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# SYNTHESIS OF 2-SUBSTITUTED 3,5-DIBROMOTHIOPHENES THROUGH BASE-CATALYZED HALOGEN DANCE REACTION OF 2,5-DIBROMOTHIOPHENE

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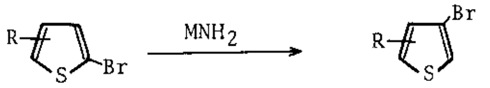
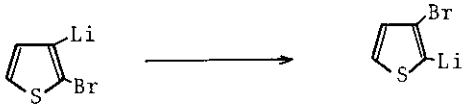
Abstract —— Treatment of 2,5-dibromothiophene with LDA in THF at -78°C, followed by quenching with electrophiles afforded the corresponding 2-substituted 3,5-dibromothiophenes in good yield.

It is well known that 2-bromothiophenes are easily convertible to 3-bromothiophenes on treatment with metal amide in liquid ammonia[1,2] (eq. 1). Furthermore, 2-bromo-3-lithiothiophene, generated from 2-bromo-3-iodothiophene, underwent a rapid halogen-metal exchange reaction similar to the base-catalyzed halogen dance (BCHD)[3]. This reaction is noted for the other thienyllithium compounds to ultimately give the stable 2-lithiothiophene derivatives[3] (eq. 2).



eq. 1



eq. 2

However, lithiation of 2,5-dibromothiophene (1) with lithium diisopropylamide (LDA) in THF or ether at -70°C was known to give 2,5-dibromo-3-lithiothiophene (2) which behaved like a normal lithium reagent and 2,5-dibromo-3-trimethylsilyl thiophene (3) was obtained by quenching with trimethylchlorosilane[4]. We examined the same reaction during the investigation of a synthesis of 3-substituted 2,5-dibromothiophenes, which would be useful precursors giving poly-substituted thiophenes. The lithiothiophene formed in this reaction was found to be 3,5-dibromo-2-lithiothiophene (4), which would be derived from 2 by BCHD mechanism. The results of our studies are described in this paper. (Scheme 1).

Scheme 1

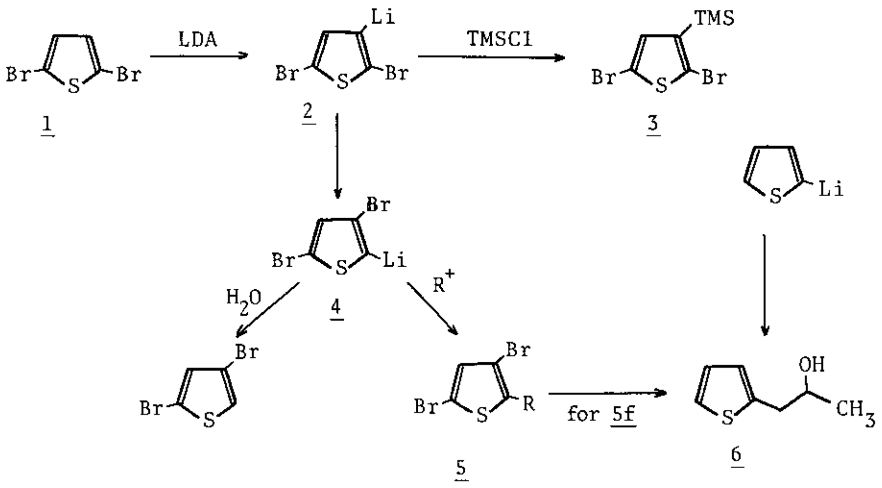
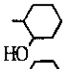
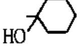


Table 1. 2-Substituted 3,5-Dibromothiophenes (5a)-(5j)

| 5 | R | Yield (%) | bp (torr) | $^1$H NMR ($CDCl_3$) δ 4H |
|---|---|---|---|---|
| 5a | $-CH_3$ | 95 | 70-75°C (2)[a] | 6.92 |
| 5b | $-CH_2CH_3$ | 80 | 90-95°C (3) | 6.80 |
| 5c | $-CH_2CH{=}CH_2$ | 68 | 108-113°C (3) | 6.97 |
| 5d | -CHO | 85 | 117-120°C (3) | 7.19 |
| 5e | -COOEt | 72 | 130-135°C (3) | 7.12 |
| 5f | $-CH_2CH(OH)CH_3$ | 73 | 136-140°C (3) | 7.00 |
| 5g | $-CH_2CH(OH)Et$ | 68 | 138-144°C (3) | 6.95 |
| 5h |  HO | 63 | 180-185°C (3) | 6.95 |
| 5i |  HO | 77 | 163-167°C (3) | 6.93 |
| 5j | $-SCH_3$ | 45 | 154-159°C (3) | 7.40 |

[a] lit.[5] bp 48-55°C (0.35-0.45)

Treatment of 1 with LDA (1.1 equi. mol, THF, -78°C, 0.5 h), followed by quenching with water at the same temperature gave 3,5-dibromothiophene in nearly quantitative yield without recovery of any trace amount of 1. This fact indicates that 2 initially generated from 1, was rapidly converted to 4 even at -78°C. The same reaction by the use of methyl iodide instead of water gave 3,5-dibromo-2-methylthiophene (5a)[5]. In a similar fashion, ethyl iodide, allyl bromide, N,N-dimethylformamide, ethyl chloroformate, propylene oxide, butylene oxide, cyclohexene oxide, cyclohexanone, dimethyl disulfide were used to give the corresponding 2-substituted 3,5-dibromothiophene (5b)-(5j), respectively. The results are summarized in the Table 1.

In addition, in order to confirm that substitutents were introduced to the 2-position, 5f was led to 1-methyl-2-(2-thienyl)ethanol (6). Treatment of 5f with n-BuLi (3 equi. mol, THF, -78°C) afforded 6[6], which was identical with the authentic sample prepared by the reaction of 2-lithiothiophene with propylene oxide, in all respects.

## REFERENCES

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6. 95 % yield, bp 75-80°C (3 torr), $^{1}$H NMR (CDCl$_3$) $\delta$ 1.22 (3H, d, J=7 Hz), 2.91 (2H, d, J=6 Hz), 3.80-4.17 (1H, m), 6.87-7.03 (2H, m), 7.20 (1H, d,d, J=6 and 1.5 Hz).

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