Tetrahedron Vol. 36, pp. 1879 to 1883

0040-4020/80/0615-1879/$02.00/0

TELE-SUBSTITUTION REACTIONS IN THE NAPHTHALENE SERIES

THE BEHAVIOUR OF 1,4 - DIMETHYL - 2 - NITRO - 3 - PHENYLSULPHONYL - AND 2,3 - BISPHENYLSULPHONYL - 1,4 - DIMETHYL - NAPHTHALENE TOWARDS SODIUM ARENETHIOLATES AND SECONDARY ALIPHATIC AMINES

M. NOVI, G. GUANTI,* C. DELL'ERBA, D. CALABRÒ and G. PETRILLO
Istituto di Chimica Organica dell'Università, C.N.R. Centro di Studio sui Diariloidi e loro Applicazioni, Palazzo delle Scienze, Corso Europa, 16132 Genova, Italy

(*Received in UK* 21 *September* 1979)

Abstract—1,4 - Dimethyl - 2 - nitro - 3 - phenylsulphonylnaphthalene (2) reacts with sodium benzenethiolate in DMSO at 120° to give 1 - methyl - 2 - nitro - 4 - phenylthiomethylnaphthalene (4) [*tele*-substitution product (TSP) of the phenylsulphonyl group] and 1,4 - dimethyl - 3 - phenylsulphonyl - 2 - phenylthionaphthalene (5) [normal substitution product (NSP) of the nitro group]. The analogous reactions of 2 with sodium 2,4,6- trimethylbenzenethiolate and of 2,3 - bisphenylsulphonyl - 1,4 - dimethylnaphthalene (3) with sodium benzenethiolate or aliphatic amines give only TSPs of the phenylsulphonyl group. In the case of the reaction of 2 with aliphatic amines both the possible TSPs (*tele*-substitution of the phenylsulphonyl or of the nitro group) were isolated in 9:1 relative yield. All the data show that the phenylsulphonyl is a leaving group far better than the nitro in such *tele*-substitution processes. The mechanism previously proposed to account for the formation of TSPs from 1,4-dimethyl - 2,3 - dinitronaphthalene is strongly supported by the obtained results.

The reactivity of 2,3-dinitronaphthalene derivatives is of some interest because of the unusual kind of displacements involved, which often are completely different from those occurring on benzene derivatives having a similar structure. For instance, while 1,2-dinitrobenzene reacts with nucleophiles to give exclusively products deriving from normal aromatic substitution (S_NAr),[1] 2,3-dinitronaphthalene furnishes 2-arylthio - 3 - nitronaphthalene [normal substitution product (NSP)] with sodium arenethiolates[2] and 1 - amino - 3 - nitronaphthalene (*cine*-substitution product) with amines.[3] Moreover, when the two positions *ortho* to the nitro groups are occupied by Me groups, whereas the benzene derivative gives the expected NSP, 1,4 - dimethyl - 2,3 - dinitronaphthalene (1) by reaction with sodium arenethiolates furnishes, besides NSP, 1 - arylthiomethyl - 4 - methyl - 3 - nitronaphthalene [*tele*-substitution product (TSP)].[4] This last kind of product is, on the other hand, the only one when 1 is treated with secondary amines.[5] To account for the formation of TSPs, we suggested[4] a mechanism involving tautomerization of 1 into 2,3-dinitro - 4 - methyl - 1 - methylene - 1,2 - dihydronaphthalene followed by attack of the nucleophile on this tautomeric form to give products. The preliminary tautomeric equilibrium of the naphthalene substrate is similar to the vinyl-allylic one, typical of olefinic systems, whose position is known to be strongly affected by the type of substituent attached to the double bond.[6,7]

