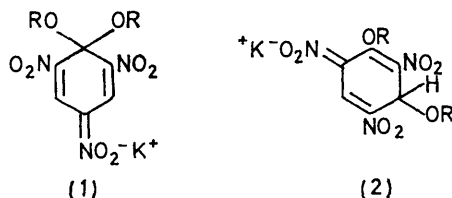


σ -Complex Formation and Aromatic Substitution with Thiolates and Nitroaryl Thioethers¹

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U.v. and ¹H n.m.r. evidence for the first *gem*-bisalkylthio-analogue of a Meisenheimer complex is reported. This substance was obtained, in equilibrium with the 1,3-bisalkylthio-analogue (which preponderates), on mixing ethyl thiopicrate with sodium ethanethiolate in dimethyl sulphoxide. These complexes are ephemeral species, however, because of a remarkable specific substitution of the *p*-nitro-group by ethanethiolate to give 1,4-bisethylthio-2,6-dinitrobenzene in high yield. In the corresponding reaction of *p*-tolyl thiopicrate with sodium toluene-*p*-thiolate, decay of Meisenheimer-type intermediates was too fast to be studied by n.m.r.; besides the product of *para*-substitution, products of *ortho*- and of *ortho*-plus *para*-substitution were detected.

In recent years Meisenheimer complexes,² which have been suggested as intermediates in aromatic substitution,^{3,4} have been the subject of n.m.r. studies,⁵ showing that addition complexes involving unsubstituted positions [*e.g.* (2) in the picryl series⁶] are also formed.



These studies have been extended to arenes carrying other activating groups such as cyano, halogeno, aza,

or annulated arene,⁵ and to five-membered heterocycles.⁷ Reactions with other nucleophilic species such as nitrogen, carbon, and sulphur nucleophiles have also been investigated.⁵ Studies with sulphur nucleophiles have concerned the interaction of aqueous sodium sulphite with trinitrobenzene,⁸ trinitroanisole,⁸ trinitrotoluene,⁹ picric acid,¹⁰ *N*-methyl-,⁸ or *NN*-dimethyl-trinitroaniline,⁸ or trinitrobenzaldehyde,⁹ and of sodium ethanethiolate or benzenethiolate with trinitrobenzene,^{11a} trinitroaniline, *N*-methyltrinitroaniline, or 2,4-dinitroaniline in methanol-dimethyl sulphoxide mixtures.^{11b} These studies⁸⁻¹¹ revealed that sulphur nucleophiles add exclusively to unsubstituted ring positions so that, although the question of whether *gem*-bisalkylthio-analogues of Meisenheimer complexes (I) can be ob-

¹ Preliminary report, G. Biggi and F. Pietra, *Chem. Comm.*, in the press.

² J. Meisenheimer, *Annalen*, 1902, **323**, 205.

³ J. F. Bunnett and R. E. Zahler, *Chem. Rev.*, 1951, **49**, 273; F. Pietra, *Quart. Rev.*, 1969, **23**, 504.

⁴ J. A. Orvik and J. F. Bunnett, *J. Amer. Chem. Soc.*, 1970, **92**, 2417.

⁵ (a) M. J. Strauss, *Chem. Rev.*, 1970, **70**, 667; (b) M. R. Crampton, *Adv. Phys. Org. Chem.*, 1969, **7**, 211; P. Buck, *Angew. Chem.*, 1969, **81**, 136; E. Bunzel, A. R. Norris, and K. E. Russell, *Quart. Rev.*, 1968, **22**, 123; R. Foster and C. A. Fyfe, *Rev. Pure Appl. Chem.*, 1966, **16**, 61.

⁶ M. R. Crampton and V. Gold, *J. Chem. Soc. (B)*, 1966, 893; K. L. Servis, *J. Amer. Chem. Soc.*, 1967, **89**, 1508.

⁷ F. Terrier, A. P. Chatrousse, R. Schaal, C. Paulmier, and P. Pastour, *Tetrahedron Letters*, 1972, 1961; D. Spinelli, V. Armanino, and A. Corrao, *J. Heterocyclic Chem.*, 1970, 1441.

⁸ M. R. Crampton, *J. Chem. Soc. (B)*, 1967, 1341.

⁹ A. R. Norris, *Canad. J. Chem.*, 1967, **45**, 175.

¹⁰ M. R. Crampton and M. El-Ghariani, *J. Chem. Soc. (B)*, 1969, 330.

¹¹ (a) J. W. Larsen, K. Amin, S. Ewing, and L. L. Magid, *J. Org. Chem.*, 1972, **37**, 3857; (b) M. R. Crampton, *J. Chem. Soc. (B)*, 1968, 1208.

