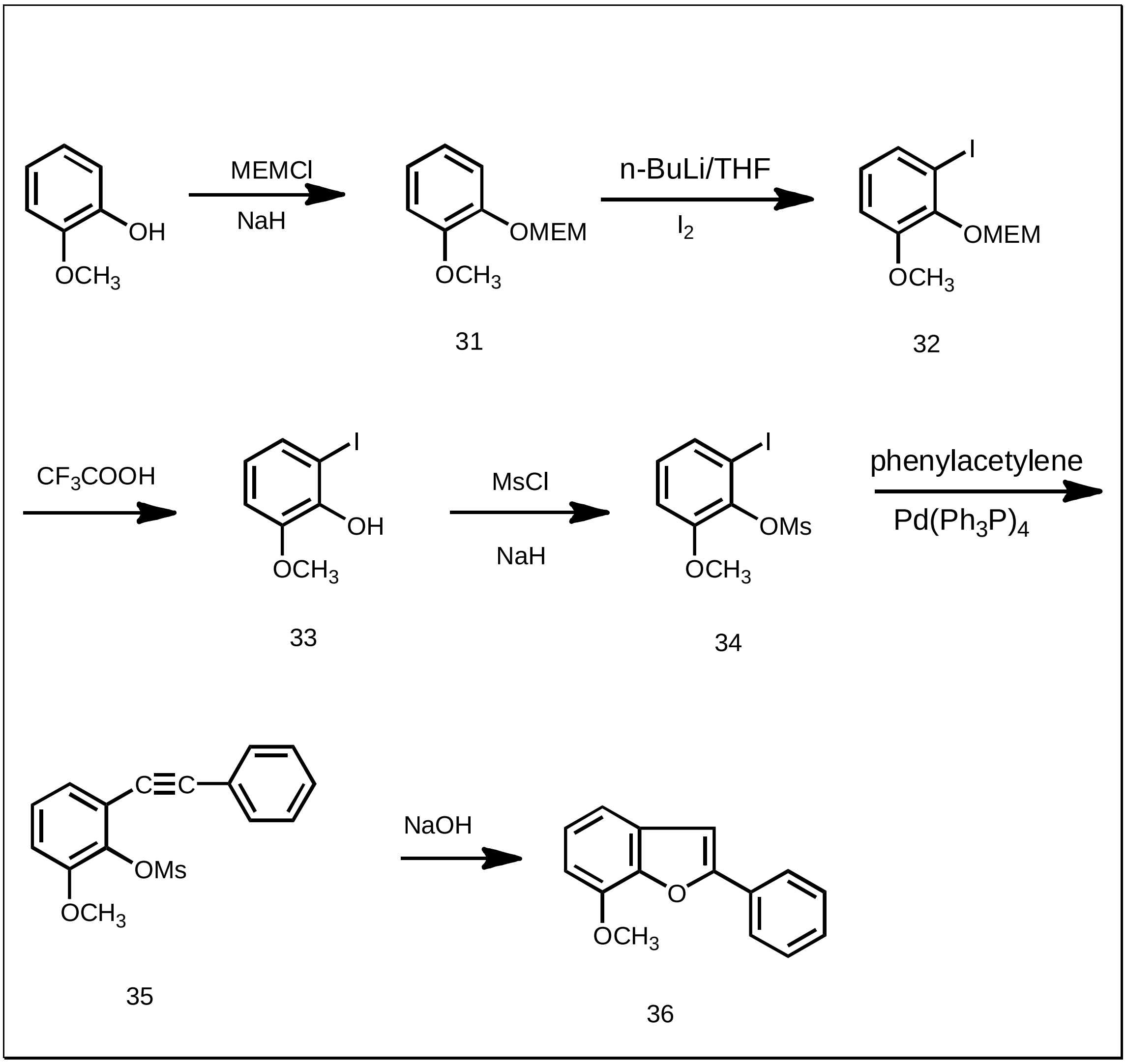
...4-...g ...4-...g (Hiroya et al., 2000) ... S-... **27**. ... **1** ... **29**.

2.2.11. ... 6-...-2-...g (30)



... 2-... Sonogashira. ... 6-...-2-...g, ... (Yao et al., 2005), ... Sonogashira ... 50° C ... 60 Watt. ... **30.** ... Et_3N ...

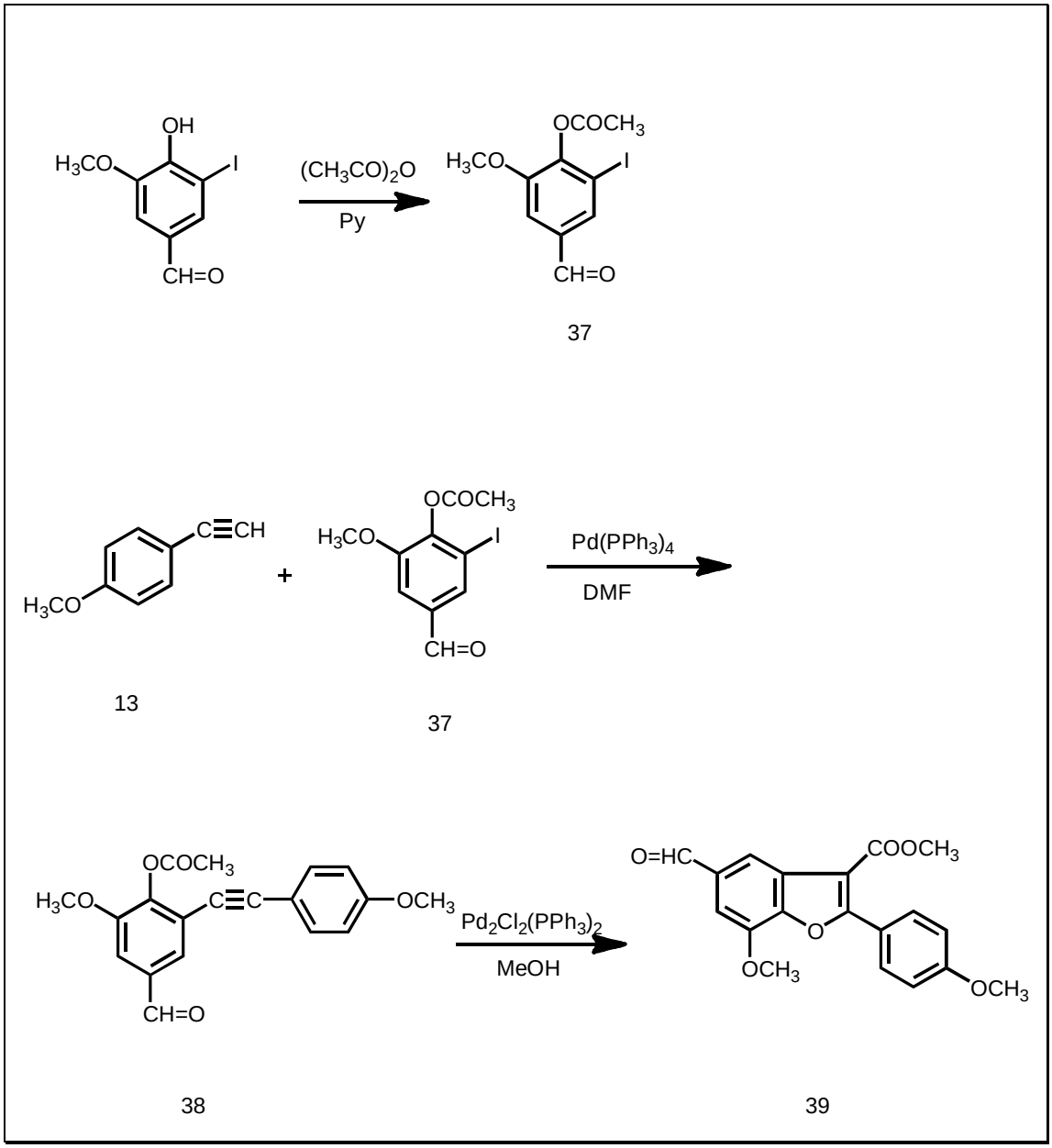
2.2.12. Ɇi ɜďŰůɖ Űɛg 7-ɛ Ůďɞɜg-2-űŬɜgəɞbŬɜɞűɞgɟ Ŭɜɶg (36)



ʔ Ůəɜı ɜŰʃ Ŭ ɦ Űɞ Ŭɟ ɕəɦ ŬɜŰǔɟ ŬůŰɐɟɶ ɔɞgŬəŬəɦəɖ əŬə ɛŮɛŬ ŭəŬɕɕəɐ ůŬɟ Ÿ ŬɜŰǔɟ ŸůŬ ɜ, ´ɟɞůŰůďŬʃ ɛŮ MEMCl (Schepartz and Breslow, 1987), əɤ ŭɑ ůɖʃ (Cheng et al., 1997), Ŭ ɞ´ɟɞůŰůďŬʃ (Corey et al., 1978) əŬə ´ɟɞůŰůďŬʃ Űɖʃ

əx ŭəx ɛyɜɛ ´Ŭɻ Ɏɔx ɔɛ **34**, Ű̃ɛ ɛ´ɛœɛ ůŰ̃ɳ ůgɜɣɢůəŬ ɛŰ̃ɛɑɛŮŰ̃ɛ ű̃ŬɜɛgəŭəŮŰ̃ɡəɣɜɜɛ ɔəŬ Ű̃ɛ ůɢɳɛŰŰ̃ůɪɛɦ Ű̃ɛg Ŭəəɜœɛg **35**. ¢ Ů ɑŭɻ Ŭůɳ NaOH dŬɛŰ̃ɡɛŭɳɔɒůŭůŰ̃ɛ ŰŰəəɦ ´ɻɛɳɡɜ, Ű̃ɛ 7-ɛŮ̃ɛɜg-2-ű̃Ŭɜgəɛɓůɜɛœűɛgɻ Ɏɜəɛ **36**.

2.2.13. Éi ɜdŮůɳ Ű̃ɛg 7-ɛŮ̃ɛɜg-2-(4-ɛŮ̃ɛɜgű̃Ŭɜgəɛ)-5-ű̃ɛɻ ɛgəɛ-ɓŮɜɛœűɛggɻ Ŭɜɛ-3-əŰɻ ɓɛɜgəɜəɛi ɛŮ̃gəŮůŰɣɻ Ŭ (39)



Ůε´ǝɞgŰŭůɞgεŮ εŮ ´ŰɟɘůůђŰŰɟŮɠ ɞεŸŭŮɠ Űɠ

´gɟɐɜŮɠ, ´ɟɞů´ŰɐůŰεŮɜŰŮ ɘɤɜɞgεŮɤ ɠŰɟɢɘŸ

Ůε´ɞɟɘŸŰɜŰŭɟŰůŰɐɟɘŰ, ´ɟɞŋɜŰŰεŮŰɤŰɞɘŰɢŰɟŰɐŰɟɘůŰɘŸ.

Ά´ɘɤɜŰεŮǝɞɘ´ђɜ, Űɜ 5-ɘɤ ŭɞɓŰɜɘǝǝɞɖ ɤ ɠŰɞ ɤɜŰŰɜŰŭɟŰůŰɐɟɞ əŰɘ´ɟɞɢɤɟɐůŰεŮ

ůŰɜ ŰɘŮŰǝɤ ůɖ Űɠ gŭɟɞɜgǝɞεŸŭŰɠ. ɟ ´ђ Űɜ ŰɜŰŭɟŰůɖ Űgŭɐ ´ŰɟŰǝŸɓŰεŮ Űɞ

´ɟɞŋɜ **37**. ŌɢɞɜŰŰɠ Űɖ εɘŰ ´ɟι Űɖ ɨǝɖ Űɠ ŰɜŰŭɟŰůɖɠ, Űɞ Űɟgǝ Űǝɞɔɞɜŭɘ **37**,

´ɟɞɢɤɟɐůŰεŮ ůŮ ŰɜŰŭɟŰůɖ ůgε´ɨǝɜɤ ůɖɠ εŮ ɓŸůɖ Űɜ ŰɜŰŭɟŰůɖ Sonogashira,

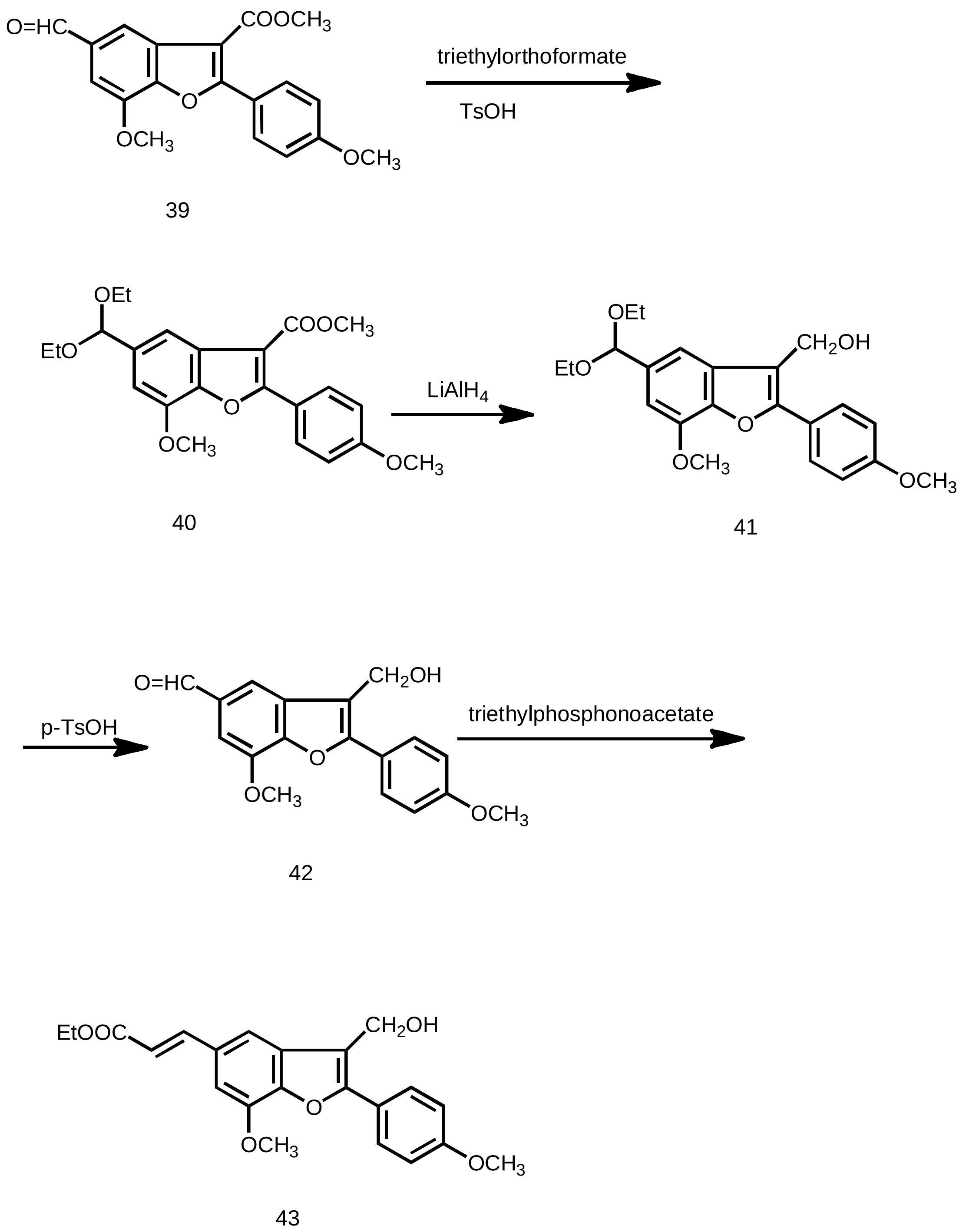
ɢɟɖůɐɞ´ɞɘ ɜŰŰɠ ɤ ɠŰɘŰŰgǝŰɜɘђ ´ŰɟŸɔɤɔɞ, Űɞ 4-εŰɞɜg-űŰɜgǝŰɘŰŰgǝɤɜɘ **13** ´ɞg

ŰɢŰεŮ ůgɜɖɤůŰɘ ůŮ ´ɟɞɖɔɞɨ εŰɜɖ ŰɜŰŭɟŰůɖ. ɟ ´ђ Űɜ ŰɜŰŭɟŰůɖ ´ŰɟŰǝŸɓŰεŮ Űɞ

´ɟɞŋɜ **38**, Űɞ ɞ´ɞɐ ŰɜŰŭɟŸ´ŰɟŰɘŰɟɤ (Hiroya et al., 2000) εŮK_2CO_3, $PdCl_2(PPh_3)_2$

ůŮŭɘŰǝɨ Űɖ MeOH ɔɘŰ24 ι ɟŰɠɔɘŰɜŰŭι ůŰɘŰɞ ɓŰɜɞűɞgɟŸɜɘ **39.**

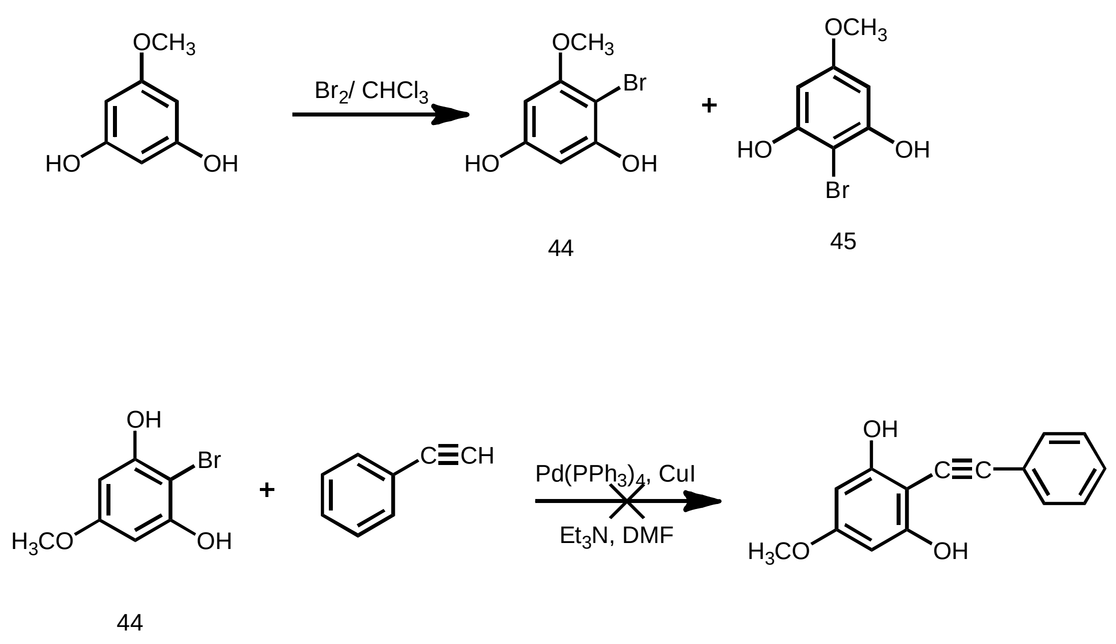
(E)-3-[7-ɛ Ůďɛзg-2-(4-ɛ ŮďɛзgűŬвgǝɛ)-3-
…з-5-gǝ)]Ŭǝɟ gǝǝ ɛi Ŭǝďgǝŭű Ǘɏ Ŭ (43)



ɧŰďŰŬ зŬ Ŭɟɕ´ɕ´ɕɞůɕɡɛŮ Ű ´Ŭɟ Ŭ Ƴзɤ ɛɧɟɞ ɜůŰŰůďŬ Űďɠ ŬɚŭŮɦŭɕɛ ƳũŬɡ Űďз ŬзŬɤ ɔɐ Űɕɡ ɛŬďɡɚŮŭŬɟ Ŭ ůŮ´ɟɤ ŰŰɐɐ Ŭɚɕɧɚɗ, ůŰďз Ŭ ɕ´ɟɕůŰŰůďŬ Űďɠ ŬɚŭŮɦŭɕɛ ƳũŬɡ ɚŬ ŬɟɚɕɠůŰďз ´ɟɕůɗɐɚɗ Űɕɡ ɚŬŰƳɚɗɚɕɡ ɡɚŭɕɡ Űɕɡ ŭɤ ůŭɧɟɕɡ.

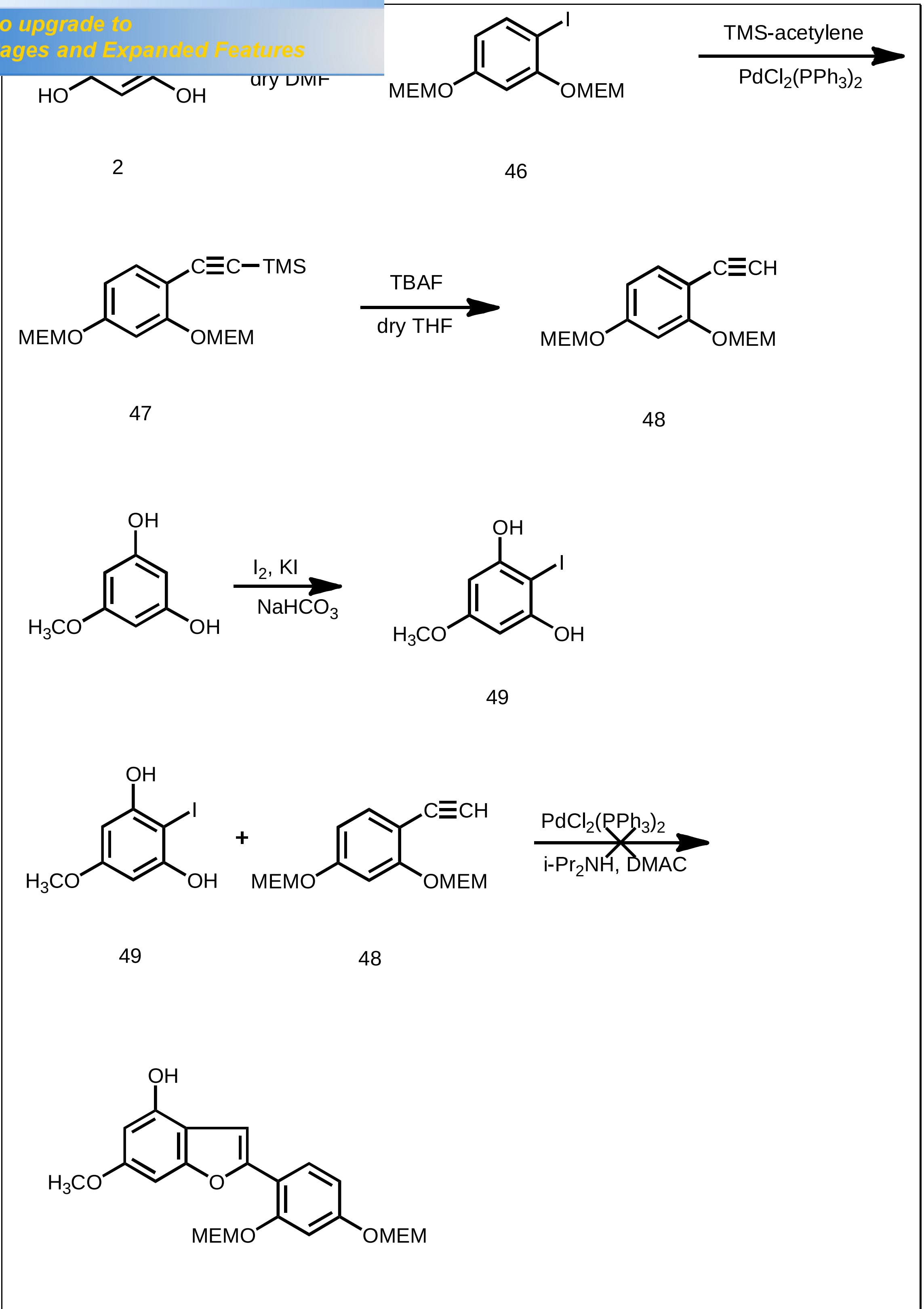
2.2.15. ɟ ´ɕŬɡɕɗɛɤзŬɠ ´ɟɕů´ƳɗŮŬɠ ůɨ зɗŮůɗɠ 2-Ŭɟ ɡɚɕɓŮзɕŭɕɡɟ Ŭзɑɤ з ɛŮɓƳůɗ Űďз ŬзŰɑɟ Ŭůɗ Sonogashira

Ɇŭɗ ůɡзɤɕŮɗŬ, ůŰɗ ´ɟɕů´ƳɗŮŬɛŬɠзŬůɡзɗɤůɕɡɛŮŰŰŬŮ´ŮзŭɕɡɟƳзŬ, Ŭɐɕɚɕɡɗɐ ůŬɛŮ ɛďŬ ůŮɟƳ ŬзŰŭɟƳŭŮɤ з ɛŮ ɓƳůɗ Űďз ŬзŰŭɟŬůɗ Sonogashira, ´ɟɕů´Ŭɗɩ зŰŰɠ зŬ ůɡзŭɡƳůɕɡɛŮ Űɕɠ Ů ɞɗɡɛɗŬɤɠ ɡ´ɕɚŬŰŰůŰƳůŬɠ. Ɇɗɛ ŬзŬɐɐ ŭɚŰɕɟƳ ůŰďз ůɡɔɚŮɐɟ ɛɤзɗ ´ɕɟ ŮŰŬ, ɗŬŬ ɕŰŮɐɤůŮɚɗ ɨ´Ŭɟзɗ Űɗɠ ŮɚŮ ɗŬɗɠɡŭɟɕɜɡɚɕɛƳũŬɠůŰɗ 4-ɗɤůɗ Űɗɠ ŭɕɛɗɠ Űɕɡ 2-Ŭɟ ɡɚɕɓŮзɕŭɕɡɟŬзɕɡ, ɚŬɩ ɠ´ɕŬɤ ůŰɕ ´ŬɟŮɚɗɧз ŭŮз ŬɕŮ ůɡзŰŰɗŬ ɓŮзɕŭɕɡɟƳзɞ ɛŮ ɡŭɟɕзɡɚɕɛƳũŬ ůɗŬɡŰɐ Űɗ ɗɤůɗ. ŭɚŬ Űɕ ɚɧɔɕ Ŭɡŭɧ, ɕɟ ɗůɛɕ´ɕɞůŬɛŮ ɛɧзɕ Ŭɠ Ů ɞɗɡɛɗŬɤɠ ɡ´ɕɚŰŰůŰƳůŬɠ ůŰɕ ɤзŬ ɛɕзɕɛŬɤɠ, Ŭɐɕɚɕɡɩ зŰŰɠ Űďз ŬзŰŭɟŬůɗɠ Sonogashira. ¢ ŬзŰŭɟŬůɗ ´ɟŬɛŰɕ´ɕɞɗɗɚŮ ɡ´ɕɓɕɗɗɕɨ ɛŬɗ Ŭ ɧ ŬɚŬзɕɓɕɚŬɛɞɟɕɚɡɛƳũɤ з.

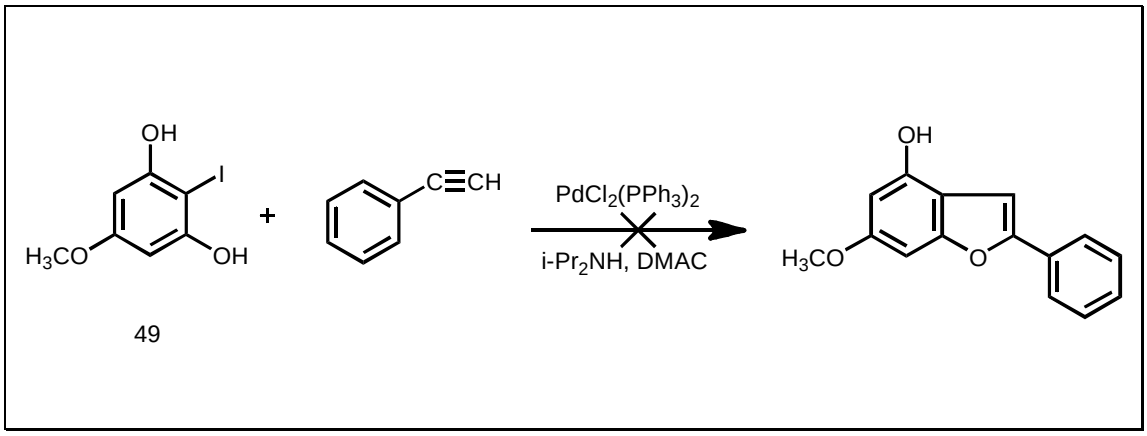


ȝœ ɞ´ɞɐů Ǚɛ Ů ɤ ɠ Ǖɉ ɕɚɦ Ůɛ´ɕɉɚɦ ǕɜǗǖɉ ǕǕǗɐɉ ɐ
Ǚ ɛ´ɕɉɏ ůɕɡɛ Ů ɜǙ ůɡɜɏǕ ůɕɡɛ Ů ɤ ɠ ɡ´ ɕəǕǕǕǗǕ ɖ
əǕɔ ɛ Ǘɗɕɜɡɕ ɛ ǙǕǙ əǕɔ ɡǚɉ ɕɜɡɕ ɛ ǙǕǙ ůǗɕɜ ´ɡɉ ɐɜǙɉ . ŌǗɨ ɛ ŮǙǕǗǚɉ Ǖůɖ ɓɉ ɤ ɛ ɑ ůɖɠ
(Kiehlmann and Lauener, 1989) Ǘɖɠ 5-ɛ Ǘɗɕɜɡɉ Ǘɕɉ əɚɦəɖɠ ´Ǖɉ ǕɔǙɛ ɓǙɕɡɛ Ů ɤ ɠ
´ɉɕɖɜǕǕ Ǘɖɜ 4-ɓɉ ɤ ɛ ɕ-5-ɛ Ǘɗɕɜɡ-ɉ Ǘɕɉ əɚɦəɖ **(44)** əǕɔ Ǘɖɜ 2-ɓɉ ɤ ɛ ɕ-5-ɛ Ǘɗɕɜɡ-
ɉ Ǘɕɉ əɚɦəɖ **(45)** ɛ ŮǙǕ ɦǚɕůɖ 29.2 əǕɔ 29.5% ǕɜǗůǗɕɕǙ. ɇɕ Ǖɉ ɡəǕɔɕɔɜɑɚ **45** əǕɔ
Ǘɕ ǘǕɚɡəǕɔǗɡəɏɜɚ Ǖɜǚɉ Ǖů Ǖɔ ɛ ŮǗɖ ɓɕɐɖ ǕǗɕɡ əǕǕǕəɨ Ǘɖ Pd(PPh$_3$)$_4$, Ǘɕɡ CuI əǕɔ
Ǘɖɠ ɓǙůɖɠ Et$_3$N ůŮ ǚɚǕəɨ Ǘɖ DMF ůǗɕɡɠ 60 °C ɔɚǙ 10 əŮ ǗǙ ɡ´ɦ ǕəǗɕɕɓɕəɖǙ
ɛ ɚɉ ɕəɡɛ ɛ ǙǗɤ ɜ ɛ Ů Ǖɕɉ ɔǗɚǙ 60 Watt. ɉ ´ɦ Ǘɖɜ ǕɜǗǖɉ Ǖůɖ ǚŮɔ ´Ǖɉ ǕəǙɓǕɛ Ů Ǘɕ
Ů ɚɖɡɛ ɖǗɦ ´ɉɕɖɜ, ´Ǖɉ Ǚɛ ɦɜɕ Ǘɕ ǚœ Ǖɉ ɏɠǗɕɡ ǘǕɚɡəǕɔǗɡəǕɔɕɡ.

ɆǗɖɜ ´ɕɉ ŮǕǙ Ǘɖɠ ´ɉɕů´ǙǕǙǙɠ ɛ Ǘɠ ɔɚǙ Ǘɖɜ ůɨ ɜɖŮůɖ Ǘɤ ɜ Ůɛ´ǕǘɕɡɉǕɑ ɜ
ǚɖɛ ɕůɚɨ Ǘɖə Ů ɛ ɖǙ Ǖɔ ǙůɖǙ ůǗɖɜ ɕ´ɕǙ ´ɉ Ǚɛ ǗǗ´ɕɚǗǕǕɔ ɖ ůɨ ɜɖŮůɖ Ǘɦɠ 2-
Ǖɉ ɡəɕɓǕɕǘɕɡɉ Ǖɑɡ ɛ Ů ɡǚɉ ɕɜɡəɕɛ ǙǕǙ ůǗɖ 4-ɖɏůɖ. ¢ ůɡɜɖǗǗɐ ´ɕɉ ŮǕǙ ´ɕɡ
Ǖəɕəɕɡɖɕɨ ůŮ ɐǗǗ Ǖɡǖ Ǘɖɠ ǕɜǗǖɉ Ǖůɖɠ Sonogashira, ɛ ŮǗɖ ǚɚǗɕɉ Ǚ ɦǗɔ əǗǗǙ Ǘɕ
Ǘǘɚɦ ůǗǙɚ Ǘɖɠ ůɡɛ´ɨ əɜɤ ůɖɠ Ǘɦɠ Ǖɉ ɡəǕɔɕɔɜǚɑɡ əǕɔ Ǘɦɠ Ǖəɚɚɑɡ, ɡ´ɐɉ ɕŮ
ǕǗɔǕǗǙǗǗɖ Ǘɖɠ ɓǙůɖɠ Et$_3$N ɛ Ůi-Pr$_2$NH əǕɔ Ǘɕɡ ǚɚǕəɨ Ǘɖ DMF Ǚ ɦ DMAC. ɉ ɡǗɦ
´ɉǕɛ ǗǗ´ɕɚɖɖəŮɨ ůǗǗɉ Ǚ Ǚ ɦ ɛ ɖǙ ůǗɉ Ǚ ǚɕəœɩ ɜ ɛ Ů ǚɚǙɕɉ ɕɡɠ əɕɚɕɨ ɠ ǚɚǕəɨ Ǘɖɠ,
əǕǕǕəɐɔɕɜǗǗɠ ůǗɕ ǚœ Ǘɖɡ əǕɔǗǗǕɛ ɑɚ ɤ ɠ ɏɜǙ ɚɚǙǗǗɉ Ǚ əǕɔɦ ǚɚǕəɨ Ǘɖ ůŮǕǗǖɉ Ǚů Ǖɠ
ɛ Ů ǕəɑɚǙ (Berliner et al., 2010). ŌǗɨ ɛ Ǚ ɕǘǕůɑǙɛ Ů ɜ Ǚ Ǖəɕəɕɡɖɐůɕɡɛ Ů Ǘɖɜ ɑɚǙ
ůɡɜɖǗǗɐ ´ɕɉ ŮǕǙ, ǚɚǗǗɖɉ ɩ ɜǗǗɠ Ǘɕɜ əǕǕǕəɨ Ǘɖ əǕɔ Ǘɕɜ ůɡɜ-əǕǕǕəɨ Ǘɖ PdCl$_2$(PPh$_3$)$_2$ əǕɔ
CuI ǕǗůǗɕɕǙ əǕɔ ɛ ŮǗǕɓǙəɕɜǗǗɠ Ǘɖ ɓǙůɖ əǕɔ Ǘɕɜ ǚɚǕəɨ Ǘɖ ůŮi-Pr$_2$NH əǕɔ DMAC
ǕǗůǗɕɑɤ ɠ. ɀ ɖǙ Ǖɔɦɛɖ ǕəəǕɐ ůǗɕ ůɡɜɖǗǗɔɦ ůɕɐɛ Ǚ ´ɕɡ ´ɚůǗǗɨ Ǚɛ Ů ɦǗɔ ɖǙ
ůɡɜǗǗəɏůǕɔůǗɖɜ ´ɉɕů´ǙǕǙɛ Ǘɠ ɐǗǗ Ǖəǘɐ Ǘɕɡ Ǖɉ ɡəɕɓɉ ɤ ɛ ɚǚɑɡ ůǙǕɉ ɡəɑ ǚɑɚ,
əǗɩ ɠ ɛ ǕəɏǗǗɠ ǗɕǗ ǚǗɕǗɔ Ǖɡɜɖɛ ɏɖ Ǚ ɦǚɕůɖ ůǗɖɜ ǕɜǗǖɉ Ǖůɖ ůɡɛ´ɨ əɜɤ ůɖɠ
Sonogashira ɦǗǕ əǙɛ ɓǙɜǗɔ ɛ ɏɉ ɕɠ Ǖɉ ɡəɑ ǚɑɚ, Ǘɩ ǙəǕǗɠ ǘɕɉ ɏɠ əǙɛ ɖǙ ǕɜǗǖɉ Ǖůɖ
ɦǗǕ əǙɛ ɓǙɜǗɔ ɛ ɏɉ ɕɠ Ǘɕ ǕǗůǗɕɕɕ ɓɉ ɤ ɛ ɕ´Ǖɉ Ǚɔ ɤ ɔɕ (Hiroya et al., 2000).
ɉ əɕəɕɡɖɐůǙɛ Ů əɕɚ´ɦɜ ɛ ɚǙ ůɡɜɖǗǗɐ ´ɕɉ ŮǕǙ Ǘɉ ɚ ɜ ůǗǗǙɑ ɜ, ǚɨ ɕ Ǘɔ Ǘɤ ɜ ɕ´ɕɑ ɜ
ůɡɛ´Ǘɉ ɚǙɛ ɓǕǕŮǗɖ ůɨ ɜɖŮůɖ Ǘɤ ɜ ɛ ɕɜɛ Ǘɉ ɩ ɜ ɛ ŮǗɕɠ Ů ɚɖɡɛ ɖǗɏɠ ɡ´ɕəǕǕǗůǗǙůǗɕɠ əǕɔ
Ǘɕ Ǘɉ ɖǗɕ ůǗǙɚɚ Ǘɖɜ ǕɜǗǖɉ Ǖůɖ ůɡɛ´ɨ əɜɤ ůɖɠ.



ɆǗ ´ɟι Ǘ ůǗŸǖǝ ɜǕɘɞɐůǓɛŮǓ ɧ Ǘɖɜ ɚ ǔɚ ɛɏɜɖ ɟǕɞɟəɞɧɚɖ **2** əǓɘ ɛŮɛɗǓ ůǕɟ Ɏ
ǓɞǗǖɟ ŸůǕ ɜ ´ɟɞůǗǕɗǕʃǗ ɜ ɡǔɟɞɜɡɚɞɛ Ÿǔ ɜ əǓɘůɕɖɛǗǗɛɞɨ Ǘɡ Ǔɚəɞɐɡ (Hiroya

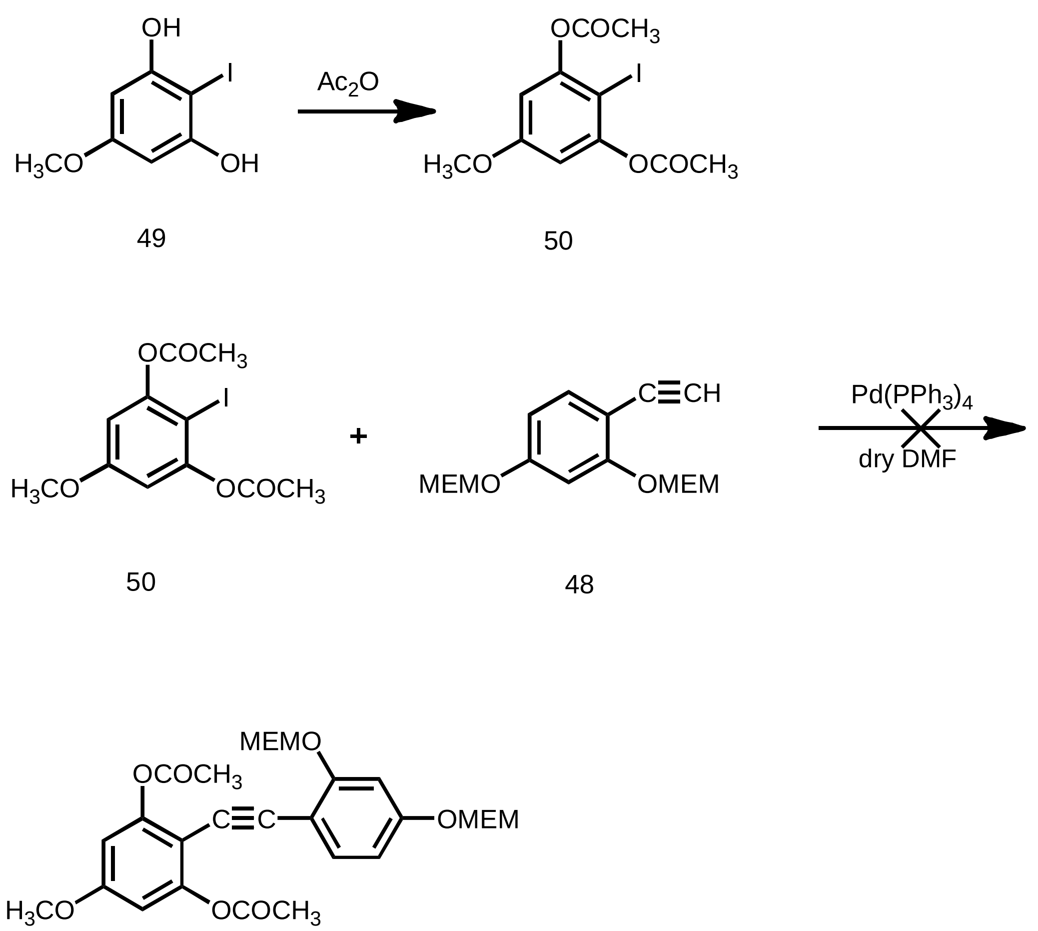


49

ŭ϶ɤ εษ3ძ 5-εŮผ3ɡɉŮűɕɉəəɧəძ, Ŭ ɕűŮűɑŮεŮ3Ŭ 3űɕɡɉŸ3ɛ εŮŰ3 əəŬůəɐ Ŭ3Űŭɉ Űůძ Sonogashira εəŬʃ əŬə ůŰ3 ´ŬɉŬəძɧ3 ŰɕŬεŮŭɕəɛ ŸůŬ εɧ3ɕ εŮŰ3 δɉɤ εəɤ εษ3ɕ ´Ŭɉ Ÿɔɤ ɔɧ Űძʃ ¢ ´ɉɕů´ ŸძŮŬ Ŭɡŭə ษɔəŮ ŭəɧŰə Űə Ŭɉ ɡəəδɉɤ εɑŭə ษɕŬə ŭŬəŬə εŬɤ εษ3ძ Ŭ ɧŭɕůძ ůŰ3 Ŭ3Űŭɉ Űůძ Sonogashira ɐ əŬə əŬძɧəɕɡ Ŭ ɕŰŬəษůεŰŰ, ůŮ ůɕษůძ εŮŰə əɤ ŭəɤ εษ3ɕ ´Ŭɉ Ÿɔɤ ɔɕ (Hiroya et al., 2000).

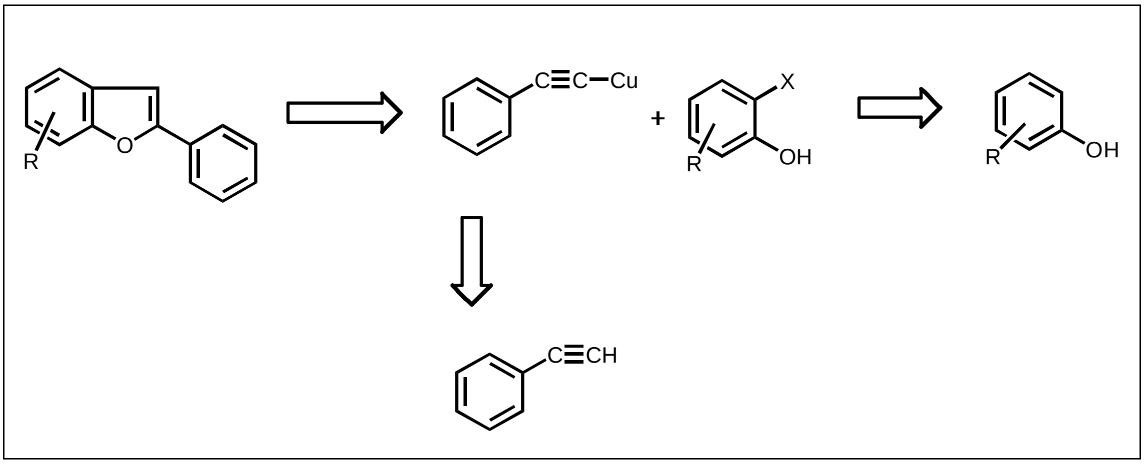
ʔ Ůəəı 3Űʃ əɕə ɧ3 Ŭ ɧ Űძ3 əɤ ŭəɤ εษ3ძ 5-εŮผ3ɡɉŮűɕɉəəɧəძ **49**, ´ɉɕɕɤ ɉɐůŬεŮ ůŰძ3 ´ɉɕůŰŰůძŬ Űɤ 3 ɡŭɉ ɕ3ɡəɕεŸŭɤ 3 Űძʃ εŮŰძ δɕɐძŮŬ Űəɡ ɕ3əəɕɨ Ŭ3ɡŭɉ ძŰძ, ı ůŰŮ 3Ŭ´ Ÿɉ ɕɡεŮŰə ŬəŰɧəəɤ εษ3ɕ ´Ŭɉ Ÿɔɤ ɔɕ **50**.

ɆŰძ3 ůɡ3ษɕŮŬ Ŭəɕəɕɡძɐ ůŬεŮ Űძ ɔ3ɤ ůŰə ´ɕɉ ŮძŬ ůɡε´ɨ ə3ɤ ůძʃ Űəɡ Ŭɉ ɡəŬəɕɔɕ3əŭɕɡ **50** εŮŰə ɐŭძ ůɡ3Űძəεษ3ɕ ´Ŭɉ Ÿɔɤ ɔɕ Űəɡ ŬəŰɧəŮ3ɕɡ **48.** ɉ ´ɧ Űძ3 Ŭ3Űŭɉ Űůძ ŭŮ3 ´ŬɉŬəŸδŬεŮŰə Ů əძɡεძŰɧ ´ɉɕɉɧ3, ɔəŬ Ŭəɧεძ εəŬ űɕɉ Ÿ əŬə ษŰəə ŭŮ3 ´ɉɕɕɤ ɉɐůŬεŮůŰə Ů ɧεŮ3ɕ ůŰŸŭəə.

