Synthetic Communications: An International Journal for Rapid Communication of Synthetic Organic Chemistry
Publication details, including instructions for authors and subscription information:
http://www.tandfonline.com/loi/lsyc20

A Convenient Synthesis of Thiophenes from β, γ-Epoxycarbonyl Compounds

Kyung-Tae Kang [a] & Jong Sun U [a]
[a] Department of Chemistry , Pusan National University , Pusan, 609-735, Korea
Published online: 23 Sep 2006.

To cite this article: Kyung-Tae Kang & Jong Sun U (1995) A Convenient Synthesis of Thiophenes from β, γ-Epoxycarbonyl Compounds, Synthetic Communications: An International Journal for Rapid Communication of Synthetic Organic Chemistry, 25:17, 2647-2653, DOI: 10.1080/00397919508011811

To link to this article: http://dx.doi.org/10.1080/00397919508011811

SYNTHETIC COMMUNICATIONS, 25(17), 2647-2653 (1995)

A CONVENIENT SYNTHESIS OF THIOPHENES FROM β,γ-EPOXYCARBONYL COMPOUNDS

Kyung-Tae Kang* and Jong Sun U

Department of Chemistry, Pusan National University, Pusan 609-735, Korea.

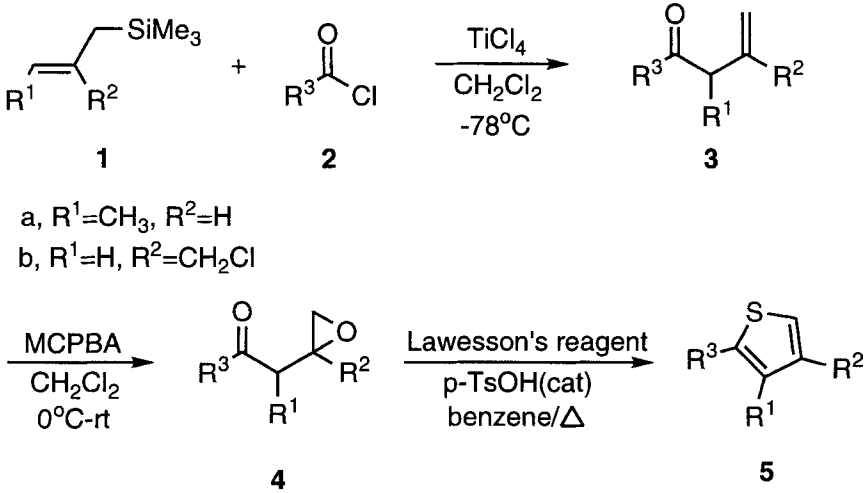
Abstract: β,γ-Epoxycarbonyl compounds were converted to thiophenes when treated with Lawesson's reagent in the presence of a catalytic amount of p-toluenesulfonic acid.

β,γ-Epoxycarbonyl compounds are useful precursors of furans.[1] Recently, we have reported on a facile synthesis of β,γ-epoxycarbonyl compounds by epoxidation of allylic ketones[1b] which were readily obtained from the Lewis acid-mediated reaction of allylsilanes with acid chlorides.[2] We report herein on the direct conversion of epoxycarbonyl compounds to thiophenes.

The allylsilanes, 2-(chloromethyl)-3-(trimethylsilyl)propene (**1a**)[3] and crotyltrimethylsilane (**1b**)[4] react with various acid chlorides in the presence of one equiv of $TiCl_4$ at -78 °C to afford the corresponding allylic ketones **3** in high yields. Isomerization of **3** to conjugated enones by acids was not observed at all under the reaction conditions. However, the allylic ketones **3g-j**, where R^1=CH_3, were readily isomerized to conjugated enones during chromatographic