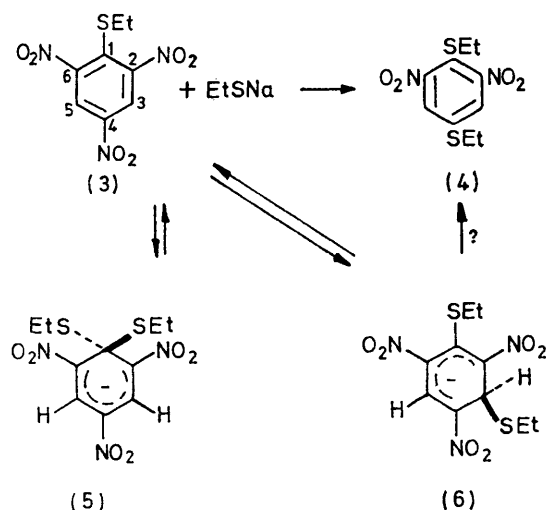
tained has never been raised, it is implied that they may not be obtainable when unsubstituted ring positions are available.

We report here our observations¹ on a system (ethyl thiopicrate-sodium ethanethiolate) analogous to those of Meisenheimer,² with sulphur in place of both the ether and the alkoxide oxygen atoms. We have also studied the interaction of *p*-tolyl thiopicrate with sodium toluene-*p*-thiolate.

RESULTS AND DISCUSSION

When ethyl thiopicrate (3) (10^{-5} mol l⁻¹) was mixed with a small volume of a solution of sodium ethanethiolate in dimethyl sulphoxide at 24° under nitrogen, giving a 1.1 to 10-fold excess of the salt, a deep red colour immediately developed and then rapidly faded. Under these conditions two u.v. absorptions [λ_{max} 464 (log ϵ ca. 4.0) and 545 nm (ca. 4.2)] were seen which are typical of 1:1 Meisenheimer complexes.^{5a} In contrast, when a 200-fold excess of sodium ethanethiolate was used, stable coloured solutions were obtained with a single u.v. maximum at 525 nm (log ϵ ca. 4.1), typical of 2:1 Meisenheimer complexes.

In a preparative experiment with 0.3M-reagents the colour was allowed to fade completely, then water was added to give a yellow crystalline precipitate of the substitution product (4), which was obtained in high



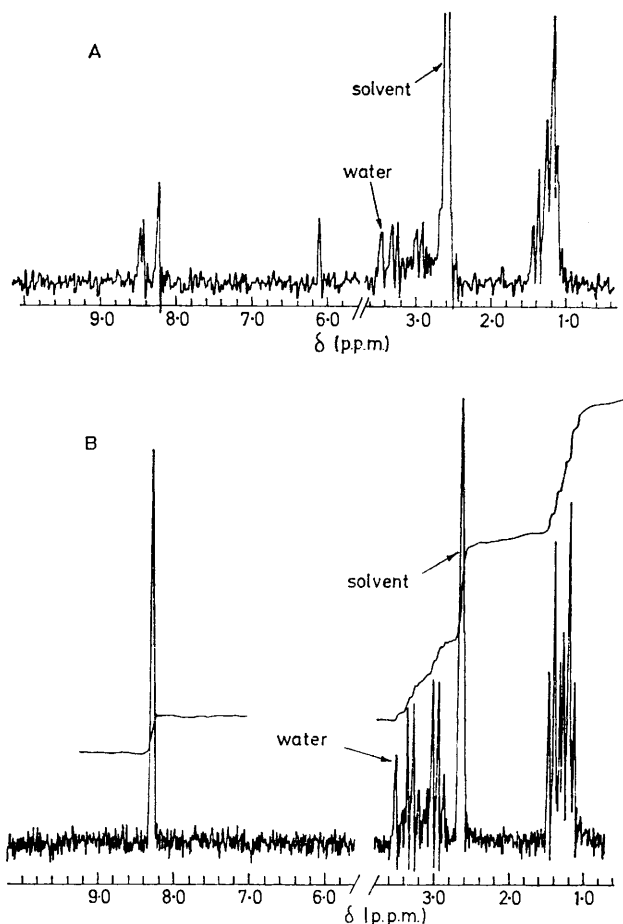
yield. The presence of a single sharp ¹H n.m.r. absorption (δ 8.23 p.p.m.) in the aromatic region shows that the product is not the *ortho*-substituted derivative which would possess two non-equivalent aromatic hydrogen atoms.

