Pergamon

PII: S0040-4039(97)01183-0

Tetrahedron Letters, Vol. 38, No. 30, pp. 5315-5318, 1997

0040-4039/97 $17.00 + 0.00

Preparation of Benzofurano-, Benzothieno-, Indolo-3-Sulfolenes as Precursors for Heteroaromatic *o*-Quinodimethanes

Chung-Wen Ko and Ta-shue Chou*
Institute of Chemistry, Academia Sinica, Taipei and
Department of Chemistry, National Taiwan University, Taipei, Taiwan, R.O.C.

Abstract: Efficient routes have been developed for the synthesis of benzothieno-3-sulfolene **15**, benzofurano-3-sulfolene **16**, and *N*-tosylindolo-3-sulfolene **18**. These compounds are ideal precursors for the corresponding heteroaromatic *o*-quinodimethanes. © 1997 Elsevier Science Ltd.

The chemistry of heteroaromatic *o*-quinodimethanes **1** (HAQD's) has drawn increasing interests from organic chemists in the past few years.[1] One of the general strategies toward the generation of these reactive species is using heteroaromatic-fused 3-sulfolenes **2**[2] as their precursors. There are several advantages of this methodology. For example, the extrusion of SO_2 is usually performed at moderately high temperatures under totally neutral conditions so that the corresponding HAQD's generated *in situ* can be trapped in good yield. About a dozen heteroaromatic-fused 3-sulfolenes have been demonstrated to be good precursors for HAQD's.[1,3] The HAQD's of benzothiophene[4], indole[5] and benzofuran[6] were generated by 1,4-elimination and flash vacuum pyrolysis strategies. However, benzofurano-3-sulfolene and benzothieno-3-sulfolene are still unknown so far. Although *N*-acetylindolo-3-sulfolene is known,[7] it was only an SO_2 trapping product of the indolo-*o*-quinodimethane. Therefore, we wished to prepare the fused 3-sulfolene of these heteroaromatics efficiently and study the generation of the corresponding HAQD's from them.