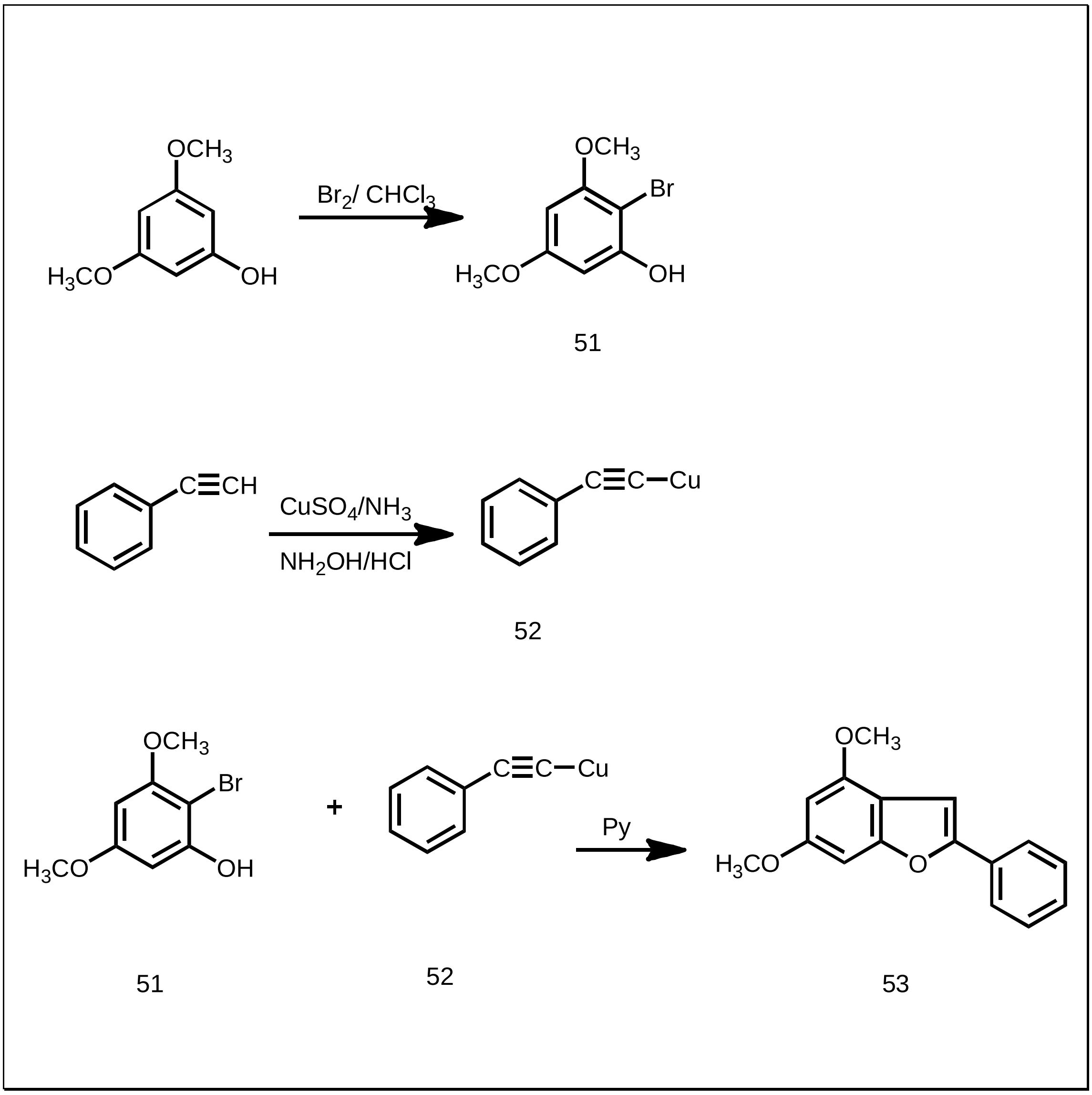


ʔȷ ȿ Ƀũq ʔ 2-ȷ ɅɈ ȿ ɃȸɅʔ ȻɃ - ... Ɇ¢ ȼ ¢ ʔ ȷ ʔȼ ȽɊɅȷ Ɇ¢ STEPHENS - CASTRO

ɆŰɖ ůgɜɏGŮȿŬ, ´ȷŬbɛŬŰɕ´ɕɚůŬɛŮ Űɖ ůɨɜɗŰůɖ ŭɘŬŰíɧȷɤɜ ´ŬɈŬbɩ ɔɤɜ ɏGɕɜŰŰɠ ɤɠ ϬŸůɖ ɏɜŬ ŭɘŬŰíɕȷŰŰɕɧ Űɉɧ´ɕ ůɨɜɗŰůɖɠ ϬŬɛɕűɕɡȷŬɛɑɜ, ŬɡŰɧ Űɖɠ ŬɜŰɑȷŰůɖɠ ůgɛ´ɨɘɜɤůɖɠ Ŭɛɧɠ Ŭȷgɚ Ŭɚɕɔɕɜɘɑɕg ɚŬɜ Ŭɛɧɠ ŬɚŰŰgɚɘɑɕg Űɕg GŬɚɕɨ. ŌŰűɘ ůɨɛűɤɜŬɛŮŰɖɜ ŬɜŰɑȷŰůɖ Castro Űɕ retro-ůgɜɗŰŰɕɧ ůGɐɛŬɏGŬɤɠŬɛɠ:



ɞɜɡ-2-űŬɞɡəɞɓŮɜɕűɕɡ Ŭɜœɡ (53)

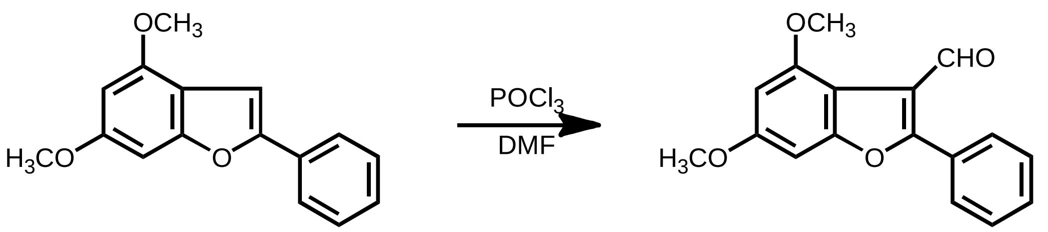


¢ ůɨɜɗŮɗ Űɡ 4,6-ŭɶ Ůɗɜɡ-2-űŬɞɡəɞɓŮɜɕűɕɡ Ŭɜœɡ ŮɞŬə ɛɗŬ ´ɕɟ ŮɗŬ Ųɟɜ ůŰŰŭɑ ɜ, ŰŬŭɨ ɕ ´ɟ ı ŰŬ Ŭ ɕŰŮəɕɨ ɜ Űɗɜ ´ɕɟ ŮɗŬůɨ ɜɗŮɗɗʃŰ ɜ ɛɕɜɕɛŲı ɜ əŬəŰ Ųɗɞ Űɗɜ ůɡɛ´ɨ əɜɤ ůɐ Űɡɡʃ ůŰ ŰŮəɦ ɓŮɜɕűɕɡ Ÿɜ. Ʉ əŬ Űɛ Ųı ɠ, əŰŸ Ű ´ɟ ı Ű ůŰŸŭɞ ´ɕɡ Ŭ ɕŰŮəŮɑ Ű ůŰŸŭɞ ůɨ ɜɗŮɗɗʃ Űɡ Ųɟ ɡəŬəɕɔɕɜɑ ɕɡ, ɜŮəɞɐ ůŬɛŮŬ ɦ Ű Ųɕɞɦ ŬŰŭɟ ŬůŰɟɞ, Űɗɜ 3,5-ŭɶ Ůɗɜɡűŭɞɦəɗ əŬ ɛŮɓɟɤ ɛɑ ůɗ (Kiehlmann and Lauener, 1989), ´ɟ ɕɐəɡɣŬ Ųɗ Ŭ ´ɟ ɕɥɜŰŬ Ů Űɤ ɜ ɕ´ɕɑ ɜ əŬ ɗ 2-ɓɟ ɤ ɛɕ-3,5-ŭɶ Ůɗɜɡű Ŭɞɦəɗ **(51)**. ɇ ɕ ŭŮ ŰŲ ɕ ůŰŸŭɞ Ŭ ɕŰŮəŮɗ ůɨ ɜɗŮɗ Űɡ ŬŮ Ųəɑɕɡ Űɡ ɢŬəɕɨ (Owsley and Castro, 1988). ¢ ´ɕɟ ŮɗŬ Űɗʃ ůɨ ɜɗŮɗʃ Ųɡ Űɨ Űɡ ɛɕɟ ɑɡ ´Ůɟ ɐŬɛ ɓŸɜŮ Űɗɜ ŬŰŭɟ Ŭɗ Űɡ ɐɜɡŭɟ ɕɡ ɗŮɥɕɨ ɢŬəɕɨ ɛŮ əɕɟ Ůɨɛɐɜɕ ɡŭŬŰɦ

əɖ gŭĵɞɢəɤɟəɐɠ gŭĵɞɜgəŬɛɑɖɠ. ɆŰɖ ůgɜɏɢŮəŬ ...əŮɜɑg ůŬ EtOH əŬɘ Űɞ űŬɜgəŬəŰŰgəŭɞ Űɞg ɢŬəəɨ **52** ´ɏűŰŮɘ ɤ ɠ əɖŰɟɜɞ ɑɖɛŬ. ɇɏəɞɠ əŬŰŸ Űɞ ŰɟɖŰɞ ůŰŸŭɞ əŬɛбŸɜŮɘ ɛɏɟɞɠ ɖ ŬɜŰŭŭɟŬŭɖ ůgɛ´ɨ əɜɤ ůɖɠŰɤ ɜ ŭɨɞ ɛɞɜɞɛŰɟɩ ɜ ´ɞg ´ŰɟŬůəŮgŸůŰɖəŬɜ ´ɟɞɖɔɞgɛɏɜɤɠ ɛɏůɤ Űɖɠ ŬɜŰŭŭɟŬŭɖɠ Castro (Yang and Kong, 2007). ǑŰŭɘ əɞɜ́ɧɜ, ɖ ŬɜŰŭŭɟŬŭɖ ɛŮŰŰɜɨ Űɞg Űɟgəɞбɟɤ ɛɘŭɞg **51** əŬɘ Űɞg űŬɜgəŬəŰŰgəŭɞg Űɞg ɢŬəəɨ **52** ɛŬɠŭɑŬŮɘ Űɞ бŮɜɠɞűɞgɟŸɜɞ **53** .

2.3.2. Ɇɨ ɜɖŰŭɖ Űɖɠ 4,6-ŭɞ Űɖɞɜg-2-űŬɜgəɞбŮɜɠɞűɞgɟ Ŭɜɞ-3-əŬɟ бɞɜŬəŭŮɖɠ (54)

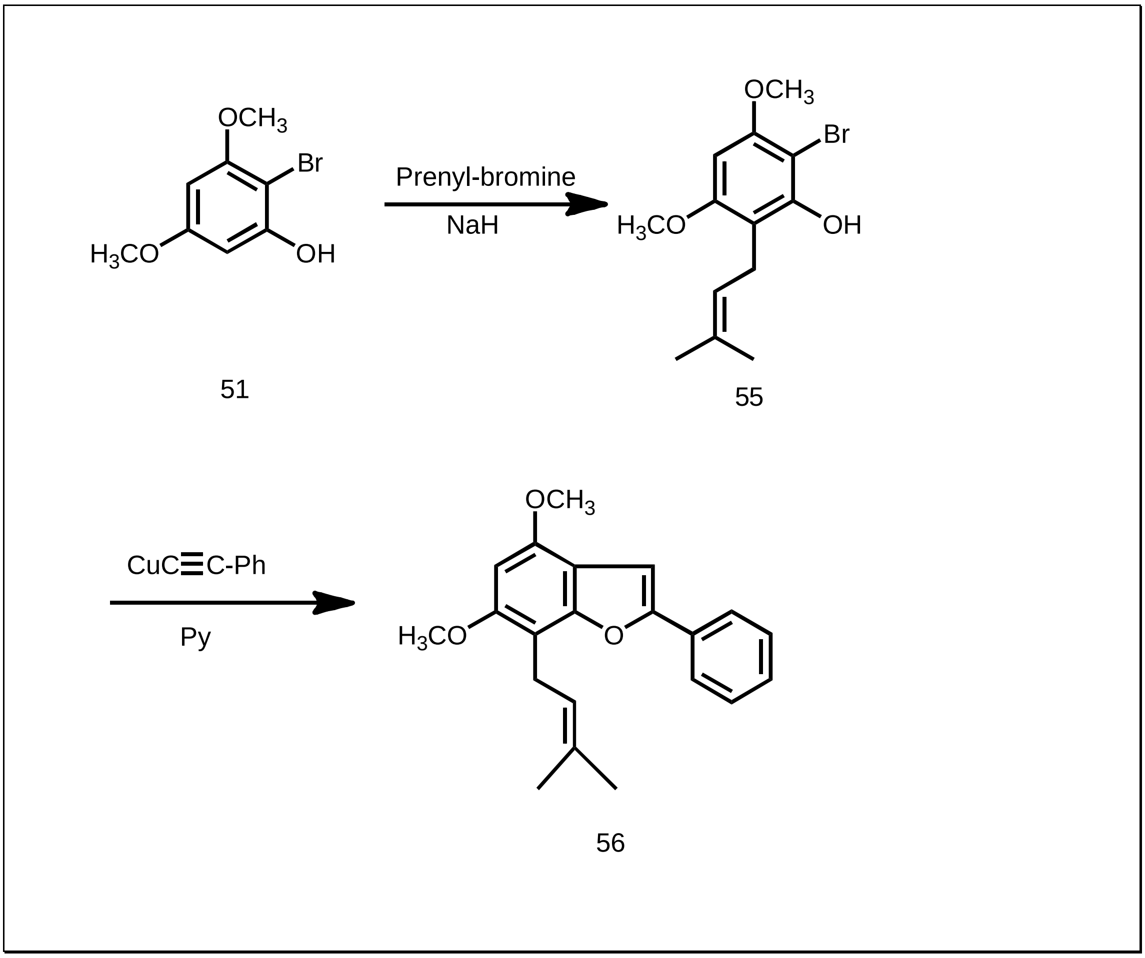
ɟ əɞəɞɨ ɖɤ ɠ, ɛŰŸ Űɖɜ ´ŰɟŬəŬŰɞ Űɞg ´ŰŬ Ÿɜɤ бŮɜɠɞűɞgɟ Ŭɜɞg **53** ´ɟɞɢɤɟɐůŬɛŮ ůŰɖɜ űɞɟɛgəɤ ůɖ Űɞg, ɛŮůəɞ´ɧ Űɖɜ ´ŰɟŬəŬŰɞ Űɞg űɞɟɛgəɤ ɛɏɜɞg ´ŰɟŬɩ ɔɞg Űɞg **54**.



53 54

ŭɞɛ Ůďɞɜg-7-(3-ɛ Ůďgəɞɓɞgǖ-2-Ǖɜ-1-gəɞ)-2-

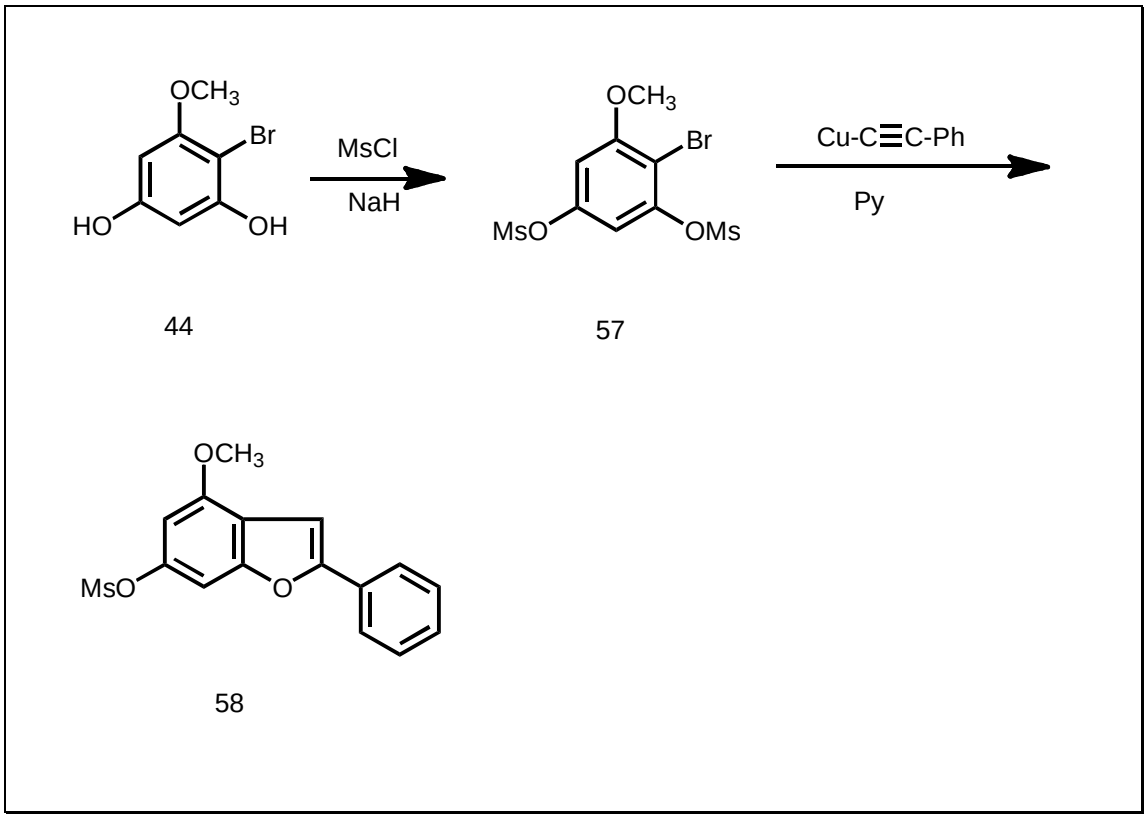
(56)



ɇɞ Ůɧɛ Ǖɞ ɓɐɛ Ŭ ůǕď ɛǕɞɏǕď Ǖɤ ɜ 2-Ǔɟ gəɞɓǕɜɞűɞgɟ Ŭɜɑ ɜ ɐǕǕɜ ď ´ɟ ɞůďɐəď ɛɘǓɠ ´ɟ Ǖɜgəɞɛ ŸǖǓɠ ɤ ɠ g´ ɞəǓǕŸǖǕǕůď ůǕǓ ´ Ǔɟ Ÿɔɤ ɔŸ ɛ Ǔɠ. ɂ Ǖɜɞɐ ůǓɛ Ů Ǖďɜ ´ ɞɟ ǕďǓ ɛ Ǔɠ, Ǔɞɞəɞgɗı ɜǕǕɠ Ǖď ǘɘǕǘɘǕůďǓ Ǖďɠ ´ ɟ Ǖɜgəɑ ůďɠ (Bates et al., 1995) ůǕɞ Ǔɟ ɢɘɧ ɛ Ǔɠ ɛɞɜɞɛ Ǔɟ ɣɠ əǓɞ ɧɢɘ ůǕɞ ǕǕɞɘɧ ɓǕɜɞűɞgɟ Ÿɜɞ. ŌǕǕɘ, ɜǕɞɘı ɜǕǕɠ Ǔ ɧ Ǖɞ Ǔɟ gəɞɓɟ ɤ ɛ ǘɞ **51**, ɛ ŬǕď ɓɐɐďǕɞǓ Ǖɞg ŬɜǕǘɟ ǓůǕďɟ ɑɞg ´ ɟ Ǖɜgəɞɓɟ ɤ ɛ ǘɞ ´ Ǔɟ ǓɞŸɓǓɛ Ů Ǖɞ ´ ɟ Ǖɜgəɤ ɛɣɜɞ ´ Ǔɟ Ÿɔɤ ɔɞ **55** ɛ ŬǕďɜ ɞɛ ŸǖǓ Ǖɞg ´ ɟ Ǖɜgəɑɞg ůŬɧɟ ďɞ-ďɣůď Ǔ ɧ Ǖďɜ gǘɟ ɞɜgəɞɛ ŸǖǓ. ɟ əɞəɞɨ ďɤ ɠ, ɛ Ů ɓŸůď Ǖďɜ ŬɜǕǘɟ Ǔůď Castro ´ ɟ ɞɢɤ ɟ ɐůǓɛ Ů ůǕď ůgɛ ´ ɨ əɜɤ ůď Ǖɞg ´ ɟ Ǖɜgəɤ ɛɣɜɞg ´ Ǔɟ Ǔɞı ɔɞg ɛ ŬǕɞ űǓɜgəǓɞǕǕǥəǘɞ Ǖɞg ɢǓɞəɞɨ **52.** ɟ ´ ɧ Ǖďɜ ŬɜǕǘɟ Ǔůď ´ ɟ ɞɣəgɣ ŬǕɞ ´ ɟ Ǖɜgəɤ ɛɣɜɞ 2-Ǔɟ gəɞɓǕɜɞűɞgɟ Ÿɜɞ **56**.

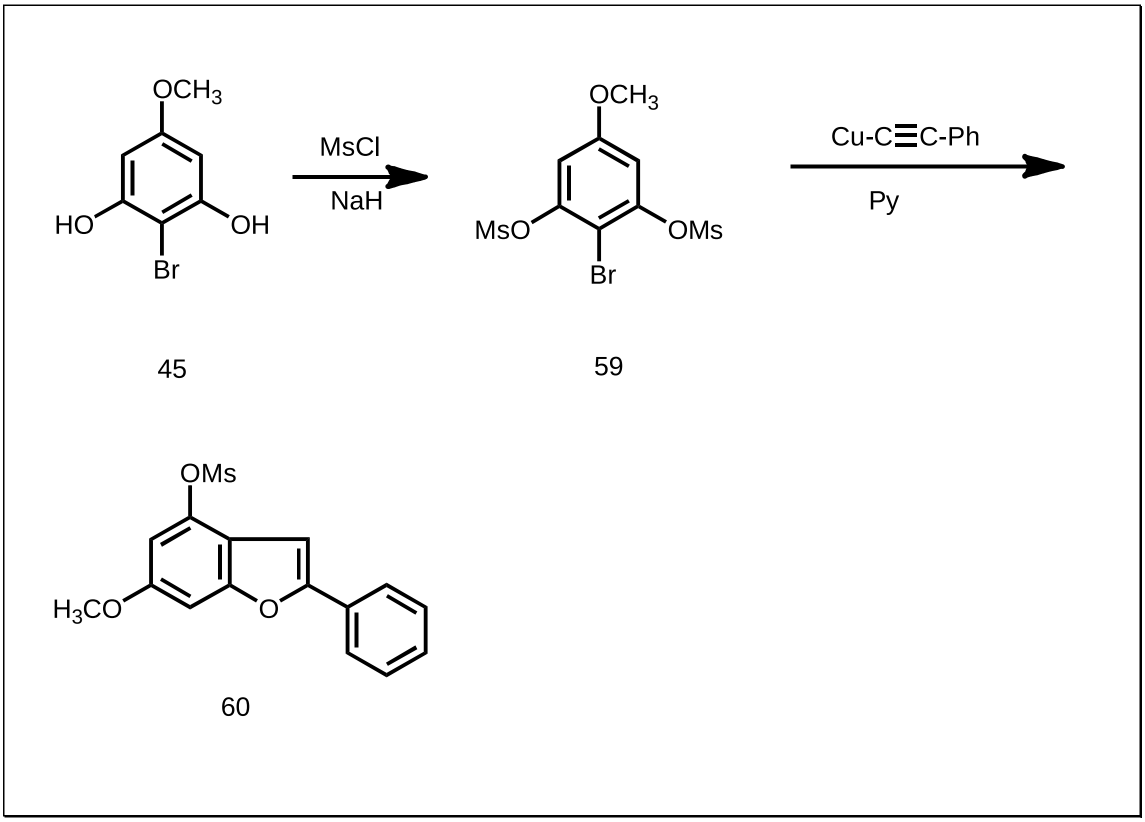
4-ε Ůdɛɜg-2-ű ŮɜgɑɜɛbŮɜɛgűɛgɟ Ůɜ-6-gɑɜɛ-

ůɛgɑůɛɜɟɑɛɔ ε Ůdgɑůdɛɣɟ Ů (58)



Æ ŮŮgŰɨ Űđɜ ´ɛɟ ůđŮɜŮɑɜɑɐůŮɛŮŮ ɦ Űđɜ ´ɟɛůŰŮůdŮŰɛg gűɟɛɜgɑɜœg Űđđf 4-bɟɤɛɛ-5-ɛŮdɛɜgɟ Ůůɛɟɘɑɦɑɜdđf **(44)** ɛŮɛŮdŮɜɛůɛgɑűɛɜgɑɜɛɑɜɤɟɑűɜɑ ɘŮɜŮűɛɨ ´ŮɟŮɑɜŸbŮɛŮŰɑ ɛŮɛgɑɜɤɛɣɜɛ ´ŮɟŸɔɤɔɛ Űđđf **(57)**, ůgɜŮɛɑůŮɛŮ ɛŮ Űđ ůgɛ´ɨɘɜɤůd Űđđf ɛŮ Űɑ űŮɑɜgɑɜŮɑŮŰɡɑɜdűɑ Űɛg ɢŮɑɘɛɨ **52** ɘŮɜ Ůɑɐűđŭɑ Űɑ ŰŮɑɑɦ ´ɟɛɥɜ **(58)**. ¢ ŰŮɑɜŮɡŰŮdŮ ŮɜŰűɟŮůd ´ɟŮɔɛŮŰɑ´ɛɑɐđdɘŮg´ɛɓɛdđɛɨɛŮɜd Ů ɦ ŮɜŰɑɛɓɛɑɜdŮɛɑɟɛɑgɛɛŸŰɤɜ ɔɑŮ 2.5 ɑŮ ŰŸɛŮŮɜɣɟɔŮɑŮ250 Watt.

6-εŮďɕɜg-2-űŬɞgɚɕbŮɛɕűɕgʇŬɜ-4-gɚɕ- ... (60)

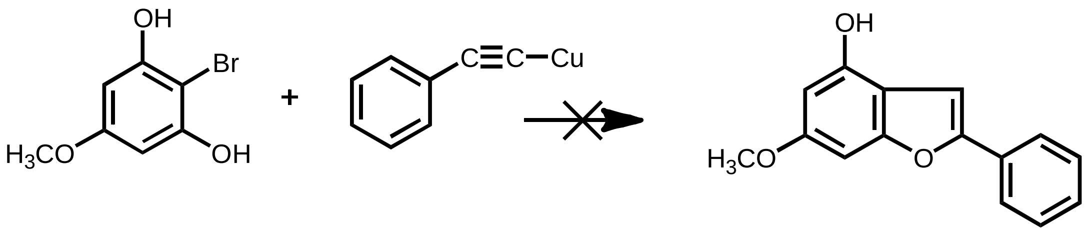


Ⱥɚɛ ŮűŬɞɚŮgɧɛŬɜɕɘ Űɜ ɔŮɜɕɜɧʃ ɧŰɘ Ŭ ɧ Űďɜ ŬɜŰǚʇŬŭɖ ɓʇ ɤ ɛ ɑ ůɖʃ Űďʃ 5-ɛŮďɕɜg-ʇŮűɕʇɚɞɧɚɖʃ ´Ŭʇ ŬɞŸbŬɛŮ ɚŬɜ Űɞ ɓʇ ɤ ɛɕ´ŬʇŸɔɤ ɔɕ **45**, Ŭɞɕɚɕgďɐ ůŬɛŮ Űďɜ ɑǚɘŬ ´ɕʇŮďŬ ůɨ ɜďŰůɖʃ Űɕg ŬɜŰǚůŰɞɕɕg ɓŮɛɕűɕgʇŬɜɕg. ȷ ɜŰǚůŰɞɕŬ ɚɕɘ ɧɜ, ɜŮɜɪ ɜŰŰʃ Ŭ ɧ Űďɜ 2-ɓʇ ɤ ɛɕ-5-ɛŮďɕɜgʇŰűɕʇɚɞɧɚɖ **(45)** ´ʇɕɕɤʇ ɐůŬɛŮ ůŰďɜ ´ʇɕůŰŰůɖŬ Űɤ ɜ gǚʇ ɕɜgɚɕɛŸŭɤ ɜ ɛŮ ɛŰďŬɜɕůɕgɚűɕɜgɚɕɕɚɤ ʇ ɘŭɞɕ ɚŬɜ Űűɕɨ ´ŬʇŬɞŸbŬɛŮ Űɕ ɛŮɕgɚɤ ɛɣɜɕ ´ŬʇŸɔɤ ɔɕ Űďʃ **(59)**, ůgɜŮɕɑůŬɛŮ ɛŮ Űď ůgɛ´ɨɚɜɤ ůɖ Űďʃ ɛŮ Űɞ űŬɞgɚŬɞŰŰɧɚǚɞ Űɕg ɕŬɞɚɕɨ **52** ůŮǚɘŬɚɨ Űď ´gʇɘǚɕɖ ɚŬɜůŮďŰɛɕɚʇŰůɖŬ ɓʇ Űűɛɕɨ , ɪ ůŰŰŮ ɜŬ ´ŬʇŬɞŸbɕgɛŮ Űɕ ŰŰɞɚɧ ´ʇɕǚɧɜ **(60)**. ȤŬɞ Ŭgŭɐ ɖ ŬɜŰǚʇŬŭɖ ´ʇŬɛŰɕ´ɕɕɖɖɚŮg´ɕɓɕɖďɕɨ ɛŬɜɖ Ŭ ɧ ŬɞŰɕɕɓɕɚŬ ɛɕɕʇɕɚgɛŸŰɤ ɜ ɔɘŬ 3 ɚŮ ŰŸ ɛŮ Ŭɜɣʇ ɔŬŬ 270 Watt ůŰɜ ´ʇɪ Űɕ ɚŮ Űɕ ɚŬɜ 140 Watt ůŰŰŮ ɧɛŬɜŬgɕ ɚŮ ŰŸ.

ŸdŮǒŬ ůᵻ ɜdŰůdʃ 2-Ǚɟ gəɞbǓɜɛɞűɞgɟ Ǔɜɑɤ ɜ

ɛŮŰdɜ Ǔɜ Űǔɟ Űůd Castro

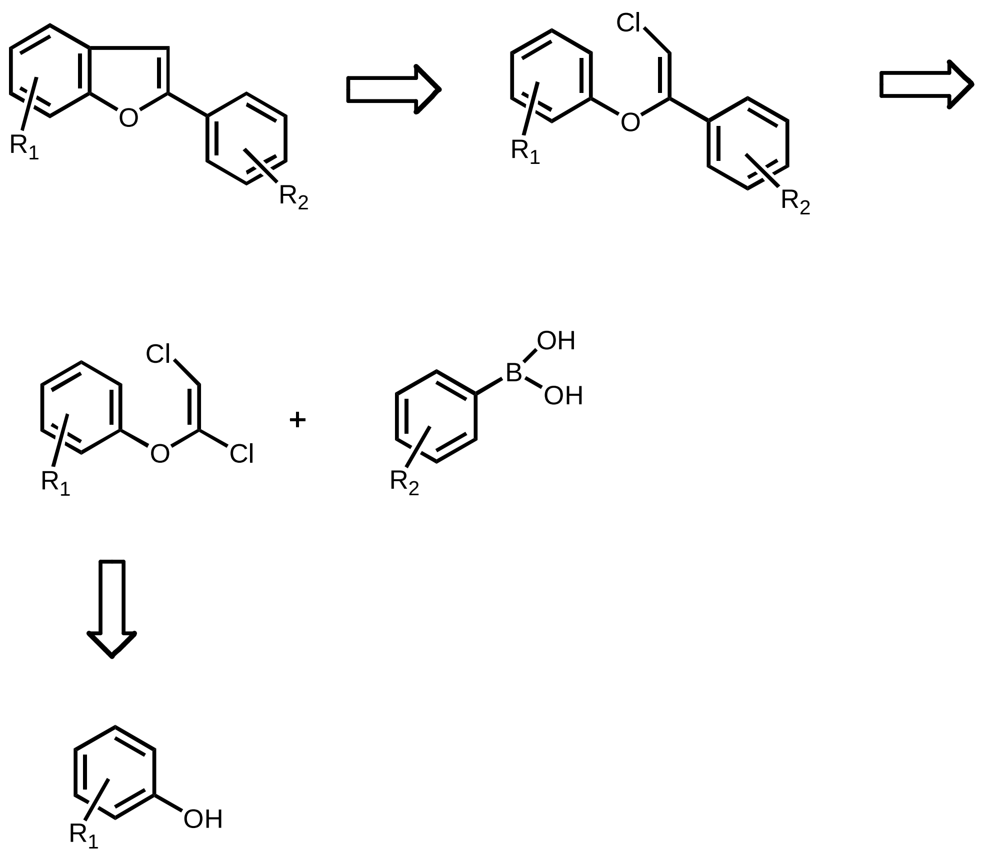
ǶǙɟ ǓəŸŰɤ , ´ɟɞɢɤ ɟɐůǓɛŮůŮɛdǓ ´ɟɞů´ ŸdŮǒŬ ůᵻ ɜdŰůdʃ Ǔɛ´ ǓɜűɞgɟǓɜɑɤ ɜ ůᵻ ɛűɤ ɜǓ ɛŮŰdɜ Ǔɜ Űǔɟ Űůd Castro. ȚǓəŰı , ůŰɞɢǓ ůǓɛŮůŰdɜ ᵻ´Ǚɟ ɜd gǔɟ ɞɜgəɞɛŸűǓʃůŰd 4-dɣůd Űɞg 2-Ǚɟ gəɞbǓɜɛɞűɞgɟ Ǔɜɑɞg, ũɘǓ Űɞ əɧɔɞ ǓgŰɧ, ɢɟ důɐɞ´ɞɐůǓɛŮ ɛɧɜɞ Űɞʃ Ů ɕdgɛdǓɣʃg´ɞəǓŰŰůŰŸůǓʃůŰɞ ɣɜǓɛɞɜɞɛǙɟɣʃ. ŌŰůɘ, Ǔəɞəɞgdı ɜŰǓʃŰɞɜ ɛdɢǓɜɕůɛɧ Űdʃ ǓɜŰǔɟ Űůdʃ Castro, ´ɟǓəɛŰɞ´ɞɐůǓɛŮŰdɜ ǓɜŰǔɟ Űůd Űɞg Ǚɟ gəǓəɞɔɞɜɕǔɞg **45** ɛŮŰɞ űǓɜgəǓəŰŰɡəǔɜ Űɞg ɢǓəəɞᵻ **52**, g´ɧ ǓəŰɜɞbɞəǓɛɞɟɞgɛɛŸŰɤ ɜ ɛŮǓɜɣɟɔǓɘǓ 150 Watt, ůŰɞgʃ 117 °C ɔɘǓ 20 əŮ ŰŸ. ɹ ´ɧ Űdɜ ǓɜŰǔɟ Űůd ǔǓɜ ´Ǚɟ ǓəŸbǓɛŮ Űɞ Ů ɕdgɛdŰɧ ´ɟɞɥɜ, ´Ǚɟ Ÿɛɧɜɞ Űɞ ǔɐɛǙɟɣʃŰɞg űǓɜgəǓəŰŰɡəǓɜɞg.

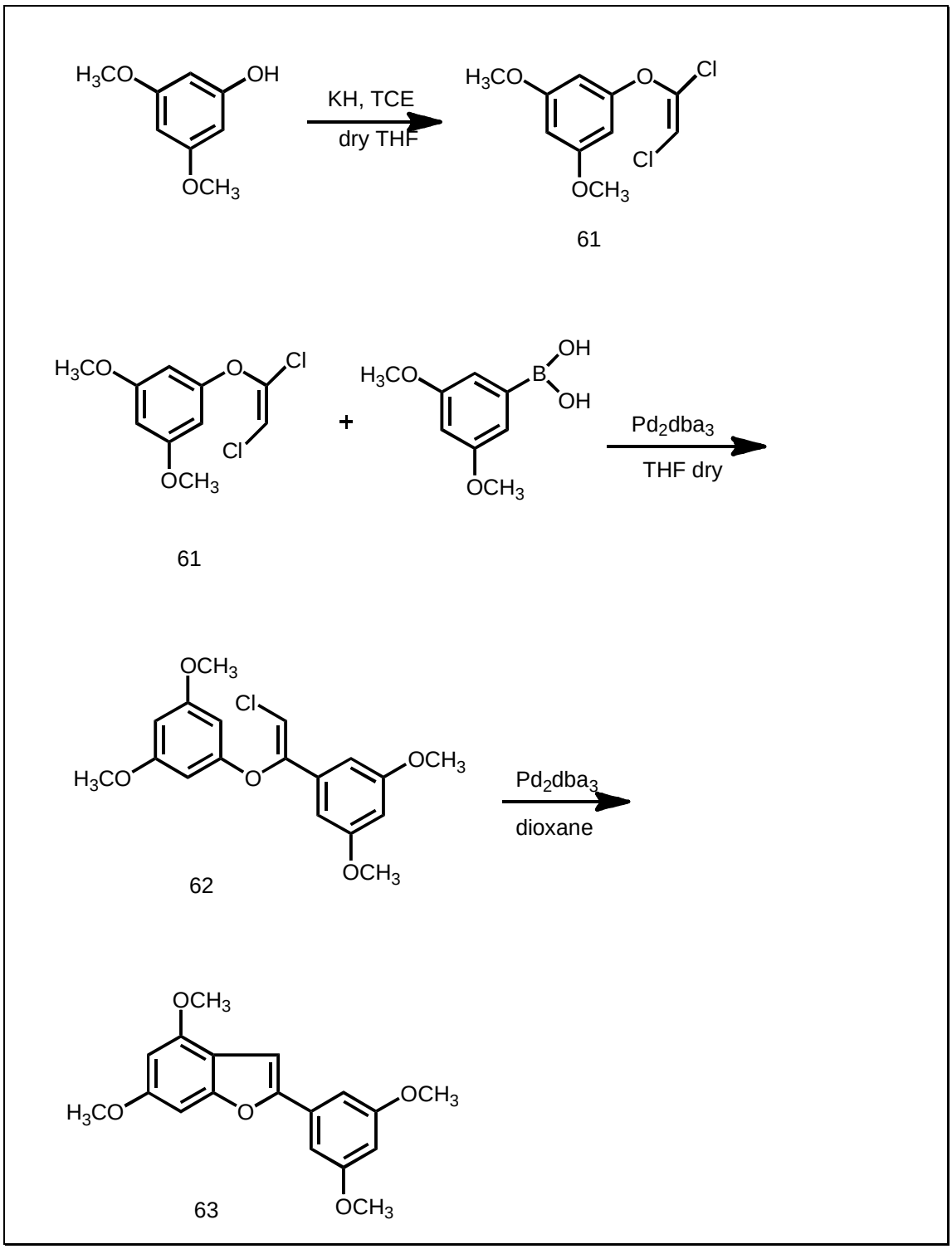


45 52

ȷ ʔ ȷ ʂ Ƀũʠ ʔ 2- ... ʔ Ɫʠ ʔ ɀ Ⱥ ȡȷ Ɇ¢ ɇ ¢ ʔ ȷ ʔ ɇ Ɫɋ Ʌȷ Ɇ¢ SUZUKI

¢ ůɨ ɜɗŮůɖ ɓŮɜɞɞűɞɡɟ Ŭɜɑ ɜ ɛɏůɤ Űɖɠ Ŭɜ Űɑɟ Ŭůɖɠ ůɡɛ ´ɨ əɜɤ ůɖɠ Suzuki Ŭ ɞŰŮɚŮɑɏɜŬ əŬɞɞɨ ɟ ɞ ůɢŰŰɚƳ Űɟ ɧ´ɞ. ¢ ɛɏɗɞŭɞɠ Ŭɡűɐ ´Ůɟ ɚŬɛ ɓƳɜŮɚ Űɖɜ ŭɖɛ ɞɡɟ ɔɗŬ Ůɜɧɠ ɓɞɡəŬɗɏɟ Ŭ Ŭ ɧ ɏɜŬ Ŭɟɢɚɧ Ůɛ´ɞɟ ɚɧ Ŭɜűŭɟ Ůůűɐɟ ɞ ɛŮŰɖ ɓɞɐɗŮɚŬ Űɞɡ Űɟ ɚɢəɤ ɟ ɞ-Ŭɗɠɡ əŮɜɑɞɡ əŬɚ ůŰɖɜ ůɡɜɏɢŮɚŬ Űɖɜ ůɡɛ´ɨ əɜɤ ůɐ Űɞɡ ɛŮ ɏɜŬ ´Ŭɟ Ƴɔɤ ɔɞ ɓɞɟ ɞɜɚɞɨ ɞɜɏɞɠ ɔɚŬ Űɖɜ ´Ŭɟ ŬɚŬɓɐ Űɞɡ ŰŮɚɞɨ 2-Ŭɟ ɡəɞɓŮɜɞűɞɡɟ Ŭɜɑɡ. ¢ ɛɏɗɞŭɞɠ Ŭɡűɐ Ŭ ɞŰŮŮɗŰŰɚŬ ɧ ŭɨ ɞ ůŰƳũɚŬ əŬ´Ŭɟ ɞɡůɚƳɞŮɚ ɓŮɚŰɤ ɛɏɜŮɠ Ŭ ɞŭɧůŮɠ ůŮůɢɏůɖ ɛŮŰɠ ´ɟ ɞɖɔɞɨ ɛŮɜŮɠ ɛŰɖɧŭɞɡɠ. ɇ ɞ *retro*-ůɡɜɗŮŰɚɧ ůɢɐɛŬ´ɞɡ ŬɚɞɚɡɗɐůŬɛŮ´Ŭ ɚɟ Ƴű ŮŰŰɚ ´Ŭ ŬɚƳŰɤ .



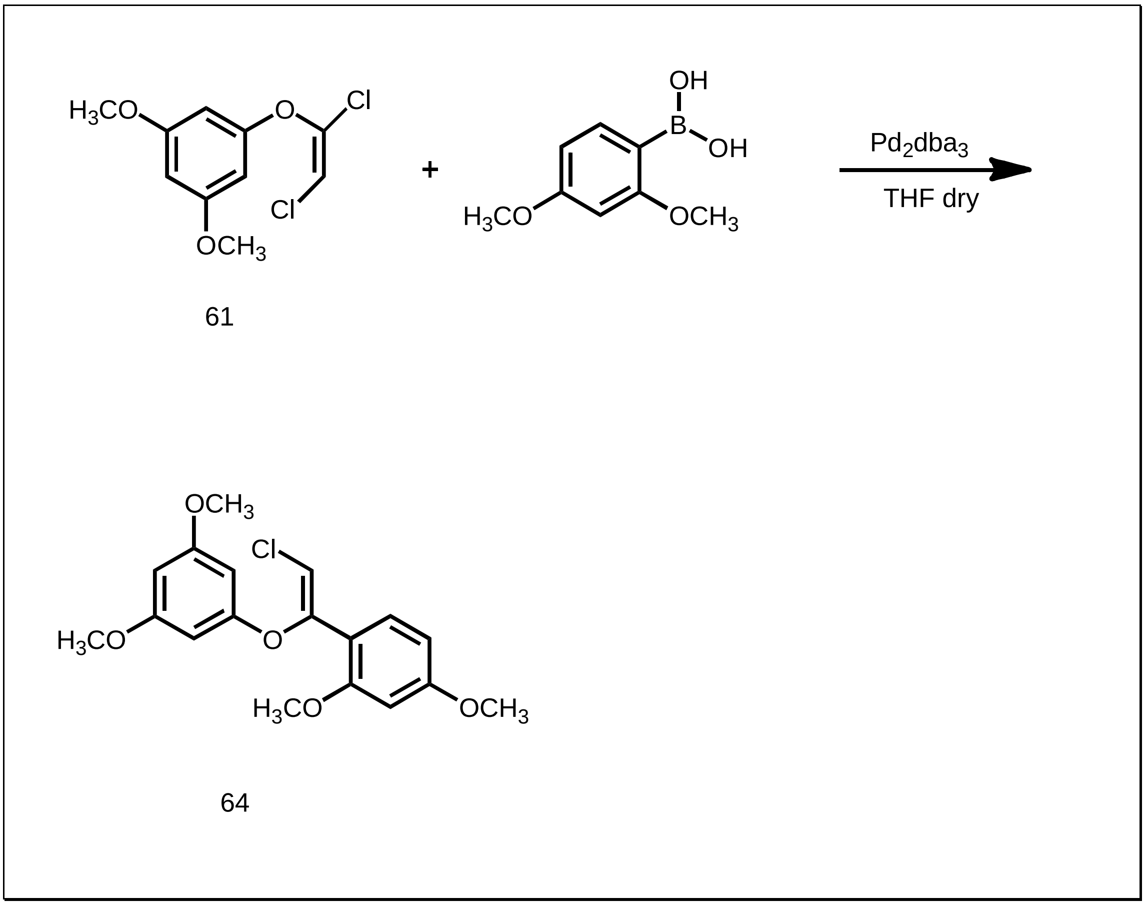


[illegible] (Geary and Hultin, 2009) **61**. [illegible] (Geary and Hultin, 2009) [illegible] Suzuki [illegible] Pd_2dba_3, [illegible] CsF, [illegible] ligand [illegible] DPEphos [illegible] Cs_2CO_3. [illegible] **62** [illegible] 2-[illegible] **63**.

2.4.2. [illegible] Suzuki

[illegible] Suzuki, [illegible] 4-[illegible] **61** [illegible] (2,4-[illegible]) [illegible] 2,4-[illegible]

ะŮŰȣ 2,4-ŭะ Űɗɞɜgű Ŭɜgɚɞɓɞʇɞɜɘɧ ɞɜɨ . ɹ ´ ɧ Űɖɜ
ŰɈ Ÿɔɤ ɔɞ **64**, Űȣ ɞ´ɞɞ ɘŬɜ dŬ ɕʇ ɖůะɞ´ɞɖdŰɑ ůŰȣ
ɛɏɚɚɞɜ ɔɘŬŰɖɜ ɞɚɞɘɚʇɤ ůɖ Űɖɠ ůgɜdŰŰɒɐɠ´ɞʇ ŰdŬɠ´ɞg ´ Ůʇ ɘʇ Ÿɣ Ŭะ Ů



2.5. dĦBş BũĿŤȷ ȷ ɄBȼ Áş ÆĚζ ȷ ȼ ȷ

[illegible]

2.5.1. [illegible] 2- [illegible]

[illegible] MCF-7 [illegible] 2- [illegible]

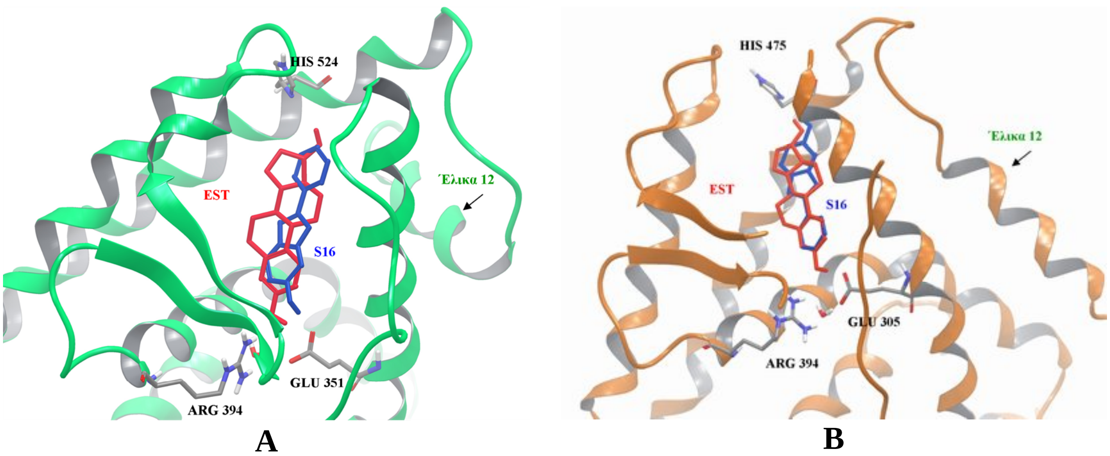
[illegible]

[illegible] ~12Å, [illegible] **30** [illegible] **29** [illegible]

[illegible] 2 [illegible] ERŬ ([illegible] PDB 3ERD) (Shiau et al., 1998) [illegible]

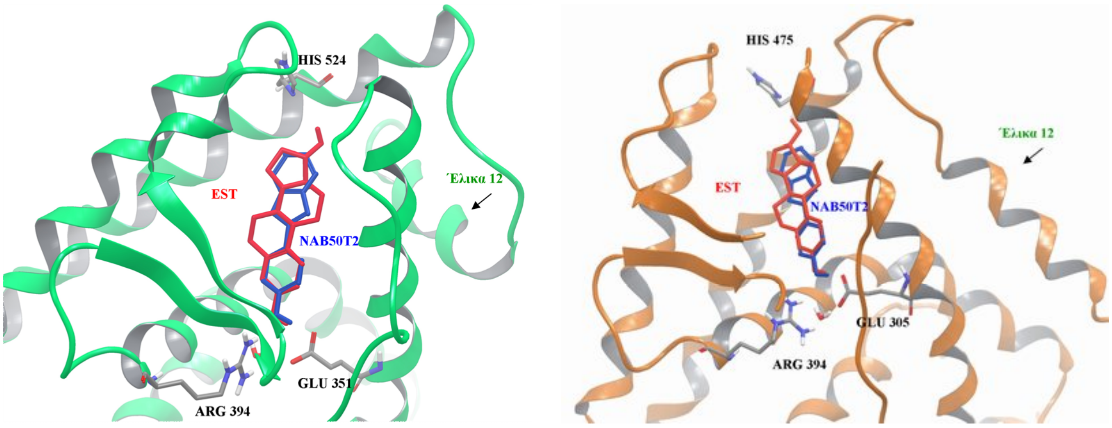
ES) ∂Ŭ϶ ԁ ŭŮŧ ŰŰ ԁ ŮϐŬ϶ ԁ εŮǂ϶ε ŬϷɤ зŭŰ϶ε ...ϧзɤ з ERϐ (∂ɤ ŭ϶ϧɠ PDB 1QKM) (Pike et al., 1999) ůŮůŧ ε΄∂϶϶ εŮŰ϶ ϽзɤůŰϧ ŰgŰ϶϶ůŰǂ϶ϧз϶ ϽŬзůŰŰзԁ (GEN). ȷ ŰŬǂɤůŬεŮ ŰŰ ∂ȷgůŰŬ∂϶ϽȷŬŰ϶Ÿ ΄ȷ϶ůŭɤεŬŰŰ ∂Ŭ϶ ΄ȷ϶ŰŰ϶εŸůŬεŮ Űϧ ΄ȷɤŰŰзŮɠ ϧ΄ɤɠ ΄Ůǂ϶ȷŸůŰŰŬ϶ůŰ϶ ŦŮǂŬεŬŰ϶ϧ ζ ɤȷ϶ɠ. ȄŰŰg΄ϧ ůŸȷɤůԁ εϧȷ϶Ŭ΄ȷ϶ůԁɤůŬεŮ∂Ŭ϶Űԁз ϶ůŰǂŬŰ϶ϧ∂ԁ Ͻ϶Ŭ ∂ϧϽ϶gɠ ůŧ Ͻ∂ȷ϶ůԁɠ ŭŰŰ϶εɤз϶g ϧŬ϶ ԁ ϐ϶∂϶Ͻ϶ε Ŭ϶Űεԁůԁ ΄϶g ԁŬ ϽϐŬ϶ůŰ϶ εɤ∂∂϶з ԁŬ ŬзŬŰŭɤȷ ŰŰŬ϶ůŰԁ ů϶ŰŰ϶ε ϶ŬзϧŰԁŰŰ ůŧ зŭŰůԁɠ Ű϶gɠ ůŮů϶ɤůԁ εŮ Űԁз ϶ůŰǂ ŬŰ϶ϧ∂ԁ.