These data suggest that thio-analogues of the Meisenheimer complexes (2) or (1) (or both) do indeed form, but do not survive because either the complexes them-

* The n.m.r. data reported here were obtained for solutions in commercial (CD₃)₂SO distilled over CaH₂. Solutions in untreated solvent, which contained large amounts of H₂O, gave the same results.

selves or uncomplexed (3) react rapidly with sodium ethanethiolate to give compound (4).

The reaction of 0.3M-reagents under nitrogen was monitored by fast-scan ¹H n.m.r. spectroscopy.* At either 60 or 100 MHz, immediately after mixing the reagents, singlets at δ 8.48, 8.43, 8.23, and 6.17, as well as complex absorptions at δ 3.4—2.4 and 1.6—0.8 p.p.m., were seen, and the signals for structure (3) [δ 9.15 (2H, s), 3.0 (2H, q), and 1.2 (3H, t)] were absent. The intensities of the signals at δ 8.48, 8.43 and 6.17 p.p.m.



N.m.r. (100 MHz) spectrum of ethyl thiopicrate (3) plus sodium ethanethiolate in (CD₃)₂SO; A, ca. 3 min after mixing; B, after 3 h

decreased while that of the signal at δ 8.23 p.p.m. increased concurrently. After 3 min this type of spectrum still persisted; however after 3 h the spectrum of (4) alone was observed (Figures A and B, respectively). Throughout, the ratio of the total area of the peaks at δ 8.48, 8.43, 8.23, and 6.17 to the area of the δ 1.6—0.8 signals was 1:3, and the ratio of the areas of the peaks at δ 8.48 and 6.17 was 1:1.

The last two signals can be attributed to the complex (6) produced by addition at the unsubstituted ring carbon atom, and the signal at δ 8.43 p.p.m. can be assigned to the *gem*-bisalkylthio-complex (5). These assignments are in agreement with chemical shift data for the

Meisenheimer complexes (1) and (2). Moreover the lack of spin-spin coupling between the cyclohexadienide protons of both structures (5) and (6) conforms to the case of the complex between trinitrobenzene and sodium ethanethiolate.¹¹

The singlet at δ 8.43 would also be consistent with a Meisenheimer complex derived from (3) by sodium ethanethiolate addition at C-4. However, in view of the high mobility of the nitro-group in nucleophilic aromatic substitution,¹² we can exclude this possibility.

Finally, although the aliphatic region of the spectrum in Figure A is not readily interpretable, the signal at δ 8.23 p.p.m. is clearly attributable to compound (4).*

The decrease in intensity of the low-field n.m.r. signals in a parallel fashion [and the extremely high rates of formation of compounds (5) and (6); see later] indicate that we are observing compounds (5) and (6) at their equilibrium ratio. The combined areas of the signals at δ 8.48 and 6.17 relative to that at δ 8.43 (Figure A) show that (6) is appreciably more stable than (5), which is just the reverse of the situation encountered with the Meisenheimer complexes (1) and (2).⁶ In the latter case the greater stability of (1) than of (2) was attributed to the release, in going to structure (1), of steric hindrance to the planarity of the nitro-groups at C-2 and C-6 in the starting aromatic compound⁶ and to the particular stability of a saturated carbon atom substituted with two electronegative groups.^{13b} Although it may be argued that reversal of the relative stabilities with our complexes is in accord with the low electronegativity of sulphur with respect to oxygen, we believe that an answer to this question is better delayed until data for a wider variety of anionic σ -complexes from thiolates are available.

In this connection, and because the factors involved in determining the relative rates of formation of the Meisenheimer complexes of types (1) and (2) are not yet fully clear,¹³ it would be interesting to have the relative rates of formation of (5) and (6) from (3). However, such data could not be obtained because these rates are extremely high (out of the range of standard stopped-flow u.v. techniques). This is also an unsuitable system for carrying out calorimetric studies, which have been of value in the area of Meisenheimer complexes.¹⁴

However we have investigated in detail the rates of formation of compound (4) and the disappearance of (5) and (6). Data at both low and high concentrations of (3) have been obtained by following either the decrease of the 545 nm u.v. absorption or the increase of the n.m.r. signal at 8.23 p.p.m. (see Table). The disappearance of the complexes (5) and (6) and the formation of (4) rigorously follow first-order kinetics. This clearly rules out a bimolecular process in which (6) would react with sodium ethanethiolate to give (4), whereas the unimolecular transformation of (6) into (4) (Scheme) cannot be excluded. If such an intramolecular trans-

formation, for which there is no experimental proof, is ruled out, compound (4) must originate exclusively from

Reaction of sodium ethanethiolate with ethyl thiopicrate (3) to give the bisethylthio-compound (4) in $(\text{CH}_3)_2\text{SO}$ or $(\text{CD}_3)_2\text{SO}$ at 24°

