Studies in Sulfur Heterocycles. Part 16:[1,2] Synthesis of [1]Benzothieno[3,2-*b*]pyrans via Tandem Reactions from 2,3-Dihydrobenzo[*b*]thiophene-3(2*H*)ones

Sukanta Kamila, Chandrani Mukherjee, Asish De*

Department of Organic Chemistry, Indian Association for the Cultivation of Science, Jadavpur, Kolkata-700032, W.B, India
E-mail: ocad@mahendra.iacs.res.in

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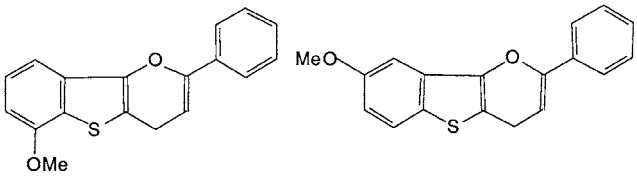
Abstract: Sequential treatment of *N*,*N*-diethyl-2-methylsulfanyl aryl amides with LDA and *p*-anisaldehyde, 1-naphthaldehyde and cinnamaldehyde afforded the corresponding thioaurones. Heating the thioaurones derived from cinnamaldehyde, above 200 °C resulted in electrocyclic ring closure and sigmatropic shift in tandem to give substituted [1]benzothieno[3,2-*b*]pyran. Treatment of *N*,*N*-diethyl-2-methylsulfanyl-5-methoxy benzamide and crotonaldehyde gave 4-methyl-8-methoxy[1]benzothieno[3,2-*b*]pyran via conjugate nucleophilic addition and ring closure in one pot. Possible mechanistic pathways are discussed.

Key words: thioaurones, electrocyclic ring closure, sigmatropic shift, benzothiopyran

Recently we reported[3,4] the synthesis of substituted thioindoxyls, key intermediates in the synthesis of diversely substituted benzo[*b*]thiophenes, through side-chain deprotonation and instantaneous intramolecular nucleophilic attack on the carbonyl carbon by the incipient anion. After the publication of our initial results,[3] Cabiddu[5] reported the formation of thioindoxyls from commercially available ethyl-2-methyl sulfanyl benzoates, following the same principle and the conversion of the thioindoxyls into their 2-arylmethylidene or 2-alkylmethylidene derivatives, commonly known as thioaurones. This prompts us to report our initial findings in this area.

Resurgence of interest in thioaurones,[6] in recent times is due to their manifold uses.[5] We developed a one-pot synthesis of thioaurones from *N*,*N*-diethyl-2-methylsulfanyl aryl amides as shown in Table 1.[7] When compounds **1** and **2** were heated in a silicone oil bath at 210 °C (bath temperature) for 7 hours, a brown mass was obtained in each case which, on chromatography over silica gel, afforded colourless crystalline compounds [eluant: EtOAc:light petroleum (3:17)]. The carbonyl peaks were absent in the IR spectra. In the proton NMR spectra apart from the methoxy signals, a two proton multiplet was present for both the compounds at δ = 2.88 to 3.22 ppm. The aromatic region showed the presence of a six proton multiplet and three doublet of doublets. In the ^{13}C NMR there were signals due to six quaternary carbons of which three are considerable down field. Signals due to methyl and methylene carbons were present in appropriate places. On the basis of spectroscopic and analytical data, the resulting compounds were assigned the structures 2-phenyl-6-methoxy[1]benzothieno[3,2-*b*]pyran (**6**) and 2-phenyl-8-methoxy[1]benzothieno[3,2-*b*]pyran (**7**) respectively.[8]

It is interesting to note that the signal due to C-2 in each case appears at δ = 186.8 ppm. This considerable downfield shift is explained by its attachment to the ring oxygen atom, phenyl ring and the double bond. On the other hand the signal due to C-3 appears at δ = 83.3 and 83.4 ppm for compounds **6** and **7**. This upfield shift is accounted for by substitution pattern. COSY and HMBC spectra established the assignments beyond doubt (Figure 1).



6 **7**

Figure 1

Formation of these two tricyclic compounds is accounted for by a plausible mechanistic pathway shown in Scheme 1. The pathway consists of electrocyclic ring closure (of *cis*oid conformation) and [1,3]hydrogen shift in tandem. Severe geometrical constraints associated with antarafacial shift suggests the possibility of an alternative two stage mechanism, the exact nature of which is under investigation.