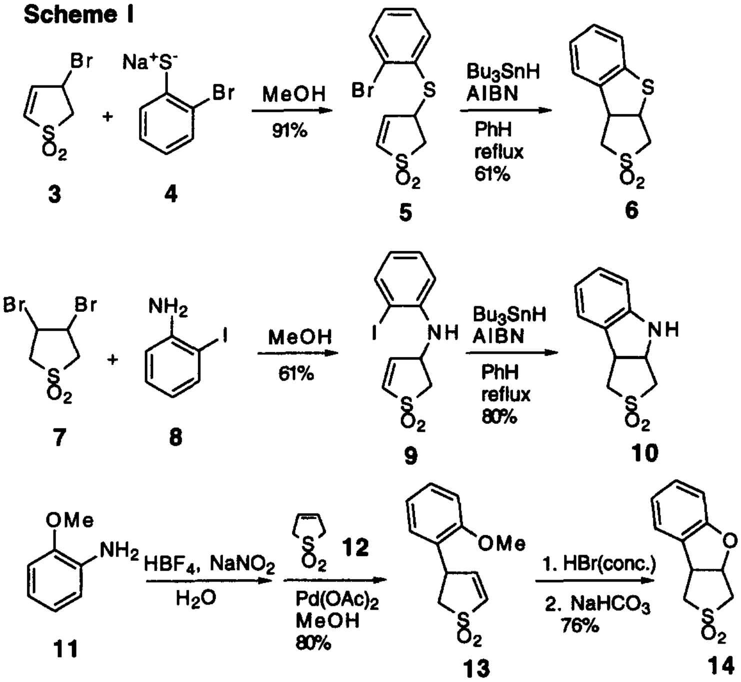
1

2

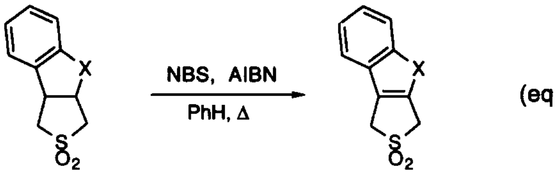
Our strategy involved the preparation of dihydro heterocycles at first of which the subsequent aromatization could lead to the target molecules. It was reported that 4-bromo-2-sulfolene **3**[8] undergoes direct substitution reaction with thiophenoxide in good yield. Therefore, we treated **3** with *o*-bromothiophenoxide **4** in MeOH and obtained the desired substitution product **5** in 91 % yield (**scheme I**). Radical cyclization of **5** initiated by Bu_3SnH and AIBN in refluxing benzene proceeded smoothly to afford **6** in 61 % yield. By a similar strategy, compound **7**[9] was reacted with *o*-iodoaniline **8** to give product **9** in 61% yield. Since the reaction involved double dehydrobromination and subsequent conjugate addition,[8] a large excess (8 eq) of **8** was used to assure good yield. Cyclization of **9** to **10** could be achieved by radical process in 80% yield.

It is known that the reaction of either **3** or **7** with a phenoxide yields only the unstable thiophene 1,1-dioxide *via* elimination reactions.[8] Therefore, a different route was used for the preparation the dihydrofuran system **14**. Treatment of *o*-anisidine **11** with nitrous acid[10] followed by the addition of 3-sulfolene **12** and a catalytic amount of $Pd(OAc)_2$ produced the coupling product **13** (72%). Demethylation of **13** and subsequent base-induced cyclization gave the desired product **14** in 76% overall yield.

Scheme I



Aromatization of heterocycles can be accomplished in many ways. However, not all of these methods are useful for the preparation of aromatic-fused 3-sulfolenes because these target molecules may lose SO_2 if the conditions involve high temperatures.[2] Therefore, indirect aromatization was considered. When **6** was treated with NBS in the presence of AIBN in refluxing benzene for 1h, benzothieno-3-sulfolene **15** was obtained in 97% yield without any intermediate being detected (eq1). The reaction time was kept short to avoid possible SO_2 extrusion. Similar condition was found effective for compound **14** as well where benzofurano-3-sulfolene **16** was produced in 74% yield.



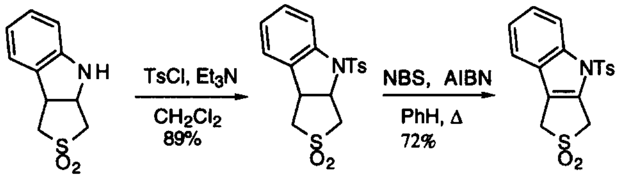
6, X= S
14, X= O

15, X= S (97%)
16, X= O (74%)

(eq 1)

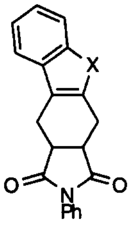
However, the reaction of **10** with NBS/AIBN did not give the desired aromatized product. The nitrogen atom on **10** might have acted as an activating group for eletrophilic aromatic substitution so that radical bromination was retarded. To solve this problem, **10** was first tosylated (TsCl, Et_3N) to **17**. The partially deactivated molecule was then treated with NBS/AIBN and the aromatization proceeded without any difficulty to give **18** in 72% yield (**scheme II**).

Scheme II

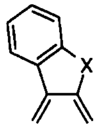


10 **17** **18**

In order to demonstrate that compounds **15**, **16**, and **18** are indeed precursors for the corresponding *o*-quinodimethanes, we treated these compounds with *N*-phenylmaleimide, a good dienophile, at 150°C. In all cases, the Diels-Alder cycloadducts **19**, **20** and **21** were produced in good yields (79%, 86%, and 80%, respectively). These results clearly evidenced the HAQD's **22**, **23** and **24** to be involved as the transient intermediates under the reaction conditions.



19, X= S
20, X= O
21, X= NTs



22, X= S
23, X= O
24, X= NTs

In summary, we have developed very efficient routes for the preparation of benzothieno-3-sulfolene **15**, benzofurano-3-sulfolene **16**, and *N*-tosylindolo-3-sufolene **18**. These compounds are all good precursors for the corresponding heteroaromatic *o*-quinodimethanes **22-24**. Further synthetic applications of these reactive species are under study.

We thank the National Science Council for financial support.

