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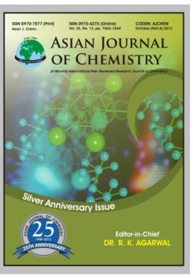

# Non-Acidic Mediated Friedel-Craft Reaction of Thiophene Using $EtAlCl_2$

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Since alkyl Lewis acids are Brønsted bases, they give a non-acidic reaction media. In this context, acylation of thiophene is investigated in the presence of $EtAlCl_2$ and non-acidic media. Besides 8 examples of thiophene, one example for pyrrole is synthesized in moderate to high yields (up to 99 %).

**Key Words: Thiophene, Acylation, Alkyl Lewis acid, Electrophilic aromatic substitution.**

## INTRODUCTION

Electrophilic aromatic substitution ($E_AS$) is one of the most used methods for obtaining new derivatives of heteroaromatics, which are high electron density of aromatic systems. The Friedel-Crafts acylation followed by a transformation has found a plethora applications in the synthesis of substituted heteroaromatics[1]. $AlCl_3$ is the most common catalyst used for this purpose[2,3]. $FeCl_3$[4], $CuFe_2O_4$[5], zeolite[6] and $SnCl_4$[7] are the other catalysts that can be given as examples. Although several catalysts are now available as mentioned above, there have been sustained efforts towards the finding of new catalysts**.** Recently, Simirnov *et al*. reported the preparation of 1,4-*bis*(2-thienyl)butane-1,4-dione with $SnCl_4$, $TiCl_4$ and $AlCl_3$ catalysts[8]. Although alkyl Lewis acids are weaker than common Lewis acids ($AlCl_3$, $FeCl_3$, *etc*.), they are also Brønsted bases[9]. Apart from its role as catalyst in the acylation reaction**,** alkyl Lewis acids were reported to be actively Brønsted base involved in acylation or other reactions[10,11]. Despite this advantage, their use is rare. To the best of our knowledge, alkyl Lewis acid is used for the first time in the acylation of heteroaromatic compounds (thiophene and furan) in this study.

## EXPERIMENTAL

$EtAlCl_2$ (1 M in hexane) and acyl chlorides were purchased from Aldrich. $CH_2Cl_2$ was distilled over $CaH_2$ prior to use. Ethyl acetate and hexane for column chromatography were used without further purification. $^1H$ and $^{13}C$ NMR were recorded with Bruker Spectroscopin Avance PDX 400 MHz using TMS (tetramethylsilane) as standard. IR spectra were recorded with JASCO FT-IR 480 plus spectrometer and selective peaks are reported. The reactions were monitored by TLC and UV-Lamp. The products were purified with Merck silica gel 5554. The yields are calculated from the isolated products. All spectroscopic data are in good accordance with the literatures.

**General procedure for acylation of thiopene:** 0.5 mL (0.0063 mol) thiophene and 0.33 mL (0.003 mol) succinyl chloride were dissolved in 20 mL dried $CH_2Cl_2$ at 0 ºC under inert atmosphere. 9.45 mL (0.0095 mol) $EtAlCl_2$ was added drop by drop to that solution. After mixing 2 h at 0 ºC, the mixture was quenched with sat. $NH_4Cl$ and extracted 3 times (total 50 mL) with $CH_2Cl_2$. The combined organic phase was dried with $Na_2SO_4$ and concentrated under reduced pressure. Upon purification with flash column (hexane; ethyl acetate, 4;1), the product **3** was isolated (750 mg, 99 % yield).

**Methyl(2-thienyl)methanone (1)[12]:** ($R_f$ = 0.24) $^1H$ NMR δ 7.69-7.65 (m, 1H), 7.61 (dd, *J* = 4.9, 1.0 Hz, 1H), 7.13-7.09 (m, 1H), 2.54 (s, 3H). $^{13}C$ NMR δ 189.95, 144.54, 133.45, 132.11, 127.93, 26.76. IR :1660, 1517, 1414, 1356, 1274, 1062, 858, 726, 592.

**1,2-*Bis*(2-thienyl)ethanone (2)[13]:** ($R_f$ = 0.26) $^1H$ NMR δ 7.72-7.67 (m, 1H), 7.57-7.51 (m, 1H), 7.15-7.09 (m, 1H), 7.04 (dt, *J* = 6.9, 3.4 Hz, 1H), 6.90-6.82 (m, 2H), 4.28 (s, 2H). $^{13}C$ NMR δ 143.33, 134.04, 132.45, 128.06, 126.90, 126.79, 125.04, 40.23. IR : 1661, 1517, 1414, 1354, 1237, 1059, 856, 700.