When *N*,*N*-diethyl-2-methylsulfanyl-5-methoxy benzamide was treated sequentially with LDA and crotonaldehyde, a gummy product was obtained which upon repeated chromatography afforded a thick liquid which did not show any absorption due to a carbonyl group in the IR spectrum. ^{1}H NMR spectrum showed two three proton signals at δ = 3.89 and 1.61 ppm as singlet and doublet respectively. On the basis of analytical and spectral data, this compound is assigned the structure 4-methyl-8-methoxy[1]benzothieno[3,2-*b*]pyran (**8**) which is formed via three reactions taking place in tandem viz. formation of thioindoxyl, conjugate nucleophilic addition and ring closure as shown in Scheme 2.

We have reported above a new approach towards the synthesis of benzothieno[3,2-*b*]pyran. These compounds

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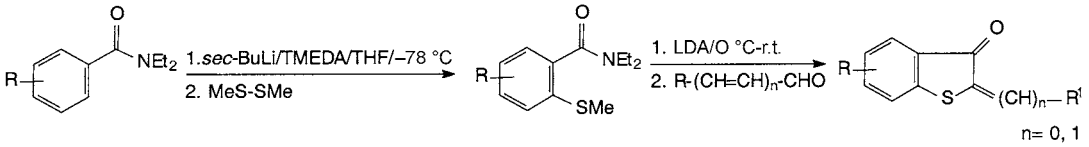
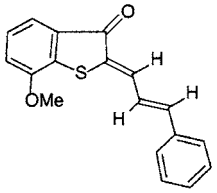
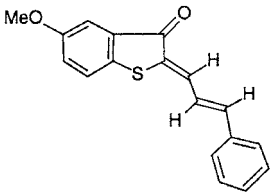
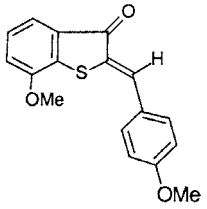
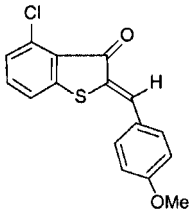
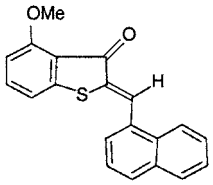
Table 1 One-Pot Synthesis of Thioaurones from *N*,*N*-Diethyl-2-methylsulfanyl Aryl Amides



Entry	Compounds	Yield (%)
1		83
2		74
3		84
4		78
5		69

belong to a system of which there are only few reports and their formation in one pot reaction is particularly convenient. Work is in progress for synthesising more compounds of this class and more in depth study of the mechanisms.

Acknowledgement

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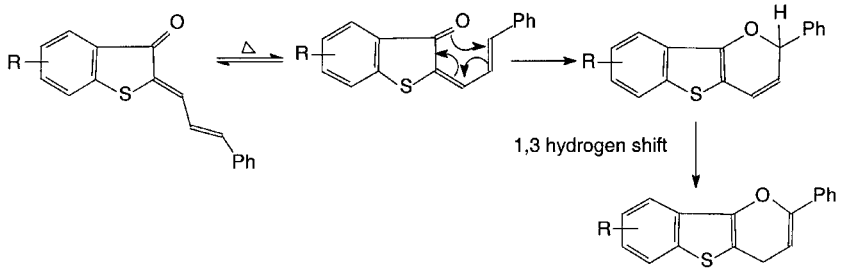

Scheme 1

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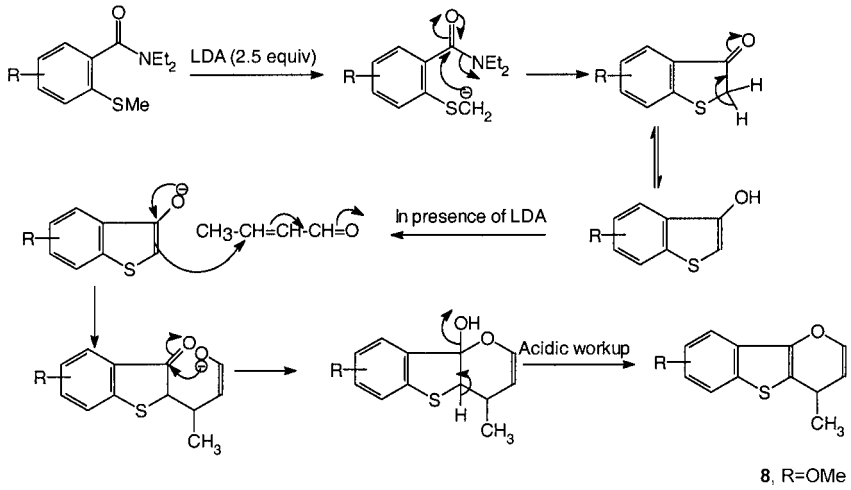