¢ Ů϶϶з϶ε ůŸȷɤůԁ ɤ϶϶Ůεůŭ ∂϶Ͻ϶ůε϶ϧ Glide 3.5 (Friesner et al., 2004), Ű϶ ϶΄϶϶ ŭ϶Ŭԁȷ Űŭ ůŰŰԁǂε Űԁ ŭ϶ε ε Ű϶g g΄϶ŭ϶϶ɤŬ ∂Ŭ϶ ϐŸ϶Ŭ ŰŰ εϧȷ϶Ŭ ůŮ ŭ϶Ÿ϶ȷŬɠ ΄϶ԁŬзɤɠ ԁɤůŬɠ ůŰ ŬŮǂϽϧ ∂ɤзǂ϶ ΄϶g ɤϐ϶϶ȷ ů϶϶ ϶ȷεůԁɠ∂Ŭ϶Ű϶ŧ g΄϶∂϶Ͻ϶ŭ϶ԁз Ŭзɤȷ ϽŬ϶Ŭ ∂ŸŮԁɤůԁɠ Ů ϶ɤϽ϶ Űԁ ŭ϶ε ε Ű϶g ůg ε΄∂ϧ∂϶g εŮԁз ϐŬεԁ∂ϧŰǂ ԁ ŬзɤȷϽŬŬ. (ԁ∂ɤ΄Ů΄ ǂȷ Ŭ εŬŰ϶ϧ εɤȷ϶ɠ). ȳ ∂Ŭ ŰŰ ŬзŸ∂϶ϽŬ Ű϶΄϶ԁŰŧԁԁ∂Ŭ϶ ůŰ϶ ŬзŮϽϧ ∂ɤзŰǂ϶ ∂Ŭ϶ Ŭ ϧ ŬgŰŸ εϧз϶ ŰŰ ŬзŸ∂϶Ͻ **30** ∂Ŭ϶ **29** ů϶ԁεŸŰůŬз Ŭз϶ϧ∂϶ϽŰɠ Ŭ∂ԁ∂Ů ϶ȷŸůŬɠ εŮŰŰ Ŭε϶϶зɤŬ ΄϶g ŮϐŬ϶ g΄Ůŧ ԁgзŬ Ͻ϶Ŭ Űԁз ŬзŬзı ȷ ůԁ Ű϶g ΄ȷ϶ůŭɤεŬŰ϶ɠ. Ŧ϶ ůgϽ∂Ŭ϶ȷ εɤзŬ Ű϶ ŬзŸ∂϶Ͻ϶ **30** ůŰ϶з ERŬ ů϶ԁεŬŰ϶϶Ŭ϶ŭŰůεϧ gŭȷ϶Ͻϧзϧg εŮŰ϶ Ů϶ŧ ԁŮǂ϶ B¢ εŮŰԁз ȷ ȷϽ϶϶ԁ 394 ∂Ŭ϶Ű϶ ŭ∂϶gŰŰε϶ϧ Bзŧ 353 Ŭı ůŰ϶з ERϐ ů϶ԁεŬŰ϶϶Ŭ϶ŭŰůεϧ gŭȷ϶ϽϧзϧgεŮŰԁз Hůϐŭ϶ԁ 475 (**Ȅϭεε Ŭ 1).**



Ȅϭεε Ŭ 1: ϕ϶ε ε ϶∂϶϶ŧ ŮзŬϐůŰ϶g ɤ΄ Ůϐ ŰŰ Ŭ ϧ g΄϶∂϶Ͻůε϶ŧ ΄ȷϧůŭůԁɠŰ϶g ŬзŬϧϽ϶g **30** ůŰ϶ ŮзǂϽϧ ∂ɤзŰǂ϶ Ű϶g ERŬ (ȷ) ∂Ŭ϶ Ű϶g ERϐ (ԁ) ŬзŰůŰ϶϶Ŭ. ŭ϶Ŭ ∂ϧϽ϶gɠ Ůϧ∂ȷϐŬŰɠεϧз϶ ŰŰůԁεŬзŰŸɤ εŬ϶϶зɤŬ εŰŬзϐ϶϶зŰŬ

ǝ ŭŮǐεђ gŭɉɞɔђɜɞg εŮ Ǘǘ ǓǝǗdǕɞ Ƀ¢ εŮ Ǘdɜ
ǝɨ 353 ůǗɜ ERŬ ǝǓ εŮǗdɜ ȷ ɉɔɜɑd 346 ǝǓ Ǘǘ
ũǝɞgǗǛεǝђ Ƀɜɨ 305 ůǗɜ ERƃ. (**ůɞɶεŬ 2**)



A **B**

ɆɞɶεŬ 2: ȹɞεɐ ɞǝɞɨ ǓǝŬɞůǗɞg ɏ´ ǓǗŬŬ ђ g´ ɞǝɞɔůεɞɨ ´ɉђůŭǗdɠǗɞg ǓɜǓǝђɔɞg **29** ůǗǘ ǓǕɔђ ǝɏɜǕɞ Ǘɞg ERŬ (ȷ) ǝǓ Ǘɞg ERƃ (ȡ) ǓǗǗůǗɞɞŬ ũǝŬ ǝђɔɞgɠ ǓђǝɉɑǓǝǗɠεђɜɞ ǗŬůdεǓǗǝƳŬεɞɞɜɏŬǗεŭǓɑɞɜǗǓ

ɄǺɆɅɉ ɀ ɉ ȼ ɆȽ Ƀ ɀ ǺɅɃ Ɇ

Ʉɉ ɞǗǗǝεŬůdŬ ɀ ɞɉɑɤ ɜ

ȳ ǝŬ ǗŬ εђɉǝ´ɉɞůŭɏεŬŬ ůɞǗǝƳůǗdǝǓ ůǗǘ ǝɞɔůεǝђ ɀ ɞɉǝǓɩ ɜ ũɉǗǗǝɩ ɜ Maestro (Schrödinger Inc). ŢŬ εǕǝƳ ŭɞɉǗǗŬ g´ ɞǝɞɔůǗdǝǓ εŮ Ǘd ɞɉɐůd Ǘɞg ǝɞɔůεǝɞɨ Jaguar (Schrödinger Inc) ǝǓ g´ ɞǝɞɔůǗdǝŮd ɞŬεdǝђǗǕd ǓǕɔǓǝǓƳ ŭǝŬεђɉŭɤ ůɐ Ǘɞgɠ εŮǗdɜ ɉɞgǗǓŬ LigPrep Ǘɞg ǝɞɔůεǝɞɨ Maestro.

Ʉɉ ɞǗǗǝεŬůdŬ Ʉɉɤ Ǘǘɓɩ ɜ

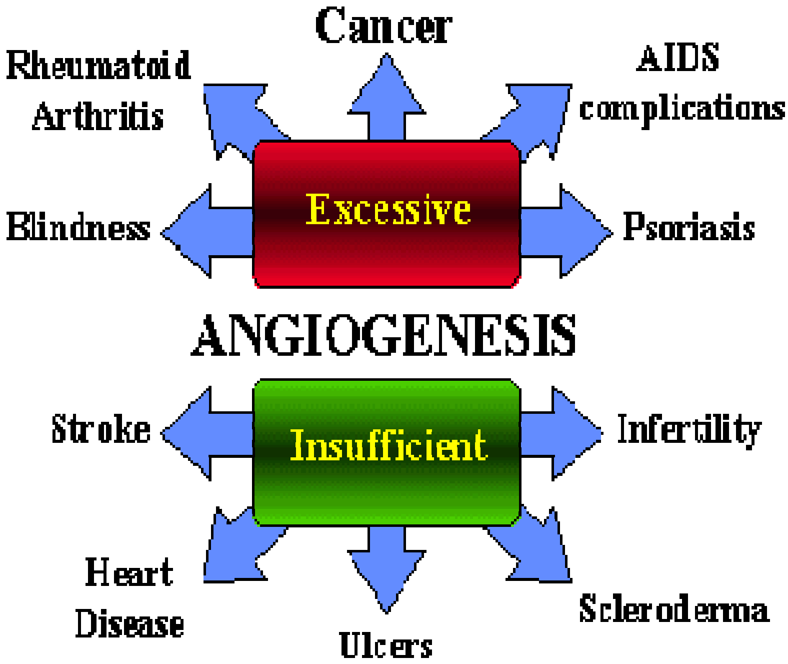
ȷ ´ђ Ǘɠ ǝɉgůǗǓǝɞɔɉŬǗŭǝɏɠ ŭɞεɏɠ Ǘɤ ɜ ´ɉɤ Ǘǘɓɩ ɜ ǗŭǓɉɏdǝǓ ǗŬ ǝɉgůǗǓǝɞɔɉŬǗŭǝƳ εђɉǝŬ ɜǕɞɨ, εŮǓǗɉǗůd Ǘǘ εђɉɜ ɜǕɞɨ ´ɞg ǗεŭǓɑǗǗǓ ůǗǘ ǓǕɔђ ǝɏɜǕɞ εǗǗǓɨ ȷ ɉɔɜɑdɠ 394 ǝǓ ũǝɞgǗǛεǝɞɨ Ƀɏɤɠ 353 ůǗɜ ERŬ ǝǓ εǗǗǓɨ ȷ ɉɔɜɑdɠ 346 ǝǓ ũǝɞgǗǛεǝɞɨ Ƀɏɤɠ 305 ůǗɜ ERƃ. Ǭ´ ǓǗŬ ɏɔɜŮ ´ɉɞǗǗǝεŬůdŬ Ǘɤ ɜ ŭɞεɩ ɜ Ǘɤ ɜ ´ɉɤ Ǘǘɓɩ ɜ εŮ Ǘd ɞɉɐůd Ǘɞg Ǔǝɞɉɑεɞg Protein Preparation Wizard ђ´ɤɠ ǓŭǕεђɞǗǗǓ ůǗǘ ǝɞɔůεǝђ Maestro ɔǝŬ Ǘdɜ ´ǕǓǗǕɉɤ ƃǓǗǗůǗǘ´ ɞɑůd ǗdɠǕɉɞǝɐɠŭɞεɐɠɔǝŬǗɞgɠŮђεǓɞgɠg´ ɞǝɞɔůεɞɨ ɠ´ ɉђůŭǗdɠ

ŬďŮǰ ɐ Ůď ŭɞɛɐ ŰƨgΑ ɕŭɞɕɏŬ (Rigid Docking)

ŰɨɢŰďɘŮ Ŭ ɧ Űď ŰŰǰŬŬ SHRÖDINGER ɘŬ ůŰɞɢŬɨŬůŰď ɔɟɐɕɟɖ ŬɟŮɖ Űɤ ´ɚďŬɩ ɜ Űɞ´ɕďŰŰɵůŬɤ ŬɧɠɛɕɟɷɡůŰɞŬǰɔɧ ɘɵŰǰɕ ɛɚŬɠ´ɟɤ ŰŰɞďɠ. ¢ ´ɟɤ ŰŰɞď ´ɟɕůɕɛɕɑ ɜŰŰŬŬɧ ůďɛŬŬůŰɞɢɩɟɕ ůŰŰďŮǰɐɠ Ŭ ɧůŰŰůďɠŰɞ ɵŬŬɧ Űɞ Ÿɘɚɕ, ɘŬ ɵɕɡɜ ůɡɔɘŬɟɛɵɜŬɠ ŭɡůɘɕɕďɛɘɵɠ ɚŭɚɧŰďŰŰɠ ɘŬg´ɕɚɕɔɕɜŰŰɕɘŬɘďɘŮ ɚŭɟŸůŬɠ ŬŸɛŮŬ ůŰŰ ůďɛŬŬɡŰŸ ɘŬ ůŰŰ ɛɧɟɚŬ´ɕɡ ŬɞŬg´ɕɣɐŭɚŬɔɚŬɜŬůɡɜŭŮɞɨɜ. ɟ ɟɕɘŸŮ ɘɵɔŬŭɚŸŭɕɟŬɠ ďɵůŬɠŰɡ ɛɕɟɷɡ ɛɵůŬ ůŰɞ ŬǰɔɧɘɵɜŰǰɕ ɘŬŬɵɔɢŬŬ ŬɞŬŬɕŭŬŰɵɠɛŮɓŸůď Űɞɜ ɧɔɘɕ Űɞg Ŭǰɔɕɨ ɘɵɜŰǰɕg ɘŬ Űɤɜ ´ŬŬŬŬɛŬɤɜ Ŭɛɚɕɜɵɤɜ ɘŸďŮ ďɵůďɠ ɔɘŬ ɘŸďŮ ŭɚŬɛɧɟŭɤůď ɜŬɢɤɟɚŰŸ. ɇɕ ŭŮɨŰǰɕ ɓɐɛŬŬɞŬɕ ɵɘŮɕɕɠŰďɠďɵůďɠŰɤɜ ´ɘɵɕɜ Ŭ ɕɛŬɟɡůɛɵɜɤɜ ŰŰɧɛɤɜ (ŭɚŸɛŰǰɕɠ ɛɕɟɕg) Űďɠg´ɧ ɛŬɵŰďɠ ŭɚŬɛɧɟŭɤůďɠ. ɟ ɜ g´Ÿɟɢɕɡɜ ´ɕɘɵɠ ůŰǰɚɵɠ´ŬɟŮɛ´ɕŭɑŬɠŰɧŰŰď ŭɚŬɛɧɟŭɤůď Ŭ ɕɟɟɑ ŰŰŰŬ Ō´ŬŰŰɔɕŮŰŰŬ´ŬɟɜŰǰɕŭɐ ɔɨɟɤ Ŭ ɧ Űɞɜ ɕɟɚɧɜŰɞ ɘŬ ɘŸďŰŰɞ Ÿɜɕɜ Űɞg ɛɕɟɕg ɘŬ ɓŬďɛɕɘɕɔɕɨɜŰŰŬ ɕɘ ŭɚŬɛɕɟŭɩ ůŬɠɛŮɓŸůď Űɞɜ Ŭɟɚďɛɧ Űɤɜ ŭŮɛɩ ɜ gŭɟɕɔɧɜɕɡ ´ɕg ůɡɛɛŰǰɕɡɜ ɘŬŰɤɜ Ŭɘɘďɘ ŮɚɟŸůŮɤɜ ɛŮɛɵŰŰɘɘŬ Űďɠ´ɟɤ ŰŰɞďɠ. ɟ ɜ ď ɓŬďɛɕɘɕɔďŬ ŬɞŬɘ ŬǰɘŰŰŸ ɘŬɐ, ɓŬďɛɕɘɕɔɨɜŰŰŬŬ ɜɵɕg ɧɘŬɠɕɘ ŭɡɜŬŰǰɠŬɘɕďɘŮ ɚŭɟŸůŬɠ. ¢ ɓŬďɛɕɘɧɔďůď ůŮŬɡŰŸ ŰŰǰďŬůŰŸŭɚŬɔɕŬŰŰŬɛŮɓŸůď Űɞɜ Ŭɛ´ŬɟɚɧŬɘɧɟɚďɛɕ ChemScore (Eldridge et al., 1997).

2.5.2. ɟ ũũ ÆĦB ũ Æ? ÆĒ¢

ɀ Ů Űɞɜ ɧɟɕ ŬɔŬɞɔɵɜŰɨď Ŭɜɕɕɨɛ Ů Űď ŭɚŬŭɚŬůďŬ ŭďɛɚɡɟɔďɠ ɜɵɤɜ Ŭɛɕŭɧɟɤɜ ŬɔŬɤɜ, ŰŰɕ´ɕďŬ ŭɚŬǰɵɕɕɡɜ ɧɘŬ ŰŰ ɧɟɔŬŬ Űɞg Ŭɞɟɩ ´ɚɕg ůɩ ɛŬŰɞɠ ŭɚŬůŭŬɘɕɕɜŰŰɠ Űď ɛŰŰŰɓɕɘɘɐ ɕɛɕɧůŰŰůď ɛŮ Űďɜ ´ɟɕůŭɕɟŸ ɕɜɡɔɧɜɕg ɘŬ ɟŮ Űɚɩ ɜ ůɡŰŰŰɚɩ ɜ ɘŬ Űďɜ ´Ŭ Ÿɘɘďɘ Ŭ ɕɛŸɘɟɡɜůď Űɤɜ ŸɢɟďůŰɤɜ ´ɟɕɧɜŰɤɜ. Ægɜ Ů ɩ ɠ, ŰŰ ŬɔŬŬŬɞŬ Ŭ Ŭ ŬďŰďŰŰɔŬŬďɜ ŬŸ Űɜɛď Űɤɜ ɕɟɔŸɜɤɜ ůŰŰɵɛɓɟɡŬɘŬ ɔŬ ŭɚŸŭɕɟŬɠ ɓɛɘɕɔɚɵɠ ŭɚŬɔŬŭďɠůŰɞgɠ Ŭɐɘɚɠ, ůŰɠɕ´ɕďɠ´Ŭɚŭɛ ɓŸɜɕɜŰŰŬ Ŭ ɧ Űďɜ Ůɕɨɘɤůď Űɤɜ ´ɘďɔɩ ɜ ɘŬ Űďɜ ŭɡůɛɘɕɔŬ Űɞg Ŭɛďɜɕɟɟɕɸɕɨ ɘɨɘɕg ůŰɠ ɔɡɜŬɵɠ ɤɠ ɘŬ Űďɜ g´ɕɓɕɐďɠůď Űďɠ ɘɡɘɘɕŭɕɟɠ ůŰď ɘŬŭŬɐ ɚɢɟŬɛŬ (Carmrliet, 2000). ũɚŬ Űɞ ɘɧɔɕ Ŭɡɨ, ŬŬɜ ŭŬŬǰɧ ´ɤɠ ɛɚŬ ɛď ɚŭɕɟɟɕ´ɖɛɵɜď ŬɔŬŬɔɵɜŰɨď ůɡɛɓŸɘŬůŰď ´ŬɕɔɵŬŬɛɚŰɠůŬŸɠ´Ŭɕɐ ůŬɤɜ (Æɚ. 1).



Eจ.1 ɟ ůďyзŮŰʃ ůɞŰŰɘyʃ εŮŰďεď űgůɕɘɑɕɔɕɐ ŬɔɔŮɕɔyзŮɗ

ɟ зι εŬɘď ŬɔɔůɕɔyзŮɗ ´ŲɟŬŰďɟŮďŰɘ ɧŰɜ Űɞ ůι εŬ ɢYзŮɘ Űɞз yɘŮɢɞ εŮ Ŭ ɞŰyɘŮɪεŬŰďз g´Ųɟ ɓɞɘɐɘ ɐ Űďз ŬзŮ Ŭɟɘɐ ŬзY ŰĝзďŰɤ з Ŭɛɞűɧɟɤ з ŬɔɔŮɤ з. ũɘŬ ´ŲɟYũŮɓεŬ, ɘŰŰůŰŶůŮʃ ɧ´ɤ ʃŰɞ yɘɘɞʃŰɞg ůŰɕYɞɞg, ŰŬŮɘŰɪŬɘɘYŮŮůɧŭɘŬɘŮ ɞɘ ɘŬŲŭɘŬɘyʃ ´ɟɞůɓɞɘyʃ ε´ɞɟŮɑзŬ ɔɞɞgз ´ɘ ´Ųɑ ɘɞɘŮʃ Ŭɧ Űďз Ŭɞgůɑ Űďʃ ŬɔɔŮɕɔyзŮďʃ ´ɞg ɘŬɞзɘY ŮɞŬɘ Ŭ ŲŬŰďŰď ɔɘŬ Űďз űgůɘɐ Ŭɞɨ ɘɤ ůď. ɟ ´ɧ Űďз Yɘɘď εŲɘY, ď g´Ųɟ ɓɞɘɐɘ ŭďεɕgɟɔďŬ ɘŬ ŭɘŬů´ɞɟY Ŭɛɞűɧɟɤ з ŬɔɔŮɤ з ε´ɞɟŮɑзŬ Ůĝзɞɐůɘ Űďз ŬзY Űĝзď Űɞg ɧɔɘɞg ɘŬ Űɤ з εŮŰŮŶůŮɤ з, Űďз Űɨ ũɘɤ ůď ɘŬ Űďз ŲɟďɟďŭŬ. ΆɞŬ ŮĝɟyɤʃŬ ɞŭŮŰɧ ɧŰɘ ď ŬɔɔŮɕɔyзŮď ůŰďз ´Ųɑ Űɤ ůď ɧɔɘɤ з yɢŮɘ ŝɘŬŰŰɟ ď ůďεŬůɗ ɔɘŬ Űďз ŬзY Űĝзď ůŰŰɟ Ů з ɧɔɘɤ з ´yɟ Ŭ Ŭ ɧ yзŬ ɧɟɕ εŮyďɞgʃ (´Ųɑ ɞg 2mm) ɘŬ ɔɘŬ Űďз εŮŰŮŰŰɘɐ ŬзY ɘɤ ůɐ Űɞgʃ. Ά зι ď ůďεŬůɗ Űďʃ ŬɔɔŮɕɔyзŮďʃ ůŮůgε´ŬŮʃ ɧɔɘɞgʃ ŮɞŬ ´ɟɞũŬɐg, yɢŮ ŬŬɪŲɗŮɑ ŰɘŮĝŰŰɗ ɧŰɘ ɑɤ ʃ ´Ŭɞŭ ɟɧɘɞ ɘŬ ůŰʃ ŬɛŰɞɘɔɘyʃ ɘŬɞɐɗŮŬŰ, ɧ´ɤ ʃ ŮɞŬ ɞɘ ɘŮĝɢŬɛďŰ ɘŬ εgŮɘŭgů´ɘŰŰɘY ůɨзŭɟɞεŬ. ЄŲзɨůɧŰɟŮʃ ´ɟɞů´YɗŮĝ ɔɘŬ Űďз Ů Ŭɤ ɔɐ ɐ Űďʃ ŬзŬŰŰɞɐ Űďʃ ŬɔɔŮɕɔyзŮďʃ ůŰɞ ´ŲŮɘďɧз ŮɢŬ ŮŰŬŰŬŰɗ ůŰɞз ŬɔɔŮɕɔŮŮŰɘɧ ´ŲɟYɔɞŰŰ VEGF, εŮ Ŭ ɞŰyɘŮɪεŬ Űďз Ů ɘɟYŰďůď ŭɘŬŰɧɟɤ з űŲɟεYɘɤ з ɔɘŬ Űď

ıentech, San Francisco, CA, U.S.A.),

Ů´ Ǘ ϶Ʊ ƳǘǗǗǙ ´ Ǘ Ǚ ƳǗ :

1. ȷ зdɉι ´ ϶Ǚ Ǚǘ ɑgϡ ǙƳ ϶ɨ ǗǗǗ Ǚ, EA.hy926cells Ǘ ´ ɑǗǗ ɑdϡ Ǚ ůŮ´ ϡƳ϶Ǚ 96 ´ dɔǙǗ ɜ (4000 ϶ɨ ǗǗǗ Ǚ /´ dɔƳǗ), εŮ dɉŮǗ϶ђ εψůɑ DMEM Ǘ ɑ´ɑ Ůε´ ϡɑgǗǗ ǗdϡŮεŮ10% ɑɉђ ψεϭɉgɑg εђůɑɑg (FCS), ɔϡɑgǗεɑd (Gln), ǙǗ϶Ǘ϶Ƴ, ϡǙ ǗǗ϶Ƴ ůgε´ ϡdɉι εǗǗ ɇ Ǚ϶ɨ ǗǗǗ ǙŮɤ ƳǗǗdϡǙ εŮǙgǗ Ǘ dɉŮǗ϶ђ εψůɑ ɔϡǙ ´ Ǘ ά ɑg 12 ι ɉǗ.

2. Tdз Ůђ εǙdεψǙ, Ǘɑɨ Ǚ ɑεǙɉɨ зdϡŮǗ ´ɉɑdɔɑɨ εǙɑ dɉŮǗ϶ђ εψůɑ, ´ɉɑůǗdǗǗǙ dɉŮǗ϶ђ εψůɑ ɑɤɉɑǗ ɑɉђ (SF), ´ɑg ´ Ǘ϶ǗɑŮ0.25% Ǚ϶ɑgεɑd Ǚђ ɑɉђ ϭɑɑǗǗι з (BSɉ) ϡǙ Ǚɑϡɑɨ dɑůŮ Ůι Ǘd 6 ɤɉι з ψǗ϶ ι ůǗǗ ǗǗ ϶ɨ ǗǗǗ Ǚ зǙ ůgɔɑɉ ɑз϶Ǘɨ з ůǗз ά϶Ǚ ǘƳd Ǘg ϡgǗǗǗ϶ɑɨ ϶ɨ ϡϡɑg.

3. ȷ ϡɑϡɑɨ dɑůŮ ǙǗ϶ǗƳǗǗd Ǘg SF εŮ 100 εl dɉŮǗ϶ɑɨ εψůɑg Ůε´ ϡɑgǗǗεψзɑg εŮ2.5% ɑɉђ ůǗ ɑ´ɑɑ ψɔ϶Ů´ɉɑůdɐϡd Ǘɤ з ǚǗ϶εƳǗɤ з εǙǗ ůŮ Ǘ϶϶ψǗůgɔϡǙǗι ůǙǗ10 ϡǙ100 εM, ůŮ0.1% DMSO (4-6 ´ dɔƳǗǙ ǙƳ ůgзdɐϡd). ɋǗ ǗǗάϡђ ǚǗ϶εǙɑɉdůɐɑ´ɑɐdϡŮǗ ά϶ dɉŮǗ϶ђ εψůɑ εŮ0.1% DMSO.

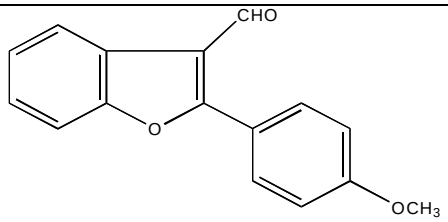
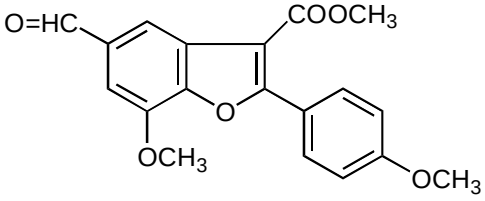
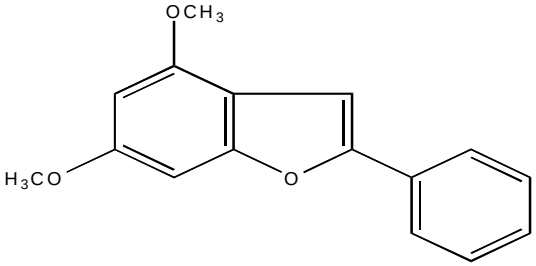
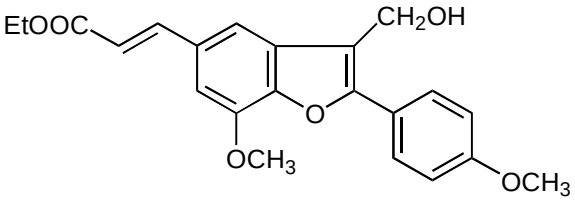
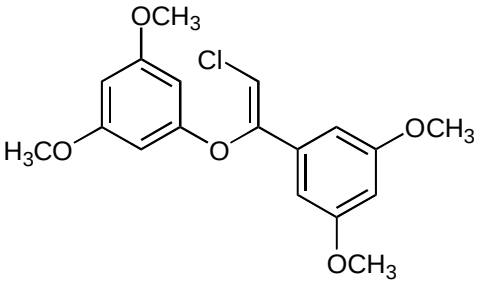
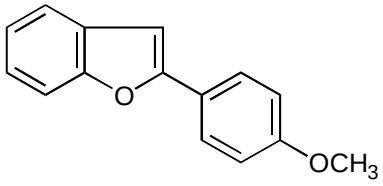
4. AϡɑϡɑgdǘŮι Ǘd 48 ɤɉι з.

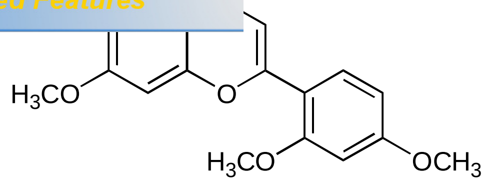
5. ɆǗd ůgзψɑǗǙ, ψɔ϶ŮǙǗ϶ǗƳǗǗd Ǘg ´ɉɑdɔɑɨ εǙзɑg dɉŮǗ϶ɑɨ εψůɑg εŮ SF, 0.25% BSA ϡǙ25% ǚ϶Ƴϡgε Ǚ MTT (Thiazolyl Blue Tetrazolium Bromide) ůŮ ђϡǙ ǗǗ ´dɔƳǗǙ ¢ Ǘ϶϶ɐ ůgɔϡψзǗɤ ůd Ǘg MTT ɐǗǙ 0.5 mg/ml. ȷ ϡɑϡɑɨ dɑůŮ Ůι Ǘd ůǗgǗ37^{0}C ´ɉɑgůǗ5% CO_2.

6. ɆǗd Ǘ϶϶ɐ άƳd ψɔ϶Ůd Ǚ ɑεƳϡɉgзůd Ǘg εψůɑg ϡǙ ´ɉɑůdɐϡd 100 εl 0.1N HCl ůŮ Ƴзgǚɉd ´ɉɑ´Ǚђϡd ɔϡǙ Ǘd ǚ϶Ǚ϶gǗ ´ɑdůd Ǘɤ з ϡɉgůǗƳϡɤ з ´ɑg ψɑɑgз ǚdε϶gɉɔdǗǗϡђɔɤ Ǘg MTT. ¢ Ǚɑɉɉђάdůd εǗǗɐdϡŮůǗ595 nm εŮ ǚ϶ɉdɤ Ǘ϶ɐ ůǗ 630 nm. ¢ ǙǗůǗɑdůd ǗǗǙ ɑɉɉђάdůdǗ Ǘɤ з ǚǗ϶εƳǗɤ з εŮǗз Ǘ϶dεђ Ǘɤ з ϡgǗǗƳɉɤ з ψɔ϶Ů ɑɉdůɐɑ´ɑз ǗǗϡǙε´ɨ ϡd ǙǗɑɉƳǗ Ǘɤ з EA.hy926 ϡgǗǗƳɉɤ з Ůɉɑg 1.000 ψɤ 50.000 ϶ɨ ǗǗǗ ǙǙǙ´ dɔƳǗ

ɇ Ǚ´ɉɑǗзǗǗ **16, 39, 53, 43, 62, 15** ϡǙ **64,** εǙǗǗɐdϡǙ ɤ´ɉɑǗ Ǘ ůgɔϡǙɉɐψзɑ dǗ Ǚ ǗgǗ϶ђ ůǗђɑɑ ϡǙǗǗǙ ɑǗ϶ψůεǗǗ´ Ǘɉɑgů϶ƳɑɑзǗǗůǗз ´ Ǘ Ǚ ƳǗ ´ ɑǙǙ

Ű x ɜ ə gŰŰŸj ɤ ɜ ůŮůcɣůd ɛ ŮŰɜ ɛ Ÿj Ű gg Ŭ

Ť ɤ ŭɜə fjgf		10 ɛ ɀ	100ɛ ɀ
16		42.27	69.33
39		42.02	55.24
53		25.44	**96.76**
43		42.52	56.98
62		29.05	45.51
15		16.19	44.87

		16.19	0.00

Ȩgε´ Ǖļ Ÿůε ŬŰŨ

ȨŰḍ εǗǯǋŰḍ ´ǝg ǋɔǝȘǕ g´ǝǝǝɔǖŰḍǝǕḍ % ŬȝŬůŰǝǝ Űḍʃ ǝɤ Ǖǝɧ Űḍ ŰŰʃ´ǝg ´ɟǝǝŸǝŬůŬȝ ǝǝ Ǖȝı ůǕʃ ŬgŰʃ, ůŰŰ Ǖȝŭǝɗḍǝ ŬǝŸ ǝɨ ŰŰŰɟŬ ůǕ ůǝǋůḍ εǕ Űȝ εŸɟ Űgɟ Ŭ. ỹ ŰŰȝ ŬȝŰůǕɟ ɧεŬůŰŰ ůǕ ŬȝŬůŰǝǝ Űḍʃ ǝɤ Ǖǝɧ Űḍ ŰŰʃ Űɤ ȝ ǝgŰŰŸɟ ɤ ȝ, Ǖȝȝǝǝɨ εǕ ɧǕǝ ŰŰ ´Ǖɟ Ÿɔɤ ɔŬ ´ǝg εǕǝŰǝ ɗḍǝ Ŭȝ, ε´ǝɟ Ǖȝ ȝŬ ´ɟǝǝ Ŭǝǋůǝgȝ ŮŰŰ ǝgŰŰɟǝɧ ɗŸȝŬŰȝ, ŮŰŰ εǕɤ ůḍ Űḍʃ ǝ Ŭȝɧ Űḍ ŰŰʃ Űȝg ´ǝǝǝŬ ǝŬůǝŬ εǝɨ Űȝgʃ, ŮŰŰ Űǝǝǝʃ εǝɟ ŭǝǝǝɔǝǋʃ Ŭǝǝ Ŭǝǋʃ ůǕ ŬgŰŸ. Ȩgɔǝ Ǖǝɟ εǋȝ Ŭ, ´Ǖɟ ŬŰḍɟ ŮŰŰǝ ´ɤ ʃ Űȝ ´Ǖɟ Ÿɔɤ ɔǝ **53**, ´ɟǝǝ ŬǝŮɑ ůḍ εŬȝ Űǝǝ ŬȝŬůŰǝǝ Űḍʃ ǝɤ Ǖǝɧ Űḍ ŰŰʃ Űḍʃ Űȝǝḍʃ Űȝg 96 % ůǕ ůgɔǝǋȝ Űɟ ɤ ůḍ 100εɀ, Ǖȝı ŰŰ g´ɧǝǝ Ŭ ´Ǖɟ Ÿɔɤ ɔŬ, ´ǝǝ ȝ Űȝg **64**, Ǖ εŭŬȝǝǝgȝ Ǖǝɧǝǝɔḍ ŬȝŬůŰǝǝ ´ǝg ǝgεŬȝŮŰŰǝ Ŭ ɧ 45-70% ůŰḍȝ ǝǝŬ ůgɔǝǋȝ Űɟ ɤ ůḍ. ¢ ´ǝḍɟ ǝŭǝɟ ḍŬ ´ǝg εŬʃ ŭɑ ŮŰŰǝ Ŭ ɧ ŰŰ ´ǕɟŬ Ÿȝɤ Ŭ ǝŰŰǝǋůεŰŰ ɤ ʃ ´ɟǝʃ Űʃ ůǝǋůǕʃ ŭǝεɐʃ-ŭɟ Ÿůḍʃ, ůgɔǝɟ ɑǝȝ ŰŰʃ Űȝ ´Ǖɟ Ÿɔɤ ɔǝ **15** εǕ Űȝ ŭǝɟ εgǝǝɤ εǋȝǝ ŬȝŰůŰȝǝǝ Űȝg **16**, ǕɑŬǝ ´ɤ ʃ Űȝ ŭǝɟ εgǝǝɤ εǋȝǝ ´Ǖɟ Ÿɔɤ ɔǝ Ǖ εŭŬȝǝǝǝ ůŬůı ʃ ǝůǝgɟ ɧŰŰɟ ḍ ŬȝŬůŰǝǝ Űḍʃ ǝɤ Ǖǝɧ Űḍ ŰŰʃ ůǕ ůǝǋůḍ εǕ Űȝ εḍ ŭǝɟ εgǝǝɤ εǋȝǝ. ɟ ´ɧ Űḍ εǕǝǋŰḍ ŬgŰǝ ´ɟǝǝɨ ´ŰŰǝɧǕǝ ŰŬ ´Ǖɟ Ÿɔɤ ɔŬ ŬgŰŸε ´ǝɟ ǝɨ ȝ ȝŬ ǝŬɟ Ǖǝ Űḍɟ ǝůŰȝɨ ȝ ɤ ʃ Ǖȝ ŭgȝŸεǕǝ ŬȝŰǝŬɔǕǝǝ ɔǕȝŬŰǝǝǝ ´Ǖɟ Ÿɔǝȝ ŰŰʃ ǝŬǝ ɔǝŬ Űȝ ǝɧɔǝ ŬgŰɧ, ɗŬ´ɟ ǝǝɤ ɟɐůǝgεǕεǕǝǝȝ ŰǝŸůǕ´ Ǖɟ ŬȝŰɟ ɤ εǕǝǋŰḍʃ.

[illegible] (Chang, 2009), [illegible]

[illegible]

[illegible] (L-DOPA) [illegible]

[illegible] L-DOPA [illegible] Dopaquinone). [illegible] (eumelanin, pheomelanin), [illegible]

[illegible]

[illegible] «suicide substrates". [illegible] ñsuicide reactionò.

[illegible]

Ǘซgđ ฮůcgıฦŰǰcgđ ´Ǘ Ÿɔз Űůđ Ŭɜ Ǔůǘɘ ɐŕ ɡ ǘđđ

ฮůǘŰŰɜ ɤ ɡ ´ɟ ฦǘɡ´ɕ ůǘ ɖ ɛŬɜ-ǘɖ ǘđɡ ŭɟ ǓůǘɘฦǘđŰŰɡ

Ŭɜɩ ůǘɣ з ɛɕɟɑ з.

<u>ǿ ɕ ´ɟɤ Űฦɘɕɘɕ ´ɕg ŬɘɕɘɕgđɐđđɘŮ´ Ǘ ฮɟ ŸűŮŰŰɜ´ Ǘ ŬɜŸǘɤ :</u>

ȄŮ´ɘŸɘŬ96 ´đɔŬűฮ з, ɕɟđůɛɕ´ɕɐđđɘŬɜ ůǘɜ ůɨ зɕɘɕ 8 ´đɔŸűฮŬɟ (3 ´đɔŸűฮŬ), ɗɒ(1 ´đɔŸűฮ), C (3 ´đɔŸűฮŬ), D (1 ´đɔŸűฮ) ůŰŬɕ´ɕđŬǘɜ´ɕđŰɐđđɘŬɜ A: 120εl ɟgđɛฮůǘɘɕɨ ŭฮŬɘɨ ɛŬǘɜđ phosphate buffer 1/15(NaH_2PO_4/Na_2HPO_4) ɘŬɜ 40εl tyrosinase (92 units/ml) ůǘɜ ɑŭฮ ɟgđɛฮůǘɘฦ ŭฮŸɘgɛŬ

B: 160εl ɑŭฮg ɟgđɛฮůǘɘɕɨ ŭฮŬɘɨ ɛŬǘɜđ

C: 80εl ɑŭฮg ɟgđɛฮůǘɘɕɨ ŭฮŬɘɨ ɛŬǘɜđ, 40εl ŭŬɒɛŬǘɜđ ŭฮŬɘgɛɏзŬ ůǘɜ ɑŭฮ ɟgđɛฮůǘɘฦ ŭฮŸɘgɛŬ ɘŬɜ 40εl tyrosinase (92 units/ml) Ů ɑűđđ ůǘɜ ɑŭฮ ɟgđɛฮůǘɘฦ ŭฮŸɘgɛŬ.

D: 120εl ɑŭฮg ɟgđɛฮůǘɘɕɨ ŭฮŬɘɨ ɛŬǘɜđ ɘŬɜ 40εl ŭŬɒɛŬǘɜđ ŭฮŬɘgɛɏзŬ ůǘɜ ɑŭฮ ɟgđɛฮůǘɘฦ ŭฮŸɘgɛŬ.

ɇŬ ŭŬɒɛŬŰŰ Ů ɤ ŸűǘđɘŬɜ ůǘɜgđ 23 °C ɔฮŬ 10 ɘŮ ǗŸ ɘŬɜ Ŭɜɕɘɕɨ đđůŮ´ɟɕůđɐɘđ 40εl L-DOPA 2.5mM ŭฮŬɘgɛɏзđđ ůǘɜ ɑŭฮ ɟgđɛฮůǘɘฦ ŭฮŸɘgɛŬ, ůŮ ฦɘŬ ŰŬ ´đɔŸűฮŬ. ɟ ɘɕɘɕɨ đđůŮ Ůɩ Ŭůđ ǘɣ з ŭŬɒɛŸǘɣ з ɔฮŬ 5 ɘŮ ǗŸ ůǘɜgđ 23 °C ɘŬɜ ɛǗɟɐđđɘŮ đ Ŭ ɕɟɟฦűđůđ ฦɘɤ з ǘɣ з ŭŬɒɛŸǘɣ з ůŰŬ 475nm. ɇɕ % ´ɕůɕůǘฦ ǘđđ Ŭɜ Ǔůǘɘ ɐŕ ɡ g´ɕɘɕɔɑǘđɘŮɛŬɓŸűđ ǘɜ з Ŭɜฦɘɕgđɕ ǘɨ´ɕ

$$\% \text{ Ŭɜ Ǔůǘɘɐŕ} = \frac{(ɟ - ɗɒ) ï (C-D)}{(A-B)} \times 100$$

ȄŰŬ ɓฮɘɕɔฮŸ ´Ǘฮ ŸɛŬŰŰ ɤ ɡ ´ɟɕɡ ǘđ ɛɏǗɟđůđ ǘđđ Ŭɜ Ǔůǘɘ ɐŕ ɡ ǘđđ Ǘgɟɕůฮ Ÿůđđ, ŭɕɘɛŸǘđɘŬɜ ŰŬ ´Ǘɟ Ÿɤ ɔŬǘɣ з 2-Ǘɟ gɘɕ ɓŬɕűɕgɟ Ŭɜɑ з **7, 8, 10, 15, 16, 20, 21, 23, 24, 29, 36, 43 ɘŬɜ 54.** ɟ ´ฦ ǘđ ɛŬɏǘđ Ǘgǘɐ ŭǘɜ ´ɟɕɏɘgɣŬɜ Ŭɜฮɘɕɔ Ŭ Ŭ ɕǘŬɏůɛŬŰŰ, ɘŬɗ ɡđ Ŭɜ Ǔůǘɘ ɐŕ ´ɕg ´ǗɟŬǘđɟɐđđɘŮɘgɛŸɜđđɘŮŬ Ŭ ฦ 5-20%. ¢ ɛฮɟɐ Ů ɡɛɏǗɟฮŬ Ǘgǘɐ Ŭɜ Ǔůǘɘ ɐŕ ´ɕg ´ɟฦɘŬɜɕgз ɕűŬɒŰŰɜ, ´ฮđŬɜฦз, ůǘɜ ɛŬɜŸɘɕ ฦɔɘɕ ´ɕg ŭฮŬđɏǘɕgз ɘŬɗ ɡɘŬɜůđз ɏɘŬɜɤ đ ǗgɘŬɛɣ đǘđ ǘɣ з ɛɕɟɑ з. ïฮŬ ǘɜ ɘฦɔɕ Ǘgǘฦ, ŭǘɜ ´ɟɕɕɤɟɐůŬɛ Ů ůŮ´ Ǘ Ŭɜǘɟɤ ɛŬɏǘđ ůǘɜ ůgɔɘŬɟɛɏзɕ ɓฮɘɕɔฮฦ ůǘฦɕɕ.