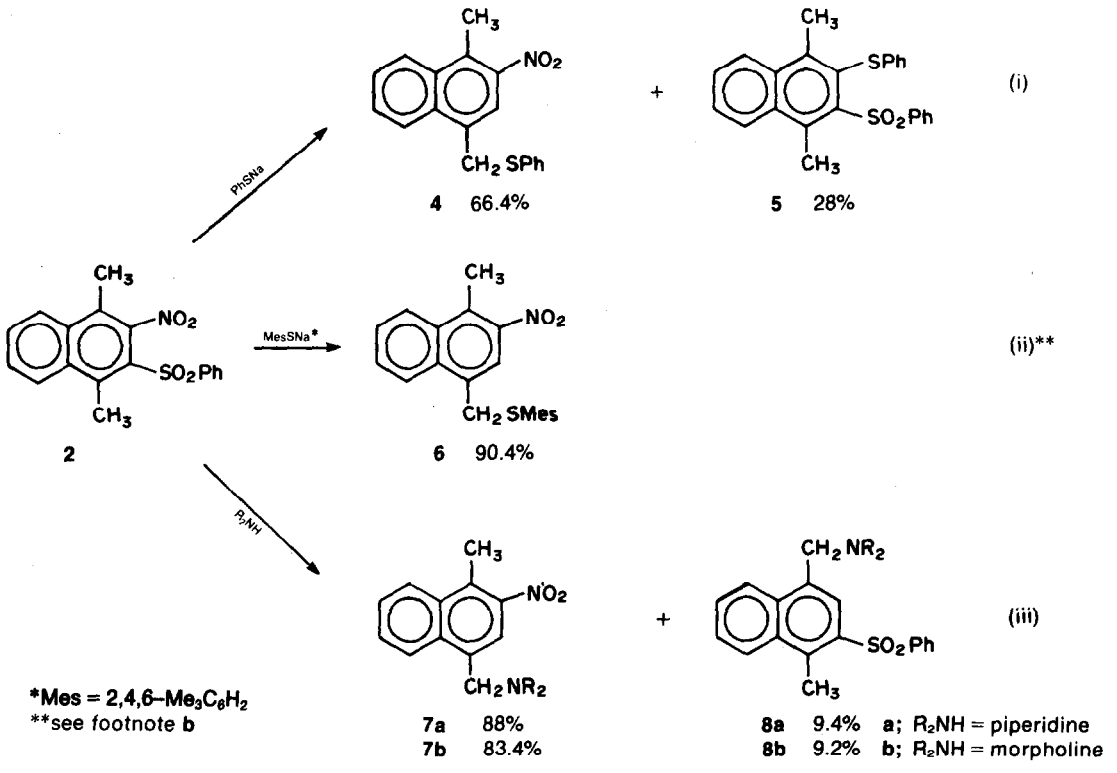
Therefore, with the purpose of studying the effect of the gradual change in 1 of the nitro with the phenylsulphonyl group on the NSP/TSP ratio, we have synthesized 1,4 - dimethyl - 2 - nitro - 3 - phenylsulphonyl - (2) and 2,3 - bisphenylsulphonyl - 1,4 - dimethyl - naphthalene (3) and studied their behaviour towards both sodium arenethiolates and amines.

RESULTS AND DISCUSSION

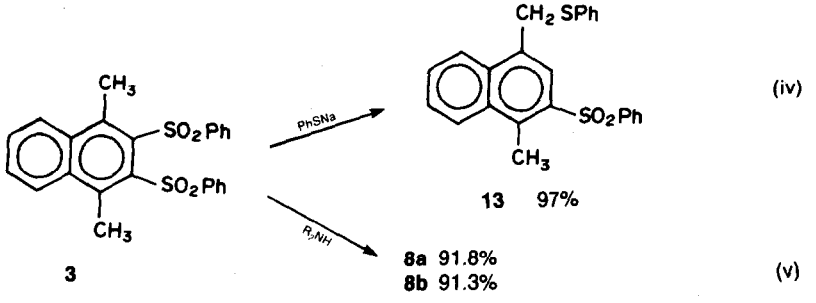
The results obtained from the reactions of 2 and 3 with two significative[4] sodium arenethiolates and secondary aliphatic amines are summarized in Schemes 1 and 2. Experiments with sodium arenethiolates were carried out in DMSO solution at 120° and those with secondary amines in neat amine at 110°[a] using experimental conditions identical to those previously[4] employed for 1. The reaction products, isolated in any case in good overall yield, were identified through their analytical and ^1H NMR data.