**1,4-*Bis*(2-thienyl)butane-1,4-dione (3)[13]:** ($R_f$ = 0.11) $^1H$ NMR δ 7.82-7.66 (m, 2H), 7.55 (dd, *J* = 4.9, 1.0 Hz, 2H), 7.06 (dd, *J* = 4.9, 3.8 Hz, 2H), 3.29 (s, 4H) $^{13}C$ δ 190.7, 143.9, 133.4, 131.9, 127.9, 33.1. IR : 1641, 1545, 1506, 1428, 1360, 1128, 751.

**(2-Thienyl)(*p*-tolyl)methanone (4)[14]:** ($R_f$ = 0.36) $^1$H NMR δ 7.72 (t, *J* = 13.5 Hz, 2H), 7.64-7.58 (m, 1H), 7.55 (dd, *J* = 3.8, 1.1 Hz, 1H), 7.26-7.18 (m, 2H), 7.07 (dd, *J* = 4.9, 3.8 Hz, 1H), 2.38 (s, 3H). $^{13}$C NMR δ 135.62, 134.20, 133.37, 129.80, 129.21, 127.74, 21.66. IR : 1704, 1632, 1513, 1413, 1289, 1048, 848, 740.

**2-Benzoylthiophene (5)[14]:** ($R_f$ = 0.28) $^1$H NMR δ 7.90-7.71 (m, 1H), 7.65-7.57 (m, 1H), 7.52 (dd, *J* = 3.8, 1.1 Hz, 1H), 7.50-7.43 (m, 1H), 7.41-7.35 (m, 1H), 7.04 (dd, *J* = 4.9, 3.8 Hz, 1H)). $^{13}$C NMR δ 187.57, 143.75, 138.20, 135.33, 134.79, 134.21, 132.13, 129.15, 128.34, 127.80. IR : 1627, 1513, 1410, 1288, 1051, 836, 721.

**(Z)-1-(2-Thienyl)but-2-en-1-one (6)[15]:** ($R_f$ = 0.37) $^1$H NMR δ 7.79-7.59 (m, 1H), 7.58-7.36 (m, 1H), 7.16-6.92 (m, 2H), 6.81-6.66 (m, 1H), 1.87 (dd, *J* = 6.9, 1.6 Hz, 3H). $^{13}$C NMR δ 181.43, 145.13, 143.67, 133.39, 131.54, 128.00, 126.88, 18.32 . IR : 1659, 1614, 1514, 1440, 1415, 1294, 1234, 1063, 907, 784.

**1,8-*Bis*(2-thienyl)octane-1,8-dione (7)[16]:** ($R_f$ = 0.15) $^1$H NMR δ 7.70-7.58 (m, 2H), 7.52 (dd, *J* = 4.9, 1.1 Hz, 2H), 7.03 (dd, *J* = 4.9, 3.8 Hz, 2H), 2.87-2.77 (m, 4H), 1.77-1.61 (m, 4H), 1.35 (dt, *J* = 14.1, 5.2 Hz, 4H). $^{13}$C NMR δ 192.06, 144.08, 132.59, 130.92, 127.41, 38.66, 28.57, 23.99 . IR : 1647, 1411, 1242, 1185, 927, 851, 727.

**(Furan-2-yl)(2-thienyl)methanone (8)[17]:** ($R_f$ = 0.28) $^1$H NMR δ 8.07 (d, *J* = 2.4 Hz, 1H), 7.62-7.53 (m, 2H), 7.33-7.25 (m, 1H), 7.07 (dt, *J* = 3.8, 3.2 Hz, 1H), 6.49 (s, 1H). $^{13}$C NMR δ 171.60, 151.26, 144.81, 141.14, 132.34, 126.73, 117.20, 111.08. IR; 1622, 1566, 1464, 1413, 1305, 808, 740. IR: 1622, 1566, 1464, 1413, 1305, 1179, 1013, 884, 808.