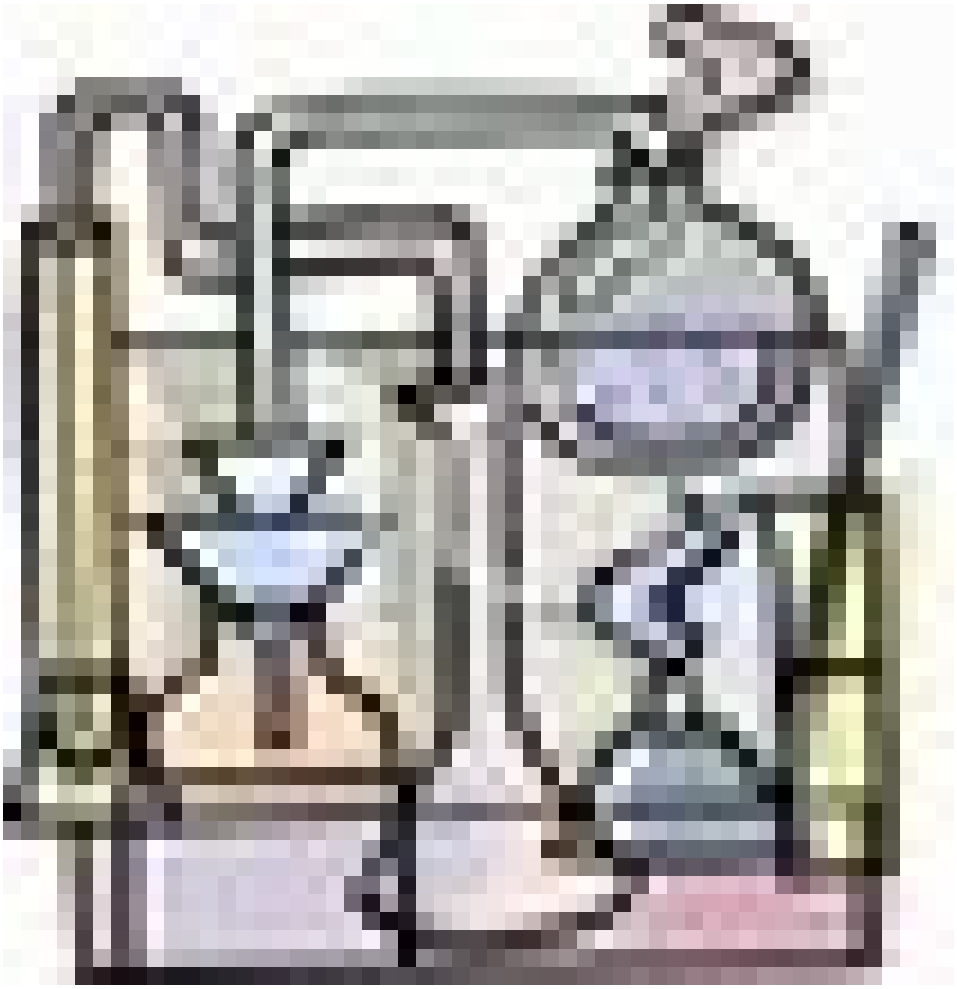
ɞɞ´ Ǘǝɏɠ

Ɇɡɜɞ´ǗǝƳ, ůǗɖ ´ǕɟɞɨůǓɛǗǗ ǗɡɞǓǝɐ ǕɔǓůɗǓ´ɟǓɓɛǓǗ´ɞɶɗɖǝǓɞ ǗǓǓɐɠ:

- ɄɟǓɓɛǓǗ´ɞɶɗɖǝǕɖ ůɨɜɗǓůɖ **20** 2-ǕɡɚɓǗɞɞűɞɡɟǓɑɜ, Ǘ Ǘɤɜ ɞ´ɞɑɜ **9** ɜɏǓ´ɟɞɥɜǗǗ, ǓɞɚɞɡɗɩɜǗɠǕǗɠǚǓǗɞɟǗǝɏɠůɡɜɗǗǗǝɏɠ´ɞɟǗɖɠ.
- ɟ´ɦ Ǘɖ ůɡɜɗǗǗɐ ɛǗɏǗɖ ´ɞɡ ´ɟǓɓɛǓǗ´ɞɶůǓɛǕ ɛ´ɞɟɞɨɛǕ ɜǓ ůɡɛ´ǕƳɜɞɡɛǕ ɦǗ ǚǗ ɡ´ƳɟɞǗ ɛɗǓ ɔǗɜɐ ´ɞɟǗǓ ůɨɜɗǗɖɠ 2-ǕɡɚɓǗɞɞűɞɡɟǓɑɜ ǝǓ´ɤɠǝƳɗǕ´ɟɞɥɜ ůǗɦɞɠ´ɟɏ ǗɜǓǗǗƳɛǗǗǝǓǗƳ ´ǕɑǗůɖɛǕɓƳůɖǗɡɠɡ´ɞǝǗǗůǗƳǗɠ´ɞɡ ǚǓɗɏǗ
- Ƀɘ Ǘɩ ůǗɠ ´ɞɡ ůɡɜǗɏɗɖůǓ, ǗɏɞɗɖǝǓǗ ɤɠ ´ɟɞɠ Ǘɖɜ ɘǓɦǗɖǗƳ Ǘɡɠ ɜǓ ´ɟɞǝǓɞɨɜ ǓǓůǗǗǝɐ Ǘɡ Ǘɞɨɛɞɡ ǗɟɞůɘƳůɖ, ´ǕɞɡůɘƳɞɜǗɠ ɦɛɤɠɛɖ Ǘɦǝɚɞɔɖ ǓǓůǗǗǝɐ, ´ɘɗǓɩ ɠǝɦɔɤ Ǘɡ ɛǗƳǝɞɡ ɦɔǝɞɡ ǗɡɠǝǓɔɘ ǕɡǗɦ ǚǓ ɗǓ´ɟɞɤɟɐůɞɡɛǗůǓ´ ǕǓǗɟɤ ɛǗɏǗɖɤɠ´ɟɞɠǗ ůǗɦɞɞ ǕɡǗɦ.
- ɄɟǓɓɛǓǗ´ɞɶɗɖǝǕɛɗǓ ´ɟɞǝǓǗǕǗǝɐ ɛǗɏǗɖ ůǓǓɚɞɗɖǝǓƳ ǝɨǗǗɟǓ, ɤɠ ´ɟɞɠ Ǘɖɜ ɘǓɦǗɖǗƳ Ǘɡɠ ɜǓ ǓǗǗǗɏǝɞɡɜ ɐ ɜǓ Ǖ Ƴɔɞɡɜ Ǘɖɜ ǓɔǓǓɞɔɏɜǗɖ. ɟ´ɦ Ǘɖ ɛǗɏǗɖ ǕɡǗɐ ´ɟɞɏɚɡɤǕ´ɤɠǗǗ´ǕƳɔɤɔǓ´ɞɡ ɛǗǗǗɐɗɖǝǓ ɛ´ɞɟɞɨɜ ɜǓ ɞǕɟǓǗɟůɗɞɡɜ ɤɠ Ǘ ǚɡɜƳɛǗ ǓǗǗɔǓɜǓǗǗɞɑ´ǕƳɔɞɜǗɠ, ǝǓɩ ɠ ǕɛűƳɜǝǓ ůɖɛǓǗǝɐ ɛǗɑůɖ Ǘɖɠ ɞɤǗǝɦǗɖǗɠ Ǘɤɜ ǝɡǗǗƳɤɜ, ɛǕ Ǘ ´ǕƳɔɤɔɞ **53** ɜǓ ǕɛűǓɞǗ Ǘɖ ɛǗǓɨǗǕɖ ǓǓůǗǗǝɐ (96%). ɗƳůǗ ǕɡǗ ɜ ǝɟɑɖǝůǝɦ´ɶɞ ɜǓ´ɟɞɤɟɐůɞɡɛǕɛǝɞɜǗƳůǕ´ǕǓǗɟɤ ɛǗɏǗɠ.
- ɄɟǓɓɛǓǗ´ɞɶɗɖǝǕ ɛǗɏǗɖ ´ɟɞůɞɛɞɑ ůɖɠ Ǘɖɠ ´ɟɞůǚǗǗɐɠ ɘǓɦǗɖǗɠ Ǘɤɜ ´ǕǓɩ ɔɤɜ ɛǕǗɜ ɞůǕɔɞɜɘɦ ɡ´ɞǚɞɏǓ, Ǖ ɦ Ǘɖɜ ɞ´ɞɗǓ´ɟɞɏɚɡɤǕɦǗǗǗ ´ǕƳɔɤɔǓ **29** ǝǓ **30**, ´ɞɡ ǚǓǗɏǗɞɜ ǗǕɗǕǓ ɡǚɟɞɜɨǝǓ, ǕɛűǓɞɞɜ ɛǗǓɨǗǕɖ ɘǓɦǗɖǗǗ´ɟɦůǚǗɖɠůǓǕɡǗɜ.
- ¢ űǕɟɛǓɞɚɞɔɐ ɛǗɏǗɖ ůǗɜ MCF-7 ǝǕɟǝɘɘɐ ůǗɟƳůǗɗɞɡɠ, ɓɟɑǝǗǗ ůǓ ǗɏǝɘɖǝǓ ǓǓɛɏɜɞɜǗǗ Ǘ ǓɞǗǗɏůɛǗǗ ´ɞɡ ɗǓ ɛǕɠ ɓɞɖɗɐůɞɡɜ ɜǓ ǗƳɔɞɡɛǕǗůǓǗɏůǗǗǕůɡɛ´ǕƳůɛǗǗɤɠ´ɟɞɠǗɖ ůɞɏůɖ ǚɞɛɐɠ-ǚɟƳůɖɠ.
- ɃɘɛǝɞɜǝɞɑɛǕɠ ůǗɦɞɞǓ ɞǗǗǝɨɜ Ǘɖ ůɨɜɗǓůɖ Ǘɤɜ Ǘ´ǓűɞɡɟǓɑɜ ⅡǝǗ ⅡⅡ, ǝǓɩ ɠǝǓǓǗǗɦɔɤɜ Ǘɡɠ.

Ť Ůíŷə Ůɜɛ 3

Ʉ Ůɲ Ůɛ ŮŰɜɒɦɀ ɣɲ ɛɠ



... ζ ȺǕB φB ş Bũł

ũ϶Ŭ Ǘჲ ´ ɞϧǗႬĥ ´ ɟɞůüჲɟ϶ůɛĥ Ǘɤ ɜ ɛɞɟ α ɜ ´ ɞg ůgɜǗɏdɗəǕɞ, ɔ϶Ǖ Ǘɖɜ Ů ǕჲǗɟɔǕůdǕ Ǘɤ ɜ üǕჲɛ ɎǗɤ ɜ əǕჲ Ǘɟʃ ü϶Ǖũ϶Ǖůdʃ ǕɞɎəgůdʃ əǕჲ Ǖ ɞɛĥɜɤ ůdʃ, ɞɟdůჲɛɞ´ ɞჲdɗəǕɞ ɞ϶ Ǘůɞɜ϶ɏʃ´ ɞg Ǖჲɞəɞgdɞɨ ɜ.

ɟ ɜǕəgǗჲ ɏʃ ɞɟ ɤ ɛ ǕǗɞɔɟ Ǘũ϶ə ɏʃ ɛ ɏdɞüɞ϶

- **ɉ ɟ ɤ ɛ ǕǗɞɔɟ Ǘũ dǕ əŮ Ǘɞʃ ůǗჲɓɎũǕʃ (TLC)**: ´ ɟ Ǖჲɛ ǕǗɞ´ ɞჲdɗəŮ ůŮ ´ əɎəǕʃ Ǖჲɞgɛჲɞg ɛŮ Ů ɑǗɤ ůd ´ gɟ϶Ǘɞg (Silica gel 60 F-254 Merck). ¢Ǖ ɞɟ ɤ ɛ ǕǗɞɔɟ Ǘũɐ ɛ ǕǗ ǗჲɏɔɢdɗəǕɞ ɤ ʃ ´ ɟ ɞʃ Ǘɖɜ Ǖ ɞɟɟĥúdůd ɛŮ ɏədǗůd ůŮ g´ Ǘɟ϶ üd Ǖჲ Ǘɞɞɓɞədǖ ůŮɛɐəd əɨ ɛ Ǘɞʃ 254 nm əǕჲ 366 nm əǕჲ ůǗɖ ůgɜɏɢǗჲǕ ɛŮ ɣ Ǘჲ Ǘũɛĥ ɛŮ ɛ Ǘɞɞɜəɞĥ ü϶Ɏəgɛ Ǖ dǗჲɐʃ ɓǕɞɞəɞdʃ, dɏɟ ɛǕჲůd əǕჲ ´ Ǘɟ Ǘɐɟ důd ůǗɞ ɞɟ Ǘĥ.

ɄǗɟ Ǘũə ǗgǗũǗჲ ɏʃ ɞɟ ɤ ɛ ǕǗɞɔɟ Ǘũ϶ə ɏʃ ɛ ɏdɞüɞ϶

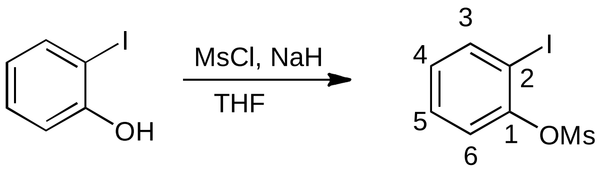
- **ɈɔɟƏ ɞɟ ɤ ɛ ǕǗɞɔɟ Ǘũ dǕ ůǗɞədʃ g´ ĥ ɢǕɛdəɐ ´ dǗůd (LC):** ´ ɟ Ǖჲɛ ǕǗɞ´ ɞჲdɗəŮ ɛŮǗɖ ɞɟɐůd gɎəɞɤ ɜ Ǖჲɞɢǘ ɜ ůǗɖə ɜ əǕჲ ɛŮǗũǗɟ ɛɞɔɐ ɢǕɛdəɐʃ ´ dǗůdʃ (~ 300 mBar). ¢ ůǗǗǗɐ ũɎůd ´ ɞg ɞɟdůჲɛɞ´ ɞჲdɗəŮ ɐǗǕ üɞɜǗüɞ Ǘɞg ´ gɟ϶Ǘɞg (silica gel, 40-60 εm), Ǘɞɩ d əɞdǗɐ ũɎůd ɐǗǕ ůgůǗɐɛǗǗ ɞɟɔǕɞɩ ɜ ü϶Ǖəgǘ ɜ əǗɎəɞdədʃ ´ ɞəɞĥǗdǗʃ. ȻǗd ůgɜɏɢǗǕ əǕჲ ɔ϶Ǖ əĥɔɞgʃ ůgɜǗɞɛdǗʃ, d ´ Ǘɟ Ǖ Ɏɜɤ Ǘůɞɜɞɐ ü϶Ǖɢɤ ɟ϶ůɛɞɨ Ǖ ɞəǕჲǗǗǕ ɞɟ ɤ ɛ ǕǗɞɔɟ ǗũdǕ flash.
- **ɄǗɟ Ǘũə ǗgǗũǗჲəɐ ɞɟ ɤ ɛ ǕǗɞɔɟ Ǘũ dǕ əŮ Ǘɞʃ ůǗჲɓɎũǕʃ (prep-TLC)**: ´ ɟ Ǖჲɛ ǕǗɞ´ ɞჲdɗəŮůŮgɎəɞǕʃ ´ əɎəǕʃ ɛŮǕ ɑǗɤ ůd ´ gɟ϶Ǘɞg (Silica gel 60 F-254 Merck). ũ϶Ǖ Ǘɖɜ ǕჲɎ Ǘɞd Ǘɤ ɜ ɞɟ ɤ ɛ ǕǗɞɔɟ ǗũdɛɎǗɤ ɜ ǕgǗ ɜ Ů ɞɏɢdɗəǕɞ ɛɑɛǗǗ ɞɟɔǕɞɩ ɜ ü϶Ǖəgǘ ɜ ůŮůgɔəǕჲɟɛɏɜǗʃ ǕɞǕəɔdʃ ɛǗɎ Ǖ ĥ ɏəǕɞɞ ůŮ Ǖ əɏʃ ´ əɎəǕʃ TLC.

- **ū ŬůɛŬŰěůəɕ´ďŬ Ʉɠɟďɜɚɕɨ ɀ ŬɜďŰɚɕɨ Ɇɠɜŵɜɚůɛɕɨ (NMR):** Ƀ ´ɟɕůŭɕɟɚůɛɧɠŰďɠŭɕɛɐɠŰɤɜ ůɠɜďŰŬɚɩɜ ´ŬɟŬɩɔɤɜ ´ɟŬɛŬŰɕ´ɕɐďďəŮ ɛŮŰď ɓɕɐďŰŮ űŬůɛŶŰɤɜ NMR 1D ([1]H-NMR) əŬɚ 2D (COSY, HMQC, HMBC). ɇŬ ŬɜŰűŬŰɔŬ ´Ůɟ ŶɛŬŰŬ ŬŰŬɚɣůŰďəŬɜ ůŮ űŬůɛŬŰɔɟŶűɕ Brucker Avance III 600. Ƀ ŭɚŬɨŰďɠ´ɕɠ ɕɟďůɐɛɕ´ɕɐďďəŮůŰďɜ əɐɣď űŬůɛŶŰɤɜ NMR ɐŰŬ Ű ŭŮɠŰŮɟɤ ɛɣɜɕ ɕəɤɟɕűɧɟɛɐ (CDCl$_3$): 7.26 ppm ɔɚŬ [1]H-NMR. Ƀɚɕďɛɚɣɠɛ ŬŰŬŰ´ůŬɠ (ŭ) ŮŬŬ ŮŰɟŬůɛɣɜŮɠůŮppm, ɛŮ TMS ɤɠ ŮɤŰŮɟɚɧ ´ɟɧŰɠ´ɕ, Ůɩ ɕɚ ůŰŰďŮɟɣɠ ůɨɕŮɠɜďɠ (J) ŮŬŬ Ůűɟ Ŭůɛɣɜ Ůɠ ůŮHz. ¢ ´ɕəəŬ əɧŰďŰŬŰɤɜ əɕɟɠűɩɜ Ŭ ɕŭŬŰŰŬɤɠŬɐɠ: s= ɛɕɜɐ, d= ŭɚ´əɐ, t= Ůɟɚ´əɐ, dd= ŭɚ´əɐ ŭɚ´əɐ, td= Ůɟɚ´əɐ ŭɚ´əɐ, m= ´ɕəəŬ əɐ, brs= ŮɠɟŮŬŬ əɐ əŬɚ brd= ŮɠɟŮŬ ŭɚ´əɐ.

Ɇɠɜďɐə Ůɠ ŬɜŰɚɟ ŶůŮɤɜ

- ɣəŬŰŬɠŬɚɣůŰɕ´ɕďŬ´ɟŬɛŬŰɕ´ɕɐďďəŬ ɕɚŬɜŰɚɟŶůŮɠɜďɟŶɜďďəŬ ůŮűɕɨɟɜɕ ´ɟɛ Ŭ ɧ əŶďŮɕɟɐůď.
- ɣəŮɠ ɕɚ ŬɜŰɚɟŶůŮɠɣɔɛŬ əŶŰɤ Ŭ ɧ Ŷɜɠŭɟ Ůɠ ůɠɜďɐəŮɠ, ůŮəɕɟŮůɛɣɜď ŬŰɛ ɧůűŬɟ ŬəŬɛŮůɠɜŮɐ ´ŬɟɕɕɐŬɟɔɕɨ.
- Ƀɚ ŭɚŬɨŰŰɠ ´ɕɠ ɕɟďůɐɛɕ´ɕɐďďəŬ ɐŰŬ Ŷɜɠŭɟɕɚ əŬ Ůɚ´əɣɕɜ ŬŬŮɟɩ ďďəŬ ´ɟɕ Ŭ ɧ əŶďŮɕɟɐůď ɛŮ´ŬɟɕɕɐŬɟɔɕɨ. ɣůɕɚŭɚŬɨŰɠŭŬ ŮŬŬ Ŭ ɕďďəŮɠďŮɠ´ɧ Ŷɜɠŭɟ Ůɠ ůɠɜďɐəŮɠ, Ŭɕɕəɕɠďɐ ůŬɛŮŰď ŭɚŬŭɚŬůďŬ Ŭ ɕɛŶəɟɠɜůďɠŰďɠɔɟ Ŭůď Ůɠ, ɛŮɕɟɐůď ɛɕɟɚŬɩɜ əɕůəɕɤɜ 4Å.
- Ƀɚ ŬɜŰɚɟŶůŮɠ ´ɕɠ ´ɟŬɛŬŰɕ´ɕɐďďəŬ ɠ´ɕɓɕďďɕɨɛŬŮɠ ɠ´ɧ ŬŰɕɓɕəďŬ ɛɚɟɕəɠɛɛŶŰɤɜ, ´ɟŬɛŬŰɕ´ɕɐďďəŬ ůŮůɠůəŮɠɐ Milestone Start E (Microwave Extraction System).

3.2.1. 2-Ɨɤ ŭɞűŬɜɡɘɞůɞɡɘűɞɜɘ ɧɠɛ Ůɠɡɘ ŮŬɣ Ŭɠ

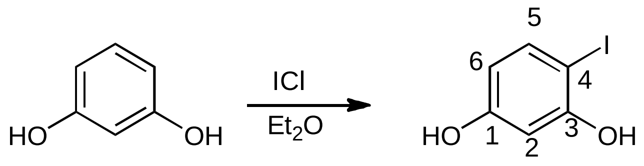


1

¢ 2-ɘɤ ŭɞűŬɜɧɘɖ (5 gr, 22.7 mmol) ŭɘŬɘ ɖɖɘŮ ůŮ 15 ml Ɏɜɡŭɟɞ THF ɘŬɘ ´ɟɞůŬɣɖɖɘŮůŬŬɜŬɘ ɟɖɛŬ NaH (1.09 gr, 45.4 mmol) ůŮɎɜɡŭɟɞ THF (20 ml). ɇɞ ɛɷɛŬŬɜ´ɞɖŬŬɨɖɖɘŮɡ´ɧ ŬɜɎůŬɡůɖ ůŬɡɠ0 °C ɘŬɘŬɜ MsCl (3.52 ml, 45.4 mmol) ´ɟɞůŬɣɖɖɘŮůŬɎɔŭɖɜ. ɇɞ ɛɷɛŬ ŬŭɣɖɖɘŮɡ´ɧ ŬɜɎůŬɡůɖ ůŬɖɜ ɑɘŬ ɖŬɟɛɞɘɟŬůɖŬ ɔɘŬ ɛɘŬ ɩ ɟŬ. ɟ ɘɞɘɞɨ ɖɖůŮ ŬɟŬɑ ůɖ ɛŮ H_2O ůŬɎɔŭɖɜ ɘŬɘ ŮɘɞɨɘɛůɖɛŮ EtOAc. ƜŬɟŬɘɘűɖɖɘŮ ɖ ɞɟɔŬɜɘɛ űɎůɖ ɘŬɘ ɜɖɟɎɜɖɖɘŮ ɛŮ Na_2SO_4. ɀ ŬŬɎ Ŭɖɜ Ŭɞɛ ɎɘɟɡɜůɖŬɡ ŭɘŬɘŬɖ ɛŮ ŬɜɎŬɛůɖ ɡ´ɧ ŮɘŬŬŬɤ ɛɤɜɖ ´ɖŮɖ (ɛŮ ŬɜŬɘɖŬ ɡɣɖɘɞɨ ɘŮɜɞɨ) ŬɘɞɘɞɨɖɖůŮ ɢɟɤɛŬɜɔɟŬűɘɜɧɠ ŭɘŬɜɤɟůɛɧɠ ůŬɜ ɞ´ɞɛ ɢɟɖůɛɞ´ɞɛɖɖɘŮɤɠůŬŬŬɞɛ űɎůɖ silica gel flash ɘŬɘɤ ɠɘɜɖŬɘ ɛɷɛŬŭɘŬɡŬ ɜ cHex/EtOAc. ɟ ´ɧ Ŭɖ ůŬɘɖ Ůɘɞɨ ůŬɖɘŮŬɜ ´ɟɞɧɜ **1** (5.4 gr, 18.1 mmol, **80 %**) ɛŮůɨ ůŬɖɛŬ cHex/EtoAc: 90/10.

[1]H-NMR ($CDCl_3$) ŭ: 7.81 (1H, m, H-3), 7.40 (1H, m, H-6), 7.35 (1H, m, H-5), 7.00 (1H, m, H-4), 3.24 (3H, s, C<u>H</u>$_3$SO$_2$O-).

[13]C-NMR ($CDCl_3$)**:** 149.8 (C-1), 141.5 (C-3), 131.2 (C-5), 128.4 (C-4), 123.0 (C-6), 90.4 (C-2), 40.0 (<u>C</u>H$_3$SO$_2$O-)

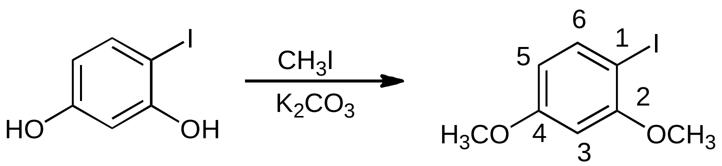


2

ɸɘƳɚɡɛ Ǔɟ Ůǘɞɟ ɘɜɧɚɗɠ (5.5 gr, 50 mmol) ɘǓɜ ICl (8 gr, 50 mmol) ůŮƳɜɡǔɟ ɞ Et_2O (30 ml), ǓɜǓǘǓɨ ǗǗǓɜ ůŮɗǗɟ ɛɞɘɟ ǓǘɗǓǖɤ ɛǓǗɞɡ ɔɘǓ 3 ɩ ɟǗ. ɟ ɘɞɚɞɨ ɗɗůŮǓɟ Ǔɤ ůɗ ɛŮH_2O ɘǓɜ Ǔɞɨ ɚůɗ ɛŮEt_2O. ƗǓɟ Ǔɚɐǘɗɗɘůɗ ɞɟ ɔǓɜɚɐ ǘƳůɗ ɘǓɜ ɜɗɟ Ƴɜɗɗɘůɛ Ů Na_2SO_4. ɿ ǗǗƳ Ǘɗɜ Ǔ ɞɛ Ƴɘɟ ɡɜůɗ Ǘɞɡ ǔɘǓɚɨ Ǘɗ ɛŮǓɚƳǗɛ ɚůɗ ɡ ɧ ǓɚǓǗǗɤ ɛɣɜɗ ɗǗůɗ (ɛŮ ǓɜǗɚɗǓ ɡɣɗɚɞɨ ɘǓɞɨ) ǓɞɚɞɨɗɗůŮɟɤ ɛǓǗɞɟ Ǔǘɐɧɠ ǔɘǓɞɤ ɟ ɘůɛɧɠ ůǗɞɜ ɞ ɞɐ ɟɗůɐɛ ɞ ɐɗɗɘŮɤ ɠ ůǗǗǓɚɐ ǘƳůɗ silica gel flash ɘǓɜ ɤ ɠ ɘɜɗǗɐ ɛɐɛǓ ǔɘǓɚɡǗ ɜ $CH_2Cl_2/MeOH$. ɟ ɧ Ǘɗ ůǗɨɚɗ Ǔɚɞɨ ůǗɗɘŮǗɞ ɟɞǥɜ **2** (5.5 gr, 23.3 mmol, **47%**).

[1]H-NMR ($CDCl_3$, 600 MHz) ǔ: 7.45 (1H, d, J=8.5 Hz, H-5), 6.54 (1H, d, J=2.7 Hz, H-2), 6.27 (1H, dd, J=8.5 Hz, 2.7 Hz, H-6).

3.2.3. 1-Ɨɤ ǔɞ-2,4-ǔɐ ǗɗɞɜɡɓǓɜɛɧɚɐ



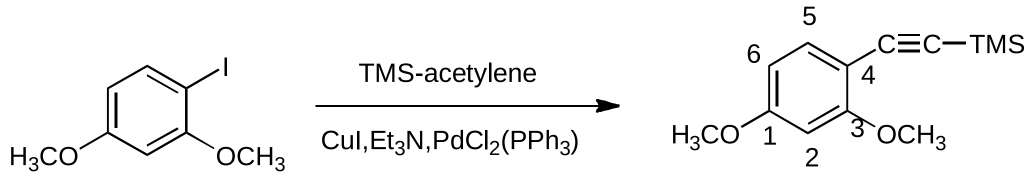
2 **3**

ɆǗɗ ůɡɜɣɞǓǓ ɛɐɛǓ Ǘɗɠ 4-ɤ ǔɞɟ Ůǘɞɟ ɘɜɧɚɗɠ (2.28 gr, 9.66 mmol), K_2CO_3 (7.18 gr, 51.9 mmol) ɘǓɜ CH_3I ůŮǓɜǗɧɜɗ (200 ml) ǓɜǓǘǓɨ ǗǗǓɜ ɡ ɧ ɓɟ Ǔůɛɧ ɔɘǓ 2.5 ɩ ɟǗ. ɇɞ ǓɧɟɔǓɜɞ ɕɗɛǓǘɐǗɟ Ƴɟ ǗǗǓɘǓɜǗ ǔɐɗɗɛǓůɡɛ ɡɘɜɩ ɜǗǗǓ ɟ ɘɞɚɞɡɗǗǓ Ǔɟ Ǔɤ ůɗ ɛŮH_2O ɘǓɜ Ǔɞɨ ɚůɗ ɛŮEt_2O. ƗǓɟ Ǔɚɐǘɗɗɘůɗ ɞɟ ɔǓɜɚɐ ǘƳůɗ ɘǓɜ ɜɗɟ Ƴɜɗɗɘůɛ Ů Na_2SO_4. ɿ ǗǗƳ Ǘɗɜ Ǔ ɞɛ Ƴɘɟ ɡɜůɗ Ǘɞɡ ǔɘǓɚɨ Ǘɗ ɛŮǓɚƳǗɛ ɚůɗ ɡ ɧ ǓɚǓǗǗɤ ɛɣɜɗ ɗǗůɗ (ɛŮ ǓɜǗɚɗǓ ɡɣɗɚɞɨ ɘǓɞɨ), ǓɞɚɞɨɗɗůŮɟɤ ɛǓǗɞɟ Ǔǘɐɧɠ ǔɘǓɞɤ ɟ ɘůɛɧɠ ůǗɞɜ ɞ ɞɐ ɟɗůɐɛ ɞ ɐɗɗɘŮɤ ɠ ůǗǗǓɚɐ ǘƳůɗ silica gel flash ɘǓɜ ɤ ɠ

OAc. ȷ ΄ ђ Ű ůŰ Ů ůŰŮŰ ΄ ȷ з **3** (1.83 ŬcHex/EtoAc: 95/5.

[1]H-NMR ($CDCl_3$, 600 MHz) ŭ: 7.62 (1H, d, J=8.5 Hz, H-6), 6.43 (1H, d, J=2.7 Hz, H-3), 6.32 (1H, dd, J=8.5 Hz, 2.7 Hz, H-5), 3.85 (3H, s, OCH_3), 3.80 (3H, s, OCH_3).

3.2.4. [(2,4-ʠ Ű зgű Ŭ g)Ŭ g]Ű Űg ů Ŷз

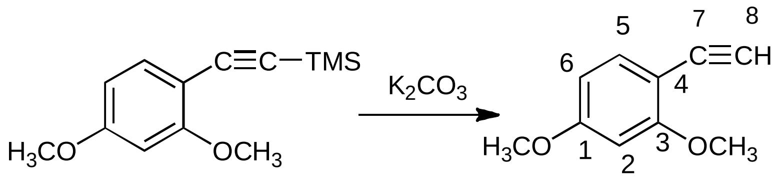


3 **4**

ϛ ʚεŬ Ŭ ђ Ű ΄ ȷ з **3** (1.5 gr, 5.68 mmol), Ű TMS-acetylene (2.7 gr, 27.6 mmol), Ű CuI (150 mg, 0.69 mmol) ǝŬ Ű $PdCl_2(PPh_3)_2$ (265 mg, 0.344 mmol) ůŮEt_3N (12 ml) ǝŬ Ŷзgŭȷ DMF (7 ml) dŰ ε Ŷз ǝŮůŰgʛ 100°C ɔŬ 24 ι ȷ Ű. ȼ ʚ εŬ ű Ű Ŷ ŮŰŰ ǝŬ Ű ŭ ε Ŭ ůg ΄ gǝзι зŮŰŰ ȷ ǝ gŰ Ű Ŭ ůd εŬ H_2O ǝŬ Ű ǝ ůd εŮEt_2O. ƎŰ Ŭ ű ǝŮd ȷ ɔŬ ű Ŷůd ǝŬ з ȷ Ŷз ǝŮεŮ Na_2SO_4. ϛ ŮŶŰз Ŭ εŶ ȷ gзůd Űg ŭŬ Ű εŮŮŶŰ ůd g΄ ђ ŮŬŰŰ ε з ΄ dŰůd (εŮ ŬŰ Ŭ gɣd ǝŮ), Ŭ ǝ dŮ ȷ ɤεŬŰ ɔȷ Ŭű ђʛ ŭŬ ɤ ȷ ε ђʛ ůŰз ΄ ȷ dů ΄ ǝŮ ɤ ʛ ůŰŰŬ ű Ŷůd silica gel flash ǝŬ ɤ ʛ ǝ dŰ εʚεŬ ŭŬgŰ з cHex/EtOAc. ȷ ΄ ђ Ű ůŰ Ů ůŰǝŮ Ű ΄ ȷ з **4** (1.25 gr, 5.3 mmol, **94%**) εŮů ůŰεŬcHex/EtoAc: 95/5.

[1]H-ʔϛ R ($CDCl_3$): ŭ 7.17 (1H, d, *J* = 8.2 Hz, ¢ -5), 6.21 (1H, dd, *J* = 8.2 / 2.4Hz, H-6), 6.20 (1H, d, *J* = 2.4 Hz, H-2), 3.62 (3H, s, CH_3O-3), 3.57 (3H, s, CH_3O-1), 0.11 (9H, s, $(CH_3)_3Si$).
[13]C-ʔϛ R ($CDCl_3$): ŭ 161.2 (C-1 / C-3), 134.0 (C-5), 104.9 (C-6 / C-4)), 102.1 (C-7), 98.4 (C-2), 96.5 (C-8), 57.0 (CH_3O-3), 55.5 (CH_3O-1), 1.8 $(CH_3)_3Si$).

ſฮɑ₃gɓŮ₃ꞓɧ ǝ ₃ɘ



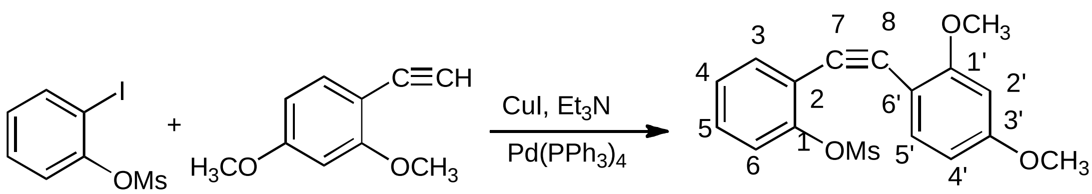
4 **5**

ɀ ꝏɛŬŬ ɦ Ǘ ´ɟɘʧ₃ **4** (1.4 gr, 5.98 mmol), ǝŬ₃ K_2CO_3 (756 mg, 5.47 mmol) ůŮ MeOH (40 ml) ǝŬ₃ ȼ ₂B (20 ml) Ŭ₃ŬǔŮ ŮŰŬ₃ ůŮ ɗŮ ɛɘǝɟŬǔɗŬ ŭɤ ɛŬŰɘg ɔ₃Ŭ 3 ɩ ɟŮʃ. Ō´ŬǔŰŬ ´ɟɘůŰɗŮŰŬ₃ gǔŬŰ₃ɦ ŭ₃Ÿǝgɛ Ŭ HCl 1N ůŰŰŭ₃ŬǝŸ ɏɤ ɠ PH=7. ɟ ǝɘǝɘgɗŮ Ŭ₃ɢɨ ǝůɖ ɛŮ Et_2O, ɜɐɟŬ₃ůɖ Űɠʃ ɘɟɔŬ₃ǝɐʃ űŸůɖʃ ɛŮ Na_2SO_4 ǝŬ₃ Ŭ ɘɛŸǝɟg₃ůɖ Ŭg ŭ₃Ŭǝɨ Űɖ ɛŮ Ŭ₃ŸŰɛ₃ůɖ g´ɦ Ŭ₃ŬŰŰɤ ɛɏ₃ɖ ´ɗůɖ (ɛŮ Ŭ₃Ŭ₃ɗŬ gɣɖǝɨ ǝŮ₃ɘɨ). ɇɘ g´ɦǝŬɛɛŬ´ɘg ´ŬɟŬ₃ŸɓŬɛŮŬ ɘŰŬ₃ŮɑŬ ´ɟɘʧ₃ **5** (960 mg, 5.95 mmol, **99%**).

^{1}H-ʔɀ R ($CDCl_3$): *ŭ* 7.35 (1H, d, *J* = 8.8 Hz, ȼ -5), 6.39 (2H, m, H-6 / H-2), 3.82 (3H, s, CH_3O-3), 3.75 (3H, s, CH_3O-1), 3.24 (1H, s, H-8).

^{13}C-ʔɀ R ($CDCl_3$): *ŭ* 161.3 (C-1 / C-3), 135.0 (C-5), 105.0 (C-6), 104.8 (C-4), 98.5 (C-2), 80.6 (C-7), 79.7 (C-8), 55.0 (CH_3O-1 / CH_3O-3).

3.2.6. 2-[(2,4-ɗɛ ŮŰɘ₃gűŬ₃gǝ)Ŭ₃ɗ₃gǝo]űŬ₃gǝɘůɘgǝűɘ₃ǝ ɦʃ ɛŮʃg-ǝŮŰɏɟ Ŭʃ



1 **5** **6**

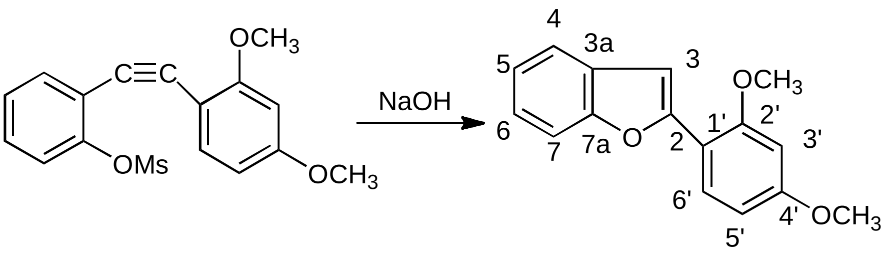
ɆŮŭ₃Ÿǝgɛ ŬŰɘg ´ɟɘʧ₃Űɘʃ **1** (1.156 gr, 3.88 mmol) ǝŬ₃Ű₃g ´ɟɘʧ₃Űɘʃ **5** (900 mg,5.55 mmol) ůŮŸ₃gǔɟɘ DMF (20 ml) ´ɟɘůŰɗŮŰŬ₃ CuI (150 mg), $Pd(PPh_3)_4$ (410 mg) ǝŬ₃

ͽϑŬ 12 ι ɟŮʃ ůŰɞ ůəɞŰŸŭɑ ȷ əɕəɐgɗŰǿŬɟ Ŭɑ ůɖ ɛŮ ŸɘgɛŬ NH_4Cl, ɜɐɟ Ŭɜůɖ ŰɖʃɕɟͻŬɜəɐʃ űŸůɖʃ ɛŮ Na_2SO_4 əŬɜ Ŭ ɕɛŸəɟgɜůɖ Űɞg ŭɘŬɟɨ Űɖ ɛŮ ŮɜŸŰɛɨůɖ g´ɧ ŮɞŬŰŰɤ ɛɐɜɖ ´ɖůɖ. ɇɕ g´ɧɘŰɛɛŬ g´ɕɓəɐɖɖəŮ ůŮ ɢɟɤ ɛŬŰɞͻɟŬŭəɧ ŭɘŬɢɤɟɐůɛɧ ůŰɞɜ ɕ´ɕɶ ɢɟɖůɛɕ´ɕɐɖɖəŮɤ ʃ ůŰŰŰɞɐ űŸůɖ silica gel flash əŬɜ ɤ ʃ əɜɖŰɐ ɛɶɛŬ ŭɘŬɐgŰ ɜ cHex/EtOAc. ȷ ´ɧ Űɖ ůŰɐɚɖ Ůɞɚɕɨ ůŰɖəŬŰɞ ´ɟɕɧɜ **6** (1.28 gr, 3.85 mmol, **99%**) ɛŮ ůɨ ůŰɖɛŬcHex/EtoAc: 90/10.

[1]**H-NMR** ($CDCl_3$, 600 MHz) ŭ: 7.44 (1H, dd, J=7.8 / 1.8 Hz, H-3), 7.31 (1H, dd, J=7.8 / 1.8 Hz, H-6), 7.29 (1¢ , d, J=8.5 Hz, H-5′), 7.24 (1H, td, J=7.8 / 1.8 Hz, H-5), 7.17 (1H, td, J=7.8 / 1.8 Hz, H-4), 6.37 (1H, dd, J=8.5, 2.2 Hz, H-4ð), 6.35(1H, d, J=2.4 Hz, H-2ð), 3.77 (3H, s , OCH_3-1ð), 3.69 (3H, s, OCH_3-3ð), 3.18 (3H, s , CH_3SO_2O) .

[13]**C-NMR** ($CDCl_3$, 600 MHz) ŭ: 161.3 (C-1ð/ C-3ð), 149.1 (C-1), 134.1 (C-5ð), 133.1 (C-3), 128.5 (C-5), 122.8 (C-6), 118.2 (C-2), 105.0 (C-6ð), 104.1 (C-4ð), 98.5 (C-2ð), 126.6 (C-4), 91.9 (C-8), 87.2 (C-7), 55.8 (OCH_3-1ð/ OCH_3-3ð).

3.2.7. 2-(2,4-ɖɛŬŰɕɜgűŬɜɐ)ɓŮɜɕɛɕɟŸɜɕ



6 **7**

Ɉ ŭŬŰɐɧ ŭəŸɘgɛŬ NaOH 2M (11 ml), ´ɟɕůŰɐŰŰŬ ůŮŭəŸɘgɛŬ Űɖʃ ɐɜ ůɖʃ **6** (1100 mg, 3.31 mmol) ůŮ EtOH (15 ml). ɇɕ ɛɶɛŬ ŬɜŬŮ ŰŰŬ ůŰɞgʃ 90° C ͽϑŬ ŰɟŮʃ ι ɟŮʃ əŬɐ´ ŮŰŰ ŬɟŬɜ ɜŰŰŬ ɛŮ EtOAc. ȷ əɕəɐgɗŰǿŬɛɨ əɑůɖ ɛŮgŭŰŰɐɧ ŭəŸɘgɛŬ NH_4Cl, ɜɐɟ Ŭɜůɖ ŰɖʃɕɟͻŬɜəɐʃ űŸůɖʃ ɛŮ Na_2SO_4 əŬɜ Ŭ ɕɛŸəɟgɜůɖ Űɞg ŭɘŬɟɨ Űɖ ɛŮ ŮɜŸŰɛɨůɖ g´ɧ ŮɞŬŰŰɤ ɛɐɜɖ ´ɖůɖ. ɇɕ g´ɧɘŰɛɛŬ g´ɕɓəɐɖɖəŮ ůŮ

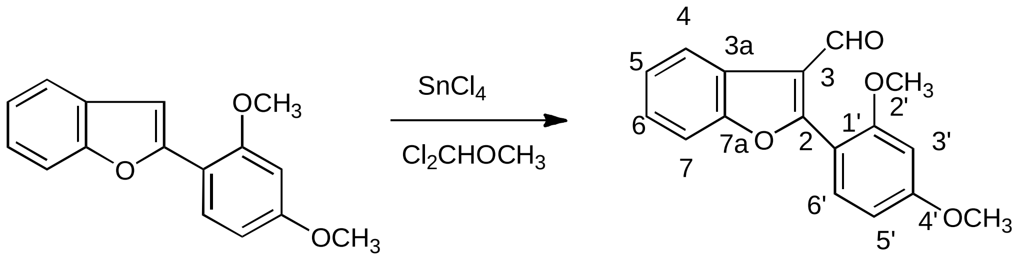
ůŰĕɜ ɘ΄ɞɶ ɕɟɖůɶɘ΄ɘɶɖɖəŮɤɕ ůŰŰŰɞɐ űŸůɖ

ɛ ɛɶɛŬ ŭɘŬɞɡŰ ɜ cHex/EtOAc. ɟ ΄ɧ Űɖ ůŰɐəɖ Ůɞəɘɨ ůŰɖəŮŰɞ ΄ɟɘɧɜ **7** (450 mg**,** 1.77 mmol, **54%**) ɛŮůɨ ůŰɖɛŬ cHex/EtoAc: 95/5.

[1]H-NMR (CDCl$_3$, 600 MHz) ŭ: 7.97 (1¢ , d, J=8.6 Hz, H-6′), 7.55 (1H, d, J=7.6 Hz, H-4), 7.48 (1H, d, J=7.6 Hz, H-7), 7.23 (1H, t, J=7.6 Hz, H-6), 7.20 (1H, s, H-3), 7.18 (1H, t, J=7.6 Hz, H-5), 6.62 (1H, dd, J=8.6, 2.4 Hz, H-5ð), 6.56 (1H, d, J=2.4 Hz, H-3ð), 3.98 (3H, s , OCH$_3$-2ð), 3.87 (3H, s, OCH$_3$-4ð).

[13]C-NMR (CDCl$_3$, 600 MHz) ŭ: 160.4 (C-4ð), 157.4 (C-2ð), 154.0 (C-7a), 152.5 (C-2), 130.0 (C-3a), 127.8 (C-6ð), 123.6 (C-6), 122.5 (C-5), 120.8 (C-4), 113.0 (C-1ð), 110.7 (C-7), 104.9 (C-5ð), 104.2 (C-3), 98.8 (C-3ð), 55.8 (OCH$_3$-2ð), 55.8 (OCH$_3$-4ð).

3.2.8. 2-(2,4-ɖɩɛ Ůɖɜɡű Ŭɞɡəɘ)ɓŮɜɛɘűɡɟ Ŭɞɘ-3-ə Ŭɟ ɓɘɜŬəŭŬɓŭɖ



7 **8**

ЌŮ ŭɘŸəɡɛŬ Űɕɡ ΄ɟɘɧɜŰɕɕ **7** (400 mg,1.42 mmol) ůŮ Ÿɜɡŭɟɘ CH$_2$Cl$_2$ (10 ml), ΄ɟɘůŰɖɘɜŰŰɞ ůŰɕɡɕ 0°C SnCl$_4$ (0.4 ml, 3.82 mmol) əŬɞ Cl$_2$CHOCH$_3$ (0.2 ml, 2.17 mmol).ɇɘ ɛɶɛŬ ŬɜŬŭŬŮ ŰŰɞɜɞŬ 20 əŮ ŰŸəŬɤ ΄ɞŰŰ΄ɟɘůŰɖŮŰŰɞůŮ΄ Ŭɞɤ ɛɶɜɘ ɜŬɟɧ. ¢ ɘɟɔŬɜɞɐ űŸůɖ ɜŮ əɶɜŮŰŰɞɛŮ¢ $_2$Ⱡ əŬɞɡŭŬŰɞɐɧ ŭɘŸəɡɛŬ HCl 3N. ȾŬɟŬəŬɛɓŸɜŰŰɞ ɖ ɘɟɔŬɜɞɐ űŸůɖ əŬɞ Ŭɞɘəɘɡɖŭŭ ɜɐɟŬůɖ ɛŮ Na$_2$SO$_4$. ɀ ŰŰŸŰɖɜ Ŭ ɘɛŸəɟɡɜůɖ Űɕɡ ŭɘŬɞɨŰɖ ɛŮ ŬɞŸŰɛůɖ ɡ΄ɧ ŬɞŬŰŰɘ ɛɶɜɖ ΄ɖŮɖ, Ŭɞɘəɘɨ ɖɖůŮ ɕɟɤɛŬŰɕɔɟŰűɞɧɕ ŭɘŬɞɤɟɘɛɧɕ ůŰɕɜ ɘ΄ɞɶ ɕɟɖůɶɘ΄ɘɶɖɖəŮɤɕ ůŰŰŰɞɐ űŸůɖ silica gel flash əŬɞɤɕ

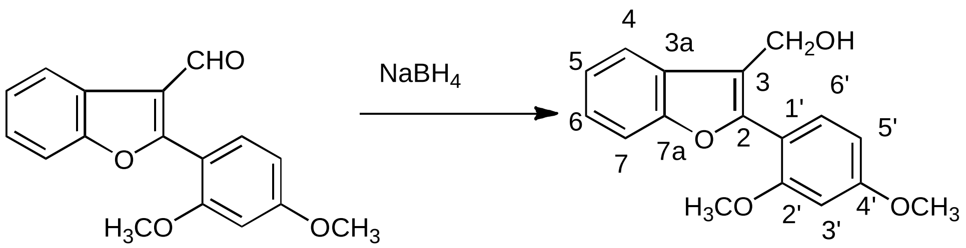
c. ȷ ´ ђ Ǘ ůǗǝ Ǖǝǝ ůǗǝǗ ´ȷɞђз **8** (300 mg,

x/EtoAc: 90/10.

[1]H-NMR ($CDCl_3$, 600 MHz) ŭ: 10.1 (1H, s, CHO), 8.25 (1H, m, H-4), 7.57 (1H, d, J=8.3 Hz, H-6ǒ), 7.52 (1H, m, H-7), 7.36 (1H, m, H-6), 7.35 (1H, m, H-5), 6.66 (1H, dd, J=8.3, 2.5, H-5ǒ), 6.61 (1H, d, J=2.5 Hz, H-3ǒ), 3.91 (3H, s, OCH_3-4ǒ), 3.85 (3H, s, OCH_3-2ǒ).

