REACTION OF N,N'-THIONYLDIIMIDAZOLE WITH THIOLS: A SULFUR TRANSFER REACTION[1]

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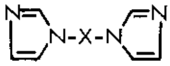
Abstract —— Reaction of N,N'-thionyldiimidazole with thiols effects the formation of disulfides and trisulfides. These results are rationalized by assuming that the thiols react with N,N'-thionyldiimidazole to produce the disulfides and N,N'-thiobisimidazole which subsequently reacts with the starting thiols to give the trisulfides.

N,N'-Carbonyldiimidazole (Ia) and N,N'-thionyldiimidazole (Ib) have been known as valuable synthetic reagents.[2] In spite of their versatility as reactive intermediates, the reaction of thiols with compound Ia or Ib has not been known to date. We now wish to report the formation of the disulfide and the trisulfide by the action of the thiol with compound Ib which sharply contrasts with that of alcohols or phenols.

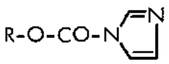
The alcohol (II) or the phenol (II) react with compound Ia or Ib to give the ester (III) or the sulfite (IV), respectively.[2a] With this concept in mind, we examined the reaction of the thiol with compound Ia or Ib.



(Ia) X = CO
(Ib) X = SO

R-OH

(II)

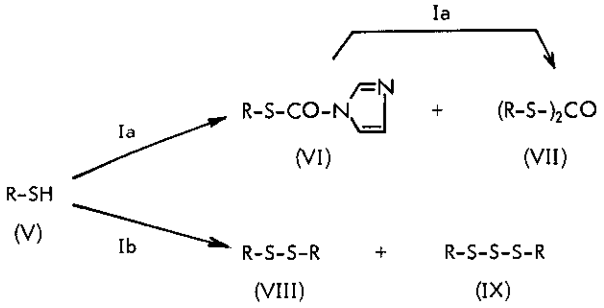


(III)

$(R\text{-}O\text{-})_2SO$

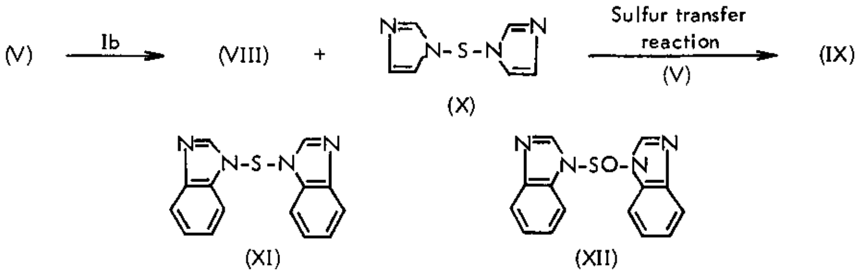
(IV)

The reaction of 4-methylthiophenol (Va) with compound Ia in dichloromethane at room temperature gave the ester (VIa, 33%, mp 104-106°C) and the carbonate (VIIa, 22%, mp 91-93°C), which was also obtained by the action of compound Ia to compound VIa in 79% yield. This behaviour of the thiol was similar to that of



a: p-Me-Ph b: o-MeCO-Ph c: Ph
d: 2,4,5-TriCl-Ph e: PhCH$_2$- f: p-NO$_2$-Ph

the alcohol or the phenol. On the other hand, surprisingly, the reaction of 2-acetylthiophenol (Vb) with compound Ib (1.5 mol. eq.), which is formed in situ, at room temperature in dichloromethane afforded a mixture of the two products (68%, weight/weight), which was separated into the disulfide (VIIIb)[3] and the trisulfide (IXb).[4] This interesting result prompted us to examine the reaction of the other thiols (Vc-f) with compound Ib. The reactions of compounds Vc-e with compound Ib under similar conditions gave a mixture of the disulfides (VIIIc-e)[5] and the trisulfides (IXc-e)[6] in good yield as expected. The reaction of p-nitrothiophenol (Vf) with compound Ib afforded di(p-nitrophenyl)sulfide (VIIIf) alone in 70% yield. Although all the disulfides (VIIIc-e) were isolated in pure state, only the trisulfide (IXc) could not be separated due to the liquid in pure state and remained in the mixture of the disulfide and the trisulfide appearing like one component in TLC. The spectral data (^{1}H-NMR, IR) of this mixtures did not contradict the existence of the trisulfide.