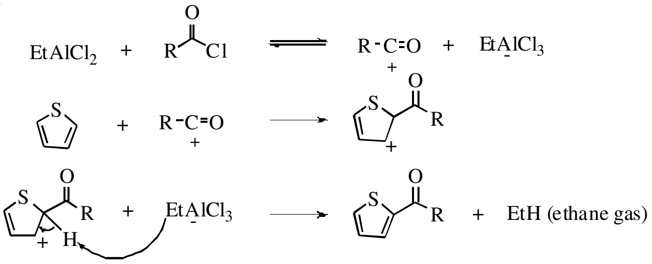
**1-(1*H*-Pyrrol-2-yl)ethanone (9)[18]:** ($R_f$ = 0.22) $^1$H NMR δ 6.98 (td, *J* = 2.8, 1.4 Hz, 1H), 6.81 (ddd, *J* = 3.8, 2.4, 1.4 Hz, 1H), 6.14 (dt, *J* = 3.8, 2.4 Hz, 1H), 2.36 (s, 3H). $^{13}$C NMR δ 187.95, 132.13, 125.43, 117.31, 119.42, 25.53. IR: 1645, 1547, 1428, 1364, 1129, 1045, 841, 773.

## RESULTS AND DISCUSSION

Snider and co-workers accomplished many Lewis acid catalyzed reactions using alkyl Lewis acids. They reported that proton-initiated rearrangements do not occur since alkyl Lewis acids give a non-acidic reaction media due to basicity of alkyl parts, which are proton scavengers and rapidly turn into ethane or methane gases[19]. When alkyl-acid chlorides are employed in the acylating agent, the formation of acidic proton is thus not to be expected.

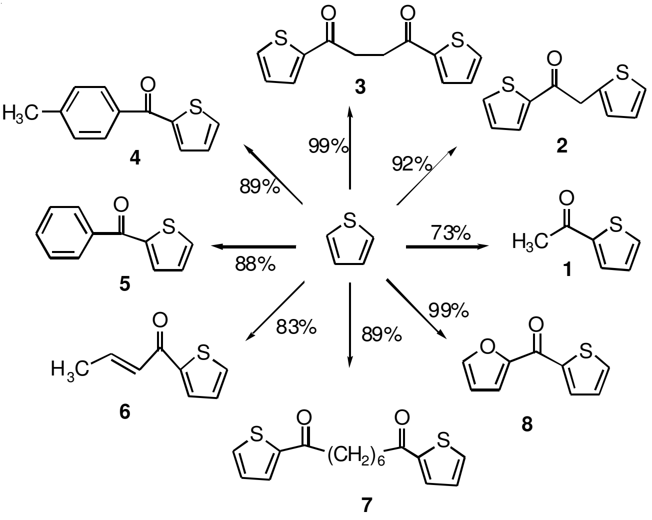
On the other hand, Watt and co-workers reported that acylation of ferrocene with acryloyl chloride would not yield the corresponding unsaturated ferrocenyl ketone, instead afforded propanoyl ferrocene and ferrocenophane derivative using AlCl$_3$ as a catalyst. They synthesized acryloylferrocene in two steps starting from ferrocene[19,20]. In first step, 3-chloropropanoylferrocene was obtained through the Friedel-Crafts acylation and in second step, dehydrochlorination of 3-chloropropanoyl ferrocene *via* silica gel (column chromatography) afforded acryloylferrocene. However, Dogan and co-workers[11] have synthesized acryloylferrocene in one step using EtAlCl$_2$/Me$_3$Al Lewis acids. The aforementioned attributes have prompted us to use EtAlCl$_2$ as lewis acid in Friedel-Crafts acylation of thiophene.

We speculated that during the acylation of thiophene, ethyl anion abstract the hydrogen form thiophene during the aromatization or after the aromatization (**Scheme-I**). It is clear that the reaction media is non-acidic because ethyl anion have neutralized the proton produced during the acylation.



**Scheme-I:** EtAlCl$_2$ as Brønsted base in $E_AS$ reaction

Among eight derivatives of thiophene synthesized (**Scheme-II**), 1,4-*bis*(2-thienyl) butane-1,4-dione (**3**) is the most commonly used one because it is the precursor for SNS type conductive polymers[2,21]. Therefore, we searched the optimization condition for **3**. The best yield observed was 0.15 M of succinyl chloride and 0.315 M of thiophene were used. On the other hand, the catalyst loading showed that the highest yield obtained when 1.5 equivalent of EtAlCl$_2$ was used in accord with thiophene.



**Scheme-II:** Thiophene derivative syntheses in the presence of EtAlCl$_2$

Different routes are available leading to 1,4-*bis*(2-thienyl)-butane-1,4-dione (**3**)[22-24]. Among these methods, the Friedel-Craft reaction, which is the first reported by Merz and Ellenger albeit with long reaction period (24 h), is mostly used[25]. Recently, the reaction time has been reduced under forcing conditions (reflux)[21].