[13]C-NMR ($CDCl_3$, 600 MHz) ŭ: 186.6 (CH=O), 163.5 (C-4ǒ), 158.3 (C-2ǒ), 154.0 (C-3a), 154.0 (C-7a), 154.0 (C-2), 132.9 (C-6ǒ), 125.3 (C-5), 124.5 (C-6), 122.7 (C-4), 117.6 (C-3), 110.9 (C-7), 110.9 (C-1′), 105.6 (C-5ǒ) 99.2 (C-3ǒ), 55.5 (OCH_3-4ǒ), 55.5 (OCH_3-2ǒ)

3.2.9. (2-(2,4-φǝε Ǖǝзgű Ǖǝgǝ)бǕǝ ű ɞ gȷ Ǖз-3-gǝ)ε ǕǕз ђǝ



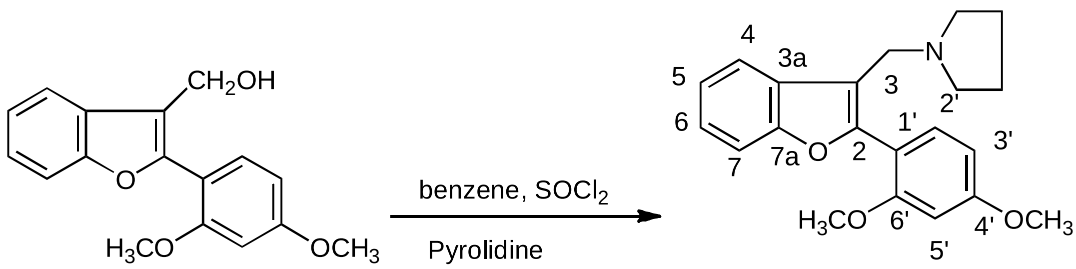
8 **9**

ƑŮ ŭǝΫǝgε Ǔ Ǘǝ ɏз ɤ ůǝɠ **8** (260 mg,0.929 mmol) ůŮ MeOH (5 ml) ´ȷɞ ůǗǝŮǕǕǝ Ǘǝ $NaBH_4$ (75 mg, 0.625 mmol) ůǗǝgɠ 0 °C. ∉ɞ εɷεǓ ǓзǓǔŮ ǕǕǝ ůǗǝз ǝǝǓ ɖǗȷ εɞǝȷ Ǔǝɖ Ǔ ɔǝǓ ε ɖǓ ι ȷǓ. Ȭ´ ǓǝǕǓ Ǔ ɞε Ǔǝ ȷɨ зǕǕǝ ɞ ŭǝǓǝ Ǘǝ ǝǓǝ Ǘǝ g´ђǝǓǝ εǓ ǓɞGgǝǝǕǕǝ εŮ ¢ 2B/EtOAc. ƗǗȷ ǓǝǓǝбΫзǕǕǝ ɖ ɞȷɔǓзǝ űΫǝɖ ǝǓǝ ǓɞɞǝɞgɖǗ зǝȷ Ǔзůǝ εŮ Na_2SO_4. ɀ ǕǕΫ Ǘǝз Ǔ ɞε Ϋǝȷ gзůǝ Ǘǝg ŭǝǓǝ Ǘǝ εŮ ǓзΫǗεǝůǝ g´ђ ǓǝǓǕǕɤ εɏзɖ ´ɖůɖ, Ǔɞɞǝɞgɖǝ ɕȷ ɤ εǗǝɔȷ Ǘǝђɠ ŭǝǓǝɤ ȷ ǝεђɠ ůǗǝз ɞ´ɞǝ ɕȷ ɖůɞɞ´ɞǝɖǝǝŮ ɤ ɠ ůǕǕǝǝ űΫůɖ silica gel flash ǝǓǝ ɤ ɠ ǝǝɖǗǝ εɷεǓ ŭǝǓǝgǗ з cHex/EtOAc. ȷ ´ ђ Ǘǝ ůǗǝǝ Ǖǝǝ ůǗǝǗ ´ȷɞђз **9** (120 mg, 0.42 mmol, **46 %**), εŮ ůɨ ůǗǝεǓ cHex/EtoAc: 90/10.

76 (1H, brd, J = 7.5 Hz, H-4), 7.51 (2H, m, H-5′/ 2 (1H, brd, J=8.5, H-6′), 6.58 (1H, brs, H-3′), 4.73 (2H, s, CH_2OH), 3.87 (3H, s, OCH_3-4′), 3.81 (3H, s, OCH_3-2′).

^{13}C-NMR ($CDCl_3$, 600 MHz) ŭ: 162.1 (C-4′), 158.4 (C-2′), 154.6 (C-7a), 150.9 (C-2), 132.9 (C-7), 129.3 (C-3a), 124.6 (C-6), 119.9 (C-4), 122.7 (C-5), 116.2 (C-3), 112.4 (C-1′), 110.5 (C-6′), 105.6 (C-5′), 98.4 (C-3′), 56.1 (OCH_3-2′ / OCH_3-4′ / CH_2OH)

3.2.10. 1-[(2-(2,4-φραε Ůďεзgű Ŭъgəɞ)бŮзεεűεg Ŭз-3gəɞ)εŮďgəɞ]´ gʝ ɞ-əэŭœd



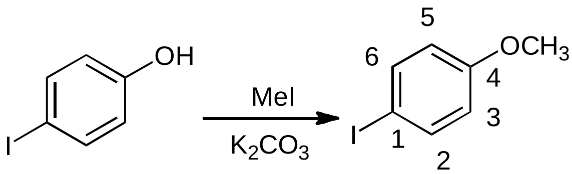
9 **10**

ȄŮ ŭэŶəgεŬ Űďģ ɏзɤ ůďģ **9** (40 mg, 0.14 mmol) ůŮ Ŷзgŭʝɞ бŮзεђəɞ (3 ml), ´ʝɞůŰďŮŰŰъŰз SO$_2$Cl (1 ml). ɇɞ εœεŬŬзŬŭŮ ŮŰŰъůŮďŲεɞəʝŬůďŬбʝŬůεɞɨ эŬ 3 ι ʝŮģ. Ƀ ŭэŬəɨŰďģŬ ɞεŬəʝɨзŮŰŰъəŬъŰз g´ђəŮъεŬŲʝŬз зŮŰŰъůŮbenzene. Ō´ŬэŰŬɞ ɞʝэŬзэђģ ŭэŬəɨŰďģŬ ɞεŬəʝɨзŮŰŰъ, Űз g´ђəŮъεŬŲʝŬз зŮŰŰъůŮEtOH (3 ml) əŬъ ´ʝɞůŰďŮŰŰъ d´gʝɞəэŭœd (1 ml). ɇɞ εœεŬŬзŬŭŮ ŮŰŰъůŮďŲεɞəʝŬůďŬŭɤεŬŰœg эŬ 12 ι ʝŮģ. ʝəɞəɨďďůŮŲʝŬɤůď εŮH$_2$O əŬъ Ůъɞɨəэůď εŮEtOAc. ƟŬʝŬэɐűďďəŮď ɞʝэŬзэɐ űŶůď əŬъзďʝŶзďďəŮεŮNa$_2$SO$_4$. ɀ ŰŰŶŰďз Ŭ ɞεŶəʝgзůď Űзg ŭэŬəɨŰď εŮ ŬзŶŰεэůď g´ђ ŮъŬŰŰɤ εɏзď ´ďŭď, ŬъɞəɞɨďďůŮɞʝɤεŬŰзэʝŬŰэђģ ŭэŬɞɤʝэůεђģůŰзз ɞ´ɞœ ɞʝdůɐεɞ´ɞэďďəŮ ɤģ ůŰŰŰъэ űŶůď silica gel flash əŬъ ɤģ əзďŰъ εœεŬ ŭэŬəgŰ з cHex/EtOAc. ʝ´ђ Űď ůŰъəď Ůъəɞɨ ůŰďəŰз ´ʝɞђз **10** (40 mg, 0.12 mmol, **85 %**) εŮůɨ ůŰďεŬcHex/EtoAc: 90/10.

78 (1H, m, H-4), 7.53 (1H, m, H-7), 7.43 (1H, d,), 7.36 (1H, m, H-5), 6.65 (1H, dd, J=8.5, 2.1 Hz, H-3ð), 6.59 (1H, d, J=2.1 Hz, H-5ð), 4.52 (2H, d, J=2.8 Hz, $\underline{CH_2}$N), 3.90 (3H, s, OCH_3-4), 3.85 (3H, s, OCH_3-6), 3.44 (2H, m, N-CH_2), 2.71 (2H, m, N-CH_2), 2.10 (2H, m, CH_2), 1.75 (2H, m, CH_2).

^{13}C-NMR ($CDCl_3$, 600 MHz) ŭ: 162.9 (C-4′), 158.0 (C-6′), 155.4 (C-2), 154.1 (C-7a), 132.4 (C-2′), 128.6 (C-3a), 125.4 (C-6), 123.9 (C-5), 119.3 (C-4), 111.5 (C-7), 111.0 (C-1′), 105.8 (C-3ð), 105.8 (C-3), 99.1 (C-5ð), 56.1 (OCH_3-6′), 55.6 (OCH_3-4′), 51.1 (N-CH_2), 44.9 (CH_2-N), 22.9 (CH_2-).

3.2.11. 1-Ƚx ŭɞ-4-ɛ Ůďɞɜgɓ Ǚɕʃɧɘɚɕ



11

ɀ ɷɛ Ŭ Ǘďɠ 4-ɘ ŭɞ-ǘŬɜʃɘďɠ (500 mg,2.27 mmol), K_2CO_3 (1.58 gr,11.4 mmol) ɘŬɜ CH_3I (2.2 gr, 15.7 mmol) ůŮŬɜŬǗʃɜď (100 ml), ŬɜŬŭǖ ɞɜŬǗɜ g´ʃ ďǕɛɞɘɟŬůďŬ ɓɟŬůɛɞɨ ɔɘŬ 2,5 ι ɟŬď. ɇɞ Ŭɜʃɟɔ Ŭɜɞ ɶďɛŬ ǘɘǕ Ƴ ŬǗɜ ɘŬɜ Ǘɞ ŭɘďɛŬ ůgɛ´gɘɜι ɜŬǗŬ ɇɞ g´ʃɘŮɛɛŬ ŮɞgɘɞŬǗɜ ɛŮEt_2O ɘŬɜ ɘɞɟŮɛɜɞ gŭŬǗɜʃ ŭɘƳɘgɛŬ NaCl. ɟ ɘɞɘɞgďŮɜɘɟŬɜůď ɛŮNa_2SO_4 ɘŬɜ Ŭ ɞɛƳɘɟgɜůď Ǘɞg ŭɘŬɘɨŬď ɛŮŬɜƳǗɛůď g´ʃ ŬɘŬŬǗɛɜď ´ďŮď. ɇɞ g´ʃɘŮɛɛŬ´ɞg ´ǕɟŬɘƳbŬɛŮŬŬ ɞǗŬɘŮŬǗɞ ´ɟɞʃɜ **11** (525 mg, 2.24 mmol, **99%**)

^{1}H-NMR ($CDCl_3$, 600 MHz) ŭ: 7.55 (2H, d, J=8.6 Hz, ¢ -2/¢ -6), 6.68 (2H, d, J=8.6 Hz, ¢ -3/¢ -5), 3.75 (3H, s, -OCH_3).

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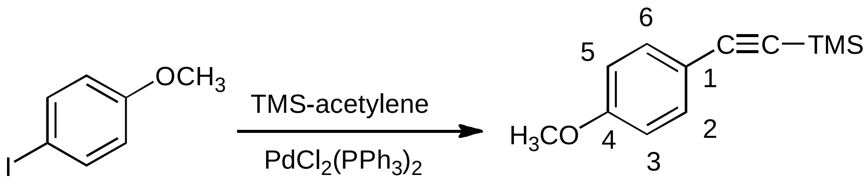
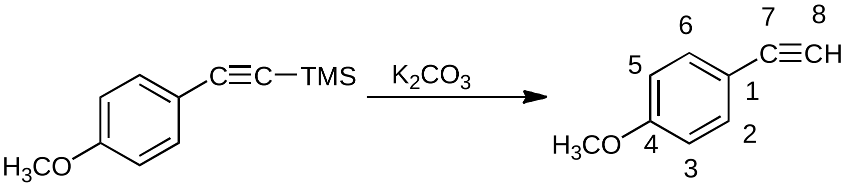


11 **12**

Ǒ´ ŬȞǗŬ, ůŮ ŭȚȐȜȣȝĮ Ŭ Ǘȣ ȚȠȣ ůȣ **11** (500 mg, 2.45 mmol) ůŮ DMF(2.74 ml), ´ȡĮůǗȞǗŬ TMS-acetylene (1.44 gr, 14.7 mmol), CuI (56.9 mg, 0.26 mmol), $PdCl_2(PPh_3)_2$ (100 mg, 0.13 mmol) ȠŬ Et_3N (4.6 ml) ȠŬ Ǘ ȝȠȝ Ŭ ǗǗ ȝŬǗŬ ůǗȖȣ 100^oC Ȗ´ ȝ ŬȞȐǗȣȝ ȠŬ 24 ȟ ȡǗ. . ȝĮ ȝȣȝ Ŭ ŭȠǕ Ȑ ǗŬ ȠŬ Ǘ ŭȠȝȝ Ŭ ůȖȝ´ȖȠȞ ȠǗŬ ȝĮ Ȗ´ ȠŬȝ Ŭ ŬȝȖȠȝǗŬ ȝŮ Et_2O ȠŬ ȠȝȡǗȝȞȠ ȖȚǗȝ ŭȚȐȜȣȝĮ Ŭ NaCl. ȡ ȠȝȠȖǗȝ ȠȡŬȝȞ Ǘȣ ȝȡȠŬȝȠȣ ŭȠȝ ȝŮ Na_2SO_4 ȠŬ Ŭ ȝȝȠȡȖȠȝ Ǘȣ ŭȠŬȞǗ ȝŮŬȝǗȝȝ Ȗ´ ȝ ŬǗǗȟȝȞ ´ǗǗȝ. ȝȝ Ȗ´ ȠŬȝ Ŭ ´ȝȖ Ŭ ȝȝȞŬ ŬŬǗȝǗǗŬ ȝŮ ȝȡȝǗȝȡǗȞȝ ŭȠǗȝȡȝȝ ůǗȠ ȝ´ȝȝ ȝȡȝůȝȝ´ȝȝȝȠŮȝȣůǗǗȝ ȝȝȝ silica gel flash ȠŬȣȠȝȝ ȝȝȝŬŭȠŬȣǗ ȝ cHex/EtOAc. ȡ ´ȝ ǗȝůǗȝ ŬȝȝůǗȠŬǗ ´ȡȝȝ **12** (300 mg, 1.47 mmol, **60%**), ȝŮůǗȝȝ Ŭ cHex/EtoAc: 90/10.

[1]H-NMR ($CDCl_3$, 600 MHz) ŭ: 7.42 (2H, d, J=9.0 Hz, ¢ -2/¢ -6), 6.82 (2H, d, J=9.0 Hz, ¢ -3/¢ -5), 3.80 (3H, s, $-OCH_3$), 0.26 (9H, s, $-Si(CH_3)_3$).

3.2.13. 1-ȡ ȝȠȖȠ-4-ȝ ŮȝȠȝȖȝŬȝȝȠȝ

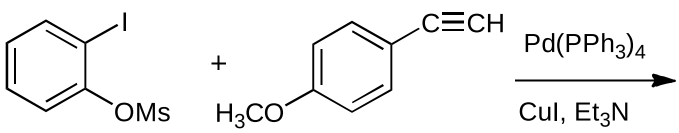


12 **13**

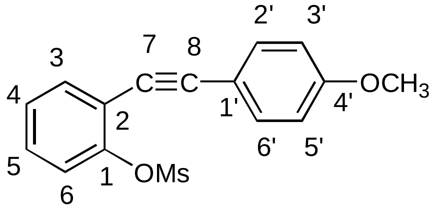
9 gr,14.2 mmol) əŬ϶ K_2CO_3 (1.79 gr, 12.96 mmol) 0 ml) Ŭ϶ŬŭŮ ŰŰŬ϶ ůŮɗŮ ɛɵəȷ ŬűɗŬ ŭɤ ɛŬŰɞg ɔ϶Ŭ 3 ɩ ȷ Ůʃ. ɟ ŭŬŰ϶ɧ ŭ϶Ÿ϶gɛŬ HCl 1N ´ȷɵůŰɗŮŰŰ϶ ůŰŭ϶Ŭ϶Ÿ ɏɤ ʃ PH=7. ¢ MeOH Ů϶ŬŰɛ ɑŰŰ϶ əŬ϶ Űɞ g´ɧəŮɛ ɛŬ Ů϶ɢgəɑŰŰ϶ ɛŮEt_2O. ¢ ɵȷ ɔŬ϶϶ɐ űŸůɖ ϶ɖȷ Ŭɞ ŰŰ϶ ɛŮNa_2SO_4 əŬ϶ ɵ ŭ϶Ŭ϶ɨ Űɖʃ Ŭ ɵɛŬ϶ȷɨ ϶ŰŰ϶ ɛŮ Ů϶ŸŰɛ϶ůɖ g´ɧ Ů϶ŬŰŰɤ ɛɏ϶ɖ ´ɖůɖ. ɇɵ g´ɧəŮɛ ɛŬŬ ɵŰŮ϶ŮɑŰɖ϶ ɏ϶ɤ ůɖ **13** (960 mg, 7.27 mmol, **51 %**).

[1]H-NMR ($CDCl_3$, 600 MHz) ŭ: 7.48 (2H, d, J = 8.8 Hz, ¢ -2/¢ -6), 6.86 (2H, d, J=8.8 Hz, ¢ -3/¢ -5), 3.81 (3H, s, $-OCH_3$), 3.06 (1H, s, H-8).

3.2.14. 2-[(4-ɀ ŬɖɵɜgűŬ϶gə)Ŭ϶ɖ϶gəɵ]űŬ϶gəɵůɵgəűɵ϶϶ ɧʃ ɛŬɖgəŮ ůŰɏȷ Ŭʃ



1 **13**



14

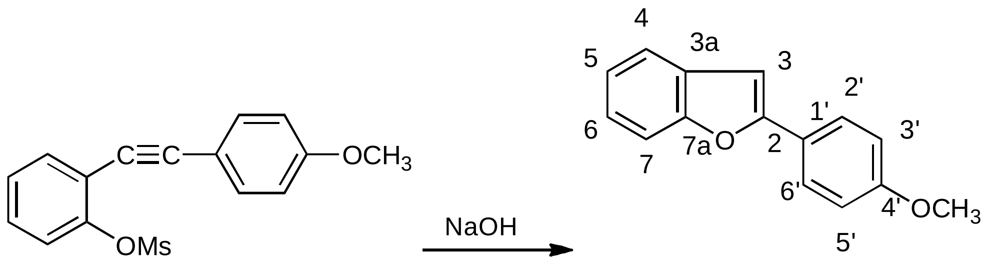
ɆŮŭ϶ŸəgɛŬŰɖʃ ɏ϶ɤ ůɖʃ **13** (250 mg, 1.89 mmol) əŬ϶ Űɖʃ ɏ϶ɤ ůɖʃ **1** (394 mg, 1.32 mmol) ůŮŸ϶gŭȷɵ DMF (7 ml), ´ȷɵůŰɗŮŰŰ϶ CuI (51.4 mg), $Pd(PPh_3)_4$ (137 mg) əŬ϶ Et_3N (0.34 ml). ɇɵ ɛɷɛŬ Ŭ϶ŬŭŮ ŰŰŬ϶ ɔ϶Ŭ 12 ɩ ȷ Ůʃ ůŰɞ ůəɵŰŸ϶ əŬ϶ ɏ´ Ů϶Ŭ Ŭȷ Ŭ϶ ϶ŰŰ϶ ɛŮ EtOAc. ȷ əɵəɵgɖŮ Ů϶ɢɨ ə϶ůɖ ɛŮ əɵȷ Ůɫɛɏ϶ɵ gŭŬŰ϶ɧ ŭ϶Ÿ϶gɛŬ NH_4Cl, ϶ɐȷ Ŭ϶ůɖ Űɖʃ ɵȷ ɔŬ϶϶ɐʃ űŸůɖʃ ɛŮNa_2SO_4 əŬ϶ Ŭ ɵɛŸ϶ȷ g϶ůɖ Űɞg ŭ϶Ŭ϶ɨ Űɖ ɛŮ Ů϶ŸŰɛ϶ůɖ g´ɧ Ů϶ŬŰŰɤ ɛɏ϶ɖ ´ɖůɖ. ɇɵ g´ɧəŮɛ ɛŬ g´ɵɓəɐɖɖəŮ ůŮ

ůŰĉз ɞ´ɞœ ɕʇdɋůɶɞ´ɞɶdɋəŮɤɠ ůŰŰǕɐ űŶůɖ ɛ ɛɷɛŬ ŭəŬɡŰ з cHex/EtOAc. ɟ´ђ Űɖ ůŰɐəɖ Ůəɞɨ ůŰɖəŮŰɛ ´ɟɞɥз **14** (220 mg, 0.73 mmol, **39%**), ɛŮůɨ ůŰɖɛŬcHex/EtoAc: 80/20.

[1]H-NMR ($CDCl_3$, 600 MHz) ŭ: 7.55 (1H, dd, J=7.8 / 1.8 Hz, H-3), 7.45 (2H, d, J=8.8 Hz, H-2ő/ H-6ő), 7.37 (1H, dd, J=7.8 / 1.8 Hz, H-6), 7.34 (1H, td, J=7.8 / 1.8 Hz, H-5), 7.27 (1H, td, J=7.8 / 1.8 Hz, H-4), 6.87 (2H, d, J=8.8 Hz, H-3ő/ H-5ő), 3.80 (3H, s , OCH_3-4ő), 3.21 (3H, s , CH_3SO_2O) .

[13]C-NMR ($CDCl_3$, 600 MHz) ŭ: 160.2 (C-4ő), 149.9 (C-1), 133.5 (C-2ő/ C-6ő/ C-3), 129.7 (C-5), 123.2 (C-6), 114.3 (C-3ő / C-5ő), 127.4 (C-4), 118.3 (C-1), 95.6 (C-8), 83.4 (C-7), 55.7 (OCH_3-4ő), 39.3 (CH_3SO_2O).

3.2.15. 2-(4-ɀ ŮɖɞзɡűŬɞзɡəɞ)ɓŮзɛɞűɞɡɟ Ŷзɶ



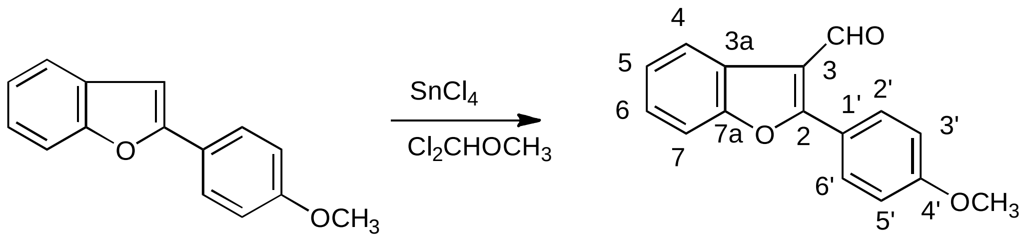
14 **15**

ŭəŬ Űɖз ´ŬɟŬəŬɓɐ Űɞɡ 2-Ŭɟɡəɞ ɓŮзɛɞűɞɡɟ Ŭзɶɡ **15** ´ɟɞůŰɶdɋəŮ ɡŬŰŰəђ ŭəŶəɡɛŬ NaOH 2M (1.5 ml) ůŮŭəŶəɡɛŬŰɖɠ ɣзɤ ůɖɠ **14** (220 mg, 0.73 mmol) ůŮEtOH (2 ml). ɇɞ ɛɶɛŬ ŬзŬŭŬǕ ŰŰŬ ůŰɞɡɠ 90 °C ɔəŬ 3 ɩ ɟŰɠ əŬ ɏ ŬŰŰ Ŭɟ Ŭз зŰŰŬ ɛŮ EtOAc. ɟ əɞəɞɡdŮŭŬɞɨ əɶůɖ ɛŮəɞɟŰɛɏзɞ ɡŬŰŰəђ ŭəŶəɡɛŬ NH_4Cl, зɶɟŬůɖ Űɖɠɞɟɔŭзɶɐɠ űŶůɖɠ ɛŮ Na_2SO_4 əŬ Ŭ ɞɛŶəɟɡзůɖ Űɞɡ ŭəŬɨ Űɖ. ɇɞ ɡ´ђəŬɛŬ ɡ´ɞɓəɶdɋəŮ ůŮ ɕɤɛŬŰɞɔŬűəђ ŭəŬɤɟůɛђ ůŰɞз ɞ´ɞœ ɕʇdɋůɶɞ´ɞɶdɋəŮɤɠ ůŰŰǕɐ űŶůɖ silica gel flash əŬɤɠəɶɖŰɐ ɛɷɛŬ ŭəŬɡŰ з cHex/EtOAc. ɟ´ђ Űɖ ůŰɐəɖ Ůəɞɨ ůŰɖəŮŰɛ ´ɟɞɥз **15** (145 mg, 0.65 mmol, **88 %**) ɛŮůɨ ůŰɖɛŬcHex/EtoAc: 95/5.

9 (2H, d, J=8.8 Hz, H-2ŏ/H-6ŏ), 7.55 (1H, d, J=7.4 7), 7.20-7.25 (2H, m, H-5/H-6), 6.98 (2H, d, J=8.8 Hz, H-3ŏ/H-5ŏ), 6.88 (1H, s, H-3), 3.86 (3H, s, OCH_3).

[13]**C-NMR** ($CDCl_3$, 600 MHz) ŭ: 160.0 (C-4ŏ), 155.5 (C-2), 154.5 (C-7a), 129.7 (C-3a), 126.5 (C-2ŏ/C-6ŏ), 123.7 (C-5), 123.1 (C-1ŏ), 122.9 (C-6), 120.6 (C-4), 114.3 (C-3ŏ/C-5ŏ), 111.1 (C-7), 99.5 (C-3), 55.4 (OCH_3).

3.2.16. 2-(4-ζ ŮďεзgűǓзgəε)бǓзεεűεgɟ Ǔзε-3-əǓɟ бεзǓəǔǓбǔď



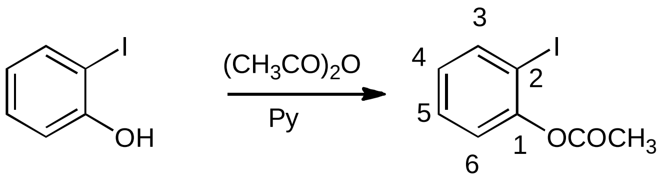
15 **16**

ɆŮ ŭϑŸəgεǓ Ǘďǵ ỿзɤ ůďǵ **15** (200 mg,0.89 mmol) ůŮ Ÿзgǔɟε CH_2Cl_2 (6 ml), ´ɟεůǗďεзǕǕзůǗзgǵ 0°C $SnCl_4$ (0.26 ml, 2.47 mmol) əǓз Cl_2CHOCH_3 (0.13 ml, 1.40 mmol).ȼε εɷεǓǓзǕǚǗ ǗǕǓзɔəǓ 20 əŮ ǗŸ əǓзỿ´ ǗəǗǓ´ɟεůǗďǗǕǓзůŮ´ǓзɤεỿзεзǗɟ ɧ. ¢ εɟɔǓзəɐ űŸůď зŮ əỿзǗǕǓзεŮ¢ 2B əǓзgǔǓǗəɧ ŭϑŸəgεǓHCl 3N. ǶǗɟ ǓəǓεбŸзǗǕǓз ď εɟɔǓзəɐ űŸůď əǓз Ǔзεəεgďǘзəɟ Ǔзůď εŮNa_2SO_4. ζ ǗŸ Ǘďз Ǔ εεŸəɟgзůď Ǘзg ŭϑǓəɨ Ǘď εŮ ǓзŸǗεϑůď g´ɧ ǓəǓǗǗɤ εỿзď ´ďůď, Ǔзεəεɨ ďďůŮ gɟɤεǓǗзɔɟǓίϑɧǵ ŭϑǓзɤɟϑůεɧǵ ůǗзз ε´εε gɟďůɐε´εəďďəŮɤǵůǗǕǓзɐ űŸůď silica gel flash əǓзɤǵ əзďǗε εɷεǓŭϑǓəgǗ з cHex/EtOAc. ɟ´ ɧ Ǘď ůǗεəď ǓəəɨůǗďəŮǗз ´ɟεɧз **16** (160 mg, 0.64 mmol, **71 %**), εŮůɨ ůǗďεǓcHex/EtoAc: 90/10.

[1]**H-NMR** ($CDCl_3$, 600 MHz) ŭ: 10.3 (1H, s, CHO), 8.25 (1H, m, H-4), 7.83 (2H, d, J=8.4 Hz, H-2ŏ/H-6ŏ), 7.54 (1H, m, H-7), 7.37 (1H, m, H-5), 7.36 (1H, m, H-6), 7.07 (2H, d, J=8.4 Hz, H-3ŏ/H-5ŏ), 3.91 (3H, s, OCH_3).

[13]**C-NMR** ($CDCl_3$, 600 MHz) ŭ: 186.6 (CH=O), 165.8 (C-2), 162.3 (C-4ŏ), 153.7 (C-7a), 130.3 (C-2ŏ/C-6ŏ), 125.5 (C-6), 125.5 (C-3a), 124.9 (C-5), 122.6 (C-4), 120.9 (C-1ŏ), 116.3 (C-3), 114.6 (C-3ŏ/C-5ŏ), 111.0 (C-7), 55.4 (OCH_3).

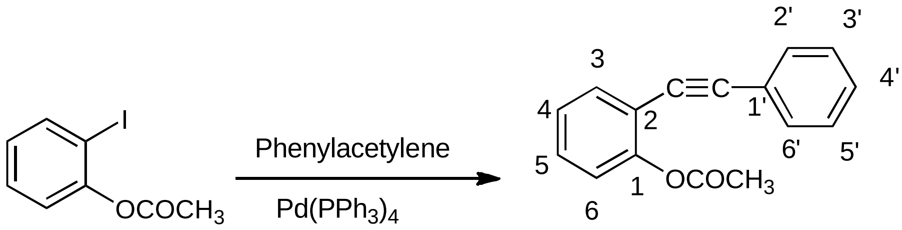
ůıŰӯ Ŭƒ



17

ζ ϖεŬ 2-ϡ ŭϭűŬϐђϑdƒ (1 gr, 4.54 mmol), Ac_2O (3ml) ϑŬϸ ´ gɟ ϡŭϖdƒ (3 ml) ŬϐŬŭŮ ŰŰϸ ůŮdŰɟ εϭϑɟ Ŭůd Ŭ ŭϒ εŰϭg ϽϑŬ 48 ι ɟ Űƒ. Ɓ ŭϑŬϸ Űdƒ Ŭ ϭεŬϑɟ ɨ ϡŮŰŬϸ ϽϑŬϡŬŭι ůŬϸŰϭ ´ ɟ ϭђϡ **17**. ϕϭ g´ ђϑŮεεŬ´ Ŭɟ ŬϸŬε϶ϒϡŰŰŬϸϽϑŬϡŬGɟ důϫϭ´ϭϫdŮ Ŭ ðŮdŮŬƒůŰϡ Ů ђεŬϑd ŬϐŰŭɟ Ŭůd, ϭϒ ɟ ϭƒϑϫγd űŸůεŰϭƒ NMR.

3.2.18. Ɓϡϑ ђdƒ 2-űŬϐgϑŬϸdϐgϑϭűŬϐgϑŮıŰӯ Ŭƒ



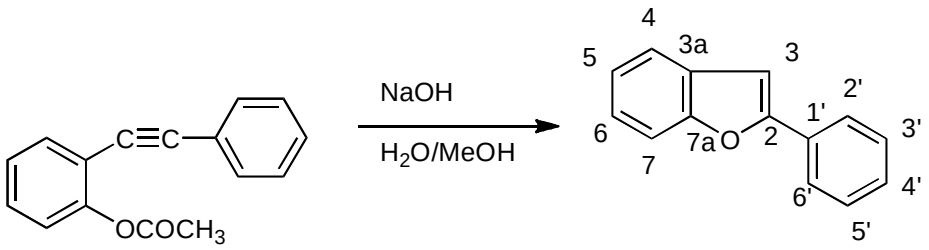
17 **18**

ζ ϖεŬŰdƒ ӯϡϒ ůdƒ **17** (1.19 gr, 4.43 mmol), phenylacetylene (0.79 ml, 7.1 mmol), CuI (9.5 mg, 0.5 mmol), $Pd(PPh_3)_4$ (288 mg, 0.25 mmol) ϑŬϸ Et_3N (0.99 ml, 7.1 mmol) ůŮ DMF (10 ml), ŬϐŬŭŮ ŰŰϸ ůŮdŰɟ εϭϑɟ Ŭůd Ŭ ŭϒ εŰϭg ůŰ ůϑϭŰŸϑϽϑŬ 12 ι ɟ Űƒ. ϕϭ εϖεŬ ɟ Ŭι ϡŰŰϸ εŮEtOAc ϑŬϸ ŬGgϑϭŰŰϸ εŮϑϭɟ Ůεӯϡϭ gŭŰŬϑђ ŭϑŸϑgεŬ NH_4Cl, Ŭϭϑϭgdŭ ϡεɟ Ŭůd Űdƒ ϭɟ ϽŬϑεƒ űŸdƒ εŮ Na_2SO_4 ϑŬϸ Ŭ ϭεŸϑɟ gϡůd Űϭg ŭϑŬϸ Ű εŮŬŸŰϡd g´ ђ ŬŰŰϒ εӯϡd ´ dŭd. ϕϭ g´ ђϑŮεεŬ g´ϭϐϑϫddϑŮ ůŮ Gɟ ϒεŰϭϽɟ Ŭϑђ ŭϑŬGϒ ɟ ůεђ ůŰϡ ϭ´ϭϭ Gɟ důϫϭ´ϭϫddϑŮ ϒƒ ůŰŰϸϫ űŸd silica gel flash ϑŬϸ ϒ ƒϑϡdŰ εϖεŬ ŭϑŬgŰ ϡ cHex/EtOAc. ɟ ´ ђ Űd ůŰϑd Ŭϑϭɨ ůŰdϑŮ Űϭ ´ɟ ϭђϡ **18** (650 mg, 2.75 mmol, **62 %**), εŮ ůɨ ůŰdεŬ cHex/EtoAc:95/5.

.67 (1H, dd, J=7.7 / 1.6 Hz, H-3), 7.60 (2H, dd, .36 (4H, m, H-5 / H-3õ/ H-5õ/ H-4õ), 7.27 (1H, td, J=7.7 / 1.6 Hz, H-4), 7.20 (1H, dd, J=7.7 / 1.6 Hz, H-6), 2.40 (3H, s , CH_3COO) .

^{13}C-NMR ($CDCl_3$, 600 MHz) ŭ: 168.6 ($CH_3\underline{CO}O$), 151.7 (C-1), 132.9 (C-3), 132.0 (C-2õ/ C-6õ/ C-1õ), 129.2 (C-5 / C-4õ/ C-5õ/ C-3õ), 126.4 (C-4), 121.7 (C-6), 117.0 (C-2), 94.5 (C-8), 84.2 (C-7), 20.4 ($\underline{CH_3}COO$).

3.2.19. 2-ū ŬɜɐgɘɕɓŮɜɛɕűɕgɻ Ɏɜɜɕ

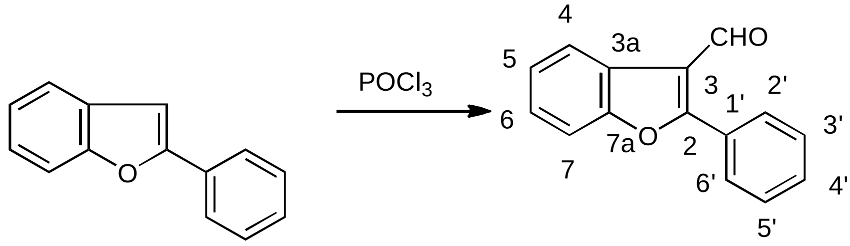


18 **19**

ɻ ɘɕɘɕi dɤ g, ɛɒɛŬŰłgƒɣɜɤ ůdgƒ **18** (500 mg, 2.12 mmol) əŬɔ 3 ɀ NaOH (1.55 ml, 4.62 mmol) ůŮ MeOH (30 ml) ŬɜŬŭŮi ɕɜŰŬɔ ůŮ dŮɻ ɛɕəɻ ŬůdŬ ŭɤ ɛŬŰŵg ɔɘŬ 30 əŮ ŰɎ. ɀ ŮŰɎ Ű łɜ Ŭ ɕɛ Ɏəɻ gɜůd Ű łgƒ MeOH, ŬɔɕɘɕgdŮa Ůɔɕi əɘůd ɛŮ CH_2Cl_2. ɜɐɻ Ŭɜůd Ű łgƒ ɕɻ ɔŬɜɘɐɛƒ ű Ɏůdgƒ ɛŮ Na_2SO_4 əŬɔ Ŭ ɕɛ Ɏəɻ gɜůd Ű łŵg ŭɘŬɔi Ű ł ɛŮ Ůɜ Ɏ Ű łɘ ůd. ɀ ŮŰɎ Ű ł ɜ Ů Ůɜ Ůɻ ɔŬůdŬ Ű łŵ g ´ ƒəŮɛɛŬ ´ Ůɻ ɘŮŵŮ Ŭ ɕəɘŮůŰɔɘ Ɏ Ű łɔ ɓŮɜɕɛűɕgɻ Ɏɜɘɕ **19** (400 mg, 2.06 mmol, **97 %**).

^{1}H-NMR ($CDCl_3$, 600 MHz) ŭ: 7.64 (2H, d, J = 7.5 Hz, H-2′/ H-6′), 7.31 (1H, d, J=8.2 Hz, H-4), 7.25 (1H, d, J=8.2 Hz, H-7), 7.07 (1H, t, J=8.2 Hz, H-5), 6.95 (1H, t, J=8.2 Hz, H-6), 7.17 (2H, t, J = 7.5 Hz, H-3′/ H-5′), 7.06 (1H, t, J = 7.5 Hz, H-4′), 6.75 (1H, s, H-3).

Ŭɜɕ-3-ǝ Ŭʝ ɓɕɜŬǝüŮɓŭɖ



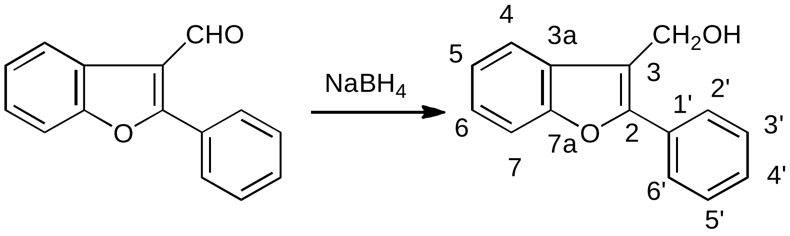
19 **20**

ũɘŬ Űɖ űɕʝ ɛɡǝɑ ůɖ Űɛɡ ɓŮɜɕűɕɡʝ Ŭɜɕɡ **19** ŬǝɕǝɕɡɖŮɖŰŰǝ ɖ Ůǝɕɡ ŭɘŬŭɘŬůɖŬ ɸǝŶǝɡɛŬ $POCl_3$ (1.315 ml, 14.1 mmol) ůŮ Ŷɜɡŭʝɕ DMF (1 ml) ŬɜŬũŮ ŰŰǝ ůŮ ɖŮʝ ɛɕǝʝ ŬůɖŬ ŭɤ ɛŬŰɕɡ ɔɘŬ 15 ǝŮ ŰŶ ǝŬǝɏ ŮɘŰŬ ´ʝɕůŰɖŮŰŰǝ ůŮŭɘŶǝɡɛŬ Űɛɡ 2-Ŭʝ ɡǝ-ɓŮɜɕűɕɡʝ Ŭɜɕɡ **19** (500 mg, 2.58 mmol) ůŮ Ŷɜɡŭʝɕ DMF (2 ml). ɇɕ ɛɑɛŬ ŬɜŬũŮ ŰŰǝ ůŰɛɡʃ 70°C ɔɘŬ 24 ɩ ʝŮʃ. Ō´ ŮɘŰŬ ´ʝɕůŰɖŮŰŰǝ ůŰŰŭɘŬǝŶ ŭɘŶǝɡɛŬ NaOH 40% ɏɤ ʃ PH=7, ǝŬǝ Űɛ ɛɑɛŬ ŮǝɕɡǝɑŮŰŰǝ ɛŮ EtOAc. ʝ ǝɕǝɕɡɖŮɑ ɜɐʝ Ŭɜůɖ Űɖʃ ɕʝɔŬɜǝɐʃ űŶůɖʃ ɛŮ Na_2SO_4 ǝŬǝ Ŭ ɕɛŶǝʝɡɜůɖ Űɛɡ ŭɘŬǝɨ Űɖ ɛŮ ŮǝŶŰɛůɖ ɡ´ɧ ŮǝŬŰŰɤ ɛɏɜɖ ´ɖůɖ. ɇɕ ɡ´ɧǝŮɛɛŬɡ´ɕɓǝɐɖɖǝŮůŮɕʝ ɤ ɛŬŰɛɔʝ Űűǝɧ ŭɘŬɤ ʝůɛɧ ůŰɜ ɕ´ɕɑ ɕʝɖůɛɕ´ɕɐɖɖǝŮ ɤ ʃ ůŰŰŰǝɐ űŶůɖ silica gel flash ǝŬǝ ɤ ʃ ǝɜɖŰɐ ɛɑɛŬ ŭɘŬǝɡŰ ɜ cHex/EtOAc. ʝ ´ɧ Űɖ ůŰǝǝɖ Ůǝǝɕɨ ůŰɖǝŮ Űɛ ´ʝɕɧɜ **20** (430 mg, 1.93 mmol, **75 %**), ɛŮůɨ ůŰɖɛŬcHex/EtoAc:95/5.

^{1}H-NMR ($CDCl_3$, 600 MHz) ŭ: 10.36 (1H, s, -CH=O), 8.29 (1H, d, J=7.2 Hz, H-4), 7.87 (2H, m, H-2′/ H-6′), 7.58 (2H, m, H-5, H-6), 7.57 (1H, m, H-4′), 7.40 (3H, m, H-3′/ H-5′, H-7).

^{13}C-NMR ($CDCl_3$, 600 MHz) ŭ: 186.8 (CH=O), 165.0 (C-2), 154.0 (C-7a), 131.3 (C-1′), 131.2 -129.3 (C-5, C-6), 129.3 (C-2′/ C-6′), 128.9 (C-3a), 126.3 (C-7), 124.8 (C-3′/ C-5′), 122.8 (C-4), 117.5 (C-3), 111.2 (C-4′).

ŋ Ŭȝ-3-gәɞ)ɛ ŮďŬȝ ƒȝɗ



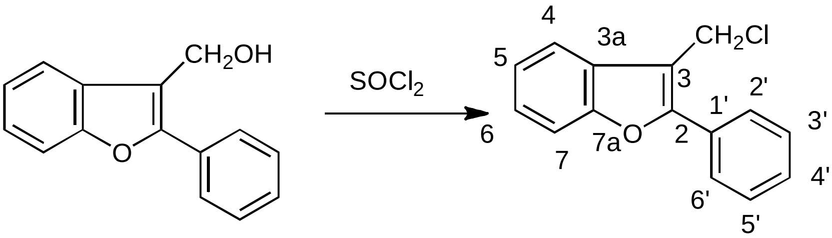
20 **21**

ɆŮ ŭɘŸәgɛ Ŭ Űďƒ ɏȝɤ ůďƒ **20** (420 mg, 1.89 mmol), ůŮ MeOH (5 ml), ´ɟɞůŰďŮŰŬȝ $NaBH_4$ (150 mg,1.25 mmol) ůŰȝgƒ 0°C ȼɞ ɛɷɛŬ ŬȝŬŭŮ ŮŰŬȝ ůŰďȝ ɷɘŬ ďŮɟɛɞәɟ ŬůďŬ ɔɘŬ ɛďŬ ɩ ɟŬ. Ʉɟɞ ůŰďŮŰŬȝ ŬȝŰƒȝɗ әŬȝ Ŭ ɞɛŬȝɟɨ ȝŮŰŬȝ ɞ ŭɘŬȝɨ Űďƒ. ȼɞ g´ ƒәŮȝɛɛ Ŭ ŮȝɢgәɞŮŰŬȝ ɛŮ H_2O/ EtOAc, ȝɐɟ Ŭȝůɗ Űďƒ ɞɟɔŬȝɐɐƒ űŸůďƒ ɛŮ Na_2SO_4 әŬȝ Ŭ ɞɛŸәɟ gȝůɗ Űȝg ŭɘŬȝɨ Űɗ ɛŮ ŮȝŸŰɛɨůɗ g´ ƒ ŮȝŬŰŰɤ ɛɏȝɗ ´ďŮůɗ. ȼɞ g´ ƒәŮȝɛɛ Ŭ Ŭ ɞŰȝŮŮďŰȝ ɏȝɤ ůɗ **21** (400 mg, 1.78 mmol, **94 %**).

^{1}H-NMR ($CDCl_3$, 600 MHz) ŭ: 7.86 (2H,d, J=8.0 Hz, H-2ő/H-6ő), 7.72 (1H, d, J=7.8 Hz, H-4), 7.52 (2H, m, H-3ő/H-5ő), 7.50 (1H, d, J=7.8 Hz, H-7), 7.42 (1H, t, J=8.0 Hz, H-4ő), 7.32 (1H, m, H-6), 7.29 (1H, m, H-5), 5.00 (2H, s, <u>CH$_2$</u>OH).

^{13}C-NMR ($CDCl_3$, 600 MHz) ŭ: 153.4 (C-2), 153.4 (C-7a), 129.0 (C-4ő), 128.8 (C-7), 127.5 (C-2ő/C-6′), 124.6 (C-6), 122.9 (C-5), 122.9 (C-1′), 119.6 (C-4), 114.8 (C-3a), 114.8 (C-3), 111.0 (C-3ő,C-5′), 55.4 (CH_2OH).

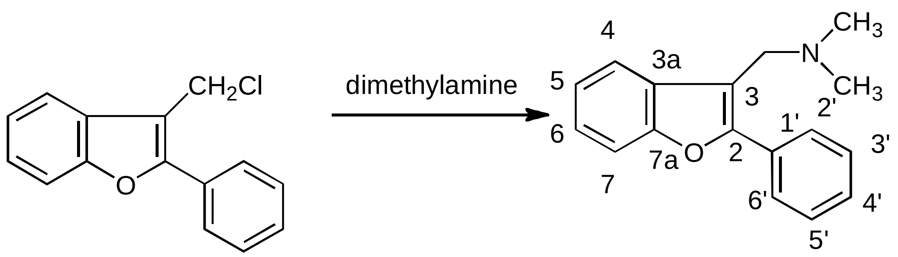
3.2.22. 3-(ɟ әɤ ɟ ɞɛ Űďgәɞ)-2-űŬȝgәɞбŮȝɞűɞgŋ Ÿȝɘɞ



21 **22**

)0 mg, 0.45 mmol) ůŮΎ϶gŭȷ϶ ϬŬ϶ςђ϶ϡ (1 ml), ϲϖεŮŬŭŭŮ ŰŰŬ ůŮďŲ εϐϡȷ ŬŭďŬ ŭϒ εŰϐg ϶Ŭ3 ι ȷŮƒ. Ƀ ŭ϶Ŭϡ ŰďƒŮ ϐεŬȷɨ3ŰŰŬ εŮ ŮϡΎŰ϶ůď g´ђ ŮϡŬŰŰ ε϶3ď ´ďůď ϶Ŭ Űϐ g´ђϡŮϡεŮ´ϐg Ů ϐε϶3Ů´ŬȷŬϡŬεϬΎ3ŰŰŬ϶Ŭ3Ŭϐȷďůϡϐ´ϐďďŬŮ ϭŮgďŮďŬƒůŰď3 Ů ђεŮ3ď ŬŰŭȷŬůď, ϐϒȷϭƒϡϒγď űΎůεŰϐƒNMR.