$10^2[\text{EtSNa}]/\text{M}$	$10^2[(\text{O}_2\text{N})_3\text{C}_6\text{H}_2\text{SEt}]/\text{M}$	$10^3k_{\text{obs}}/\text{s}^{-1}$
0.010	0.011	3.5 ^a
0.010	0.060	3.5 ^a
0.010	0.144	3.4 ^a
30	30	3.6 ^b

^a From the decrease of the u.v. absorption at 545 nm in $(\text{CH}_3)_2\text{SO}$. ^b From the increase of ¹H n.m.r. absorption at δ 8.23 p.p.m. in $(\text{CD}_3)_2\text{SO}$.

the attack of sodium ethanethiolate at C-4 of compound (3). The rate of this reaction should be extremely high, since the equilibria shown in the Scheme are so far displaced towards (5) and (6) that equilibrium constants could not be measured. Experiments with added alcohols, in order to have a detectable amount of (3) at equilibrium,^{11b} are not feasible with our system. In fact, on mixing compound (3) with sodium ethanethiolate in methanol, we obtained, instead of (4), a compound of m.p. 305–306° which probably originates from reductive dimerisation of (3).

This behaviour, which sharply contrasts with that of the corresponding oxygenated Meisenheimer complexes, where stable (1) is the final product, may be attributed to electron acceptance by the *para*-sulphur atom involving *d*-orbital participation. We ascribe the remarkable activation of C-4 to a dipole effect operating maximally in the C(4)–C(1) direction for molecular symmetry reasons. We think that this is also the reason for the unexplained specificity of substitution of the *para*-fluorine atom in the compounds $\text{MeS}\cdot\text{C}_6\text{F}_5$ and $p\text{-XC}_6\text{H}_4\cdot\text{S}\cdot\text{C}_6\text{F}_5$ by both sulphur and oxygen nucleophiles.¹⁵

We have also investigated the interaction of sodium toluene-*p*-thiolate with *p*-tolyl thiopicrate in dimethyl sulphoxide. However, the decay of the Meisenheimer-type complexes was so fast in this case that it could not be investigated by n.m.r. spectroscopy. Three products [1,3-dinitro-2,5-bis-*p*-tolylthiobenzene (50%), 3,5-dinitro-1,2-bis-*p*-tolylthiobenzene (20%), and 3-nitro-1,2,5-tris-*p*-tolylthiobenzene (10%)], the structures of which are well supported by the ¹H n.m.r. data (Experimental section), were isolated. Thus the product of *para*-substitution predominates (the product of double substitution must almost wholly arise from attack of sodium toluene-*p*-thiolate on 1,3-dinitro-2,5-bis-*p*-tolylthiobenzene), but this case contrasts with that of ethyl thiopicrate where at most a few percent of the product of *ortho*-substitution could have passed undetected by n.m.r. spectroscopy. Partial destruction of molecular symmetry in the case of *p*-tolyl thiopicrate,

¹² F. Pietra and D. Vitali, *J.C.S. Perkin II*, 1972, 385.

¹³ (a) F. Millot and F. Terrier, *Bull. Soc. chim. France*, 1971, 3897; (b) C. F. Bernasconi, *J. Amer. Chem. Soc.*, 1970, **92**, 4682; 1971, **93**, 6975.

¹⁴ K. Amin and J. H. Fendler, *J. Amer. Chem. Soc.*, 1971, **93**, 2910.

* Owing to solubility and viscosity problems introduced by the very high concentrations of the reagents required, the n.m.r. spectrum of the 2 : 1 complex(es) could not be obtained.

owing to out-of-plane rotation of one nitro-group to release repulsion with the bulky *p*-tolyl substituent, may tentatively be suggested as the cause of the decreased selectivity for attack at the *para*-position in this case. With a fluorine atom in place of the nitro-group ($\text{MeS}\cdot\text{C}_6\text{F}_5$ and *p*- $\text{XC}_6\text{H}_4\cdot\text{S}\cdot\text{C}_6\text{F}_5$) only substitution of the *para*-fluorine by EtO^- or PhS^- was observed.¹⁵

EXPERIMENTAL

M.p.s were taken on a Kofler hot-stage apparatus. U.v. spectra were recorded with a Unicam SP 800 spectrophotometer. ¹H N.m.r. spectra were run on a Varian S-60T or on a JEOL SP 100 spectrophotometer with tetramethylsilane as internal standard.