As shown in Scheme 1, compound 2 reacted with sodium benzenethiolate to give 1 - methyl - 2 - nitro - 4 - phenylthiomethyl- (4) (TSP) and 1,4 - dimethyl - 3 - phenylsulphonyl - 2 - phenylthio - naphthalene (5) (NSP) in *ca* 2.4:1 molar ratio [run (i)]. The formation of 5 involves a preferential normal substitution (NS) of the nitro group and this apparently contrasts with the results reported[8] for nucleophilic substitutions occurring on other aromatic *o* - nitro - arylsulphonyl derivatives where is the arylsulphonyl which preferentially behaves as leaving group. Moreover a control experiment, performed under the same conditions used for 2, showed that 2-nitrophenyl phenyl sulphone reacted with sodium benzenethiolate to give quantitatively 2-nitrophenyl phenyl sulphide via NS of the phenylsulphonyl group. However it has been also shown[9] that the behaviour of aromatic *o*-nitro-sulphones towards nucleophiles is

[a]The reaction of 3 with piperidine or morpholine for practical reasons was carried out in DMSO solution instead of in neat amine. Control experiments showed that, as found for 1,[4] both qualitatively and quantitatively there was no difference between the two ways of carrying out the reaction. The former was preferred because of the low solubility of 3 in neat amine.



Scheme 1.



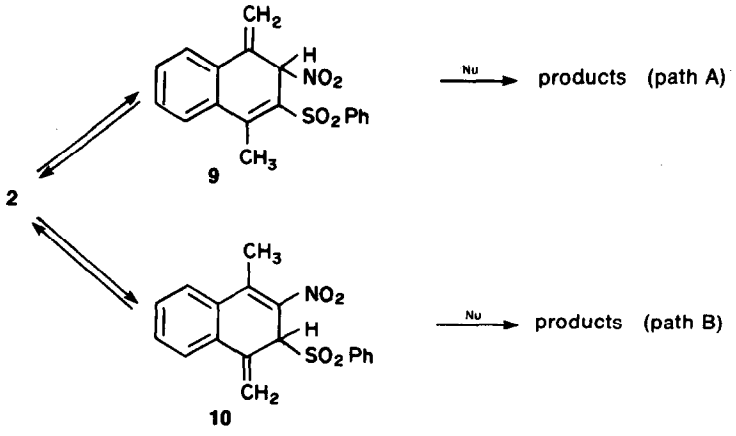
Scheme 2.

highly complex as the preferred centre of reaction varies with the arrangement of substituents in the aromatic substrate. The presence of the two Me groups in the 1,4-positions can be the cause for the preferential NS of the nitro group in **2** as it is well known that, unlike the sulphonyl group which mainly operates through inductive effect and does not require coplanarity of the C_{Ar}–S bond with aromatic ring to exert a conjugative effect,[10] the activating power of the nitro group is lowered by steric hindrance from *o*-substituents.[9,11] As regards the *tele*-substitution (TS) process involved in the reaction (i), it must be noted that the yield in TSP (66.4%) is appreciably higher than the one found[4] in the analogous reaction on **1** (16%). This fact and the exclusive formation of **4** of the two possible TSPs (namely **4** and 4 - methyl - 3 - phenylsulphonyl - 1 - phenylthiomethylnaphthalene **13**) emphasizes that the phenylsulphonyl is a nucleophugic group far better than the nitro in such a kind of process.

This considerable mobility of the phenylsulphonyl group in TS processes is also evidenced by reactions (ii) and (iii) where **2** reacts with sodium 2,4,6-trimethylbenzenethiolate to give practically[b] only **6** and with secondary amines to furnish a mixture of the two possible TSPs **7** and **8** in *ca* 9:1 molar ratio.