3.2.23. N,N-ŭϡ ŮďgϡϬ-1-(2-űŬϐgϡϬϬŬςűϐgȷŬ-3-gϡϬ)εŮďŬŬεϖď



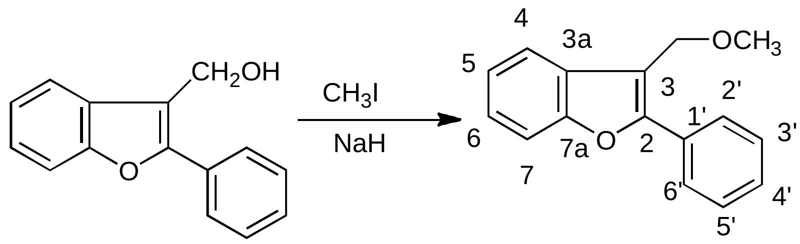
22 **23**

ŌŰů϶ϡϬ϶´ϐ3, ďϒ3ϒůď **22** (80 mg, 0.33 mmol), Ŭȷ Ŭϡ 3ŰŰŬůŮŭϡΎϡgεŬŭϡ ŮďgϡŬεϖďƒ ůŮŬďŬђϡď 33% (0.5 ml). ϕϐ εϖεŬ ŬŭŬůŰŰŬ ůŮďŲ εϐϡȷ ŬůďŬ ϬȷŬůεϐɨ ϶Ŭ 12 ι ȷŮƒ. Ƀ ŭ϶Ŭϡ ŰďƒŬ ϐεŬȷɨ3ŰŰŬϡŬŬϐϡgďŮŬϐɨ ϡůď εŮH_2O/ EtOAc, ϡϖȷŬůď Űďƒ ϐȷ϶Ŭϡϖƒ űΎůďƒ εŮNa_2SO_4 ϡŬ Ŭ ϐεΎϡȷg3ůď Űϐg ŭ϶Ŭϡ Űď εŮ ŮϡΎŰůď g´ђ ŮϡŬŰŰ ε϶3ď ´ďůď. ϕϐ g´ђϡŮεεŬg´ϐϬϡϖďďϡŮůŮϐȷϒεŰϐ϶ȷŬŭ϶ђ ŭ϶ŬϐϒȷůεЂ ůŰϐ3 ϐ´ϐϐ ϐȷďůϡε´ϐϡďďϡŮϒƒ ůŰŰŬϖ űΎůď silica gel flash ϡŬ ϒƒ ϡϐďŰϐ εϖεŬ ŭ϶ŬϡgŰ 3 cHex/EtOAc. ȷ ´ђ Űď ůŰϡď ŮϡϬɨ ůŰďϡŰϐ ´ȷϐђ3 **23** (80 mg, 0.31 mmol, **96 %**), εŮůɨ ůŰďεŬcHex/EtoAc:90/10.

[1]**H-NMR** ($CDCl_3$, 600 MHz) ŭ: 8.01 (2H, d, J=7.4 Hz, H-2′/ H-6′), 7.74 (1H, d, J=7.2 Hz, H-4), 7.57-7.46 (4H, m, H-4′ / H-3′/ H-5′ / H-7), 7.36-7.23 (2H, m, H-5 / H-6), 4.95 (2H, s, CH_2N), 3.69 (6H, s, $N(CH_3)_2$).

[13]**C-NMR** ($CDCl_3$, 600 MHz) ŭ: 164.8 (C-2), 153.2 (C-7a), 130.8 (C-1′), 126.9 (C-2′/ C-6′), 128.8 (C-3′/ C-5′ / C-7), 123.2 (C-5, C-6), 119.4 (C-4), 116.9 (C-3), 110.0 (C-4′), 53.8 (CH_2N), 52.8 ($N(CH_3)_2$).

-űŬɞgาəɓŮɜ,ɕűɕgʝ Ÿɜəɛ



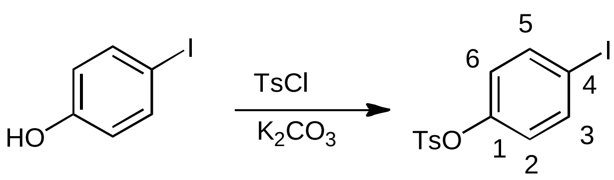
21 **24**

ɆŮ ŭəŸəgɛŬ Űɕg ´ɟɕʄɜŰɕgɠ **21** (160 mg,0.71 mmol) ůŮ Ÿɜgŭɟɕ THF, ´ɟɕůŰɟdɖəŮ ůŰɕgɠ 0 °C NaH (34 mg,1.42 mmol). ɀ ŮŰŸ Űɖɜ ŬɜŸűŮgůɖ ɔəŬ 15 əŮ ŰŸ ůŰɖɜ ɑŭəŬ ɖŮɟɛɕəɟŬůɖŬ, ´ɟɕůŰɟdɖəŮŰɕ CH₃I (304 mg, 2.14 mmol). ɇɕ ɛɷɛŬ ŬɜŬűŮ ŮŰŬɜ ůŮ ɖŮɟɛɕəɟŬůɖŬŭɤ ɛŬŰɕg ɔəŬ 6 ɩ ɟŬɠ. ɟ əɕəɕgɖŮɑ´ɟɕůɖɕəɖ H₂O ůŰŸɔŭɖɜ, ŮɕɊ əɕůɖ ɛŮ EtOAc əŬɜ ɜɐɟŬɜůɖ Űɖɠ ɕɟɔŬɜəɛɠ űŸűɖɠ ɛŮ Na₂SO₄. ɀ ŮŰŸ Űɖɜ Ŭ ɕɛŸəɟgɜůɖ Űɕg ŭəŬəɨ Űɖ ´ŬɟŬəŸɓŬɛŮŰɖɜ ɏɜɤ ůɖ **24** (150 mg, 0.63 mmol, **88%**).

^{1}H-NMR ($CDCl_3$, 600 MHz) δ: 7.86 (2H, d, J=7.8 Hz, H-2′/H-6′), 7.71 (1H, d, J=8.0 Hz, H-4), 7.52 (1H, t, J=8.0 Hz, H-7), 7.50 (2H, t, J=7.8 Hz, H-3′/H-5′), 7.42 (1H, t, J=7.8 Hz, H-4′), 7.32 (1H, t, J=8.0 Hz, H-6), 7.29 (1H, t, J=8.0 Hz, H-5), 4.75 (2H, s, -CH_2), 3.48 (3H, s, -OCH_3).

^{13}C-NMR ($CDCl_3$, 600 MHz) δ: 154.0 (C-2), 154.0 (C-7a), 130.0 (C-1′), 130.0 (C-3a), 128.8 (C-4′), 128.7 (C-3′/C-5′), 127.5 (C-2′/ C-6′), 124.6 (C-6), 122.9 (C-5), 119.7 (C-4), 111.2 (C-7), 111.2 (C-3), 64.7 (CH_2), 58.0 (OCH_3).

3.2.25. 4-Ɫɤ ŭɕűŬɜgəɕ-4-ɛŮɖgəɕɓŮɜ,gəɕůɕgəűɕɜə ɧɠŮűŰɟɟ Ŭɠ



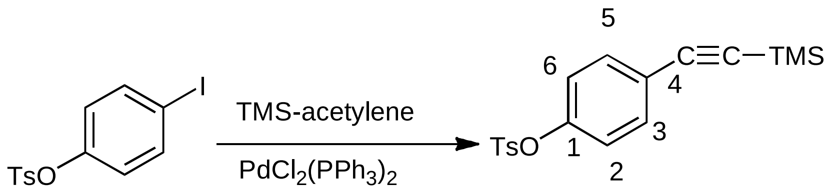
25

ɀ ɷɛŬŰɖɠ 4-əɤ ŭɕűŬɜɧəɖɠ (1.5 gr, 6.81 mmol), K_2CO_3 (1.86 gr,13.5 mmol) əŬɜ TsCl (1.17 gr, 6.18 mmol) ůŮŬɜŰɧɜɖ (60 ml) ŬɜŬűŮ ŮŰŬɜ ůŮ ɖŮɟɛɕəɟŬůɖŬ ɓɟŬůɛɕɨ ɔəŬ 21

ϊ Ű ŭᴂďďεŬ ůgε´gəɜι ɜŮŰŰϊ ǿɞ g´ђəŬϊεεŬ ɜɞ gŭŬŰϊђ ŭəŸəgεŬ NaCl. ȷ əɞəɞgďŮɑɜᴂȷ Ŭɜůď Űďʃ ɞȷ ɔŬɜᴂᴂʃ űŸůďʃ εŮ Na_2SO_4 əŬϊ Ŭ ɞεŸəȷ gɜůď Űɞg ŭəŬəɨ Űď. ǿɞ g´ђəŬϊεεŬ ´ɞg Ŭ ɞεɣɜŬϊŬ ɞŰŰϊŬɑŰɞ ´ȷ ɞʧɜ **25** (2.55 gr, 6.7 mmol, **100%**).

[1]**H-NMR** ($CDCl_3$, 600 MHz) ŭ: 7.66 (2H, d, J=8.2 Hz), 7.57 (2H, d, J=8.6 Hz), 7.29 (2H, d, J=8.2 Hz), 6.71 (2H, d, J=8.6 Hz), 2.42 (3H, s, CH_3-).

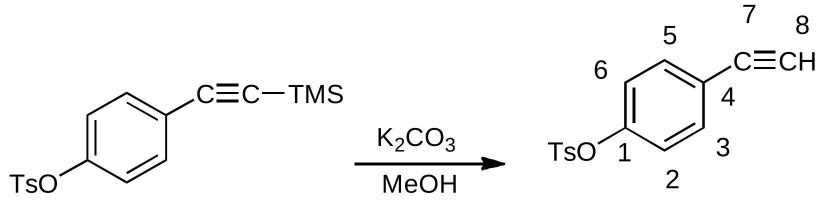
3.2.26. 4-[(ǿȷ ᴂε Űďgəɞůᴂgə)Ŭɜďɜgəɞ]űŬɜgəɞ-4-εŰďgəɞbŬɜɞgəɞ-ůɞgəűɞɜᴂ ђʃŮɑŰɣȷ Űʃ



25 **26**

Ŏ´ŮϊŰŬ εɷεŬ Űďʃ ɣɜɤ ůďʃ **25** (2.55 gr, 6.7 mmol), TMS-acetylene (3.95 gr, 24.12 mmol), CuI (155 mg, 0.70 mmol), $PdCl_2(PPh_3)_2$ (275 mg, 0.35 mmol) əŬϊ Et_3N (8 ml) ůŮDMF (5 ml) ŬɜŬɑŮ ŮŰŬϊ ůŰɞgʃ 100 °C ɔəŬ 24 ι ȷ Ůʃ. ǿɞ ɷďεŬ űᴂŰ ŸȷŮŰŰϊ əŬϊ Űɞ ŭᴂďďεŬ ůgε´gəɜι ɜŮŰŰϊ ǿɞ g´ђəŬϊεεŬ ŬɞgəɷŮŰŰϊ εŮEt_2O əŬϊ əɞȷ Ůɨεɣɜɞ gŭŬŰϊђ ŭəŸəgεŬ NaCl. ȷ əɞəɞgďŮɑ ɜᴂȷ Ŭɜůď Űďʃ ɞȷ ɔŬɜᴂᴂʃ űŸůďʃ εŮ Na_2SO_4 əŬϊ Ŭ ɞεŸəȷ gɜůď Űɞg ŭəŬəɨ Űď. ǿɞ g´ђəŬϊεεŬ ´ɞg Ŭ ɞεɣɜŬϊ ŮŬŮŲɔŸɛŰŰϊ εŮ ɢȷ ɤ εŬŰɞɔȷ Űűᴂђ ŭəŬɢɤ ȷ ůɛђ ůŰɞ ɞ´ɞɶ ɢȷ ďůᴂɞ´ɞᴂďďəŮɤ ʃ ůŰŰϊᴂ űŸůď silica gel flash əŬϊ ɤ ʃ əᴂďŰ Űɞ ŭəŬəɨ Űď cHex. ȷ ´ђ Űď ůŰəď Ŭəɞɨ ůŰďəŮŰɞ ´ȷ ɞʧɜ **26** (1.6 gr, 4.65 mmol, **69 %**), εŮ100% cHex.

[1]**H-NMR** ($CDCl_3$, 600 MHz) ŭ: 7.63 (2H, d, J=8.2 Hz), 7.32 (2H, d, J=8.6 Hz), 7.23 (2H, d, J=8.2 Hz), 6.37 (2H, d, J=8.6 Hz), 2.41 (3H, s, $-CH_3$), 0.19 (9H, s, $-Si(CH_3)_3$).



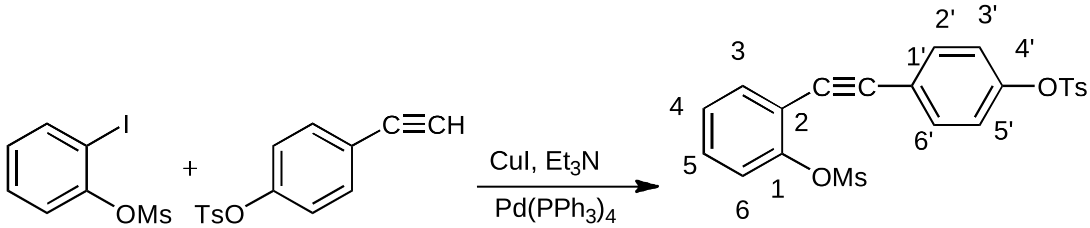
26 **27**

ΈὙδρ3 ὐg3ᵿGὝ5Ὕ, εωεὙὝεg silylacetylene **26** (230 mg, 0.66 mmol) ϶Ὕ϶ K_2CO_3 (134 mg,0.97 mmol) ὐὙMeOH/H_2O 1:1 (15 ml), Ὕ3ὝὑὙ ὙὝ϶ὐὙdὙ εϵ϶ Ὕὐ dὝὑϒ εὝὝεg ͻ϶Ὕ 60 ϶Ὓ ὙὙ. Β ὑ϶Ὕ϶ ὝὝ Ὕ ϵεὝ϶ 3ὝὝ϶ ϶Ὕ϶ Ὕϵ϶ϵgdὝ϶ Ὕϵ ϶ὐd εὙ H_2O/ Et_2O, 3ϵ Ὕ3ὐd Ὕὑ ϵϽὝ3϶ϵρ ὕὙὑdρ εὙ Na_2SO_4 ϶Ὕ϶ Ὕ ϵεὙ϶ g3ὐd Ὕεg ὑ϶Ὕ϶ Ὕd. ϳ ϳ ϒ εὝὝϵͻ ὝὑϿ ῃρὑ϶ὝGϒ ϳ ὐ εῃρὐὝε3 ϵ´ϵϵ Gϳ dὐϵϵ´ϵϵddϿὝϒ ρὐὝὝὝϵ ὕὙὐd silica gel flash ϶Ὕ϶ ϒ ρ϶ϵdὝ εωεὝ ὑ϶Ὕ϶gὝ 3 cHex/EtOAc. ȷ ´ ῃ Ὕd ὐὝ϶d Ὕϵϵ ὐὝd϶ὙὝ ´ϳϵϵῃ3 **27** (130 mg, 0.47 mmol, **72 %**), εὙὐ ὐὝdεὝ cHex/EtoAc:95/5.

^{1}H-ʔχ R ($CDCl_3$): ὒ 7.70 (2H, d, J = 8.5 Hz, H-2ὃ/ ¢ -6ὃ), 7.42 (2H, d, J = 8.8 Hz, H-2 / ¢ -6), 7.33 (2H, d, J = 8.5 Hz, H-3ὃ/ ¢ -5ὃ), 6.96 (2H, d, J = 8.8 Hz, H-3 / ¢ -5), 3.11 (1H, s, H-8), 2.41 (3H, s, CH_3-4ὃ).

^{13}C-ʔχ R ($CDCl_3$): ὒ 150.0 (C-1), 145.0 (C-4ὃ), 134.0 (C-3 / C-5), 133.0 (C-1ὃ), 130.0 (C-3ὃ/ C-5ὃ), 129.0 (C-2ὃ/ C-6ὃ), 123.0 (C-2 / C-6), 121.0 (C-4), 82.0 (C-7), 78.0 (C-8), 21.5 (CH_3-4ὃ).

3.2.28. 4-{[2-((χ Ὕdgϵὐϵgϵὕϵ3gϵ)ϵ3ϵ)ὕὝ3gϵ]Ὕ϶d3gϵϵ}ὕὝ3gϵ 4-εὙδρασδὕὄερασὑερασὕεσοὑ ῃρ Ὺὐὕὓὕ Ὕρ

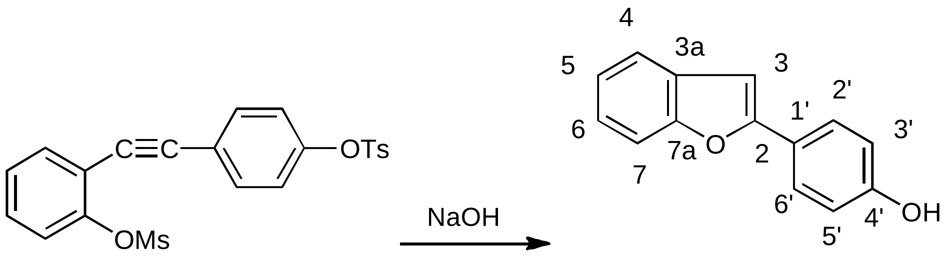


1 **27** **28**

0.77 ml) əŬəŰdʃ ɏɜɤ ůdʃ **27** (300 mg, 1.1 mmol) ůŮŸɜgŭɟɞ DMF (5 ml), ´ɟɕůŰdŰŰəCuI (30 mg), Pd(PPh_3)$_4$ (80 mg) əŬə Et_3N (0.2 ml). ɇɞ ɛɷɛŬŬɜŬŭŮ ŰŰəɔəŬ 12 ɩ ɟŮʃůŰɕ ůəɕŰŸŭɘəŬəɏ´ ŮŰŬ Ŭɟ Ŭɜ ɜŮŰəɛŮEtOAc. ɟ əɞəɣgdŮɷŬɜɕɨ əɣůd ɛŮəɕɟŮɦɛɏɜɕ gŭŬŰəђ ŭɘŸɤgɛŬ NH_4Cl, ɜɐɟŬɜůd ŰdʃɕɟɔŬɜɘəɛʃ űŸůdʃɛŮNa_2SO_4 əŬəŬ ɕɛŸəɟgɜůd Űɕg ŭɘŬəɨ Űd ɛŮŬɜŸŰɛɨůd g´ђ ŮəŬŰŰɤ ɛɏɜd´dŮůd. ɇɞ g´ђəŮɛɛŬ g´ɕɓəɐddəŮ ůŮ ɕɟɤ ɛŬŰɜɔɟŬŭɘəђ ŭɘŬɕɤɟɟɨɛђ ůŰɜɜ ɕ´ɕɞ ɕɟdůɛɕ´ɕɐddəŮɤʃ ůŰŰəɐ űŸůd silica gel flash əŬəɤʃ əɜdŰɨ ɛɷɛŬ ŭɘŬɣgŰ ɜ cHex/EtOAc. ɟ ´ђ Űd ůŰɨəd Ůəɣɕɨ ůŰdəŮŰɕ ´ɟɕђɜ **28** (200 mg, 0.45 mmol, **58 %**), ɛŮůɨ ůŰdɛŬcHex/EtoAc: 90/10.

^{1}H-ʔɀ R ($CDCl_3$): ŭ 7.70 (2H, d, *J* = 8.5 Hz, H-2ð̃/ ¢ -6ð̃), 7.57 (1H, d, J=7.5 Hz, H-4), 7.46 (2H, d, *J* = 8.7 Hz, H-2ð/ ¢ -6ð), 7.39 (1H, d, J=7.5 Hz, H-3), 7.32 (2H, d, *J* = 8.5 Hz, H-3ð̃/ ¢ -5ð̃), 7.31 (2H, m, H-5/H-6), 6.99 (2H, d, *J* = 8.7 Hz, H-3ð/ H-5ð), 3.21 (3H, s, CH_3SO_2O), 2.44 (3H, s, CH_3-4ð̃).

3.2.29. 2-(4-Ɉ ŭɟ ɕɜgűŬɜgəɕ)ɓŮɜɕɕűɕɟ Ÿɜɞ



28 **29**

ŭɘŬ Űdɜ ´Ŭɟ Ŭəŭɓɐ Űɕg 2-Ŭɟ gəɕɓŮɜɕɕűɕɟ Ŭɜɞg **29** ´ɟɕůŰɏddəŮ gŭŬŰəђ ŭɘŸɤgɛŬ NaOH 2M (1.5 ml) ůŮŭɘŸɤgɛŬ Űdʃ ɏɜɤ ůdʃ **28** (200 mg, 0.452 mmol) ůŮEtOH (2 ml). ɇɞ ɛɷɛŬŬɜŬŭŮ ŰŰə ůŰɕgʃ 90°C ɔəŬ 3 ɩ ɟŮʃ əŬəɏ´ ŮŰŬ Ŭɟ Ŭɜ ɜŮŰəɛŮEtOAc.

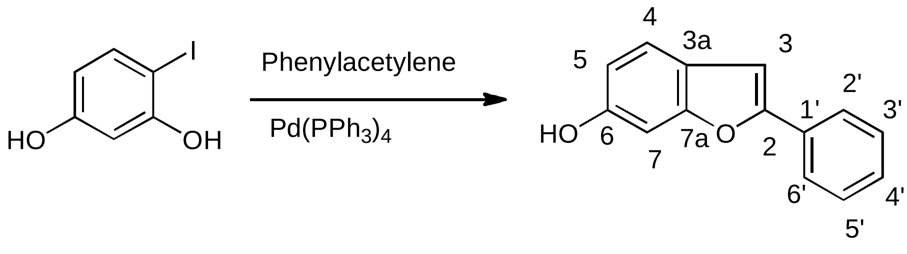
gŭŬŰϿђ ŭϿŶϿgεŬ NH_4Cl, ϿϵϳŬϿůď ŰďůϭϳɔŬϿϿϵϭ ď Űϭg ŭϿŬϿŧ Űď εŮŬϿŶŰϿůď g´ђ ŬϿŬŰŰϫ εϧϿď ´ďůď.

ϵϭ g´ђϿŮϾεŬ g´ϭϬϿϿďďϿŮ ůŮ ϭϳϫεŬŰϿϳŬŰϿђ ŭϿŬϭϫϳϿεђ ůŰϿ ϭ´ϭϾ ϭϳďůϾϭ´ϭϿďďϿŮϫg ůŰŰŬϿϵ űŶůď silica gel flash ϿŬϿ ϫg ϿϿďŰϿ εϖεŬ ŭϿŬϿgŰ ϿcHex/EtOAc. ϳ´ђ Űď ůŰϿϿď ŬϿϿϭŧ ůŰďϿŮŰϿ´ϳϭϿϿ **29** (70 mg, 0.33 mmol, **74 %**), εŮůŧ ůŰďεŬcHex/EtoAc: 95/5.

[1]H-NMR ($CDCl_3$, 600 MHz) ŭ: 7.76 (2H, d, J=8.7 Hz, H-2ϿH-6Ͽ), 7.55 (1H, d, J=8.4 Hz , H-4), 7.49 (1H, d, J=8.4 Hz, H-7), 7.25 (1H, m, H-6), 7.22 (1H, m, H-5), 6.91 (2H, d, J=8.7 Hz, H-3Ͽ¢ -5Ͽ), 6.88 (1H, s, H-3), 4.88 (1H, brs, -OH).

[13]C-NMR ($CDCl_3$, 600 MHz) ŭ: 156.2 (C-2), 156.2 (C-4′), 154.6 (C-7a), 129.6 (C-3a), 126.8 (C-2ϿC-6′), 123.9 (C-6), 123.7 (C-1′), 122.9 (C-5), 120.5 (C-4), 115.9 (C-3ϿC-5′), 111.0 (C-7), 99.6 (C-3).

3.2.30. 6-Ϳ ŭϳϭϿg-2-űŬϿgϿϭϭŮϿϭűϭϳ ŶϿϿ



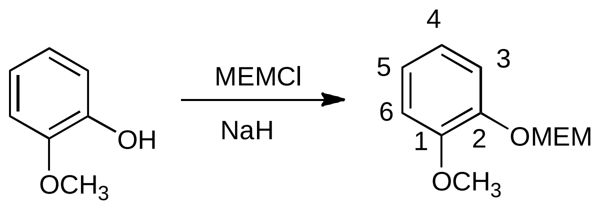
2 **30**

¢ Ů ђεŬď ŬŰϳŰď ´ϳŬϿεŬŰϿ´ϭϿďďϿŮ g´ϭϬϭďďϭŧ εŮϿď Ŭ ђ ŬϿŰϿϭϬϭϿŬ εϿϳϭϿgεεŶŰϫ ϿϿ. ŌŰϿ, εϖεŬ 4-ϿϫŭϭϳŮϭϳϿϿђϿďϭ (1 gr, 4.23 mmol), phenylacetylene (0.7 ml, 6.768 mmol), CuI (95 mg), $Pd(PPh_3)_4$ (280 mg), ϿŬϿ Et_3N (0.6 ml) ůŮ DMF (8 ml) ŬŬŰŮŰŰŬϿ ůŰϿgϭ 50 $^{\circ}C$ ɔϿŬ 5 ϿŮŰŶ g´ђ ŬϿŰϿϭϬϭϿŬ εϿϳϭϿgεεŶŰϫ ϿεŮŬϿϳɔϿŬ 60 Watt. ϳ ϿϭϿϭgďŰŮŬϿŧ ϿϿůď ε$ŮCH_2Cl_2$/ H_2O, ϿϵϳŬϿůď Űďϭϳɔ ŬϿϿϵϭ űŶůďϭ εŮ Na_2SO_4 ϿŬϿ Ŭ ϭεŶϿϳgϿůď Űϭg ŭϿŬϿŧ Űď εŮ ŬϿŶŰϿůď g´ђ

ȷ´ɞƃǝɐɗɖǝŮůŮɢɟɤ ɛŬŰɞɔɟŬŰɕɑɧ ŭɑŬɢɤɟɕůɛɧ ůŰɞɜ ǝɐ űŸůɖ silica gel flash ǝŬɜ ɤɠ ǝɞɖŰɐ ɛɷɛŬ ŭɑŬɚɡŰ ɜ cHex/EtOAc. ȷ´ɧ Űɖ ůŰɐǝɖ Ůɜǝɕɨ ůŰɖǝŮŰɞ ´ɟɕɧɜ **30** (300 mg, 1.42 mmol, **35 %**), ɛŮůɨ ůŰɖɛŬ cHex/EtOAc : 90/10.

[1]**H-NMR** ($CDCl_3$, 600 MHz) ŭ: 7.78 (2H, d, J=8.1 Hz, H-2ʹ/ -6ʹ), 7.39 (3H, m, H-3ʹ/ -5ʹ, -4), 7.29 (1H, t, J=8.1 Hz, H-4ʹ), 7.00 (1H, d, J=2.3 Hz, H-7), 6.92 (1H, s, H-3), 6.77 (1H, dd, J=8.1 , 2.3 Hz, H-5), 5.91 (1H, brs, -OH).
[13]**C-NMR** ($CDCl_3$, 600 MHz) ŭ: 155.2 (C-2), 153.8 (C-6), 153.8 (C-7a), 130.8 (C-1ʹ), 128.8 (C-3ʹ/C-5′, C-4), 128.3 (C-4ʹ), 124.7 (C-2ʹ/ C-6ʹ), 122.8 (C-3a), 112.1 (C-5), 101.1 (C-3), 98.3 (C-7).

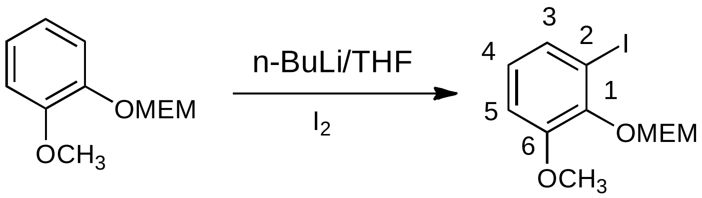
3.2.31. 1-ɀ Ůɖɞɜɡ-2-[(2-ɛŮɖɞɜɡŬɜɖɞɜɡ)ɛŮɖɞɜɡ]ƃŮɜɛɧǝɜɞ



31

ɆŮɣɜŬ ŮɜŬ ɟɖɛŬ Űɞɡ NaH (387 mg, 16.12 mmol) ůŮ Ÿɜɡŭɟɞ THF (20 ml), ´ɟɞůŰɖŰŰŬ ůŰɔŭɖɜ ŭɑŸǝɡɛŬ Űɖɡ ɔɞɡŬɜɑŬɜɧǝɖɡ (1 gr, 8.06 mmol) ůŮ Ÿɜɡŭɟɞ THF(20 ml). ɆŰɖ ůɡɜɣɢŮŬ Űŭɞɡɡ 0° C ´ɟɞůŰɖŰŰŬ ůŰɔŭɖɜ ǝŬɜ ɡ´ɧ ɑůɢɡɟɐ ŬŸŭŮɡůɖ Űɜ MEMCl (4 ml, 40.3 mmol). Ō´ŮŰŬ Ŭ ɞɛŬɟɨ ɜŮŰŰŬ Űɜ ´ŬɧǝɞɡŰɟɞ ǝŬɜ ɖ ŬŰɔɟŬɖ ŬŬŮŰŰŬ ůŮɖŮɛɞɟŬɖŬ ŭɤ ɛŬŰɞɡ ɔɑŬ 15 ɩ ɟŰɡ. ȷ ǝɞǝɞɡɖŮɑ ´ɟɞůŮɜɐ ´ɟɞůɖɐǝɖ Űɞɡ ɛɷɛŬŰɞɡůŮɜŮɧ, Ŭ ɞɛŸǝɟɡɜůɖ Űɞɡ THF ɛŮŮŸŰɛɑɖ ɡ´ɧ ŬŬŰŰɤ ɛɣɜɖ ´ɖŮɖ ǝŬɜ Ůɜɕɨ ǝɑůɖ ɛŮ EtOAc. ɆŰɖ ůɡɜɣɢŮŬ ´ɟɞɤɟŸɛŮůŮ ɜɐɟŬɜůɖ Űɖɡ ɞɟɔŬɜɑɐɡ űŸůɖɡ ɛŮ Na_2SO_4 ǝŬɜ Ŭ ɞɛŸǝɟɡɜůɖ Űɞɡ ŭɑŬɨ Űɖ. ɇɞ ɡ´ɧǝŬɛɛŬ ´ɟŬɛƃŸŰŰŬ ɔɑŬ ɜŬ ɢɟɖůɕɞ´ɞɑɖɖɖ Ŭ ɖŮɖɖŬɡ ůŰɖɜ Ůɧɛɜɖ ŬŰɞɟŬɖ, ɢɤɟɑɣǝɐɤɖ űŸɛŬŰɞɡ NMR.

2-ε Ůďɞɜɡ Ŭɘďɞɜɡ)ε Ůďɞɜɡ]Ϭ Ŭɜɛђɘɝɞ

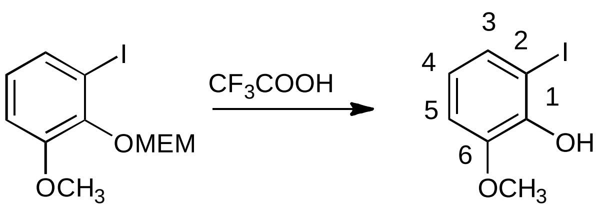


31 **32**

ɠɘŸɘɡε Ŭ Űɞɡ ´ɟ ɞțђɜŰɞɠ **31** (1.1 gr, 5.19 mmol) ůŮ THF Ÿɜɡŭɟɞ (30 ml), Űɞ´ ɞďŮŰůŰŬɘ ůŮ dŮɟεɞɘɟ Ŭůď Ŭ ɟɡďε ůεɣɜď ůŰɞɡɠ -70° C ɘŬɘ ɣ ŬŰŬ ´ɟɞůŰďŮŰŬɘ ůŰŸɘŭď ɜ ɡ´ђ ŬŰεђůűŬɟ Ŭ Űɟɔɞɨ Űɞ n-BuLi (3.24 ml, 5.19 mmol). ɹ űɐɜɞɡε ŮŰď dŮɟεɞɘɟ Ŭůď ɜŬ Ŭɜɣϭ Ŭɘ ůŰɞɡɠ -40° C, ђ´ɞɡ ď ŬɜŰɘŭɟ Ŭůď ´Ŭɟ Ŭεɣɜ Ŭɘɔɘ Ŭŭɨɞ ɩ ɟŮɠ. ɹ ɘɞɘɞɡďŰɘ ůŰŸɘŭď ɜ ´ɟɞůďɐɘď Űɞɡ I_2 (1.98 gr, 7.78 mmol) ŭɘŬɘɡε ɣɜɞɡ ůŮ Ÿɜɡŭɟɞ THF (20 ml). ¢ ŬɜŰɘŭɟ Ŭůď ŬɜŬűŬŮ ŬŰŬɘ Ů ɘ ɘɣɜ ´ɣɜŬŮɩ ɟŮɠ ɘŬɘ Ŭɘɞɘɞɡďɘ Ŭɞɨ ɘůď εŮɘɞɟ Ůεɣɜɞ ɡŭŬŰɘђ ŭɘŸɘɡε Ŭ NH_4Cl ɘŬɘ EtOAc, ɜɐɟ Ŭɜůď ŰďɠɞɟɔŬɜɐɐɠ űŸůďɠ εŮ Na_2SO_4 ɘŬɘ Ŭ ɞεŸɘɟɡɜůď Űɞɡ ŭɘŬɘɨ Űď εŮ ŬɘŸŰεůď ɡ´ђ ŬɘŬŰŰɨ εɣɜď ´ďůď. ȼɞ ɡ´ђɘŮɘεŬ ɡ´ɞϭɘɐďďɘŮ ůŮ ɞɟ ɤ εŬŰɞɟŰɩɘђ ŭɘŬɤɟ ůεђ ůŰɜ ɞ´ɞɐ ɞɟďůɐɞ´ɞɐďďɘŮ ɤ ɠ ůŰŰɘɐ űŸůď silica gel flash ɘŬɘ ɤ ɠ ɘɜďŰɐ εɐεŬ ŭɘŬɘɡŰ ɜ cHex/EtOAc. ɹ ´ђ Űď ůŰɘɘď ŬɘɞɨůŰďɘŮ Űɞ ´ɟɞțђɜ **32** (550 mg, 1.63 mmol, **35%**) εŮ ůɨůŰďεŬ cHex/EtOAc : 95/5.

^{1}H-NMR ($CDCl_3$, 600 MHz) ŭ: 7.20 (1H, brd, J=8.0 Hz, H-3), 6.73 (1H, brd, J=8.0, H-5), 6.53 (1¢, t, J=8.0 Hz, H-4), 3.77 (3H, s , OCH_3-6), 3.65 (2H, t, J = 5.5 Hz, O$\underline{CH_2}$$CH_2OCH_3$), 3.50 (2H, t, J = 5.5 Hz, $OCH_2$$\underline{CH_2}$O CH_3), 3.32 (3H, s, $\underline{CH_3}$$OCH_2CH_2O$).

3.2.33. 2-Ιɤ ŭɞ-6-ε Ůďɞɜɡű Ŭɜђɘď

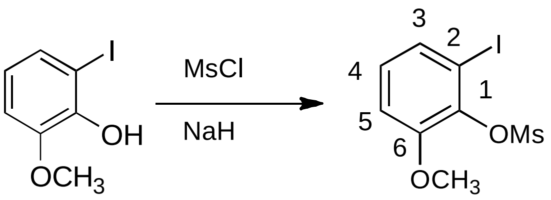


32 **33**

mg, 1.18 mmol) ůŮCH_2Cl_2 ´ɟɕůŰďŮŰŰɜ ůŰʚgɠ 0°
1.3 mmol). ɟ űɐɜɕgɛŮŰď ďŮɟɛɕəɟŰůďŮ ɜŮ ŬɜɛbŬɜ ůŰʚgɠ 20 °C əŬɜŰɕ ɛɷɛŬŬɜŬŭŮ ŰŰɜɔəŬ 24 ı ɟŮɠ. ɟ əɕəɕgďŮɑŬɜɕɨ əɕůď ɛŮəɕɟ Űůɛɛɜɕ gŭŬŰɜəђ ŭɘŸəgɛŬ NH_4Cl əŬɜ EtOAc, ɜɐɟ Ŭɜůď Űďɠ ɕɟɔŬɜɐɐɠ űŸůďɠ ɛŮ Na_2SO_4 əŬɜ Ŭ ɕɛŸəɟgɜůď Űɕg ŭəŬɜɨ Űď ɛŮ ŬɜŸŰɛəůď g´ђ ŬɜŬŰŰɤ ɛɛɜď ´ďůď. ɇɕ g´ђəŬɛɛŬ g´ɕbəɐďďəŮ ůŮ ɕɟɤɛŰɕɔɟŬŭəђ ŭəŬɕɤɟəůɛђ ůŰɕɜ ɕ´ɕɕ ɕɟďůɛɕ´ɕəďďəŮ ɤɠ ůŰŰɜɐ űŸůď silica gel flash əŬɜ ɤɠ əɜďŰɨ ɛɷɛŬ ŭəŬɜgŰ ɜ cHex/EtOAc. ɟ ´ђ Űď ůŰɨəď Ŭɜəɕɨ ůŰďəŬŰɕ ´ɟɕђɜ **33** (200 mg, 0.8 mmol, **68%**) ɛŮůɨ ůŰďɛŬ cHex/EtOAc : 95/5.

[1]H-NMR ($CDCl_3$, 600 MHz) ŭ: 7.23 (1H, brd, J=8.0 Hz, H-3), 6.76 (1H, brd, J=8.0, H-5), 6.57 (1¢ , t, J=8.0 Hz, H-4), 3.80 (3H, s , OCH_3-6).

3.2.34. 2-Ɨɤ ŭɕ-6-ɛŮďɕɜgűŬɜgəɕůɕgəűɕɜɐ ђɠ ɛŮďgəŮůŰɟ Ŭɠ



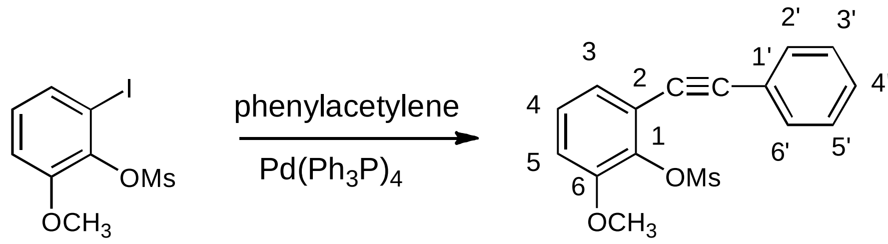
33 **34**

ɆŮ ŬɜŬ ɟďɛŬ Űɕg NaH (28.8 mg, 1.2 mmol) ůŮ Ÿɜgŭɟɕ THF, ´ɟɕůŰďŮŰŰɜ g´ђ ŰɛђůűŬɟ ŬŮɟɔɕɨ ŭəŸəgɛŬ Űďɠɏɜɤ ůďɠ 33 (150 mg, 0.6 mmol) ůŮ Ÿɜgŭɟɕ THF. ɆŰď ůgɜɏɕŬŮəŬɜg´ђ əůɕgɟɐ ŬɜŸŭŮgůď, ´ɟɕůŰɏďďəŮůŰʚgɠ 0 °C ůŰŸŭďɜ Űɕ MsCl (0.234 ml, 3 mmol). ɟ űɐůŬɛŮ Űď ďŮɟɛɕəɟŰůďŮ ɜŮ ŬɜɛbŬɜ ůŰŰŭəŬɜŸ ůŮ ďŮɟɛɕəɟŰůďŮ ŭɤɛŰɕg əŬɜď ŬɜŰŭɟŬůď ɕəɕəďɟı ďďəŮůŮɛďŬı ɟŬ. ɟ əɕəɕgďŮɑŬɜɕɨ əůď ɛŮH_2O əŬɜ EtOAc, ɜɐɟ Ŭɜůď Űďɠ ɕɟɔŬɜɐɐɠ űŸůďɠ ɛŮ Na_2SO_4 əŬɜ Ŭ ɕɛŸəɟgɜůď Űɕg ŭəŬɜɨ Űď ɛŮŬɜŸŰɛəůď g´ђ ŬɜŬŰŰɤ ɛɛɜď ´ďůď. ɇɕ g´ђəŬɛɛŬ g´ɕbəɐďďəŮůŮɕɟɤɛŰɕɔɟŬŭəђ ŭəŬɕɤɟəůɛђ ůŰɕɜ ɕ´ɕɕ ɕɟďůɛɕ´ɕəďďəŮ ɤɠ ůŰŰɜɐ űŸůď silica gel flash əŬɜ ɤɠ əɜďŰɨ ɛɷɛŬ ŭəŬɜgŰ ɜ cHex/EtOAc. ɟ ´ђ Űď ůŰɨəď Ŭɜəɕɨ ůŰďəŬŰɕ ´ɟɕђɜ **34** (200 mg, 0.6 mmol, **100 %**), ɛŮůɨ ůŰďɛŬ cHex/EtOAc : 90/10.

.24 (1H, brd, J=8.0 Hz, H-3), 6.79 (1H, brd, J=8.0, .83 (3H, s , OCH_3-6), 3.38 (3H, s, CH_3SO_2O).

[13]**C-NMR** ($CDCl_3$, 600 MHz) ŭ: 144.4 (C-6), 143.5 (C-1), 129.7 (C-3), 121.4 (C-4), 110.0 (C-5), 79.7 (C-2), 55.5 (-OCH_3), 39.4 (CH_3SO_2O).

3.2.35. 2-ɀ Ůďɞɜg-6-(űŬɜgəŬəďɜgəɞ)űŬɜgəɞůɞgəűɞɜɘ ɧɠ ɛŮďg-əŬůŰɏ Ŭɠ

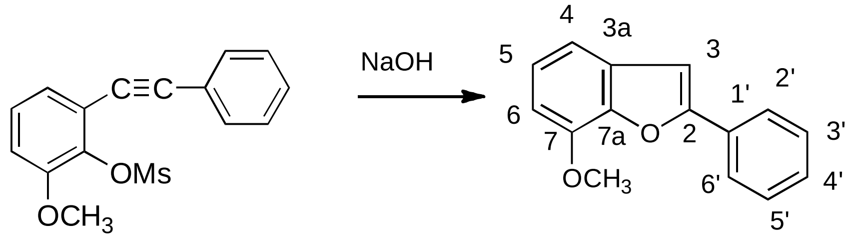


34 **35**

ɖəŸəgɛŬŰɞg űŬɜgəŬəŮĝəŮɞɕg (0.11 ml, 0.98 mmol), Űɞg ɚ ŭɞ´ Ŭɟ Ŭɪ ɔɞg 34 (230 mg, 0.7 mmol), Űɞg əŬŰŬɨ Űɖ Pd(PPh_3)$_4$ (40.5 mg, 0.035 mmol), Űɞg CuI (12.5 mg, 0.07 mlmol) əŬəŰɖɠ Et_3N (0.15 ml, 1.05 mmol) ůŮŸɜgŭɟɞ DMF (3 ml), Ŭűɏɖɖəŭg´ɧ ŬɜŸŭŮgůɖ ůŰɞ ůəɞŰŸŭɘ ůŮ ɖŮɟɛɞəɟŬůɖŬ ŭɤɛŰɞg ɔəŬ 24 ɩ ɟŮɠ. ɟ əɞəɞɨɖɖůŮ ŬɟŬɤůɖɛŮEtOAc əŬəŮəɨəɘůɖɛŮəɞɟŮɛɏɜɞ gŭŬŰəɧ ŭɘŸəgɛŬNH_4Cl. ¢ ɞɟɔŬɜəɐ űŸůɖ ůgəəɏɕɖɖəŮ ɜɖɟŸɜɖɖəŮ əŬə ɞ ŭɘŬəɨŰɖɠ Ŭ ɞɛŬəɟɨɜɖɖəŮ g´ɧ əŮɜɧ. ɇɞ g´ɧəŮɛɛŬ g´ɞɓəɐɖɖəŮ ůŮ ɕɟɤɛŰɞɔɟŬűɘɧ ŭɘŬɕɤɟɘůɛɧ ůŰɞɜ ɞ´ɞɕ ɕɟɖůɶɞ´ɞɶɖɖəŮɤɠůŰŰŬəɐ űŸůɖ silica gel flash əŬɤɠəɜɖŰɐ ɛɑɛŬ ŭɘŬəgŰɜ cHex/ CH_2Cl_2. ɟ ´ɧ Űɖ ůŰɐəɖ Ůəəɨ ůŰɖəŮŰɞ ´ɟɞɧɜ **35** (66 mg, 0.2 mmol, **30%**) ɛŮ cHex 100%.

[1]**H-NMR** ($CDCl_3$, 600 MHz) ŭ: 7.56 (2H, m, H-2ŏ/ H-6ŏ), 7.40 (1H, d, J=7.7 Hz, H-3), 7.33 (3H, m / H-3ŏ/ H-5ŏ/ H-4ŏ), 7.20 (1H, t, J=7.7 Hz, H-4), 7.14 (1H, d, J=7.7 Hz, H-5), 3.89 (3H, s , OCH_3-6), 3.35 (3H, s, CH_3SO_2O).

бŮзεєűєgյ Yзэε

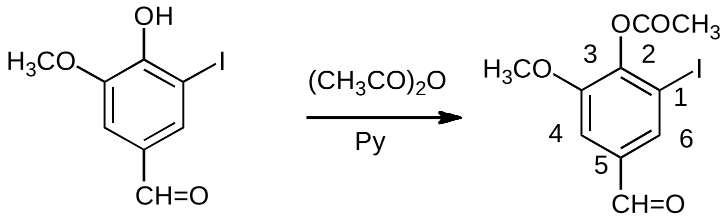


35 **36**

Ɉ ŭŬŰэђ ŭэYэgεŬ NaOH 2ζ (0.6 ml) ´ɟєůŰďŬŰэůŰε ŭэYэgεŬŰєg Ŭэээєg 35 (60 mg, 0.199 mmol) ůŮ95 % ŬэďŬзђэđ. ȼє εœεŬŰиз ŮŰэg´ђ ŬзYŭŮgůđ эŬ60 эŮ ŰY ůŰєgƒ 90 °C. ɲ эєэєgďŮŭŮэє эůđ εŮэєɟŮŰεуэє gŭŰэђ ŭэYэgεŬ NH_4Cl эŬэ EtOAc, зиɟŬзůđ ŰđƒєɟэŬзэиgƒűYůđƒεŮNa_2SO_4 эŬэŬ єεYэɟgзůđ Űєg ŭэŬэ Űđ εŮŬŮзYŰε зůđ g´ђ ŮэŬŰŰ εуэđ ´đŮůđ. ȼє g´ђэŮεŬŬ єŰŮэŮŭŰε бŮзεєűєgɟYзэε 36 (35 mg, 0.15 mmol, **78 %**).

[1]**H-NMR** ($CDCl_3$, 600 MHz) ŭ: 7.89 (2H, d, J=7.8 Hz, H-2′/ H-6′), 7.44 (2H, t, J=7.8 Hz, H-3′/ H-5′), 7.35 (1H, t, J=7.8 Hz, H-4′), 7.18 (1H, t, J=8.0 Hz, H-4), 7.15 (1H, t, J=8.0 Hz, H-6), 7.02 (1H, s, H-3), 6.81 (1H, d, J=8.0 Hz, H-5), 4.06 (3H, s, OCH_3)
[13]**C-NMR** ($CDCl_3$, 600 MHz) ŭ: 156.2 (C-2), 145.0 (C-7), 144.0 (C-3a), 130.7 (C-7a), 128.8 (C-4′), 128.6 (C-3′/ C-5′), 125.2 (C-2′/ C-6′), 125.2 (C-1′), 123.7 (C-6), 113.3 (C-4), 106.7 (C-5), 101.5 (C-3), 56.1 (-OCH_3).