High yields were observed for (furan-2-yl)(2-thienyl)-methanone (**8**) and succinylthiophene (**3**) (99 % for each) while the lowest yield (73 %) was obtained for acetyl thiophene (**1**) (**Scheme-II**). Even in the case of more long substrates, such as suberoylthiophene (**7**) and crotonoylthiophene (**6**) good yields (up to 89) were obtained. Our protocol can be extended to the acylation of other aromatics. For this purpose, 1-(1*H*-pyrrole-2-yl)ethanone (**9**) was synthesized with the yield of 90 %. Unfortunately, acylation of pyridine and pyrrole with

$EtAlCl_2$ catalyst did not give any products. The reason for this unreactivity may come from the reluctance of pyridine towards the $E_AS$ reactions and acidic proton of pyrrole.

## Conclusion

In summary, 8 derivatives of thiophene were synthesized *via* electrophilic aromatic substitution rection in the presence of $EtAlCl_2$. The yields are in moderate to good yields. The success of the reaction was probably due to the Brønsted basicity of $EtAlCl_2$. Easy work-up and short reaction period can be said as other advantages over the present methods. The current methods have either long reaction times, or have forced conditions. Moreover, our protocol is also suitable for multimolar preparations.

## REFERENCES

1. D.E. Pearson and C.A. Buehler, *Synthesis*, 533 (1972).
2. A. Cihaner, O. Mert and A.S. Demir, *Electrochim. Acta*, **54**, 1333 (2009).
3. L.F. Schweiger, K.S. Ryder, D.G. Morris, A. Glidle and J.M. Cooper, *J. Mater. Chem.*, **10**, 107 (2000).
4. A.I. El-Khawaga, M.F. El-Zohry and M.T. Ismail, *Phosphorus Sulfur Silicon*, **33**, 25 (1987).
5. R. Parella, N. Amitkumar and S.A. Babu, *Tetrahedron Lett.*, **54**, 1738 (2013).
6. F. Richard, H. Carreyre and G. Perot, *J. Catal.*, **159**, 427(1996).
7. H. Matsubara, S. Yasuda and I. Ryu, *Synlett*, **2**, 247 (2003).
8. V.I. Smirnov, A.V. Afanas'ev and L.I. Belen'kii, *Chem. Heterocycl. Comp.*, **46**, 1199 (2011).
9. B.B. Snider, D.J. Rodini, M. Karras, T.C. Kirk, E.A. Deutsch, R. Cordova and R.T. Price, *Tetrahedron*, **37**, 3927 (1981).
10. B.B. Snider and A.C. Jackson, *J. Org. Chem.*, **47**, 5393 (1982).
11. Ö. Dogan, V. Senol, S. Zeytinci, H. Koyuncu and A. Bulut, *J. Organomet. Chem.*, **690**, 430 (2005).
12. M. Cai, G. Zheng and G. Ding, *Green Chem*., **11**, 1687 (2009).
13. M. Jaspars, B.J. Morrison and O.C. Musgrave, *Tetrahedron*, **59**, 4153 (2003).
14. J.-Y. Chen, S.-J. Chen, Y.-J. Tang, C.-Y. Mou and F.-Y. Tsai, *J. Mol. Catal. A*, **307**, 88 (2009).
15. F. Manjolinho, M.F. Grünberg, N. Rodriguez and L.J. Gooßen, *Eur. J. Org. Chem.*, **25**, 4680 (2012).
16. J.H. Billmann and F.H. Travis, *Proc.-Indian Acad. Sci. Chem. Sci.*, **54**, 101 (1944).
17. H. Li, M. Yang, Y. Qi and J. Xue, *Eur. J. Org. Chem.*, **14**, 2662 (2011).
18. A.B. Zaitsev, E.Y. Schmidt, A.M. Vasil'tsov, A.I. Mikhaleva, O.V. Petrova, A.V. Afonin and N.V. Zorina, *Chem. Heterocycl. Comp.*, **42**, 34 (2006).
19. T.D. Turbitt and W.E. Watts, *J. Organomet. Chem.*, **46**, 109(1972).
20. T.H. Barr and W.E. Watts, *Tetrahedron*, **24**, 3219 (1968).
21. E. Yildiz, P. Camurlu, C. Tanyeli, I. Akhmedov and L. Toppare, *J. Electroanal. Chem.,* **612**, 247 (2008).
22. A.B. Merrill and E. Legoff, *J. Org. Chem.,* **55**, 2904 (1990).
23. W.Y. Leung and E. Legoff, *Synth. Commun.,* **19**, 787 (1989).
24. J. Kagan and S.K. Arora, *Heterocycles*, **20**, 1937 (1983).
25. A. Merz and F. Ellenger, *Synthesis*, 462 (1991).