*To whom correspondence should be addressed

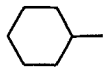
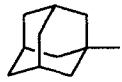
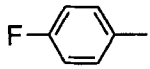
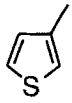
purification on silica gel.[5] With the allylic ketones **3a-f**, where R^1=H, no such isomerization arised. Epoxidation of **3** with 2 equiv of m-chloroperoxybenzoic acid (MCPBA) in dichloromethane at 0 °C~room temperature afforded β,γ-epoxy-carbonyl compounds **4** in high yield after purification (SiO_2, CH_2Cl_2). When a benzene solution of **4** with Lawesson's reagent in the presence of a catalytic amount of p-toluenesulfonic acid was refluxed for 1h, thiophenes **5** were produced. The order of addition of Lawesson's reagent and p-toluenesulfonic acid was important; when p-toluenesulfonic acid was added prior to Lawesson's reagent, a certain amount of furans were formed along with the corresponding thiophenes.[6] Following the intermediate products isolation procedure 2-isobutyl-4-chloromethylthiophene (**5a**) was obtained in 57% yield based on the starting allylsilane **1a**.[7]



The three step procedures, the $TiCl_4$-promoted reaction of the allylsilane **1** with an acid chloride, epoxidation with MCPBA, and cyclization process to thiophene could be performed successively without isolation of the intermediate

products. The consecutive procedure gave the thiophene **5a** in better overall yield (64%, Table 1, entry 1) compared to the intermediate isolation procedure (57%). The examples in Table 1 attest to the generality of the process. Both 2-substituted-4-chloromethylthiophenes (**5a-f**) and 2-substituted-3-methylthiophenes (**5g-j**) can be prepared in good yields.

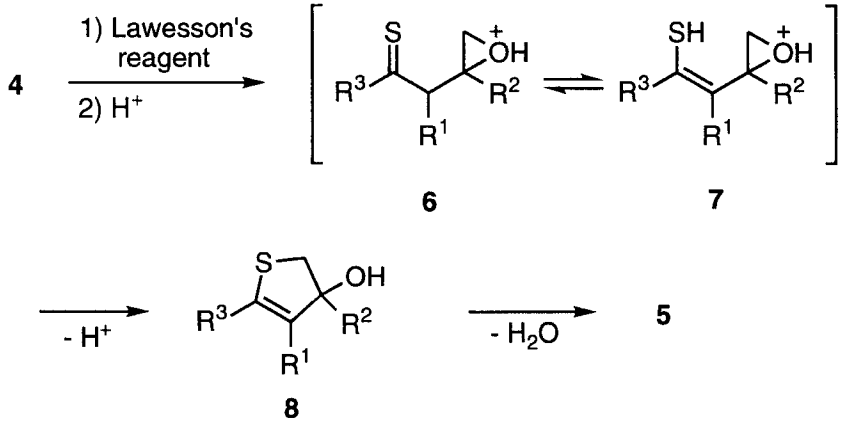
Table.1 Synthesis of Thiophenes **5**[a]

Thiophene **5**	R^1	R^2	R^3	Overall Yield,[b] %
a	H	CH_2Cl	$(CH_3)_2CHCH_2$	64
b	H	CH_2Cl		63
c	H	CH_2Cl		57
d	H	CH_2Cl	$MeO_2CCH_2CH_2$	42
e	H	CH_2Cl		56
f	H	CH_2Cl		52
g	CH_3	H	$(CH_3)_2CHCH_2$	72
h	CH_3	H	$MeO_2CCH_2CH_2$	63
i	CH_3	H	Ph	83
j	CH_3	H		70

[a]The three step reactions were carried out in seqence without isolation of the intermediate products (see text).

[b]Isolated yields (not optimized).

The reaction presumably proceeds through an acid catalyzed cyclization of the epoxythiocarbonyl intermediates **6** or their enethiol tautomers **7** initially formed from the reaction of **4** with Lawesson's reagent. The cyclization, despite of a disfavored 5-endo-trig process, could be effectively assisted by the nature of the second-row element sulfur.[8]



In summary, the present reaction sequence provides a facile and regioselective synthesis of various substituted thiophenes by using properly designed allylsilanes.