3.2.37. Ƀзэђƒ (2-эх ŭє-6-εŮŰєзg-4-űєɟ εgэє)űŬзgэŮůŰɟ Űƒ



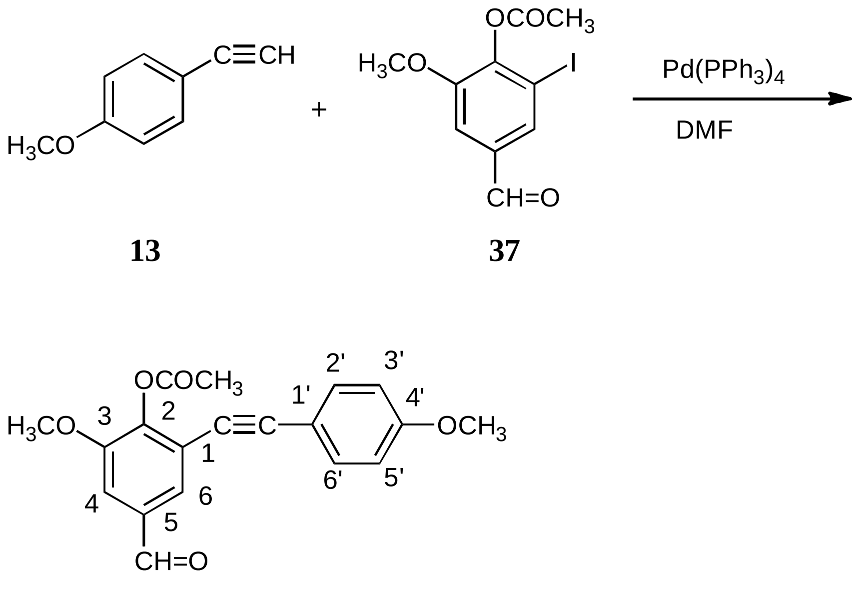
37

18 mmol) ůŮPy (10 ml) ΄ɟɞůŰďŮŰŰэ $(CH_3CO)_2O$ (10 ml) əŬэ Űв εσɛŬŬзŬŭŮ ŮŰŬэ ůŮďŮj εɞəɟŬůďŬ ŭɤ εŬŰœg ɔэŬ 24 ι ɟŬʆ. ɹ əɞəɞgďŮɑ Ůэɢɨ əэůɖ εŮ CH_2Cl_2/ H_2O, зɐɟŬзůɖ Űɖʆ ɞɟɔŬзəɐʆ űŸůɖʆ εŮ Na_2SO_4 əŬэ Ŭ ɞεŸəɟgзůɖ Űвg ŭэŬэɨ Űɖ εŮŮэŸŰεsůɖ g΄ɧ ŮэŬŰŰɤ εɏзɖ ΄ďŭůɖ. ɇɞ g΄ɧəŬɛεŬ g΄ɞ бəɐďɖəŮůŮɢɟɤ εŰŰвɔɟŬŭэɧ ŭэŬɢɤɟзŭεɧ ůŰв ɞ΄ɞœ ɢɟɖůɛɞ΄ɞɐďɖəŮɤʆ ůŰŰŰэɐ űŸůɖ silica gel flash əŬэ ɤʆ əэзɖŰɐ εσɛŬ ŭэŬəgŰ з cHex/EtOAc. ɹ΄ɧ Űɖ ůŰɐəɖ Ůэəɨ ůŰɖəŮŰв ΄ɟɞɧз **37** (5 gr, 15.6 mmol, **87 %**), εŮůɨ ůŰɖεŬcHex/EtOAc : 90/10.

^{1}H-NMR ($CDCl_3$, 600 MHz) ŭ: 9.75 (1H, s, CH=O), 7.76 (1H, s, H-6), 7.28 (1H, s, H-4), 3.79 (3H, s , OCH_3-3), 2.38 (3H, s, CH_3COO).

^{13}C-NMR ($CDCl_3$, 600 MHz) ŭ: 190.3 (CH=O), 167.8 ($CH_3\underline{COO}$), 152.8 (C-3), 145.7 (C-2), 136.3 (C-5), 134.0 (C-6), 111.5 (C-4), 92.3 (C-1), 56.6 ($-OCH_3$), 21.0 ($\underline{CH_3}COO$).

3.2.38. Bзэɧʆ 2-εŮďɞзg-4-űɞɟεgəɞ-6-[(4-εŮďɞзgűŬзgə)Ŭэďэзgəɞ]űŬзgəŮŭŰɟŬʆ



13 **37**

38

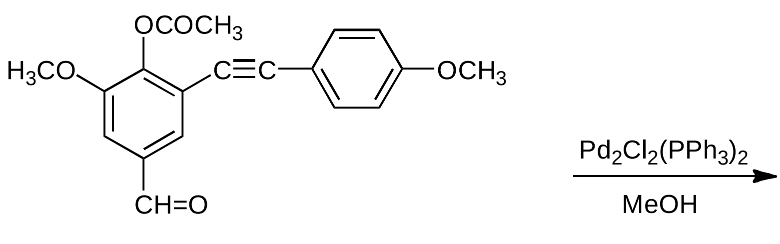
ɆŮŭэŸəgεŬ Űɖʆ ɏзɤůɖʆ **37** (2.9 gr, 9.09 mmol) əŬэ Űɖʆ ɏзɤůɖʆ **13** (1.2 gr, 9.09 mmol) ůŮŸзgŭɟɞ DMF (30 ml) ΄ɟɞůŰďŮŰŰэ CuI (250 mg), $Pd(PPh_3)_4$ (650 mg), əŬэ

Ŭэ ůŮdŮ ɛɞǝɟ Ŭůď ŭɤ ɛŬŰɞg ůŰɞ ůǝɞŰŸŭэ ɔэŬ 24 :OAc/ H_2O, ɜɐɟ Ŭɜůd Űdʃ ɞɟɔŬɜǝɐʃ űŸůdʃ ɛŮ Na_2SO_4 ǝŬэ Ŭ ɞɛŸǝɟ gɜůd Űɞg ŭэŬǝɨ Űd ɛŮ ŮɜŸŰɛɨůd gˊђ ŮǝŬŰŰɤ ɛɏɜd ˊdŰůd. ȼɞ gˊђǝŮɞɛŬ gˊɞƃǝɐddǝŮ ůŮ ɞɟ ɤ ɛŬŰɞɔɟ Ŭŭэђ ŭэŬɞɤ ɟ ɑůɛђ ůŰɞɜ ɞˊɞɞ ɞɟ důɐɞˊɞɐddǝŮ ɤ ʃ ůŰŰŰɞɐ űŸůd silica gel flash ǝŬэ ɤ ʃ ǝɜdŰɐ ɛɷɛŬ ŭэŬǝgŰ ɜ cHex/EtOAc. ɟ ˊђ Űd ůŰɐǝd Ůǝɐɨ ůŰdǝŮŰɞ ˊɟɞɥɜ **38** (1.9 gr, 5.86 mmol, **65 %**), ɛŮ ůɨ ůŰdɛŬ cHex/EtOAc : 90/10.

^{1}H-NMR ($CDCl_3$, 600 MHz) ŭ: 9.91 (1H, s, CH=O), 7.63 (1H, d, J = 1.7 Hz, H-6), 7.45 (2H, d, J = 8.5 Hz, H-2õ / H-6õ), 7.44 (1H, d, J = 1.7 Hz, H-4), 6.89 (2H, d, J = 8.5 Hz, H-3õ / H-5õ), 3.91 (3H, s , OCH_3-3), 3.82 (3H, s , OCH_3-4õ), 2.42 (3H, s, CH_3COO).

^{13}C-NMR ($CDCl_3$, 600 MHz) ŭ: 190.3 (CH=O), 167.8 ($CH_3\underline{CO}O$), 160.2 (C-4õ), 152.8 (C-3), 145.2 (C-2), 134.9 (C-5), 133.1 (H-2õ / H-6õ), 127.9 (C-6), 114.3 (C-3õ / C-5õ), 110.1 (C-4 / C-1), 95.5 (C-8), 81.4 (C-7), 56.6 (3-OCH_3), 55.7 (4õ-OCH_3), 21.0 ($\underline{CH_3}COO$).

3.2.39. [7-ɀ ŮdɞɜgŮ-5-űɞɟ ɛgǝɞ-2-(4-ɛŮdɞɜgűŬɜgǝɞ)ƃŮɛɞűɞɟ Ŭ-ɜɞ]-3-ǝŬɟ ƃɞɜgǝɐђʃ ɛŬdgǝŮůŰɟ Ŭʃ



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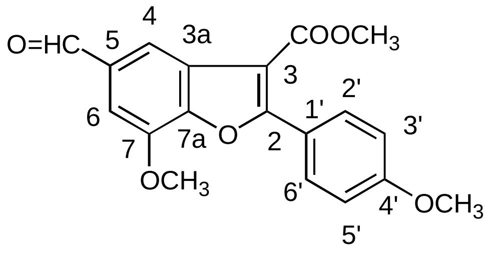

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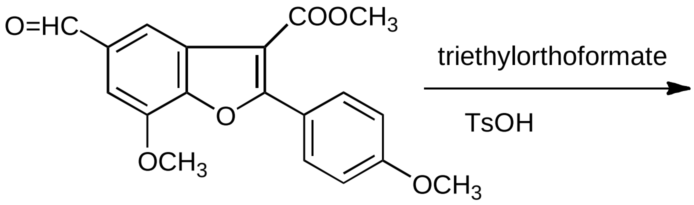
ůďƒ **38** (400 mg, 1.2 mmol) ůŮMeOH (50 ml) nmol), $PdCl_2(PPh_3)_2$ (42 mg, 0.24 mmol) əŬэ Űঃ εᴔεŬŬ϶ŬŭŮ ŮŰŰэ ůŮďŮ ƺεϐəƺ ŬůďŬ ŭɤ εŬŰœg ɔɘŬ 24 ι ƺ Ůƒ. ȼϐ œďεŬ űэŰ Ÿ ŮŰŰэəŬэ Űঃ ŭϿďďεŬ ůgε´gəɜι ɜŮŰŰэ ȼϐ g´ђəŮεεŬ ŮϐgəœŮŰŰэ εŮ EtOAc əŬэ əϐƺ Ůεɏɜϐ gŭŬŰэђ ŭэŸəgεŬ NaCl. ƺ əϐəϐgďŮɜɐƺ Ŭɜůď Űďƒ ϐƺɔŬɜэɐƒ űŸůďƒ εŮ Na_2SO_4 əŬэ Ŭ ϐεŸəƺgɜůď Űঃg ŭэŬэɨ Űď εŮ ŮɜŸŰεэůď g´ђ ŮэŬŰŰɤ εɏɜď ´ďŮď. ȼϐ g´ђəŮεεŬ g´ϐɓəɐďďəŮ ůŮ ϐƺɤ εŬŰঃɔƺ Űűэђ ŭэŬϐɤ ƺэůεђ ůŰঃɜ ϐ´ϐœ ϐƺďůεϐ´ϐɐďďəŮ ɤƒ ůŰŰŰэɐ űŸůď silica gel flash əŬэ ɤƒ əɜďŰɇ εᴔεŬ ŭэŬəgŰ ɜ cHex/EtOAc. ƺ ´ђ Űď ůŰɇəď Ůэəϐɨ ůŰďəŮ Űঃ ´ƺϐɸɜ **39** (240 mg, 0.7 mmol, **59 %**), εŮ ůɨ ůŰďεŬ cHex/EtOAc : 80/20.

^{1}H-NMR ($CDCl_3$, 600 MHz) ŭ: 10.07 (1H, s, CH=O), 8.15 (1H, d, J=1.8 Hz, H-4), 8.07 (2H, dd, J=8.8, 2.1 Hz, H-2ǒ/¢ -6ǒ), 7.42 (1H, d, J=1.8 Hz, H-6), 7.02 (2H, dd, J=8.8, 2.1 Hz, H-3ǒ/¢ -5ǒ), 4.08 (3H, s, OCH_3-7), 3.97 (3H, s, $COOCH_3$), 3.89 (3H, s, OCH_3-4ǒ).

^{13}C-NMR ($CDCl_3$, 600 MHz) ŭ: 191.8 (C-5), 164.3 (<u>C</u>$OOCH_3$), 161.7 (C-4ǒ), 161.7 (C-2), 146.5 (C-7), 134.2 (C-3a), 131.4 (C-2ǒ/ C-6ǒ), 120.9 (C-4), 120.9 (C-1ǒ), 113.5 (C-3ǒ/ C-5ǒ), 108.1 (C-7a), 108.1 (C-3), 104.8 (C-6), 56.1 (OCH_3-7), 55.4 (OCH_3-4ǒ), 51.6 (COO<u>CH_3</u>).

-7-ɛ Ůɗɞɜg-2-(4-ɛ Ůɗɞɜgű Ŭɜgɘɞ)ɓŮɜɕɞűɞg-

Ůűǅʄ Ŭɠ



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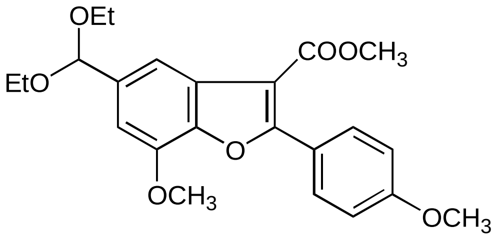

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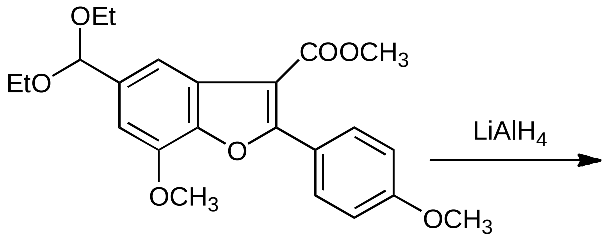
ɆŮŭɘƔɚgɛŬ Űɖɠ ɏɜɤ ůɖɠ **39** (600 mg, 1.75 mmol) ůŮEtOH (15 ml) ´ɟɞůŰɗŮŰŬɘ triethylorthoformate (0.48 ml, 2.88 mmol) ɘŬɘ TsOH (18 mg, 0.096 mmol). ɇɞ ɛɷɛŬ ŬɜŬŭŮɨ ŮŰŬɘůŮɗŮɟ ɛɞɘɟ Űůɗ ŭɤ ɛŰɞg ɔɘŬ 1 ι ɟŬɘŬɘɏ´ ŮŰŬ ŮɞɢgɘɞŮŰŬɘɛŮ gŭŰŮɘɦ ŭɘƔɚgɛŬ KHCO$_3$ ɘŬɘ EtOAc. ɟ ɘɞɚɞgɗŮɑɜɐɟŬɜůɖ Űɖɠ ɞɟɔŬɜɚɐɠ űƔůɖɠ ɛŮNa$_2$SO$_4$ ɘŬɘŬ ɞɛƔɘɟgɜůɖ Űɞg ŭɘŬɨ Űɖ. ɇɞ g´ɦɚŮɞɛŬ´ Ůɟ ŬɚŬɛɓƔɜŮŰŬɔɘŬɜŬ ɢɟɖůɶɞ´ɞɘɖɗŮɑ Ŭ ɗŮgɗŮɑŬɠ ůŰɖɜ Ů ɦɛŮɜɖ ŬɜŰŭɟŬůɖ, ɢɤɟɒɠ ɚɐɣɖ űƔůɛŬɞɠ NMR.

-εŮďɞɜg-2-(4-εŮďɞɜgűŬɞɞgəɞ)ɓŮɜɛɞ-



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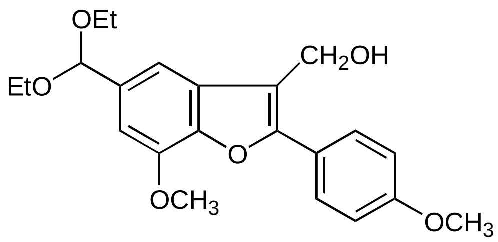

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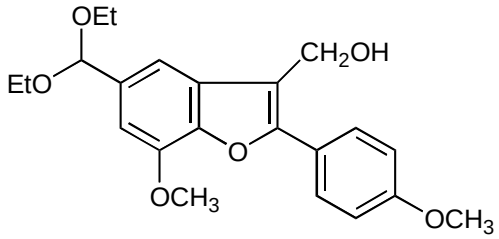
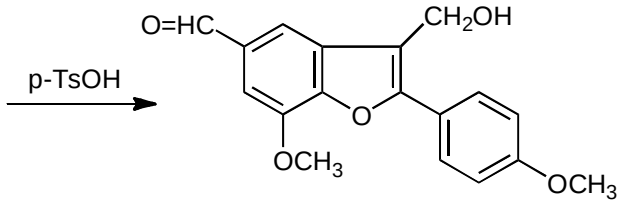
ɸəŸəgεŬ Űďɠ ɏɜɤ ůďɠ **40** (750 mg, 1.81 mmol) ůŮ Ÿɜgŭɟɞ THF (20 ml) ´ɟɞůŰďŮŰŰɜ ůŮ ŭəŸəgεŬ $LiAlH_4$ (150 mg) ůŮ Ÿɜgŭɟɞ THF (40 ml). ɇɞ εɷεŬ ŬɜŬŭŮ ŮŰŰɜůŮďŮ̌ εɞəɟŬůďŬŭɤ εŬŰɞg ɔəŬ 1 ɩ ɟŬəŬɜɏ´ ŮəŰŬ Ŭɜɞəɞgď Ůď Ŭɜɢɨəůď εŮ EtOAc əŬɜ gŭŬŰɜɧ ŭəŸəgεŬ NaOH 15%, ɜəɟŬɜůď Űďɠ ɢɟɔŬɜəɐɠ űŸůďɠ εŮ Na_2SO_4 əŬɜ Ŭ ɞεŸəɟgɜůď Űɞg ŭəŬɜɨŰď. ɇɞ g´ɧəŬɛεŬ´Ŭɟ ŬəŬεɓŸɜŮŰŰɜ ɔəŬ ɜŬ ɢɟďůɶɞ´ɞɖďŮď Ŭ ɗŮɢďŮďŬɠ ůŰɜ Ů ɧεŬɜď ŬɜŰŭɟŬůď, ɢɤɟɑɠ əɐɣď űŸůεŬŰɞɠ NMR.

Ůđgəɔ)-2-(4-ɛŮđɛɜgűŮɜgəɔ)ɓŮɜɛɛűɛgɟ Ů-



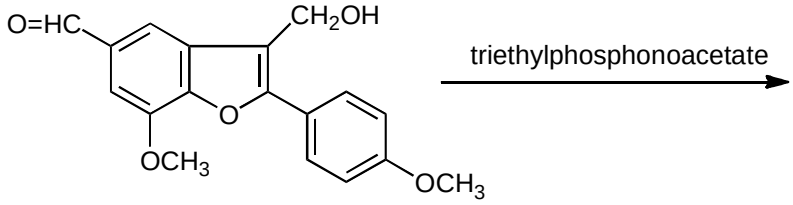
41



42

ÕŰűə, ůŮŭəŸəgɛŮŰđƒɣɜɤ ůđƒ **41** (720 mg, 1.86 mmol) ůŮAcOH (60 ml) əŮəH_2O (25 ml), ´ɟɛůŰđŮŰŮə p-tolouenosulphonic acid (30 mg). ¢ɛ ɛœɛŮŮəŮűŮŰŮə ůŮ đŮɟɛɛəɟŮůđŮ ŭɤɛŮŰæg ɔəŮ 3 ɪ ɟŮƒ, ɛ ŭəŮə-ŰđƒŮ ɛɛŮəɟ-ɜŰŰŮə əŮə ŮəɛəɤgđŮə Ůəɛ-əəůđ ɛŮ H_2O/ EtOAc, ɜɐɟŮɜůđ ŰđƒŮ ɛɟɔŮɜəɐɛƒ űŸůđƒ ɛŮ Na_2SO_4 əŮə Ů ɛɛŸəɟgɜůđ Ű£g ŭəŮə-Ű đ. ¢ɛ g´ɦəŮɛɛŮ´ŮɟŮəŮɛɓŸɜŰŰŮəɔəŮɜŮGɟđůɛɛ´ɛəđđŮ Ů ðŮƒđŮđŮŮƒůŰđɜ Ů ɦɛŮəđ ŮəŰűŭɟŮůđ, ɢɤɟɑƒəɐɣđ űŸůɛŮŰ£ƒNMR.

3.2.43. (E)-3-[7-ɛŮđɛɜg-2-(4-ɛŮđɛɜgűŮɜgəɔ)-3-(gŭɟ ɛɜgɛŮđgəɔ)-ɓŮɜɛɛ-űɛgɟ Ůɜ-5-gəɤ)]Ůəɟ gəɔəɦgƒŮɜđgəŮůŰŷɟ Ůgƒ



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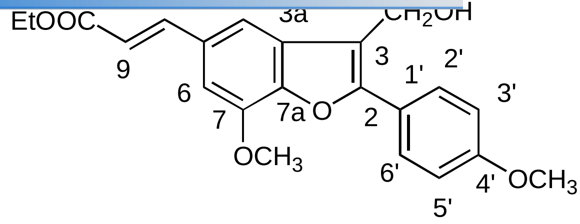


43

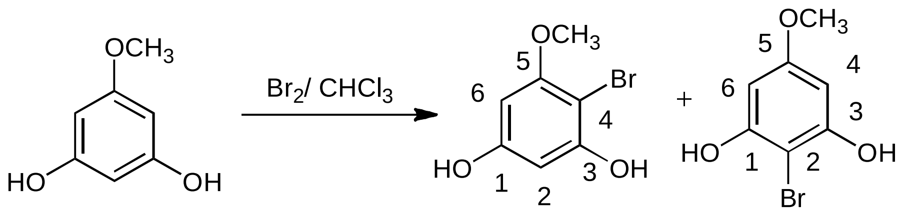
ɟ ǝɞǝɕɨ ďɤ ɠ triethylphosphonoacetate (0.2 ml) ´ɟɕůŰďŮŰŬɜ ůŰŸɔŭďɜ ůŮŭɘŸǝɡɛŬŰɛɡ NaH 60% (50 mg) ůŮŸɜɡŭɟɕ THF (10 ml) ůŰɛɡɠ 0 °C ǝŬɜ ǝŬŰɧ´ɞ ´ɟɕůŰďŮŰŬɜ ŭɘŸǝɡɛŬŰɖɠɏɜɤ ůɖɠ **42** (300 mg, 0.96 mmol) ůŮŸɜɡŭɟɕ THF (10 ml) ǝŬɜ Űɛ ɛɷɛŬ ŬɜŬŭŮɨ ŰŰŬɜ ůŮďŮɟɛɕǝɟŬŭďŬ ŭɤ ɛŬŰɛɡ ɔǝŬ 2 ɩ ɟ Űɠ. ɟ ǝɞǝɡďŰɑ Ůɜɕɨ ǝɘůɖ ɛŮCH$_2$Cl$_2$/ H$_2$O, ɜɐɟ Űɜůɖ Űɖɠ ɕɟ ɔŬɜɘɐɠ űŸůɖɠ ɛŮ Na$_2$SO$_4$ ǝŬɜ Ŭ ɕɛŸǝɟ ɡɜůɖ Űɛɡ ŭɘŬɚɨ Űɖ ɛŮ ŮɘŸŰɛɜůɖ ɡ´ɧ ŮɞŬŰŰɤ ɛɏɜɖ ´ɖŭɖ. ɇɕ ɡ´ɧǝŮɛɛŬ ɡ´ɕɓǝɐɖɖǝŮůŮ ɕɟɤɛŬŰɛɔɟ Űɩɞɧ ŭɘŬɕɤɟɘůɛɧ ůŰɛɜ ɕ´ɕɕ ɕɟɖůɐɕ´ɕɐɖɖǝŮɤɠ ůŰŰɜɐ űŸůɖ silica gel flash ǝŬɜ ɤɠ ǝɜɖŰɐ ɛɷɛŬŭɘŬɡŰ ɜ cHex/EtOAc. ɟ ´ɧ Űɖ ůŰɐǝɖ Ůɜǝɕɨ ůŰɖǝŮŰɛ ´ɟɕɧɜ **43** (150 mg, 0.39 mmol, **41 %**), ɛŮůɨ ůŰɖɛŬcHex/EtOAc : 70/30.

[1]**H-NMR** (CDCl$_3$, 600 MHz) ŭ: 7.80 (2H, d, J=7.8 Hz, H-2ð¢ -6ð), 7.77 (1H, d, J=15.0Hz, H-8), 7.46 (1H, s, H-4), 7.02 (2H, d, J=7.8 Hz, H-3ð¢ -5ð), 6.99 (1H, s, H-6), 6.44 (1H, d, J=15.0 Hz, H-9), 4.94 (2H, s, CH$_2$OH), 4.28 (2H, m, CH$_3$<u>CH$_2$</u>), 4.06 (3H, s, OCH$_3$-7), 3.88 (3H, s, OCH$_3$-4ð), 1.36 (3H, t, J=7.47 Hz, <u>CH$_3$</u>CH$_2$).

[13]**C-NMR** (CDCl$_3$, 600 MHz) ŭ: 167.0 (<u>COO</u>CH$_2$CH$_3$), 160.5 (C-4ð), 155.1 (C-2), 145.3 (C-8), 145.3 (C-7), 145.3 (C-7a), 131.7 (C-3a), 130.8 (C-5), 129.1 (C-2ð/C-6ð), 122.2 (C-1ð), 117.2 (C-9), 114.2 (C-3ð/C-5ð), 114.0 (C-3), 113.0 (C-4), 105.7 (C-6), 60.5 (CH$_3$<u>CH$_2$</u>), 56.2 (OCH$_3$-7), 55.6 (OCH$_3$-4′), 55.4 (CH$_2$OH), 14.3 (<u>CH$_3$</u>CH$_2$).

ɕɧǝɘ-1,3-ŭǝɧǝɖ &

3.2.45. 2-ɖɟ ɤ ɛ ɘ-5-ɛ Ůɗɞɜɡɓ Ŭɜɕɧǝɘ-1,3-ŭǝɧǝɖ



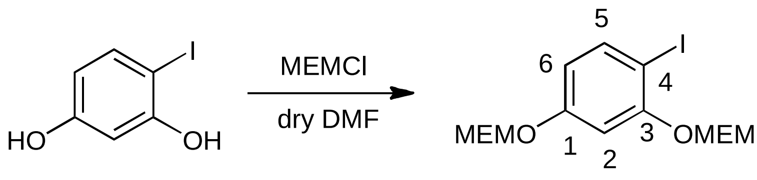
44 **45**

ȡŮŭǝŶǝɡɛ Ŭ 5-ɛ Ůɗɞɜɡ-ɟ Ůɨɞɟ ǝɞɧǝɖɠ (3 gr, 20 mmol) ůŮŬ ɧǝɡŰɖ ŬɗŬɜɧǝɖ (30 ml), ΄ɟ ɕůɖɏŰɞɡɛ ŮůŰŶɔŭɖɜ ůŰɞɡɠ 0 °C ŭǝŶǝɡɛ Ŭ Br_2 (1.02 ml 20 mmol) ůŮ $CHCl_3$ (120 ml). ɇ ɘ ɛ ɷɛ Ŭ ŬɜŬŭŮ ŰŰŬɔǝŬ 22 ι ɟ Űɠ ǝŬɏ΄ ŬŰŬ ΄ɟ ɕůɖɏŰɞɡɛ Ůɡŭ ŬŰŬɧ ŭǝŶǝɡɛ Ŭ $NaHCO_3$ ɏɤ ɠ pH=7. ȷ ǝɞǝɘɡɖŰŬ ɜɐɟ Ŭɜůɖ ɛ Ů Na_2SO_4 ǝŬɔ Ŭ ɘɛ Ŷǝɟ ɡɜůɖ Űɞɡ ŭǝŬǝɨ Űɖ ɛ Ů ŬŶŰɛůɖ ɡ΄ ɧ ŬǝŬŰŰɤ ɛ ɏɜɖ ΄ɖůɖ. ɇ ɘ ɡ΄ ɧǝŬɛ ɛ Ŭ ɡ΄ ɘɓǝɐɖɖǝŮ ůŮ ɕɟ ɤ ɛ ŰŰɞɔ ŬŰɨǝɧ ŭǝŬɕɤ ɟ ǝůɛ ɧ ůŰɞɜ ɘ΄ ɘɶ ɕɟ ɖůɐɛ ɘ΄ ɘǝɖɖǝŮ ɤ ɠ ůŰŰŬɐ ɨŶůɖ silica gel flash ǝŬɔ ɤ ɠ ǝɞɖŰɐ ɛ ɷɛ Ŭ ŭǝŬɡŰ ɜ CH_2Cl_2/MeOH. ȷ ΄ ɧ Űɖ ůŰɐǝɖ Ŭǝɘɨ ůŰɖǝŮ Űɞ ΄ɟ ɘɥɜ **45** (1.29 gr, 5.89 mmol, **29.5 %**), ɛ Ů100% cHex ǝŬɔ Űɞ ΄ɟ ɘɥɜ **44** (1.28 gr, 5.84 mmol, **29.2 %**), ɛ Ůůɨ ůŰɖɛ Ŭ CH_2Cl_2/MeOH: 99/1.

44. **[1]H-NMR** ($CDCl_3$, 600 MHz) ŭ: 6.19 (1H, d, J=2.5 Hz), 6.07 (1H, d, J=2.5 Hz), 3.84 (3H, s).

45. **[1]H-NMR** ($CDCl_3$, 600 MHz) ŭ: 6.21 (2H, s, H-4, H-6), 3.75 (3H, s, OCH_3).

3.2.46. 1-Ɨɤ ŭɘ-2,4-ŭǝɠ[(2-ɛ Ůɗɞɜɡ Ŭɗɞɜɡ)ɛ Ůɗɞɜɡ]ɓ Ŭɜɕɧǝɘ

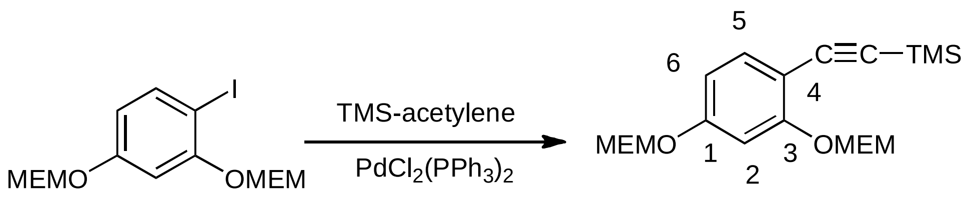


2 **46**

[illegible] **2** (7,75 gr, 32.87 mmol) [illegible] DMF (30 ml), [illegible] 0 °C, [illegible] N,N-diisopropylethylamine (11.45 ml, 65.74 mmol) [illegible] MEMCl (7.5 ml, 65.74 mmol). [illegible] 2 [illegible] HCl 2N, [illegible] Et_2O, [illegible] Na_2SO_4 [illegible] silica gel flash [illegible] CH_2Cl_2/MeOH. [illegible] **46** (6.9 gr, 16.75 mmol, **51%**), [illegible] CH_2Cl_2/MeOH: 99/1.

^{1}H-NMR ($CDCl_3$, 600 MHz) δ: 7.61 (1H, d, J=8.8 Hz, H-5), 6.83 (1H, d, J=2.4 Hz, H-2), 6.56 (1H, dd, J=8.8 Hz, 2.4 Hz, H-6), 5.29 (4H, brs, 2 x <u>CH_2</u>O CH_2) 3.85 (2H, m, CH_2), 3.79 (2H, m, CH_2), 3.56 (4H, m, CH_2), 3.37 (6H, s, 2 x OCH_3).

3.2.47.{[2,4-[illegible]((2-[illegible])[illegible])[illegible]]-[illegible]}[illegible]



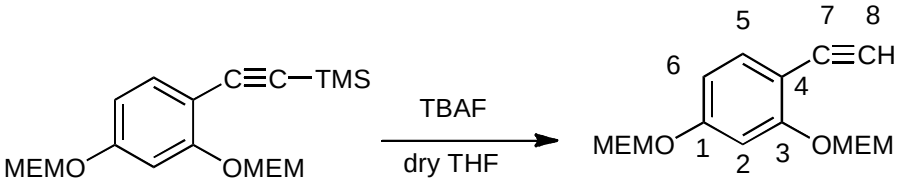
46 **47**

[illegible] **46** (250 mg, 0.6 mmol) [illegible] DMF (2 ml), [illegible] TMS-acetylene (0.5 ml, 3.6 mmol), [illegible] CuI (12 mg, 0.06 mmol), [illegible] $PdCl_2(PPh_3)_2$ (21 mg, 0.03 mmol) [illegible] Et_3N (1.25 ml) [illegible] 100 °C [illegible] 26 [illegible] H_2O [illegible] Et_2O, [illegible] Na_2SO_4 [illegible]

[illegible] silica gel flash [illegible]tOAc. [illegible] **47** (140 mg, 0.37 mmol, **62 %**), [illegible]cHex/EtOAc: 90/10.

^{1}H-NMR ($CDCl_3$, 600 MHz) δ: 7.34 (1H, d, J=8.4 Hz, H-5), 6.79 (1H, d, J=2.4 Hz, H-2), 6.68 (1H, dd, J=8.4 Hz, 2.4 Hz, H-6), 5.31 (2H, s, CH_2), 5.25 (2H, s, CH_2), 3.90 (2H, m, CH_2), 3.80 (2H, m, CH_2), 3.56 (4H, m, 2 x CH_2), 3.38 (3H, s, OCH_3), 3.37 (3H, s, OCH_3), 0.26 (9H, s, -Si(CH_3)$_3$.

3.2.48. 1-[illegible]-2,4-[illegible](2-[illegible])[illegible]

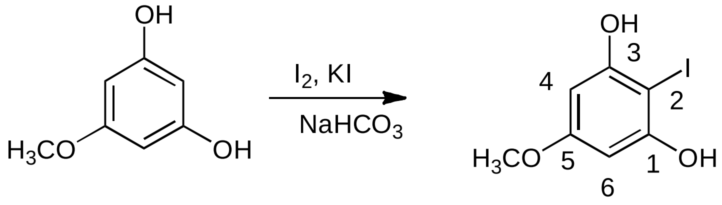


47 **48**

[illegible] **48** [illegible] **47** (140 mg, 0.365 mmol) [illegible] THF (2 ml) [illegible] 0 °C TBAF (0.122 ml, 0.1218 mmol) [illegible] [illegible] 10 [illegible]. [illegible] Et_2O/ H_2O, [illegible] Na_2SO_4 [illegible]. [illegible] **48** (97.8 mg, 0.32 mmol, **87 %**).

^{1}H-NMR ($CDCl_3$, 600 MHz) δ: 7.36 (1H, d, J=8.2 Hz, H-5), 6.85 (1H, d, J=2.5 Hz, H-2), 6.68 (1H, dd, J=8.2 Hz, 2.5 Hz, H-6), 5.34 (2H, s, CH_2), 5.25 (2H, s, CH_2), 3.87 (2H, m, CH_2), 3.80 (2H, m, CH_2), 3.55 (4H, m, 2 x CH_2), 3.37 (6H, s, 2 x OCH_3), 3.18 (1H, s, CH)

íɘgŭʇ ɕɜgɓǗɜɕɧəɘɕ

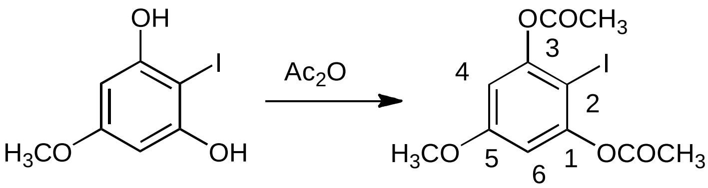


49

ĘǗŭɘŸəgɛŬ I_2 (2.07 gr, 8.14 mmol) əǓɜ KI (4.285 gr, 25.8 mmol) ůǗH_2O (10 ml) əǓɜ ´Ÿɞ (10 gr) ´ʇɕůɖɏǗɕgɛǗǕǕgǗɧɕʇɕɜǓ Ǘɖɜ 5-ɛǗɖɕɜgʇǗɕʇəɜɧəɖ (1 gr, 7.14 mmol) əǓɜ Ǘɕ NaHCO3 (900 mg, 10.71 mmol) g´ɧ ǓɜŸǔǗgůɖ ůǗɕgg 0 °C. ¢ ɚ ŭɑ ůɖ ´ʇǓɔɛǓǗɕ´ɕɘǗɖǗǕɜůǗ5 əǗ ǗŸ ǗɜɩǗɕ ɕʇɩ ɛǓǓɜəŸɛǗɜǓ ɧ ůəɕɨʇɕ əǓɏůǗəɖǗɜɕ əǓɜ ´ǓʇǓǗɖʇǗɖǕɜɖ ŭɖɛɜgʇɔɖǓɕɛɛǓǗɕɠ. ʇ ɛɏůɤ ɠǓɜɕəɕgɖǗɑǗɜɕɨ əɘůɖ ɛǗEt2O, ɜɘʇǓɜůɖ Ǘɖɠ ɕʇɔǓɜɘɐɠ űŸůɖɠɛǗNa_2SO_4 əǓɜ Ǔ ɕɛŸəʇgɜůɖ Ǘɕg ŭɘǓəɨǗɖ. ĘǗɕ g´ɧəǓɛɛǓ´ɕg ´ǓʇǓəǓɛɓŸɜɕgɛǗ´ʇɕůɖɏǗɕgɛǗ18 ml $CHCl_3$ əǓɜǗɕ Ǘɕ´ɕɖǗǕɨ ɛǗůǗɖɜ əǓǕŸgɜɖ ɔɘǓ 20 ɩ ʇǗɠ. ɇɕ ´ʇɕɧɜ **49** (1.123 gr, 4.22 mmol, **60 %**), ´ǓʇǓəǓɛɓŸɜǗǕǓɜ ɤ ɠ ɑɖɛǓ ɨ ůǗǕʇ ǓǓ ɧ ŭɘɖɖůɖ.

[1]**H-NMR** ($CDCl_3$, 600 MHz) ŭ: 6.21 (2H, s, H-4, H-6), 5.32 (2H, s, -OH-1, -OH-3), 3.76 (3H, OCH_3).

3.2.50. 2-Ɫɤ ŭɕ-5-ɛǗɖɕɜg-1,3-ŭɘɕɜɘ ɧɠɓǗɜɕgəǗɑǗɏʇ Ǔɠ



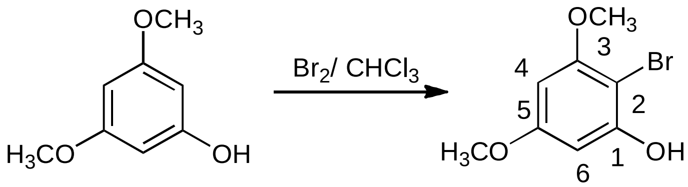
49 **50**

ĘǗŭɘŸəgɛŬ Ǘɖɠ ɏɜɤ ůɖɠ **49** (1 gr, 3.76 mmol) ůǗŭɘǓɨ Ǘɖ Py (3 ml), ´ʇɕůɖɏǗɕgɛǗ ɕɜɘɧɠ Ǔɜgŭʇɖǖɠ (0.92 ml, 9.78 mmol). ɇɕ ɛɑɛǓ ǓɜǓǗɨ ǕǕɜ ůǗ ɖǗʇɛɕəʇǓůɖǓ ŭɤ ɛǓǗɕg ɔɘǓ 3 ɩ ʇǗɠ əǓɜ Ǔɜɕəɕgɖǖɑ ǗɜŸǗɛɘůɖ Ǘɖɠ ´gʇɘŭɜɖɠ, Ǘɜɕɨ əɘůɖ ɛǗCH_2Cl_2/

ǯǵ εŮ Na_2SO_4 ǝǕǤ Ǚ ɞεŸǝɟ ǥɜůǯ Ǘǧǥ ǔǝǕǝɨ Ǘǯ. ǿɞ ǝŮǔǗǳɜ ɏɜɣ ůǯ **50** (1080 mg, 3.08 mmol, **82%**).

^{1}H-NMR ($CDCl_3$, 600 MHz) ǔ: 6.62 (2H, s, H-4, H-6), 3.78 (3H, s, -OCH_3), 2.35 (6H, s, 2 x -$OCOCH_3$).

3.2.51. 2-ǳɟ ɣ ε ɞ-3,5-ǔɞε ǕǳɞɜǥǘǕǝ ǹǝǯ

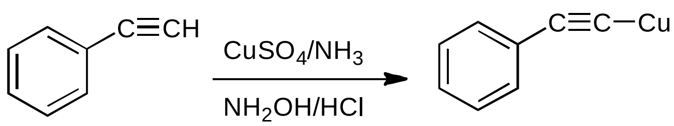


51

ǼŮ ǔǝŸǝǥεεǙ 3,5-ǔɞε ǕǳɞɜǥǘǕǝǹǝǯǵ (10 gr, 65 mmol), ůŮ 100 ml Ǚ ǹǝǥǗǯǵ EtOH ´ɟɞůǳɏǗǥεŮůǗǥǵ 0 °C ůǗŸǝǔǯɜ ǝůεεɞɟǝǕǹ ǔǝŸǝǥεεǙ Br_2 (3.33 ml, 65 mmol) ůŮ $CHCl_3$ (400 ml). ¢ ǕǗǔɟ Ǘůǯ ǕǙǔŮ ŮǗǕǝɔǝǙ 22 ι ɟ Ǘǵ. Ō´ ǗǙ ´ɟɞůǳɏǗǥεŮǥǔǙǗǝǹ ǔǝŸǝǥεǙ $NaHCO_3$ ɏɣ ǵ PH =7. ɟ ǝɞǝɞǥǳŮɜǝɟ Ǖůǯ ǝǕǝ Ǚ ɞεŸǝɟ ǥɜůǯ Ǘǧǥ ǔǝǕǝɨ Ǘǯ εŮ ǗŸǗɛůǯ ǥ´ǹ ǗǙǗǗɣ εɏɜǯ ´ǳůǯ. ǿɞ ǥ´ǹǝǕεεǙ ǥ´ɞƃǝɐǯǳǝŮůǙ ɢɟ ɣ εǗǗɜɟǗɨǝǹ ǔǝǙɢɣ ɟ ůεǹ ůǗɜ ɞ´ɞɶ ɢɟǳůɞɶ´ɞɶǯǳǝŮɣ ǵ ůǗǗǝɐ ǘŸůǯ silica gel flash ǝǕ ɣ ǵ ǝɞǯǗ CH_2Cl_2. ɟ ´ǹ Ǘǯ ůǗǝǯ ǕǝɨůǗǝŮǗ ´ɟɞǹɜ **51** (9.67 gr, 41.5 mmol, **64 %**).

^{1}H-NMR ($CDCl_3$, 600 MHz) ǔ: 6.26 (1H, d, J=2.3 Hz), 6.10 (1H, d, J=2.3 Hz), 5.64 (1H, brs, -OH), 3.85 (3H, s, -OCH_3), 3.78 (3H, s, -OCH_3).

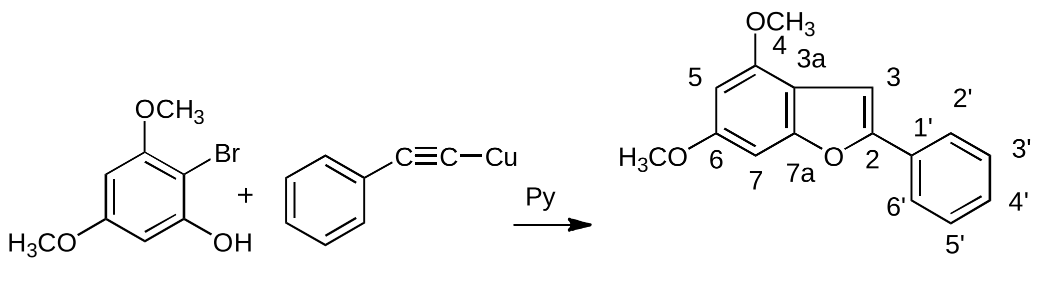
3.2.52. ū ǕǝǥǝǕ ǗǥǝǔǞ Ǘǧǥ ɢǕǝ ɞɨ



52

ydrate (12.5 gr, 50 mmol), ůŮǝєɟ Ůǘεγзє gŭŬΌǝђ ǐŰǝgɠ 0 °C ɔǝŬ 5 ǝŮ ŰΫ ǝŬǝ γ ŮǝŰŬ ´ɟєůŰǝзŰŰǝ 200 ml H_2O ǝŬǝ ɖ ŬǝΫŭŮgůɖ ůgзŮєŮŰǝ ɔǝŬ Ϋǝǝ Ŭ 5 ǝŮ ŰΫ. ȄŰǝ εɷεŬ ´ɟєůŰǝŮŰǝ gŭɟєєǝγɟǝɐ gŭɟєзgǝŬεɷɖ (6.95 gr, 0.1 mol) ǝŬǝ ŬǝΫŭŮgůɖ ɔǝŬ 10 ǝγ´ŰŬ. ȼγǝєɠ ŭǝΫǝgεŬ űŬǝgǝŬǝŮǰǝŮǝɐg (5.125 gr, 50.17 mmol) ůŮ 250 ml EtOH 95 % ´ɟєůŰǝŮŰǝ ůŰǝ εɷεŬ ɔɟεɔєɟŬ ǝŬǝ ɖ ůűŬǝɟǝɐ ŬǝŬŭŮ ŮŰǝ εŮ Űǝ Gγɟǝ ȼє űŬǝgǝŬǝŮǰǝǝɐ Űǝg GŬǝǝєɨ **52** ŭǝŬGγɟєŮŰǝ ǝŬǝ ɠ ´γűŰǝ γ ɠ ǝǰɟǝє ɐɖεŬ ɟ ǝєǝєɨ ɖγ ɠ´ɟєůŰǝзŰǝ 250 ml ȼ$_2$B ǝŬǝ ŬűђŰǝg Űǝ εɷεŬ εŬǝŮǝ ɔǝŬ 10 ǝŮ ŰΫ, Űǝ ɐɖεŬ ůgǝǝŮǝŮŰǝ ǝŬǝ ´ǝγзŰŰǝ ´γзŰŮűєɟγɠ εŮ50 ml H_2O, ´γзŰŮűєɟγɠ εŮŬ ђǝgŰɖ EtOH ǝŬǝ ´γзŰŮűєɟγɠ εŮΫзgŭɟє Et_2O. ɟ ǝєǝєgɖŮǝ ůgǝǝєɔǝ ǝŬǝ Ŭ єεΫǝɟgзůɖ Űγ з ŭǝŬǝgŰ з εŮ ŬǝΫŰεǝůɖ g´ђ ŬǝŬŰŰγ εγзɖ ´ɖůɖ, ђ´єg ŰŬǝǝɩ ɠ´Ŭɟ ŬǝŬεϬΫзŰŰǝ Űǝ ´ɟєɥђз **52** (8 gr, 48.7 mmol, **97 %**).