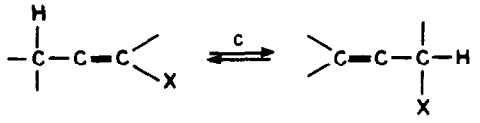
The results obtained in the reactions (i)–(iii) strongly support the mechanism previously proposed to account for the formation of TSPs.[4] At the light of this mechanism, in fact, the preferential TS of the phenylsulphonyl group needs that of the two possible TS pathways (A and B in Scheme 3) the latter is by far the preferred one. This can arise either from a more facile formation of tautomer **10** with respect to **9** or from a lower reactivity of the latter in the step leading to products. A more facile formation of **10** can be explained

[b] A little amount (*ca* 6% by weight) of unidentified by-products was also isolated in the reaction (ii) (Experimental). All attempts to effect their separation both by chromatography and crystallization proved futile and, on the other hand, the very complex ^{1}H NMR spectrum of the mixture did not furnish unequivocal information.



Scheme 3.

on the basis of the results found[6] for tautomeric equilibria of olefins of type **11** to which **2** can be formally related. It has been shown, in fact, that the nature of the hetero-

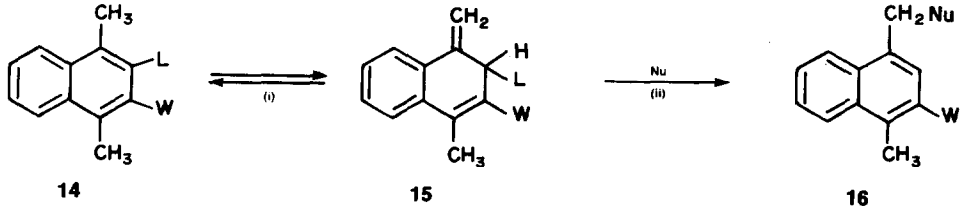


function X is decisive in determining the position of the equilibrium C. The isomer possessing the vinyl structure is generally favoured if it is stabilized by conjugation. Thus in the case of α, β-unsaturated nitro olefins[6,7] the vinylic isomer is more stable than the allylic one. On the contrary[6,12] the equilibria of unsaturated sulphones favour the allylic isomers owing to the low conjugation between the olefinic double bond and the sulphone group and the electronwithdrawing power (-I effect) of this group which destabilizes the α,β-double bond.[12a] On the basis of these considerations it is evident that, between the two possible tautomeric forms **9** and **10**, the latter is the more stable one owing to the contemporary presence of the more favoured vinyl-nitro and allyl-sulphonyl systems. Moreover, both in **9** and **10** conjugation between the exocyclic double bond and the heterofunction is possible through the extended system of conjugated double bonds. This fact, because of the stronger resonance effect of the nitro, as compared to the sulphone group, not only should further stabilize **10** with respect to **9**, but also could be responsible for greater reactivity of **10** in the step leading to the TSPs.

The last point worth noting in the experiments on **2** is the absence of NSPs in the reactions (ii) and (iii) which stresses the importance of the enhancement of steric hindrance and hardness of the nucleophile in favouring the TS over the NS process as we pointed out in the preceding paper.[4]

Results of some significance were finally obtained from the reactions on compound **3**, which, by treatment with both sodium benzenethiolate and secondary amines, furnished only TSPs in almost quantitative yield (Scheme 2). The exclusive formation of the TSP **13** (without traces of NSP) in the reaction with sodium benzenethiolate is worth emphasizing as on going from **1** to **3** the substitution of two phenylsulphonyl groups for the two nitro groups makes the TSP percentage rise from 16 to 100%. Once again the presence of phenylsulphonyl groups is shown to be a significant factor in driving the reaction along the TS pathway.