Experimental

General procedure for the synthesis of thiophenes 5: To a dichloromethane (5 ml) solution of $TiCl_4$ (5 mmol) a mixture of an acid chloride **2** (5 mmol) and the allylsilane **1** (5 mmol) in CH_2Cl_2 (4 ml) was added slowly at -78 °C. After 1h, the mixture was quenched with 3N HCl and extracted with ether. The etheral extract was washed with sat. aq $NaHCO_3$ and brine, dried over Na_2SO_4, and concentrated *in vacuo*. To a dichloromethane (8 ml) solution of the crude product **3** MCPBA

(50%, 10 mmol) was added at 0 °C, and allowed to react further for 17h. After the removal of solvent, benzene (10 ml) and Lawesson's reagent (6 mmol) were added and heated to boil. After 5 min, p-toluenesulfonic acid (10 mg) was added, and refluxed for 1h. The reaction mixture was partitioned between sat. aq $NaHCO_3$ and ether, and the aqueous layer was extracted with ether. The combined organic phases were washed with water and dried over Na_2SO_4. Purification by chromatography on silica gel (carbon tetrachloride) afforded **5**.

5a : ^{1}H NMR ($CDCl_3$, 200 MHz) δ 0.97 (6H, d, J=6.6 Hz), 1.84-1.96 (1H, m), 2.66 (2H, d, J=7.0 Hz), 4.55 (2H, s), 6.79 (1H, s), 7.07 (1H, s); ^{13}C NMR ($CDCl_3$, 50 MHz) δ 22.2, 30.5, 39.3, 41.1, 121.7, 125.3, 138.0, 145.8; MS m/e 190 (M+2, 3), 188 (M^+, 7), 153 (15), 147 (23), 145 (65), 110 (52), 84 (31), 49 (100%). **5b** : ^{1}H NMR δ 1.35-1.45 (5H, m), 1.80-1.84 (3H, m), 2.03-2.06 (2H, m), 2.69-2.80 (1H, m), 4.50 (2H, s), 6.76 (1H, s), 7.00 (1H, s); ^{13}C NMR δ 26.1, 26.5, 35.4, 39.6, 41.1, 120.9, 122.5, 137.4, 153.6; MS m/e 216 (M+2, 7), 214 (M^+, 17), 179 (10), 117 (65), 84 (100%). **5c** :^{1}H NMR δ 1.75-2.07 (15H, m), 4.54 (2H, s), 6.81 (1H, s), 7.06 (1H, s); ^{13}C NMR δ 28.8, 36.3, 36.5, 41.4, 44.8, 120.8, 120.9, 137.1, 159.6; MS m/e 268 (M+2, 10), 266 (M^+, 27), 231 (21), 173 (18), 84 (100%). **5d** : ^{1}H NMR δ 2.67 (2H, t, J=15.0 Hz), 3.11 (2H, t, J=15.0 Hz), 3.68 (3H, s), 4.51 (2H, s), 6.83 (1H, s), 7.06 (1H, s); ^{13}C NMR δ 25.2, 35.5, 40.9, 51.6, 122.2, 125.1, 137.7, 144.4, 172.6; MS m/e 218 (M+2, 3), 216 (M^+, 8), 183 (25), 147 (25), 145 (88), 123 (100), 110 (79), 84 (46%). **5e** : ^{1}H NMR δ 4.55 (2H, s), 7.02-7.55 (6H, m); ^{13}C NMR δ 40.8, 115.8, 116.1, 123.1, 123.6, 127.6, 127.7, 130.35, 130.40, 139.1, 144.7, 161.0, 164.3; MS m/e 228 (M+2, 17), 226 (M^+, 46), 191 (100), 119 (56), 117 (57), 84 (96%). **5f** : ^{1}H NMR δ 4.56 (2H, s), 7.11-7.37 (5H, m); ^{13}C NMR δ 40.8, 120.1, 122.3, 123.5, 126.0, 126.4, 135.3, 138.7, 140.5; MS m/e 216