REFERENCES

1. For a recent review, see: Chou, T. S. *Rev. Heteroatom Chem.* **1993**, *8*, 65.
2. For reviews on the chemistry of 3-sulfolenes, see: (a) Chou, T. S.; Tso, H. H. *Org. Prep. Proc. Int.* **1989**, *21*, 257. (b) Chou, T. S.; Chou, S. S. P. *J. Chin. Chem. Soc.* **1992**, *39*, 625.
3. For some more recent examples HAQD's, see: (a) Chou, C. H.; Tanhnovsky, W. S.; *J. Org. Chem.* **1995**, *60*, 5449. (b) Hariri, M. A.; Pautat, F.; Fillion, H.; Domard, M.; Fenet, B. *Tetrahedron* **1995**, *51*, 9595. (c) Carly, P. R.; Compernolle, F.; Hoornaert, G. J. *Tetrahedron Lett.* **1995**, *36*, 2113. (d) Alexandrou, N. E.; Mertzanos, G. E.; Stephanidou-Stephanatou, J.; Tsoleridis, C. A.; Zachariou, P. *Tetrahedron Lett.* **1995**, *36*, 6777. (e) Hojo, M; Tomita, K; Hosomi, A. *Tetrahedron Lett.* **1993**, *34*, 485. (f) Tome, A. C.; O'Neill, P. A.; Storr, R. C.; Cavaleiro, J. A. S. *Synlett* **1993**, 397. (g) White, L. A.; O'Neill, P. M.; Park, B. K.; Storr, R. C.; *Tetrahedron Lett.* **1995**, *36*, 5983. (h) Tome, A. C.; Cavaleiro, J. A. S.; Storr, R. C. *Tetrahedron* **1996**, *52*, 1723, 1735. (i) White, L. A.; Storr, R. C. *Tetrahedron* **1996**, *52*, 3117. (j) Chou, T. S.; Chang, R. C. *J. Org. Chem.* **1993**, *58*, 93. (k) Chou, T. S.; Chang, R. C. *Heterocycles* **1993**, *36*, 2839. (l) Chou, T. S.; Tsai, C. Y. *J. Chin. Chem. Soc.* **1993**, *40*, 581. (m) Chou, T. S.; Chen, H. C.; Tsai, C. Y. *J. Org. Chem.* **1994**, *59*, 2241. (n) Chou, T. S.; Ko, C. W. *Tetrahedron* **1994**, *50*, 10721. (o) Tso, H. H.; Tsay, H.; Li, J. H. *Synth. Commun.* **1995**, *25*, 3435. (p) Tso, H. H.; Chang, Y. M.; Tsay, H. *Synth. Commun.* **1996**, *26*, 569.
4. Dyker, G.; Kreher, R.P. *Chem. Ber.* **1988**, *121*, 1203.
5. For reviews, see: (a) Pindur, U.; Erfanian-Aboust, H. *Chem. Rev.* **1989**, *89*, 1681. (b) Magnus, P.; Gallapher, T.; Brown, P.; Pappalardo, P. *Acct. Chem. Res.* **1984**, *17*, 35. see also ref. 1.
6. (a) Bedford, S. B.; Begley, M. J.; Cornwall, P.; Knight, D. W. *Synlett*, **1991**, 629. (b) Chou, C. H.; Trahanovsky, W. S. *J. Org. Chem.* **1986**, *51*, 4208.
7. Vice, S. F.; de Carvalho, H. N.; Taylor, N. G.; Dmitrienko, G. I. *Tetrahedron Lett.* **1989**, *30*, 7289.
8. Chou, T. S.; Hung, S. C.; Tso, H. H. *J. Org. Chem.* **1987**, *52*, 3394.
9. Bailey, W. J.; Cummins, E. W. *J. Am. Chem. Soc.* **1954**, *76*, 1932.
10. (a) Sengupta, S.; Bhattacharyya, S. *Synth. Commun.* **1996**, *26*, 231. (b) Harrington, P. J.; Difiore, K. A. *Tetrahedron Lett.* **1987**, *28*, 495.

(*Received in China* 22 *February* 1997; *accepted* 30 *May* 1997)