In conclusion the results obtained by gradually changing the nitro groups of 1,4 - dimethyl - 2,3 - dinitronaphthalene with phenylsulphonyl groups support the mechanism previously proposed to account for the formation of TSPs. Up to this point of our investigation the presence of an electronwithdrawing substituent (W) in *ortho* to the leaving group (L) (Scheme 4) seems to be indispensable to promote the TS process. It can be noted, in fact, that, although a tautomerization involving the residual Me-C=C-W system of **16** is in theory possible (expecially when W = $PhSO_2$) it does not further react with nucleophiles. The effect of the W group should be mainly electronic in nature (stabilization and increase of the reactivity towards nucleophilic reagents of intermediates of type **15**) although a steric effect of this group ought not to be disregarded (tautomerization of naphthalene substrates could be promoted, *inter alia*, by formation of a sterically less congested molecule). Finally, as we pointed out in the preceding paper,[4] the more puzzling point of the mechanism depicted in Scheme 4 is the step (ii) which furnishes TSPs via displacement involving a three carbon anionotropic rearrangement.[13] At the best of our knowledge, no example of nucleophilic substitution of this kind is reported to occur on allylic-type nitro or sulphonyl



Scheme 4.

derivatives. However it is likely that the substantial thermodynamic tendency of **15** to rearomatize[14] into a less congested molecule (the TSP) is the driving force for such transformation.

EXPERIMENTAL

^{1}H NMR spectra were taken on a Varian FT 80 instrument ($SiMe_4$ as internal reference). Light petroleum had b.p. 30–50°. Organic extracts were dried over Na_2SO_4 and solvents were rotoevaporated at reduced pressure below 50°. Known products were identified by comparison of their m.ps, chromatographic data and ^{1}H NMR spectra with those of authentic samples.

Materials. Sodium arenethiolates were prepared and dimethyl sulphoxide was purified as previously reported.[4]

General procedure for performing the reactions on naphthalene derivatives. The reactions were kept at suitable temp. in a thermostatic oil bath until the disappearance of the parent compound was observed by tlc.

The initial procedure for performing the *reactions with sodium arenethiolates* under N_2 have been described in a previous paper.[4] Usual working-up involves pouring of the mixture into brine, extraction with benzene, washing with 5% NaOH aq, concentration of the benzene soln and chromatography on a silica gel column.

The reactions with secondary amines were carried out in sealed ampoules using the same amine as solvent.[5] Usual working-up involves dilution of the reaction mixture with benzene, repeated washing with water to remove the excess amine, concentration of the benzene soln and chromatography on silica gel column.

Reaction of 1,4 - *dimethyl* - 2 - *nitro* - 3 - *phenylsulphonylnaphthalene* **2**

(a) *With sodium arenethiolates.* A soln of **2**[4] (0.5 g, 1.47 mmol) and sodium benzenethiolate (0.232 g, 1.2 mol equiv) in DMSO (30 ml) was heated at 120° for 3 hr. Usual working-up and chromatography, using Et_2O-light petroleum (1:1) as eluant, gave **4** (0.302 g; 66.4%), m.p. 108° (lit.,[4] 108°); and 1,4 - *dimethyl* - 3 - *phenylsulphonyl* - 2 - *phenylthionaphthalene* **5** (0.166 g; 28%), m.p. 163° from EtOH (Found: C, 71.2; H, 4.95. $C_{24}H_{20}O_2S_2$ requires: C, 71.3; H, 4.95%); δ ($CDCl_3$) 8.33 (2H, m, H-5 and H-8), 7.83 (4H, m, H-6, H-7 and H-2' and H-6' of $PhSO_2$), 7.22 (3H, m, H-3', H-4' and H-5' of $PhSO_2$), 6.91 and 6.51 (3H and 2H resp., m, PhS), 3.32 br (3H, s, CH_3) and 2.65 br (3H, s, CH_3).

An analogous reaction with sodium 2,4,6 - trimethylbenzenethiolate gave (eluant benzene-light petroleum 1:1) **6** (0.466 g; 90.4%), m.p. 91° (lit.,[4] 91–92°); and a little amount (0.03 g) of a white solid material showing a single spot by tlc. ^{1}H NMR of this material showed that it was a mixture of products, which were not further investigated as all attempts to effect their separation both by chromatography and crystallization proved futile.