(M+2, 25), 214 (M^+, 57), 179 (100), 119 (36), 117 (35), 84 (89%). **5g**: ^{1}H NMR δ 0.95 (6H, d, J=6.6 Hz), 1.80-1.96 (1H, m), 2.15 (3H, s), 2.60 (2H, d, J=7.2 Hz), 6.78 (1H, d, J=5.2 Hz), 7.06 (1H, d, J=5.2 Hz); ^{13}C NMR δ 13.8, 22.3, 30.9, 36.9, 121.0, 129.7, 133.0, 137.6; MS m/e 154 (M^+, 9), 111 (100), 84 (38), 49 (57%). **5h**: ^{1}H NMR δ 2.19 (3H, s), 2.64 (2H, t, J=7.2 Hz), 3.08 (2H, t, J=7.2 Hz), 3.70 (3H, s), 6.79 (1H, d, J=5.2 Hz), 7.04 (1H, d, J=5.2 Hz); ^{13}C NMR δ 13.4, 23.2, 35.5, 51.6, 121.5, 123.0, 133.2, 135.9, 172.8; MS m/e 184 (M^+, 7), 124 (22), 111 (100), 84 (59), 49 (70%). **5i**: ^{1}H NMR δ 2.35 (3H, s), 6.95 (1H, d, J=5.2 Hz), 7.22 (1H, d, J=5.2 Hz), 7.27-7.52 (5H, m); ^{13}C NMR δ 14.9, 123.3, 127.1, 128.5, 129.0, 131.1, 133.1, 134.8, 137.9; MS m/e 174 (M^+, 40), 115 (14), 97 (18), 84 (100), 49 (86%). **5j**: ^{1}H NMR δ 2.42 (3H, s), 6.92 (1H, d, J=5.2 Hz), 7.08-7.35 (4H, m); ^{13}C NMR δ 15.3, 123.2, 125.0, 125.5 127.4, 131.3, 133.9, 136.6, 140.5; MS m/e 180 (M^+, 8), 147 (7), 84 (80), 49 (100%).

Acknowledgement

This work was supported by the Korea Science and Engineering Foundation through the Organic Chemistry Research Center and the Basic Science Research Institute Program, Ministry of Education (BSRI - 94 - 3408).

References

1. (a) Cormier, R. A.; Grosshans, C. A.; Skibbe, S. L. *Synth. Commun.* **1988**, *18*, 677. (b) Kang, K. -T.; U, J. S.; Hwang, S. S.; Jyung, K. K. *Synth. Commun.* **1994**, *24*, 2915.
2. (a) Kang, K. -T.; U, J. S. *Synth. Commun.* **1994**, *24*, 1507. (b) Kang, K. -T.; Lee, J. C.; U, J. S. *Tetrahedron Lett.* **1992**, *33*, 4953.

3. Trost, B. M.; Buch, M.; Miller, M. L. *J. Org. Chem.* **1988**, *53*, 4887.

4. Kira, M.; Hino, T.; Sakurai, H.*Tetrahedron Lett.* **1989**, *30*, 1099.

5. For example, **3i** was readily isomerized to the corresponding conjugated enone: ^{1}H NMR (a mixture of cis and trans isomers) δ 1.880, 1.885 (3H, d, J=7.0 Hz), 1.965, 1.971 (3H, s), 6.400, 6.407 (1H, q, J=7.0 Hz), 7.35-7.65 (5H, m).

6. 2-Isobutyl-4-chloromethylfuran was produced along with **5a**: ^{1}H NMR δ 0.93 (6H, d, J=6.6 Hz), 1.89-2.03 (1H, m), 2,45 (2H, d, J=7.0 Hz), 4.43 (2H, s), 6.05 (1H, s), 7.30 (1H, s); ^{13}C NMR δ 22.3, 27.8, 37.1, 37.6, 106.4, 122.7, 138.9, 157.1; MS m/e 174 (M+2, 11), 172 (M^+, 32), 137 (25), 129 (100%).

7. **3a**: 92%; ^{1}H NMR δ 0.91 (6H, d, J=6.6 Hz), 2.02-2.22 (1H, m), 2.33 (2H, d, J=6.6 Hz), 3.28 (2H, s), 4.10 (2H, s), 5.00 (1H, s), 5.28 (1H, s). **4a**: 85%; ^{1}H NMR δ 0.90 (6H, d, J=6.4 Hz), 2.02-2.22 (1H, m), 2.30 (2H, d, J=6.4 Hz), 2.55 (1H, d, J=17.4 Hz), 2.75 (1H, d, J=4.4 Hz), 2.84 (1H, d, J=4.4 Hz), 3.15 (1H, d, J=17.4 Hz), 3.52 (1H, d, J=11.8 Hz), 3.82 (1H, d, J=11.8 Hz). **5a**: 73%.

8. Baldwin, J. E. *J. Chem. Soc. Chem. Commun.* **1976**, *734*, 736.

(Received in Japan 18 October 1994)