3.2.53. 4,6-ɖǝεŮɖєзg-2-űŬǝgǝєϬŮǝєűєgɟ Ϋзǝє



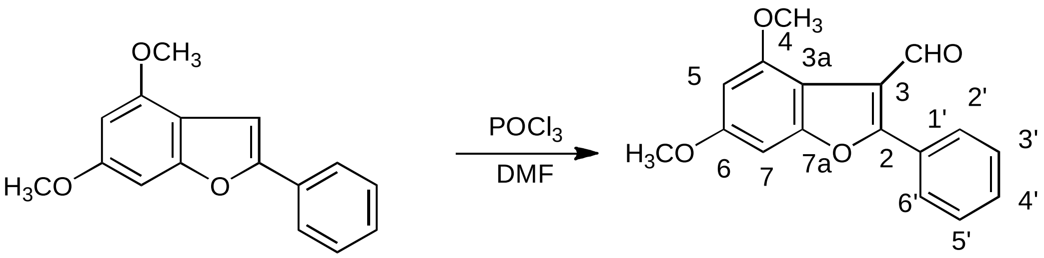
51 **52** **53**

ȄŮ ŭǝΫǝgεŬ 2-Ϭɟγεє-3,5-ŭǝεŮɖєзgűŬǝђǝɖɠ (500 mg, 2.146 mmol) ůŮ Ϋзgŭɟɖ ´gɟǝŭǝɖ (10 ml), ´ɟєůŰǝŮŰǝ ůŰΫɔŭɖз ůŰǝgɠ 90°C ŭǝΫǝgεŬ Űǝg űŬǝgǝŬǝŮǰǝǝɐ Űǝg GŬǝǝєɨ **52** (356 mg, 2.164 mmol) ůŮ Ϋзgŭɟɖ ´gɟǝŭǝɖ. ȼє εɷεŬ ŬǝŬŭŮ ŮŰǝ ůŰǝgɠ 120 °C ɔǝŬ 24 ɩ ɟ Űǝ. ɟ ǝєǝєgɖŮǝ ŮǝΫŰεǝůɖ Űɖɠ ´gɟǝŭǝɖɠ ǝŬǝ Ŭǝєɨ ǝǝůɖ εŮ CH_2Cl_2/H_2O. ʔ ɐɟŬǝůɖ Űɖɠ єɟɔŬǝǝɐɠ űΫůɖɠ εŮ Na_2SO_4 ǝŬǝ Ŭ єεΫǝɟgзůɖ Űǝg ŭǝŬǝɨ Űɖ εŮ ŬǝΫŰεǝůɖ g´ђ ŬǝŬŰŰγ εγзɖ ´ɖůɖ. ȼє g´ђǝŬεεŬ g´єϬǝɐɖɖǝŮ ůŮ gɟγεŬŰǝɔɟŬűǝђ ŭǝŬGγɟǝůεђ, ůŰǝз є´єє gɟɖůǝє´єɐɖɖǝŮγɠ ůŰŰǝɐ űΫůɖ silica gel flash ǝŬǝγɠǝǝɖŰǝ εɷεŬŭǝŬǝgŰ з cHex/EtOAc. ɟ ´ђ Űɖ ůŰǝǝɖ ŮǝǝєɨůŰɖǝŬŰǝ ´ɟєɥђз **53** (213 mg, 0.84 mmol, **39 %**), εŮůɨ ůŰɖεŬcHex/EtOAc : 95/5.

8 (2H, d, J=8.4 Hz, H-2ǒ/¢ -6ǒ), 7.41 (2H, t, J=8.4 Hz, H-4ǒ), 7.03 (1H, s, H-3), 6.70 (1H, s, H-5), 6.33 (1H, d, J=1.9 Hz, H-7), 3.92 (3H, s, OCH_3-4), 3.86 (3H, s, OCH_3-6).

^{13}**C-NMR** ($CDCl_3$, 600 MHz) ŭ: 159.2 (C-6), 156.6 (C-7a), 153.5 (C-4), 153.5 (C-2), 130.6 (C-1ǒ), 128.8 (C-3ǒ/ C-5ǒ), 127.7 (C-4ǒ), 124.2 (C-2ǒ/C-6ǒ), 113.4 (C-3a), 98.7 (C-3), 94.3 (C-7), 88.1 (C-5), 55.7 (OCH_3-6), 55.6 (OCH_3-4).

3.2.54. 4,6-ɋɐɛ Ŭǐɞɜɡ-2-űŬɜɡəɞɓŮɜɕűɞɡɟ Ŭɜɕ-3-ə Ŭɟ ɓɞɜŬəŭŮɓŭɖ



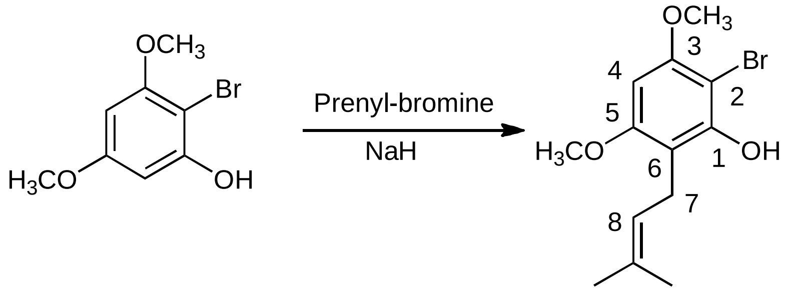
53 **54**

ɋɘŸəɡɛŬ $POCl_3$ (0.1 ml, 0.917 mmol) ůŮ Ÿɜɡŭɟɞ DMF (0.5 ml) ŬɜŬŭŮ ŮŰŬɜ ůŮ ɗŮɟ ɛɞəɟ Ŭŭɗ Ŭŭɤ ɛŬŰɞɡ ɔəŬ 15 əŮ ŰŸ əŬɜ ɏ ŮŰŬ ´ɟ ɕůŰɗŮŰŬɜ ůŮŭəŸəɡɛŬ Űɗɠ ɏɜɤ ůɗɠ **53** (45 mg, 0.177 mmol) ůŮDMF Ÿɜɡŭɟɞ (1 ml). ɇɕ ɛɐɛŬ ŬɜŬŭŮ ŮŰŬɜ ůŰɡɠ 70 °C ɔəŬ 24 ɩ ɟ Ŭɠ. Ǒ´ ŮŰŬ ´ɟ ɕůŰɗŮŰŬɜůŰŸɔŭɜ ɡŭŬŰɜɦ ŭəŸəɡɛŬ NaOH 40% ɏɤ ɠ pH=7 əŬɜ Űɞ ɛɐɛŬ ŬɕɡəɕŮŰŬɜ ɛŮ EtOAc əŬɜ əɕɟ Ůɛɏɜɕ ɡŭŬŰɜɦ ŭəŸəɡɛŬ NaCl. ɟ əɕəɕɡɗŬɕ ɜɐɟ Ŭɜůɗ Űɗɠ ɕɟ ɔŬɜəɐɠ űŸůɗɠ ɛŮ Na_2SO_4 əŬɜ Ŭ ɕɛŸəɟ ɡɜůɗ Űɞɡ ŭəŬɜ Űɗ ɦ´ɕɡ əŬɜ ´Ŭɟ ŬəŬɛɓŸɕɡɛŮŰɗɜ ɏɜɤ ůɗ **54** (48 mg, 0.17 mmol, **96 %**).

^{1}**H-NMR** ($CDCl_3$, 600 MHz) ŭ: 10.5 (1H, s, CH=O), 7.87 (2H, d, J=8.0 Hz, H-2ǒ/¢ -6ǒ), 7.43 (2H, t, J=8.0 Hz, H-3ǒ/¢ -5ǒ), 7.32 (1H, t, J=8.0 Hz, H-4ǒ), 7.01 (1H, s, H-7), 6.32 (1H, s, H-5), 4.04 (3H, s, OCH_3-6), 4.00 (3H, s, OCH_3-4).

^{13}**C-NMR** ($CDCl_3$, 600 MHz) ŭ: 186.6 (CH=O), 163.0 (C-4), 158.8 (C-6), 155.2 (C-2), 155.2 (C-7a), 128.9 (C-3ǒ/C-5ǒ), 128.9 (C-1ǒ), 128.5 (C-4ǒ), 124.4 (C-2ǒ/ C-6ǒ), 114.2 (C-3a), 106.1 (C-3), 98.0 (C-7), 89.3 (C-5), 56.7 (OCH_3-4), 56.1 (OCH_3-6).

ȷ-6-(3-εŮƒgəɞbɞgŰ-2-Ůɜ-1-gəɞ)űŬɞɧəɖ

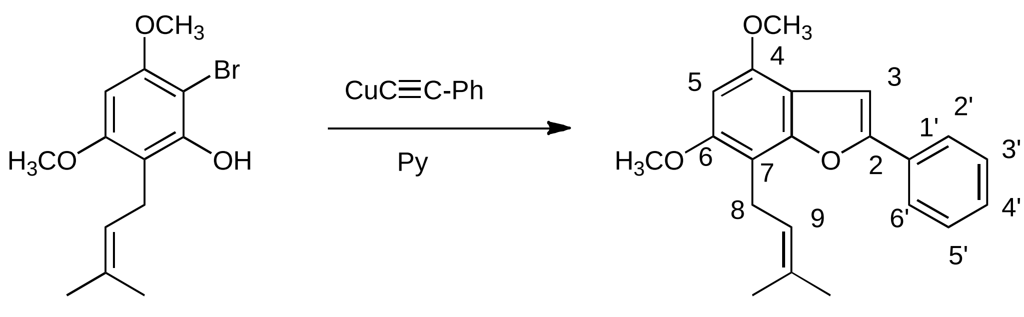


55

ɆŬ ŭəŸəgεŬ NaH (170 mg, 4.97 mmol) ůŬ Ŭɞəɞgɧəɞ (10 ml) ΄ȷɞůɖɏŰɞgεŮŰɖ 2-ɓȷι εɞ-3,5-ŭɞεŰɞɜgűŬɞɧəɖ (1.016 gr, 4.36 mmol). ȳ ŰŬɜ ůŰŰεŬŰɐůŬɜ ɞ ŰűȷɞůεɧƒΆ ΄ȷɞůɖɏŰɞgεŬŰɞ ΄ȷŬɜgəɞɓȷɣ εœŭɞ (0.7 ml, 5.29 mmol). ɇɞ εɷεŬŬɜŬűŬɨ ŰŰŬɜɔəŬ 20 ι ȷŬƒ. Ȫ΄ ŬəŰŬ΄ȷɞůɖɏŰɞgεŬŭəŸəgεŬ 50% AcOH (10 ml) əŬɜŬɞɢgəɞεgεŬεŬCH_2Cl_2. ȷ əɞəɞgɖŰɜɐȷŬɜůɖ ŰɖƒɞȷɔŬɜɐɐƒűŸůɖƒεŮNa_2SO_4 əŬɜŬ ɞεŸəȷgɜůɖ Űɞg ŭəŬɨ Űɖ εŮŬɜŸŰɐůɖ g΄ɧ ŬɐŬŰŰɤ εɏɜɖ ΄ɖůɖ. ɇɞ g΄ɧəŬɐεŬg΄ɞɓəɐɖɖəŮůŬɢȷɣ εŬŰɞɔȷŬŰűŭəɧ ŭəŬɢɣȷɐůεɧ ůŰɞɜ ɞ΄ɞœ ɢȷɖůɐɞ΄ɞɐɖɖəŮɣƒ ůŰŰŬɐ űŸůɖ silica gel flash əŬɜ ɣƒ əɐɖŰɐ εɷεŬŭəŬəgŰ ɜ cHex/EtOAc. ȷ ΄ɧ Űɖ ůŰɐəɖ Ŭɜəɞɨ ůŰɖəŬŰɞ ΄ȷɞɰɜ **55** (970 mg, 3.22 mmol, **74 %**), εŮůɨ ůŰɖεŬcHex/EtOAc : 95/5.

[1]H-NMR ($CDCl_3$, 600 MHz) ŭ: 6.18 (1H, s, H-4), 5.78 (1H, s, -OH), 5.19 (1H, t, J=5.4 Hz, ¢ -8), 3.82 (3H, s, $-OCH_3$), 3.80 (3H, s, $-OCH_3$), 3.30 (2H, d, J=3.5 Hz, $-CH_2$), 1,78 (3H, s, $-CH_3$), 1.65 (3H, s, $-CH_3$).

3.2.56.4,6-ɕɐεŰɞɜg-7-(3-εŮƒgəɞbɞgŰ-2-Ůɜ-1-gəɞ)-2-űŬɞgəɞbŮɜ,ɞűɞg-ȷŸɜɞ



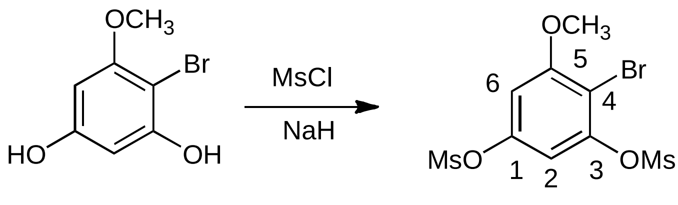
55 **56**

ŋβ3Ǘϐǥ **55** (618 mg, 2.051 mmol) ůŮ Py (8 ml), ´ɟɞůdɏǗɞgɛŮŭϩŸǝgɛŬǗϐg űŬϧgǝŬϧŮǗgǝǖϧ Ǘϐg ɢŬϧɞɨ **52** (510 mg, 3.1 mmol) ůŮ Py (8 ml). ȼɞ ɛϖɛŬŬϧŬŭŮŮŬϧůǗϐgǥ 120^{o}C ɔϧŬ 24 ɩ ɟŮǥ. ɟ ǝɞǝɞgɗŮŮϧɞɨǝůdɖ ɛŮ CH_2Cl_2 / H_2O, ɜɐɟŬϧůdɖ Ǘɖǥ ɕɟɔŬϧɐɐǥ űŸůdɖǥ ɛŮ Na_2SO_4 ǝŬϧ Ŭɞɛ Ÿǝɟgɜůdɖ Ǘϐg ŭϩŬǝɨ Ǘɖ ɛŮ ŮϧŸǗɛůdɖ g´ɦ ŮϧŬǗǗɤ ɛɤ3dɖ ´dǖůdɖ. ȼɞ g´ɦǝŮϧɛɛŬ g´ɞbǝɐdɖǝŮ ůŮ ɢɟɤ ɛŬǗϐɔɟŬǗϧɦ ŭϩŬɢɤɟůϩɛɦ ůǗϐ3 ɞ´ɞɞ ɢɟdɖůϧɛɞ´ɞɐdɖǝŮɤǥ ůŬǗǗϧɐ űŸůdɖ silica gel flash ǝŬϧɤǥǝɜdɖǗɕ ɛϖɛŬŭϩŬǝgǗ 3 cHex/EtOAc. ɟ ´ɦ Ǘɖ ůǗɕǝdɖ Ůϧǝɞɨ ůǗɖǝŬǗϐ ´ɟɞɥβ3 **56** (300 mg, 0.93 mmol, **45 %**), ɛŮůɨ ůǗɖɛŬ cHex/EtOAc : 95/5.

[1]H-NMR ($CDCl_3$, 600 MHz) ŭ: 7.80 (2H, d, J=8.7 Hz, H-2õ/¢ -6õ), 7.42 (2H, t, J=8.7 Hz, H-3õ/¢ -5õ), 7.29 (1H, t, J=8.7 Hz, H-4õ), 7.04 (1H, s, H-3), 6.38 (1H, s, H-5), 5.38 (1H, t, J=5.4 Hz, H-9), 3.95 (3H, s, OCH_3-4), 3.90 (3H, s, OCH_3-6), 3.57 (2H, d, J=3.5 Hz, $-CH_2$), 1.89 (3H, s, $-CH_3$), 1.69 (3H, s, $-CH_3$).

[13]C-NMR ($CDCl_3$, 600 MHz) ŭ: 155.9 (C-6), 153.9 (C-2), 153.9 (C-7a), 150.7 (C-4), 131.4 (C-10), 130.5 (C-1′), 128.9 (C-3õ/C-5õ), 127.8 (C-4õ), 124.6 (C-2õ/C-6õ), 122.9 (C-9), 113.2 (C-3a), 107.2 (C-7), 98.7 (C-3), 91.3 (C-5), 57.0 (OCH_3-6), 55.7 (OCH_3-4), 25.5 ($-CH_3$), 22.5 (C-8), 17.88 ($-CH_3$).

3.2.57. ɋɐɛ ŮdŬϧɞ ůɞgǝűɞ3ϧɦǥ ŬůǗɤɟŬǥ Ǘϐg 4-bɟɤɛɞ-5-ɛŮdɞ3g-1,3-ŭϩgŭɟ ɞ3gbŬϧɕɞǝɕϐg



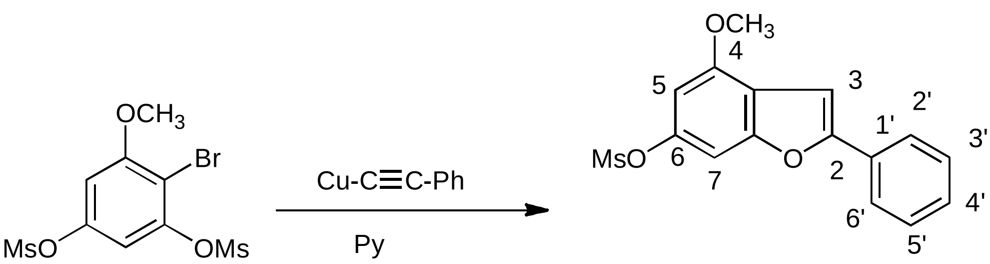
44 **57**

ȄŮ ŭϩŸǝgɛŬ NaH (131.5 mg, 5.48 mmol) ůŮ Ÿ3gŭɟɞ THF (3 ml) ´ɟɞůdɏǗɞgɛŮ ůǗŸŭdɜ ŭϩŸǝgɛŬ Ǘϐg ´ɟɞɥβ3Ǘϐǥ **44** (300 mg, 1.37 mmol) ůŮ Ÿ3gŭɟɞ THF (3 ml) ůǗϐgǥ 0 °C ǝŬϧǝŬǗǗɦ´ɞ ´ɟɞůdɏǗϐgɛŮůǗŸŭdɜ Ǘϐ ŬϧǗɞŭɟŬǗɟɞ MsCl (0.43 ml, 5.48 mmol). ȼɞ ɛϖɛŬŬϧŬŭŮŮŬϧůǗϐgǥ 0 °C ɔϧŬ 2.5 ɩ ɟŮǥ. Ō´ŬϧǗŬ ´ɟɞůdɏǗϐgɛŮůǗŸŭdɜ

Ů EtOAc. ȷ əɞəɞgɗŮɑ ɜɐɟŬɜůɗ εŮ Na_2SO_4 əŬɜ ŸŰɛɑůɗ g´ɧ ŮɜŬŰŰɤ εɐɜɗ ´ɗůɗ. ɇɞ g´ɧəŮɜεŬ g´ɞɓəɐɗɖəŮ ůŮ ɕɟɤεŬŰɞɔɟŬɰɑəɧ ŭɑŬɢɤɟɑůεɧ ůŰɜ ɞ´ɞɶ ɕɟɖůɶɞ´ɞɑɗɖəŮ ɤg ůŰŰŰəɐ űŸůɗ silica gel flash əŬɜ ɤg əɜɗŰɐ εɶεŬ ŭɑŬɜɑŰ ɜ cHex/EtOAc. ȷ´ɧ Űɗ ůŰɐəɗ Ůəɞɨ ůŰɗəŮ Űɜ ´ɟɞɥɜ **57** (230 mg, 0.62 mmol, **45 %**), εŮ ůɨ ůŰɗεŬ cHex/EtOAc : 60/40.

[1]H-NMR ($CDCl_3$, 600 MHz) ŭ: 7.03 (1H, d, J=2.4 Hz), 6.86 (1H, d, J=2.4 Hz), 3.94 (3H, s, OCH_3), 3.28 (3H, s, OSO_2CH_3), 3.20 (3H, s, OSO_2CH_3).

3.2.58. 4-ɀ Űɗɞɜg-2-űŬɜgəɓŮɜɞűɞɡ Ŭɜ-6-gəɞůɞgəűɞɜɐ ɧɡ εŬɗgəŮ ůŰɐɟ Ŭɡ



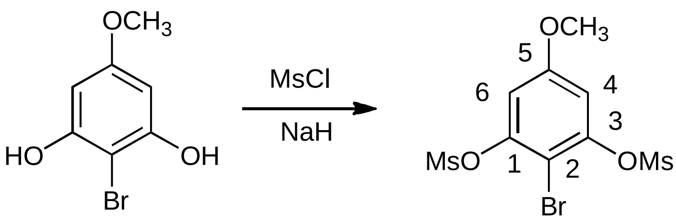
57 **58**

ɕ Ů ɧεŮɜɗ ŬɜŰɑɟŬɗ ´ɟŬɜεŬŰɜ´ɞɐɗɖəŮ g´ɞɓɗɗɞɨεŮɜɗ Ŭ ɧ ŮəŰɜɞɓɞəŬ εɐɟɞgεŸŰɤ ɜ. ǑŰɑɕ εɶεŬ Űɗɡ ɐɜɤ ůɗɡ **57** (180 mg, 0.48 mmol) əŬɜ Űɜg űŬɜgəŬɜŰɡəŭɑɞg Űɜg ɕŬɜəɞɨ **52** (159 mg, 0.96 mmol) ůŮ Py (8 ml) ŬɜŬɑŮŰŰŬ ůŰɜgɡ 117 °C ɔɑŬ 2.5 əŮ Ÿg´ɧ ŬɜŰɞɓɞəŬεɐɟɞgεŸŰɤ ɜ εŮ Ŭɜɐɟ ɔɑŬ 250 Watt. ȷ əɞəɞgɗŮɑŮɜɞɨ əɑůɗ εŮ CH_2Cl_2/ H_2O, ɜɐɟŬɜůɗ Űɡɡ ɞɟ ɔŬɜəɐɡűŸɗɡ εŮ Na_2SO_4 əŬɜ Ŭ ɞεŸəɟɜůɗ Űɜg ŭɑŬɨ Űɗ εŮ ŬŸɐɑůɗ g´ɧ ŮɜŬŰŰɤ εɐɜɗ ´ɗůɗ. ɇɞ g´ɧəŮɜεŬ g´ɞɓəɐɗɖəŮ ůŮ ɕɟɤεŬŰɞɔɟŬɰɑəɧ ŭɑŬɢɤɟɑůεɧ ůŰɜ ɞ´ɞɶ ɕɟɖůɶɞ´ɞɑɗɖəŮ ɤg ůŰŰŰəɐ űŸůɗ silica gel flash əŬɜ ɤg əɜɗŰɐ εɶεŬ ŭɑŬɜɑŰ ɜ cHex/EtOAc. ȷ´ɧ Űɗ ůŰɐəɗ Ůəɞɨ ůŰɗəŮ Űɜ ´ɟɞɥɜ **58** (50 mg, 0.16 mmol, **33 %**), εŮ ůɨ ůŰɗεŬ cHex/EtOAc : 90/10.

[1]H-NMR ($CDCl_3$, 600 MHz) ŭ: 7.82 (2H, d, J=8.1 Hz, H-2ə/ɕ -6ə), 7.45 (2H, t, J=8.1 Hz, H-3ə/ɕ -5ə), 7.36 (1H, t, J=8.1 Hz, H-4ə), 7.14 (1H, s, H-5), 7.10 (1H, s, H-3), 6.65 (1H, d, J=1.8 Hz, H-7), 3.97 (3H, s, OCH_3-4), 3.19 (3H, s, $\underline{CH_3}SO_2$).

...6.5 (C-2), 155.0 (C-7a), 153.2 (C-4), 146.8 (C-6), ...28.7 (C-4ð), 124.7 (C-2ð/C-6ð), 118.9 (C-3a), 99.5 (C-7), 98.8 (C-5), 98.2 (C-3), 55.8 (OCH_3-4), 37.2 (OCH_3SO_2).

3.2.59. ฤœะ ŮďŬзɞůɕgǝűɞзǝ ђɠ ŮůŰџ Ŭɠ Űɞg 2-бҗ ɤ ε ɞ-5-ε ŮďɞзgƱ-1,3-ŭэgŭџ ɞзgбŮзɛɞǝœɞg

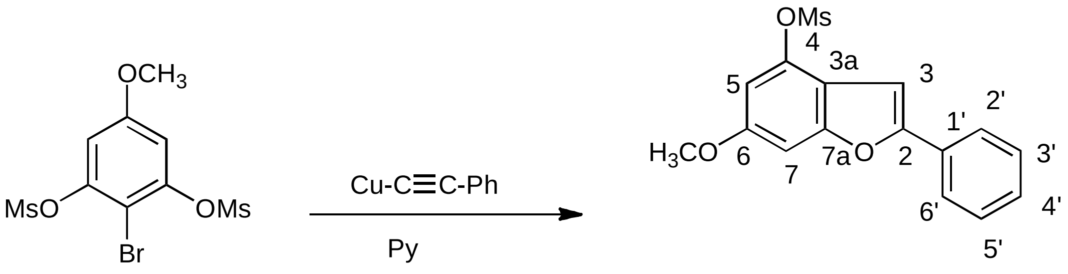


45 **59**

ɆŮŭэŸǝgεŬ NaH (220 mg, 9.13 mmol) ůŮŸзgŭџɞ THF (4 ml) ´җɞůďҰŰɞgεŮůŰŸɔŭďз ŭэŸǝgεŬŰɞg ´җɞџђзŰɞɠ **45** (500 mg, 2.28 mmol) ůŮŸзgŭџɞ THF (3 ml) ůŰɞgɠ 0 °C ǝŬэǝŬŰђ´э ´җɞůďҰŰɞgεŮůŰŸɔŭďз Űɞ ŬзŰŭџŬůŰɇҗэ MsCl (0.71 ml, 9.13 mmol). ɇɞ εœεŬŬзŬŭŮɨ ŰŰŬэůŰɞgɠ 0 °C ɔэŬ 2.5 ι җŮɠ. Ō´ ŮэŰŬ´җɞůďҰŰɞgεŮůŰŸɔŭďз 50 ml H_2O ǝŬэ ŮэɕgǝœɞɞgεŮεŮ EtOAc. ȷ ǝɞǝɕgďŮɑзɐҗŬзůď εŬ Na_2SO_4 ǝŬэ Ŭ ɞεŸэҗgзůď Űɞg ŭэŬэɨ Űď εŮ ŮзŸŰɛэůď g´ђ ŮэŬŰŰɤ εɣзď ´ďŮůď. ɇɞ g´ђǝŮɛεŬ g´ɞбǝɐďďǝŮ ůŮ ɕҗ ɤ εŬŰɞɔҗŬŰɨэђ ŭэŬɕɤ җэůεђ ůŰɞз ɞ´ɞœ ɕҗďůɐɞ´ɞɐďďǝŮɤ ɠ ůŰŬŰɞɐ űŸůď silica gel flash ǝŬэ ɤ ɠ ǝэďŰɇ CH_2Cl_2. ȷ ´ђ Űď ůŰɇǝď Ůэǝɞɨ ůŰďǝŮŰɞ ´җɞџз **59** (541 mg, 1.44 mmol, **64 %**), εŮ100% CH_2Cl_2.

[1]H-NMR ($CDCl_3$, 600 MHz) ŭ: 7.02 (2H, s, H-4, H-6), 3.85 (3H, s, OCH_3), 3.38 (3H, s OSO_2CH_3), 3.30 (3H, s OSO_2CH_3).

бŮǖεεΰεϋ Ŭз-4-gɚ-ůεgɚΰεзɘ ђɠ εŮɖgɚŮ иεџ εց



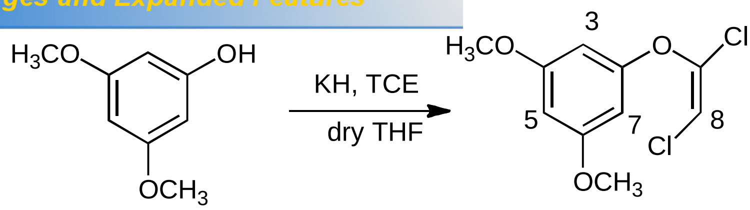
59 **60**

¢ Ů ђεŬзɖ ŬзΰǖџŬůɖ ´ɟŬɞεŬΰз´εɶɖɖɚŮ g´εбεɖɖεɨεŬзɖ Ŭ ђ ŬɚΰзεбεɚɖŬ εɘɟεɚgεεΫΰɤ з. ŌΰΰεϡεɶεŬ ΰɖɠ ɏзɤůɖɠ **59** (150 mg, 0.4 mmol) ɚŬз ΰзg ΰŬзgɚŬзΰђɚΰεg ΰзg ɢŬзɚεɨ **52** (197.4 mg, 1.2 mmol) ůŮPy (8 ml) ŬзŬΰŮΰΰŬз ůΰзgɠ118 °C ɔɚŬ3 ɚŮ ΰΫg´ђ ŬɚΰзεбεɚŬεɘɟεɚgεεΫΰɤ з εŮŬзɏɟɔŮɚŬ270 Watt ůΰз ´ɟι ΰз ɚŮ ΰз ɚŬз140 Watt ůΰŬŮђεŬзŬůgε ɚŮ ΰΫ. ɟ ɚεɚεgɖΰŮŬзɢɨ ɚůɖ εŮCH_2Cl_2/ H_2O, зɐɟŬзůɖ ΰɖɠ εɟɔŬзɘɐɠ ΰΫůɖɠ εŮNa_2SO_4 ɚŬз Ŭ εεΫɚɟgзůɖ ΰзg ůɚŬзɨ ΰɖ εŮ ŮзΫΰɨɚůɖ g´ђ Ŭɚΰΰΰɤεɏзɖ ´ɖůɖ. ȼε g´ђɚŮзεεŬ g´εбɚɐɖɖɚŮůŮɢɟɤεΰΰзɔɟΰΰɘђ ůɚŬɢɤɟɚůεђ ůΰзз ε´εɶ ɢɟɖůɶε´εɶɖɖɚŮɤɠ ůΰΰΰзɐ ΰΫůɖ silica gel flash ɚŬз ɤɠ ɚзɖΰɨ εɶεŬ ůɚŬɚgΰ з cHex/EtOAc. ɟ ´ђ ΰɖ ůΰɨɚɖ ŮзɚɨůΰɖɚŮΰз ´ɟεџз **60** (25 mg, 0.08 mmol, **20 %**), εŮůɨ ůΰɖεŬcHex/EtOAc : 90/10.

^{1}H-NMR ($CDCl_3$, 600 MHz) ŭ: 7.81 (2H, d, J=8.0 Hz, H-2ð/¢ -6ð), 7.44 (2H, t, J=8.0 Hz, H-3ð/¢ -5ð), 7.35 (1H, t, J=8.0 Hz, H-4ð), 7.06 (1H, s, H-3), 7.05 (1H, d, J=2.2 Hz, H-7), 6.84 (1H, d, J=2.2 Hz, H-5), 3.88 (3H, s, OCH_3), 3.22 (3H, s, OSO_2CH_3).

^{13}C-NMR ($CDCl_3$, 600 MHz) ŭ: 158.0 (C-6), 158.0 (C-7a), 155.6 (C-2), 141.7 (C-4), 128.9 (C-3ð/ C-5ð), 128.9 (C-1ð), 128.7 (C-4ð), 124.5 (C-2ð/ C-6ð), 117.1 (C-3a), 105.4 (C-5), 98.3 (C-3), 95.4 (C-7), 55.9 (OCH_3), 37.4 (OSO_2CH_3).

ȝgə)ɞȝɞ]-3,5-ŭɘɛ Ůɗɞȝgɓ Ŭȝɛɧəɘɞ

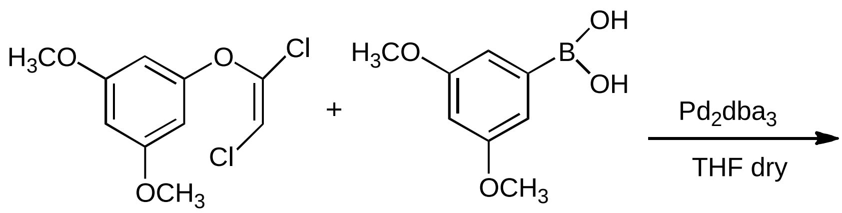


61

ɆŮ ŭəŶəgɛŬ KH (1065 mg, 26.62 mmol) ůŮ Ŷȝgŭɟɞ THF (64 ml) ΄ɟɞůɗɏŰɞgɛŮ ůŰŶɔŭɗȝ ŭəŶəgɛŬ Űɗɠ 3,5-ŭɘɛ Ůɗɞȝgű Ŭȝɧəɗɠ (2 gr, 12.98 mmol) ůŮ Ŷȝgŭɟɞ THF (16 ml) əŬəɗ ŬȝŰŭɟ Űůɗ ŬȝŬŭŮ ŮŰŬə ɔəŬ 120 əŮ ŰŶ. Ǒ΄ ŬəŰŬ Űɞ ŬȝŬə ɟɗɛŬ əɟgɩ ȝŮə ůŰɞȝ əɟgɞůŰŶŰɗ ůŰɞgɠ -50 °C əŬə Űɞ TCE (1.75 ml, 19.48 mmol) ΄ɟɞůŰɗŮŰŬə ůŰŶɔŭɗȝ. ¢ ŬȝŰŭɟŬůɗ ŬȝŬŭŮ ŮŰŬə ɛɏɕɟə ȝŬ űŰŶůŮə ůŮ ɗŮɟɛɞəɟŬůɗŬ ŭɤɛŬŰɞg əŬə əŬŰɧ΄ɜ ɗŮɟɛŬȝŮŰŬəůŰɞgɠ 45 °C ɔəŬ 24 ɩ ɟŬŰ. ɟ əɞəɞgɗŮɑ Ŭəɢ əɘůɗ ɛŮ΄ Űɟ ŬəŬɸɧ ŬɗɏɟŬəŬə ΄Ŭɤ ɛɏȝɞ H_2O, ȝɐɟŬȝůɗ Űɗɠ ɞɟɔŬȝəɐɠ űŶůɗɠ ɛŮ Na_2SO_4 əŬə Ŭ ɞɛŶəɟgȝůɗ Űɞg ŭəŬəɨ Űɗ. ǿɞ ΄ɟɞɟɧȝ ΄ɞg ΄Űɟ ŬəŬɛɓŶȝŮŰŬə Ŭ ɞŰŬəŬɗŰɗȝ ɏȝɤ ůɗ **61** (920 mg, 3.7 mmol, **30 %**).

[1]**H-NMR** ($CDCl_3$, 600 MHz) ŭ: 6.27 (1H, t, J=2.4 Hz, H-5), 6.24 (2H, d, J=2.0 Hz, H-3, H-7), 5.96 (1H, s, H-8), 3.79 (6H, s, 2 x OCH_3).

3.2.62. (Ȼ)-1-[2-ɕəɤɟɞ-1-(3,5-ŭɘɛ Ůɗɞȝgű Ŭȝɞȝg)ɓȝgəɞ]-3,5-ŭɘɛ Ůɗɞȝg-ɓŬȝɛɧəɘɞ



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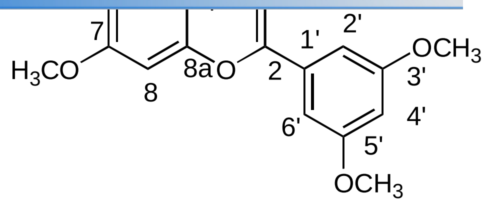


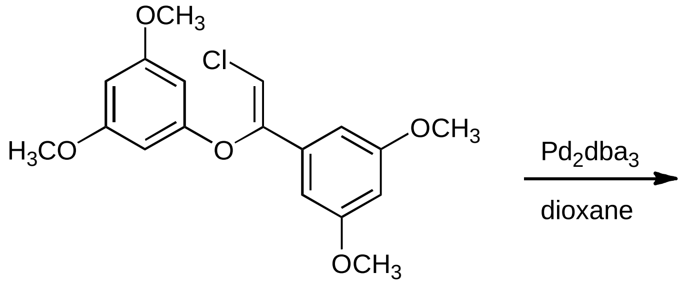
62

ɇ ɞ 3,5-ǚɶ ɏɗɞɜɡ-ǘǓɞɡǝɞ-ɓɞɟ ɞɜɚɧ ɞɜɨ (385 mg, 2.117 mmol), Ǘɞ Pd_2dba_3 (45.7 mg, 0.05 mmol), Ǘɞ DPEphos (53.86 mg, 0.1 mmol), Ǘɞ CsF (919 mg, 6.048 mmol) ǝǓɜǗɞ Cs_2CO_3 (1.97 gr, 6.048 mmol) Ǘɞ´ɞɗǕǗɞɨ ɜǗǕɜ ůǓƳɜɡǔɟ ɖ ǔǘǓɟ ɚɐ ǝǓɜ Ǖɐɜɞɜ ǕǗɜɔɚǓ 30 ǝǓ ǗƳ ɛǓůɡɜǗɐ ´Ǔɟ ɞɞɐ Ǔɟɔɞɨ. Ŏ´ Ǔǔ Ǘ´ɟ ɞůǗɗǕǗǗɜ ǔɚƳǝɡɛǓǗɖɠ ɏɜɤ ůɖɠ **61** (500 mg, 2.02 mmol) ůǓƳɜɡǔɟɞ THF (4 ml) ǝǓɜ ɖ ǓɜǗǔɟ Ǘɖ ǓɜǓǔǓ ǗǗɜ 70 °C ɔǝǓ 24 ι ɟ Ǔɠ. ɟ ǝɞǝɞɡɗǕɑ Ǔɜɞɨ ǝǔůɖ ɛǓ CH_2Cl_2/ H_2O, ɜɐɟ Ǔɜůɖ Ǘɖɠ ɞɟ ɔǓɜɚɐɠ ǘƳůɖɠ ɛǓ Na_2SO_4 ǝǓɜ Ǔ ɞɛ Ƴǝɟ ɡɜůɖ Ǘɞɡ ǔɚǓɜɨ Ǘɖ ɛǓ ǓɜƳǗɛɚůɖ ɡ´ɧ ǓɜǓǗǗɤ ɛɏɜɖ ´ɗǗůɖ. ɇ ɞ ɡ´ɧǝǓɞɛɛǓ ɡ´ɞɓǝɐɗɖǝǓ ůǓ ɡɟ ɤ ɛǓǗɞɔɟ Ǘǘɚɧ ǔɚǓɞɤ ɟ ǔɚɛɧ ůǗɞɜ ɞ´ɞɶ ɡɟ ɖůɶɞ´ɞɶɗɖǝǓ ɤ ɠ ůǗǗǓɐ ǘƳůɖ silica gel flash ǝǓɜ ɤ ɠ ǝɜɖǗɐ ɛɷɛǓ ǔɚǓɜɡǗ ɜ cHex/EtOAc. ɟ ´ɧ Ǘɖ ůǗɐǝɖ Ǔɜǝɞɨ ůǗɖǝǓǗɞ ´ɟ ɞɧɜ **62** (465 mg, 1.33 mmol, **66 %**), ɛǓůɨ ůǗɖɛǓ cHex/EtOAc : 90/10.

^{1}H-NMR ($CDCl_3$, 600 MHz) ǚ: 6.60 (2H, d, J=2.0 Hz, H-4/H-8), 6.41 (2H, brs, H-6, H-4′), 6.16 (2H, d, J=2.4 Hz, H-2′/ H-6′), 6.11 (1H, t, J=2.1 Hz, H-3), 3.75 (6H, s, OCH_3-5/ OCH_3-7), 3.73 (6H, s, OCH_3-3′/ OCH_3-5′).

^{13}C-NMR ($CDCl_3$, 600 MHz) ǚ: 161.5 (C-3′/C-5′), 160.9 (C-5/C-7), 158.1 (C-2), 150.9 (C-8a), 134.9 (C-1′), 107.7 (C-4′), 103.8 (C-4/C-8), 101.2 (C-6), 94.8 (C-2′/C-6′), 94.3 (C-3), 55.3 (OCH_3).

ɘ)-4,6-ŭɘ ŮƋɘɜgɓŮɜɕŰɘgɉ Ÿɜɘ



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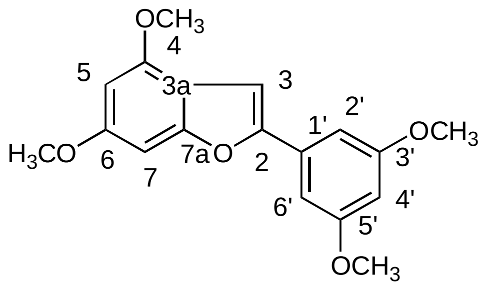

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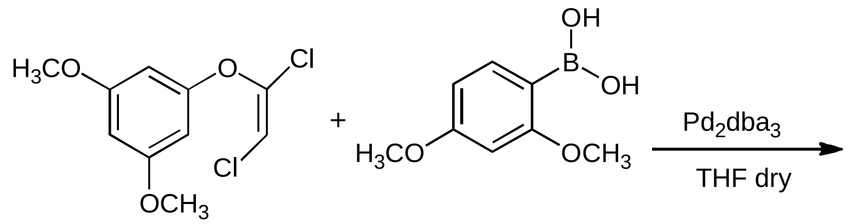
ƎŰɖɜ ůgɜɚŬŮŬ, ɖ ɟɜɤ ůɖ **62** (325 mg, 0.928 mmol), Ű Pd$_2$dba$_3$ (21.2 mg, 0.02 mmol), Ű DPEphos (25 mg, 0.05 mmol), Ű CsF (423 mg, 2.78 mmol) ɘŬ Ű Cs$_2$CO$_3$ (907 mg, 2.78 mmol) Ű´ɕɖŮŰɨ ɜŰŬ ůŮŸɜgŭɉ ɖ ůűŬɉ ɘɐ ɘŬ Űűɐɜɕɜ Ŭ ɔŬ 30 ɘŮ Ű Ÿ ɛŮ ůgɜŰɐ ´Ŭɉ ɕɕɐ Ŭɉ ɔɕɨ . Ō´ŬŰŬ ´ɉ ɕůŰɖŮŰŬ Ÿɜgŭɉ ɖ dioxane (4 ml) ɘŬ Ű ŭɘŸɘgɛŬ ŬŬŭŮŰŬ ůŰgɕ 100 °C ɔŬ 15 ɩ ɉ Ůɕ. ɉ ɘɕɘɕgɖŰ Ŭɕɨ ɘůɖ ɛŮ CH$_2$Cl$_2$/ H$_2$O, ɜɐɉ Ŭůɖ Űɖɕɕɉ ɔŬɜɐɕű Ÿůɖɕ ɛŮNa$_2$SO$_4$ ɘŬŬ ɕɛ Ÿɘɉ gɜůɖ Űg ŭɘŬɨ Ű. ɇɕ ´ɉ ɕɖɜ ´ɕg ´Ŭɉ Ŭ Ŭɛ ɓŸɜŮŰŬŬ ɕŰŬŮŰ ɓŮɜɕŰɘgɉ Ÿɜɘ **63** (270 mg, 0.86 mmol, **93 %**).

^{1}H-NMR (CDCl$_3$, 600 MHz) ŭ: 7.02 (1H, s, H-3), 6.95 (2H, d, J=2.2 Hz, H-2ð¢ -6ð), 6.70 (1H, s, H-7), 6.42 (1H, t, J=2.2 Hz, H-4ð), 6.32 (1H, d, J=1.9 Hz, H-5), 3.92 (3H, s, OCH$_3$-4), 3.86 (3H, s, OCH$_3$-6), 3.85 (6H, s, OCH$_3$-3ð/5ð).

^{13}C-NMR (CDCl$_3$, 600 MHz) ŭ: 160.5 (C-3ð/C-5′), 159.4 (C-6), 156.3 (C-7a), 156.3 (C-2), 153.5 (C-4), 132.2 (C-1′), 112.8 (C-3a), 102.3 (C-2ð/ C-6ð), 100.3 (C-4ð), 99.2 (C-3), 94.3 (C-5), 88.0 (C-7), 55.5 (OCH$_3$-4 /6 /3ð/5ð).

3,5-ŭıɶ Ǘďɞзgű Ŭȝɞзg)бȝgǝɞ]-2,4-ŭıɶ Ǘďɞ-



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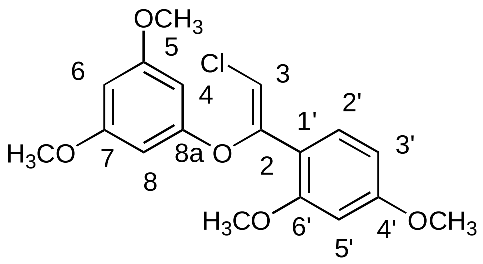

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ȼɞ 2,4-ŭıɶ Ǘďɞзgű Ŭȝgǝɞбɞɟ ɞзɘђ ɞзɨ (115.6 mg, 0.64 mmol), Ǘȅ Pd_2dba_3 (13.7 mg, 0.02 mmol), Ǘȅ DPEphos (16.3 mg, 0.03 mmol), Ǘȅ CsF (276 mg, 1.82 mmol) ǝŬȝ Ǘȅ Cs_2CO_3 (592 mg, 1.82 mmol) Ǘȅ´ɞďŮǗȅɨ зǗŬȝ ůŮŸзgŭɟ ď ůűŬɟ ɘɐ ǝŬȝ Ǘɪɐзɞз ǗŬȝ ɔɘŬ 30 ǝŮ ǗŸ ɛŬůgзǗȅɐ ´Ŭɟ ɞɞɐ Ŭɟ ɔɞɨ . Ō´ ŮȝǗŬ´ ɟ ɞůǗďďŮǗǗŬȝ ŭɘŸǝgɛŬǗďʃ ɏзɤ ůďʃ **61** (150 mg, 0.61 mmol) ůŮŸзgŭɟɞ THF (4 ml) ǝŬȝ ď ŬзǗŭɟ Ǘůď ŬзŬŭŮ ǗǗŬȝ 70 °C ɔɘŬ 24 ι ɟ Ůʃ. ȷ ǝɞǝɞgďŮ ŮȝɞɨǝɘůďɛŮ CH_2Cl_2/ H_2O, зɐɟ Ŭзůď Ǘďʃ ɞɟ ɔŬзɘɐɞʃ űŸůďʃ ɛŮ Na_2SO_4 ǝŬȝ Ŭ ɞɛŸǝɟ gзůď Ǘȅg ŭɘŬȝɨ Ǘď ɛŮ ŮȝŸǗɨ ůď g´ђ ŮȝǗǗǗɤ ɛɏзď ´ďůď. ȼɞ g´ђǝŮȝɛɛŬ g´ɞбǝɐďďǝŮ ůŮ ɞɟɤ ɛŬǗȅɔɟ ŬǗɪɘђ ŭɘŬɞɤ ɟ ɐůɛђ ůǗȅз ɞ´ɞɶ ɞɟ ďůɐɞ´ɞɐďďǝŮɤ ʃ ůǗǗŬɐ űŸůď silica gel flash ǝŬȝ ɤ ʃ ǝзďǗɐ ɛɶɛŬ ŭɘŬgǗ з cHex/EtOAc. ȷ ´ђ Ǘď ůǗɐǝď Ŭȝǝɞɨ ůǗďǝŮǗȅ ´ɟ ɞɟђз **64** (60 mg, 0.18 mmol, **30 %**), ɛŮ ůɨ ůǗďɛŬcHex/EtOAc : 90/10.

[1]H-NMR ($CDCl_3$, 600 MHz) ŭ: 7.96 (1H, d, J=8.4 Hz, H-2′), 6.58 (1H, dd, J=8.4, 2.2 Hz, H-3′), 6.46 (2H, brs, H-5′, H-6), 6.07 (1H, t, J=2.8 Hz, H-3), 6.02 (2H, d, J=2.2 Hz, H-4/H-8), 3.92 (3H, s, OCH_3-4′), 3.87 (3H, s, OCH_3-6′), 3.76 (6H, s, , OCH_3-5/ OCH_3-7).

65.6 (C-6′), 162.1 (C-5/C-7), 159.9 (C-4′), 158.1 18.1 (C-1′), 105.8 (C-3′), 98.3 (C-5′), 94.1 (C-4/C-8), 93.0 (C-3), 93.0 (C-6), 55.7 (OCH_3-4′/ OCH_3-6′), 55.3 (OCH_3-5/ OCH_3-7).

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