(b) *With secondary amines.* Compound **2** (0.4 g, 1.17 mmol) was dissolved in piperidine (5.8 ml, 50 mol equiv) and heated at 110° for 10 hr in sealed ampoule. Usual working-up and chromatography, using as eluant CH_2Cl_2–Et_2O (10:1), gave **7a** (0.292 g; 88%), m.p. 106–107° (lit.,[5] 105–107°), and 4 - *methyl* - 3 - *phenylsulphonyl* - 1 - *piperidinomethylnaphthalene* **8a** (0.042 g; 9.4%), m.p. 196–197° from EtOH–dioxane (Found: C, 72.6; H, 6.7; N, 3.7. $C_{23}H_{25}NO_2S$ requires: C, 72.8; H, 6.6; N, 3.7%); δ ($CDCl_3$) 8.6–7.3 (10H, very complex band of overlapping multiplets, aromatic protons), 3.92 br (2H, s, CH_2), 2.86 br (3H, s, CH_3), 2.48 (4H, m, piperidine 2 × CH_2-α) and 1.50 (6H, m, piperidine 2 × CH_2-β and CH_2-γ).

An analogous reaction with morpholine gave, after chromatography using CH_2Cl_2–Et_2O (20:1) as eluant, **7b** (0.279 g; 83.4%), m.p. 117–118° (lit.,[5] 117–118°), and 4 - *methyl* - 3 - *phenylsulphonyl* - 1 - *morpholinomethylnaphthalene* **8b** (0.041 g; 9.2%), m.p. 157° from EtOH (Found: C, 69.1; H, 6.0; N, 3.7. $C_{22}H_{23}NO_3S$ requires: C, 69.3; H, 6.0; N, 3.7%); δ ($CDCl_3$) 8.5–7.3 (10 H, very complex band of overlapping multiplets, aromatic protons), 3.93 br (2H, s, CH_2), 3.68 (4H, m, morpholine 2 × CH_2O), 2.84 br (3H, s, CH_3) and 2.52 (4H, m, morpholine 2 × CH_2N).

Preparation of 2,3 - *bisphenylsulphonyl* - 1,4 - *dimethylnaphthalene* **3**

The above described sulphide **5** was oxidized with peracetic acid to the corresponding sulphone. Compound **3** had m.p. 251–252° from EtOH (Found: C, 65.9; H, 4.6. $C_{24}H_{20}O_4S_2$ requires: C, 66.05; H, 4.6%); δ (CD_3COCD_3) 8.28 (2H, m, H-5 and H-8), 7.81 [6H, m, H-6, H-7 and 2 × (H-2' and H-6' of $PhSO_2$)], 7.56 [6H, m, 2 × (H-3', H-4' and H-5' of $PhSO_2$)] and 2.71 (6H, s, 2 × CH_3).

Reactions of 2,3 - *bisphenylsulphonyl* - 1,4 - *dimethylnaphthalene* **3**

In these experiments the chromatography of the mixture was unnecessary and the products obtained by extraction with benzene and evaporation of the soln were purified by crystallization.

(a) *With sodium benzenethiolate.* A soln of **3** (0.2 g, 0.46 mmol) and sodium benzenethiolate (73 mg, 1.2 mol equiv) in DMSO (12 ml) was heated at 120° for 1 hr. Usual working-up gave 4 - *methyl* - 3 - *phenylsulphonyl* - 1 - *phenylthiomethylnaphthalene* **13** (0.18 g; 97%), m.p. 141–142° from EtOH (Found: C, 71.2; H, 4.9. $C_{24}H_{20}O_2S_2$ requires: C, 71.3; H, 4.95%); δ (CD_3COCD_3) 8.19 (3H, m, H-5, H-8 and H-2), 7.62 (7H, m, H-6, H-7 and $PhSO_2$), 7.31 (5H, m, PhS), 4.72 br (2H, s, CH_2) and 2.81 br (3H, s, CH_3).

(b) *With secondary amines.* Owing to the low solubility of **3** in neat amine these reactions were carried out in DMSO solution. Thus compound **3** (0.2 g, 0.46 mmol) and amine (3 mol equiv) were dissolved in 12 ml of DMSO. The reaction was heated at 110° for 48 hr in sealed ampoule, poured into brine and extracted with benzene. The residue obtained by evaporation of the solvent was then crystallized from the proper solvent.