Materials.—Dimethyl sulphoxide (C. Erba RP) and [²H₆]dimethyl sulphoxide (Merck; 99.5%) were distilled from calcium hydride over nitrogen at 20 mmHg. Sodium ethanethiolate was prepared by dissolving sodium in ethanethiol under nitrogen at room temperature and then distilling off the excess of thiol under vacuum leaving a white solid. Sodium toluene-*p*-thiolate was prepared by dissolving 2 equiv. of sodium into a solution of di-*p*-tolyl disulphide in toluene at reflux under nitrogen and then distilling off the solvent, leaving a white solid which darkened in a few days. Ethyl¹⁶ and *p*-tolyl thiopicrate¹⁷ were prepared according to the literature.

Reaction of Sodium Ethanethiolate with Ethyl Thiopicrate.—A solution (0.6M; 1 ml) of the thiolate in dimethyl sulphoxide was added to an equal volume of 0.6M-ethyl thiopicrate in dimethyl sulphoxide at room temperature. The solution immediately became dark red. After 1 h water was added to give a yellow crystalline precipitate of 2,5-bisethylthio-1,3-dinitrobenzene (4). Identical material was obtained from extraction of the mother liquor with ether (total 0.15 g, 90%); m.p. 90—91° [from petroleum (b.p. 30—50°)] (Found: C, 41.9; H, 4.2; N, 9.8; S, 22.4. C₁₀H₁₂N₂S₂O₄ requires C, 41.7; H, 4.2; N, 9.7; S, 22.2%). The ¹H n.m.r. spectrum is shown in Figure B.

Reaction of Sodium Toluene-*p*-thiolate with *p*-Tolyl Thio-

¹⁵ J. M. Birchall, M. Green, R. Haszeldine, and A. D. Pitts, *Chem. Comm.*, 1967, 338.

picrate.—A solution (0.6M; 1 ml) of the thiolate in dimethyl sulphoxide was added to an equal volume of 0.6M-*p*-tolyl thiopicrate in dimethyl sulphoxide at room temperature. The solution immediately became dark red and quickly faded to orange-yellow. After several minutes water was added and the resulting emulsion was extracted with ether. The extract was evaporated to leave an orange oil. Preparative layer chromatography (2 mm thick silica gel activated at 110° for 1 h; eluant 1 : 1 cyclohexane-chloroform) of this oil showed four yellow bands corresponding, in order of increasing *R_F*, to *p*-tolyl thiopicrate; 3,5-dinitro-1,2-bis-*p*-tolylthiobenzene (0.050 g, 20%), m.p. 151—152° (from n-hexane) (Found: C, 58.2; H, 3.9; N, 15.6; S, 6.9. C₂₀H₁₆N₂S₂O₄ requires C, 58.2; H, 3.9; N, 6.8; S, 15.5%), δ [(CD₃)₂SO] 2.3 (3H, s), 2.4 (3H, s), 7.1 (4H, s), 7.3 (4H, s), 7.4 (1H, d, *J* 3.0 Hz), and 8.4 p.p.m. (1H, d, *J* 3.0 Hz); 1,3-dinitro-2,5-bis-*p*-tolylthiobenzene (0.125 g, 50%) m.p. 126—127° (from n-hexane) (Found: C, 58.1; H, 4.0; N, 6.8; S, 15.3. C₂₀H₁₆N₂S₂O₄ requires C, 58.2; H, 3.9; N, 6.8; S, 15.5%), δ [(CD₃)₂SO] 2.3 (3H, s), 2.4 (3H, s), 7.2 (4H, s), 7.5 (A₂' B₂' system, 4H), and 7.9 p.p.m. (2H, s); and 3-nitro-1,2,5-tris-*p*-tolylthiobenzene (0.03 g, 10%), m.p. 138—139° (from n-hexane) (Found: C, 66.3; H, 4.7; N, 2.9. C₂₇H₂₃NS₃O₂ requires C, 66.2; H, 4.7; N, 2.8%), δ [(CD₃)₂SO] 2.3 (3H, s), 2.4 (6H, s) 6.2 (1H, d, *J* 2 Hz), 7.1br (12H), and 7.6 p.p.m. (1H, d, *J* 2 Hz).

Kinetics. The kinetic results were obtained by following the reaction, either in a thermostatted u.v. spectrophotometric cuvette or in an n.m.r. tube, up to 90% completion; good, conventional first-order plots were obtained. Attempts to measure the rate of formation of intermediates were made by means of a Durrum stopped flow apparatus.

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¹⁶ C. C. Culvenor, W. Davies, and W. E. Savige, *J. Chem. Soc.*, 1952, 4480.

¹⁷ R. Passerini, *Boll. Sci. Fac. Chim. ind. Bologna*, 1950, 8, 122 (*Chem. Abs.*, 1951, 45, 7976).