Scheme 2

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(7) **Representative Experimental Procedure for the Preparation of the Thioaurones:**
N,*N*-Diethyl-2-methylsulfanyl aryl amides were treated with LDA at 0 °C under argon and after a brief interval, the aldehyde was added by syringe. The temperature was kept at 0 °C for 1 h under inert atmosphere. Usual acidic work up after this period afforded the thioaurones in very good yields.
Compound **1**: Yellowish fluffy solid, yield 83%, mp 152–153 °C. IR (KBr): 1635 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.93 (d, 1 H, *J* = 15.4 Hz), 7.67–7.64 (m, 2 H), 7.61 (s, 1 H), 7.45–7.41(m, 3 H), 7.38 (dd, 1 H, *J* = 7.9, 8.1 Hz), 7.10 (d, 1 H, *J* = 15.4 Hz), 6.97 (dd, 1 H, *J* = 7.9 Hz), 4.02 (s, 3 H). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 186.4, 165.2, 154.8, 144.6, 134.8, 133.0, 132.6, 131.3, 129.4-129.1, 126.6, 122.9, 116.4, 109.5, 53.6. Anal. Calcd for $C_{18}H_{14}O_2S$: C, 73.40; H, 4.76. Found: C, 73.48; H, 4.74.
Compound **2**: Yellowish solid, yield 74%, mp 146–147 °C. IR (KBr): 1639.4 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.80 (d, 1 H, *J* = 15.5 Hz), 7.59–7.55 (m, 2 H), 7.52 (s, 1 H), 7.37–7.35 (m, 3 H), 7.30 (d, 1 H, *J* = 2.4 Hz), 7.12 (dd, 1 H, *J* = 2.4, 8.8 Hz), 6.95 (d, 1 H, *J* = 15.5 Hz). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 186.3, 164.4, 158.1, 144.6, 134.8, 132.7, 131.8, 131.3, 129.4-129.1, 124.5,122.8, 122.1, 56.0. Anal. Calcd for $C_{18}H_{14}O_2S$: C, 73.40; H, 4.76. Found: C, 73.10; H, 4.60.
Compound **6**: Colourless needle shaped crystal, yield 78%, mp 194–195 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.55–7.42 (m, 6 H), 7.35 (dd, 1 H, *J* = 7.8, 8.5 Hz), 6.93 (dd, 1 H, *J* = 7.8 Hz), 5.70 (dd, 1 H, *J* = 3.3, 3.4 Hz), 4.00 (s, 3 H), 3.22–2.88 (m, 2 H). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 186.8, 161.5, 155.1, 138.4, 132.0, 130.7, 129.4, 129.3, 126.7, 126.6, 116.1, 115.8, 109.1, 83.2, 56.2, 44.4. Anal. Calcd for $C_{18}H_{14}O_2S$: C, 73.40; H, 4.76. Found: C, 73.50; H, 4.80.
Compound **7**: Colourless solid, yield 65%, mp 207 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.50 (d, 1 H, *J* = 8.8 Hz), 7.50–7.22 (m, 6 H), 7.10 (dd, 1 H, *J* = 2.5, 8.8 Hz), 5.67 (dd, 1 H, *J* = 3.2, 3.3 Hz), 3.78 (s, 3 H), 3.18–2.80 (m, 2 H). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 186.7, 158.1, 138.3, 134.0, 131.8, 129.5, 129.4, 129.3, 129.3, 126.9, 124.9, 121.3, 104.0, 83.4, 56.0, 44.4. Anal. Calcd for $C_{18}H_{14}O_2S$: C, 73.40; H, 4.76. Found: C, 73.50; H, 4.80.

(8) Compound **8**: Prepared in the same way as before except crotonaldehyde was used instead of aromatic aldehyde. Yellowish gummy liquid, yield 40%. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.75 (dd, 2 H, *J* = 8.9 Hz), 7.19 (dd, 1 H, *J* = 2.1 Hz), 6.99 (dd, 1 H, *J* = 2.1, 8.8 Hz), 4.88–4.84 (m, 1 H), 3.89 (s, 3 H), 2.80–2.60 (m, 1 H), 1.61 (d, 3 H). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 154.6, 140.2, 134.7, 133.8, 132.1, 125.7, 124.5, 122.5, 111.9, 108.9, 5, 29, 2. Anal. Calcd for $C_{18}H_{12}O_2S$: C, 67.24; H, 5.17. Found: C, 67.30; H, 5.40.

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