The formation of the disulfide and the trisulfide in the above reaction is rationalized as follows. In the same way as with dimethylsulfoxide,[7] the thiol

Table. Disulfides (VIII) and Trisulfides (IX)

Starting thiol	Product Disulfide	 Trisulfide	Ratio Disulfide/Trisulfide
Vb	VIIIb (mp 136-144°C)[a]	IXb (mp 171-172°C)[a]	3.9[b]
Vc	VIIIc (mp 57-58°C)[a]	IXc[c]	~1.5[d]
Vd	VIIId (mp 145-146.5°C)[a]	IXd (mp 166-168.5°C)[a]	2.4[b]
Ve	VIIIe (mp 66.5-69.5°C)[a]	IXe (mp 46-48°C)[a]	1.0[e]
Vf	VIIIf (mp 181-182°C)[a]	--	--

[a] Satisfactory elemental analyses and ^{1}H-NMR spectra were obtained. Compound VIIIc, Lit. mp 61°C, K. Vorster, *Chem. Ber.*, 1893, **26**, 2815; Compound VIIIe, Lit. mp 71-72°C, A. W. Hofmann, *Chem. Ber.*, 1887, **20**, 15; Compound IXe, Lit. mp 47-47.5°C, D. N. Harpp and R. A. Smith, *J. Org. Chem.*, 1979, **44**, 4140; Compound VIIIf, Lit. mp 181°C, K. Brand and A. Wirsing, *Chem. Ber.*, 1912, **45**, 1763.

[b] The ratio has been obtained from HPLC using a UV detector at 254 nm. The peak areas have been corrected with the absorbance at 254 nm.

[c] Not isolated compounds. Compound IXc: Lit. oil, H. Lecher, *Chem. Ber.*, 1925, **58**, 420.

[d] The ratio was obtained from HPLC using a UV detector at 254 nm.

[e] The ratio was obtained from the peak areas of methylene proton signals in ^{1}H-NMR spectra.

reacts with compound Ib to produce the disulfide (VIII) and N,N'-thiobisimidazole (X), which has been synthesized by Harpp and co-workers.[8] Then, compound X which was reported to be a sulfur transfer reagent, could react with the starting thiol to give the trisulfide (IX). Also, Harpp and co-workers have reported the formation of the trisulfide by the action of N,N'-thiobisbenzimidazole (XI)[8] to the thiol. Therefore, further evidence for the above mechanism was derived from the reaction of N,N'-thionyldibenzimidazole (XII) with compound Vb or Ve to give the mixture of the sulfides (VIIIb/IXb = 9.5; VIIIe/IXe = 0.6).

Although Harpp and co-workers[8] could not obtain the trisulfide by the action of compound X on the thiol, compound X, which formed in situ, may react with the thiol to give the trisulfide.

References

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2. (a) H. A. Staab, Angew. Chem. Internat. Edn., 1962, 1, 351, and references quoted therein; (b) M. Ogata, H. Matsumoto and S. Kida, Heterocycles, 1979, 12, 1285; (c) M. Ogata, H. Matsumoto, S. Kida and S. Shimizu, Tetrahedron Lett., 1979, 52, 5011.
3. In spite of the good yield in this reaction, the yield in isolation was low due to the difficulty of separating VIIIb (7%) and IXb (8%). Compound VIIIb: IR (Nujol) 1662 cm^{-1}, UV (MeOH) 230 nm (ε 3.70×10^4) and 329 nm (ε 8.11×10^3), NMR ($CDCl_3$) δ 2.68 (s, 6H, $2CH_3$), 7.27-8.03 (m, 4H, aromatic), $C_{16}H_{14}O_2S_2$ requires C, 63.55; H, 4.67; S, 21.21. Found: C, 63.59; H, 4.68; S, 21.16. Mp 171-172°C, MS: m/e = 302 (M^+).
4. Compound IXb: IR (Nujol) 1650 cm^{-1}, UV (MeOH) 229 nm (ε 2.81×10^4) and 329 nm (ε 8.72×10^3), NMR ($CDCl_3$) δ 2.57 (s, 6H, $2CH_3$), 7.17-8.43 (m, 4H, aromatic), $C_{16}H_{14}O_2S_3$ requires C, 57.46; H, 4.22; S, 28.76. Found: C, 57.52; H, 4.17; S, 28.57. Mp 136-144°C. Molecular weight (osmometric) requires 334.5. Found: 330.8. Although the MS spectrum of Compound VIIIb showed a molecular peak (M^+) at 302, the molecular peak (M^+) of compound IXb could not be observed.
5. Compound VIIId: UV (dioxane) 255 nm (ε 2.41×10^4), 295 nm (ε 4.12×10^3) and 304.5 nm (ε 3.91×10^3). $C_{12}H_4Cl_6S_2$ requires C, 33.91; H. 0.95; Cl, 50.05; S, 15.09. Found: C, 34.16; H, 1.21; Cl, 50.05; S, 15.29.
6. Compound IXd: UV (dioxane) 248.5 nm (ε 2.34×10^4), and 308 nm (ε 4.65×10^3). $C_{12}H_4Cl_6S_3$ requires C, 31.53; H, 0.88; Cl, 46.54; S, 21.04. Found: C, 31.48; H, 1.01; Cl, 46.31; S, 20.78.
7. T. J. Wallace, J. Am. Chem. Soc., 1964, 86, 2018.
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