Using piperidine as nucleophile **8a** (0.16 g; 91.8%) was isolated, m.p. and m.m.p. 196–197° after crystallization from EtOH–dioxane.

Analogously the reaction with morpholine gave **8b** (0.16 g; 91.3%), m.p. and m.m.p. 157° after crystallization from EtOH.

REFERENCES

[1] F. Pietra and D. Vitali, *J. Chem. Soc.* Perkin II, 385 (1972); N. Kornblum, L. Cheng, R. C. Kerber, M. K. Kestner, B. N. Newton, H. W. Pinnick, R. G. Smith and P. A. Wade, *J. Org. Chem.* **41**, 1560 (1976); J. R. Beck, *Tetrahedron* **34**, 2057 (1978).

[2] M. Novi, S. Thea, G. Guanti, C. Dell'Erba and G. Leandri, XIII*th National Meeting of the Italian Chemical Society.* ORGN 15. Merano (18–23 June 1978).

[3] D. C. Morrison, *U.S. Pat.* 3,294,838 (1966); *Chem. Abstr.* **66**, 55277p (1967); G. Guanti, S. Thea and C. Dell'Erba, *Tetrahedron Letters* 461 (1976).

[4] M. Novi, G. Guanti, S. Thea, F. Sancassan and D. Calabrò, *Tetrahedron* in press (1979).

[5] G. Guanti, S. Thea, M. Novi and C. Dell'Erba, *Tetrahedron Letters* 1429 (1977).

[6] A. J. Hubert and H. Reimlinger, *Synthesis* 97 (1969); *Ibid.* 405 (1970).

[7] H. Shechter and J. W. Shepherd, *J. Am. Chem. Soc.* **76**, 3617 (1954); Y. V. Baskov and V. V. Perekalin, *Zh. obschei Khim.* **32**, 3106 (1962); Y. V. Baskov, T. Urbanski, M. Witanowski and L. Stefaniak, *Tetrahedron* **20**, 1519 (1964); M. Bourillot, G. Ronstaing and G. Descotes, *C. R. Ser. C* **262**, 1080 (1966); G. Hesse, R. Hatz and H. Konig, *Liebigs Ann.* **709**, 79 (1967); G. Descotes, Y. Bahurel, M. Bourillot, G. Pingeon and R. Ronstaing, *Bull. Soc. Chim. Fr.* 290 (1970).

[8] A. A. Levi and S. Smiles, *J. Chem. Soc.* 1488 (1932); G. Guanti, C. Dell'Erba and P. Macera, *J. Heterocyclic Chem.* **8**, 537 (1971); D. Spinelli, G. Consiglio and R. Noto, *Ibid.* **14**, 1325 (1977) and Refs therein.

[9] J. D. Loudon and N. Shulman, *J. Chem. Soc.* 722 (1941) and Refs therein.

[10] C. Y. Meyers, B. Cremonini and L. Maioli, *J. Am. Chem. Soc.* **86**, 2944 (1964); F. G. Bordwell, *Int. J. Sulphur Chem.* **B7**, 187 (1972); H. Kloozerstiel and H. J. Backer, *Rec. Trav. Chim.* **72**, 185 (1953).

[11] J. P. Henichart, J. L. Bernier, C. Vaccher, R. Houssin, V. Warin and F. Baert, *Tetrahedron Letters* 945 (1979); P. Beltrame and P. Carniti, *Gazzetta* **103**, 723 (1973) and Refs therein.

[12a]D. E. O'Connor and W. I. Lyness, *J. Am. Chem. Soc.* **85**, 3044 (1963); *Ibid.* **86**, 3840 (1964); [b]S. T. Mc Dowell and C. J. M. Stirling, *J. Chem. Soc. B* 351 (1967); P. D. Magnus, *Tetrahedron* **33**, 2019 (1977) and Refs therein.

[13]P. B. D. de la Mare, *Molecular Rearrangements* (Edited by P. de Mayo), Chap. 2. Interscience, New York (1967).

[14]L. T. Scott and W. R. Brunsvold, *J. Org. Chem.* **44**, 641 (1979).