

Chemistry of Nitrosoimines. XV.¹⁾ Reactions of 3-Substituted 2-Nitrosoimino-2,3-dihydrobenzothiazoles with Lithium Aluminum Hydride and Diazo Compounds

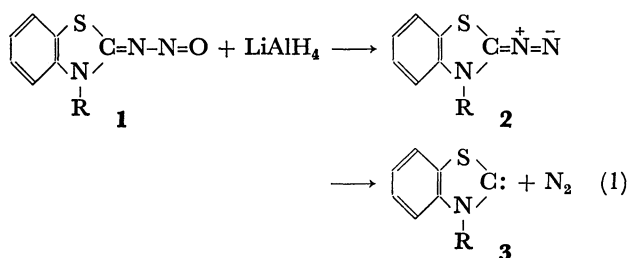
Kin-ya AKIBA, Takayuki KAWAMURA, Masahide OCHIUMI, and Naoki INAMOTO

Department of Chemistry, Faculty of Science, The University of Tokyo, Hongo, Tokyo 113

(Received December 26, 1975)

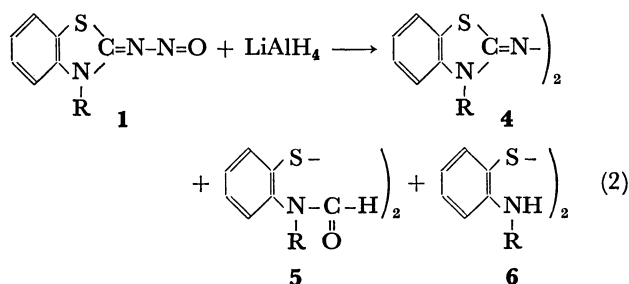
3-Substituted 2-nitrosoimino-2,3-dihydrobenzothiazoles (**1**) were reduced with lithium aluminum hydride to give the corresponding thiazolone azines and bis[*o*-(*N*-substituted *N*-formylamino)phenyl] disulfides as major products. Reactions of **1** with some substituted diazomethanes gave the corresponding unsymmetrical azine *N*-monoxides (**16**) or azines (**17**) depending on the structure of the diazomethane.

We previously reported on the reactions of 3-substituted 2-nitrosoimino-2,3-dihydrobenzothiazoles (**1**) with Grignard reagents²⁾ and organolithiums.³⁾ In this paper, we report on the reactions of **1** with lithium aluminum hydride (LAH).⁴⁾ According to the report of Zimmerman and Paskovich on the preparation of the corresponding diazo compound by the reduction of bismesityl-*N*-nitrosoiminomethane with LAH,⁵⁾ the formation of the corresponding diazo compounds (**2**) or carbenes (**3**)⁶⁾ can be expected in the reaction, together with the products of nucleophilic attack of LAH on C-2 and the sulfur of the thiazoline ring.



In order to know the reactivity of **1** toward diazo compounds or the corresponding carbenes, the reactions of **1** with some stable diazo compounds were examined under various conditions.

Reaction of **1 with LAH.** The main products of reduction of **1** with an excess amount of LAH were 3-substituted 2,3-dihydrobenzothiazol-2-one azine (**4**), bis[*o*-(*N*-substituted *N*-formylamino)phenyl] disulfide (**5**), and bis[*o*-(*N*-substituted amino)phenyl] disulfide (**6**). The yields are given in Table 1.



a) R=Ph, b) R=Me, c) R=Et

The formation of the azine (**4**) can be ascribed to the intermediacy of the diazo compound (**2**) produced by hydride attack on the nitrogen atom of the nitroso group (*path a*). On the other hand, the formation of the disulfide (**5**) can be explained by invoking the ring opened

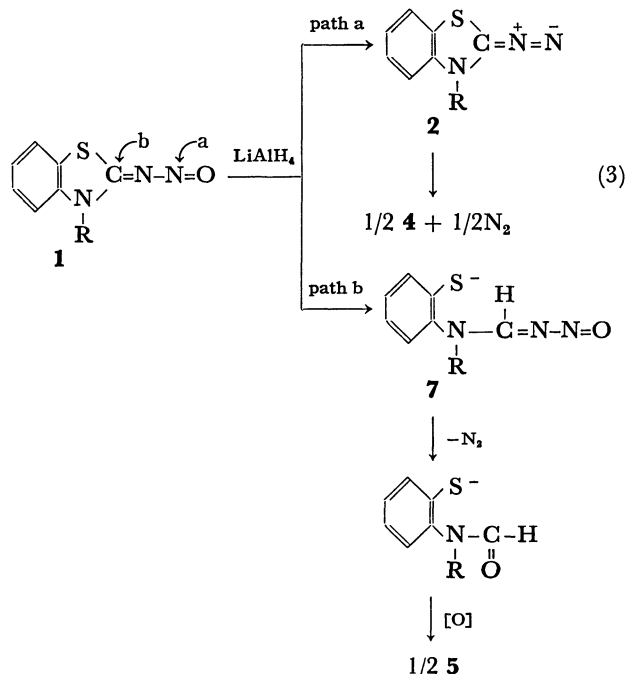
TABLE 1. REDUCTION OF **1** WITH EXCESS LITHIUM ALUMINUM HYDRIDE

1	4	5	6
a) R=Ph	16	30	20
b) R=Me	27	22	24
c) R=Et	30	28	18

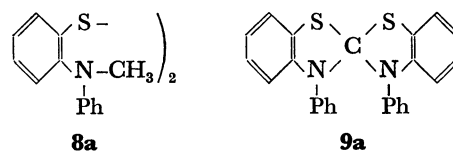
Numerical values show yields (mole %) based on charged **1**.

nitrosoimine (**7**) produced by hydride attack on the C-2 of the ring (*path b*), **7** thus formed decomposing to the corresponding carbonyl compound and nitrogen gas.⁷⁾

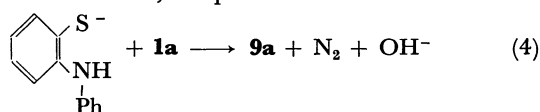
When the reaction was carried out under argon atmosphere in a closed system, the evolved gas was only nitrogen as confirmed by mass spectrometry. This supports the proposed mechanism.



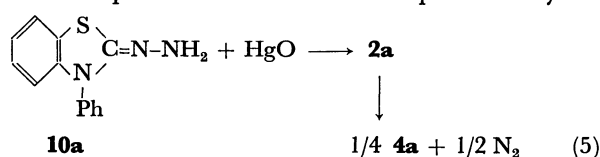
The products were scrutinized by column chromatography for the case of **1a**, two products (**8a** and **9a**)



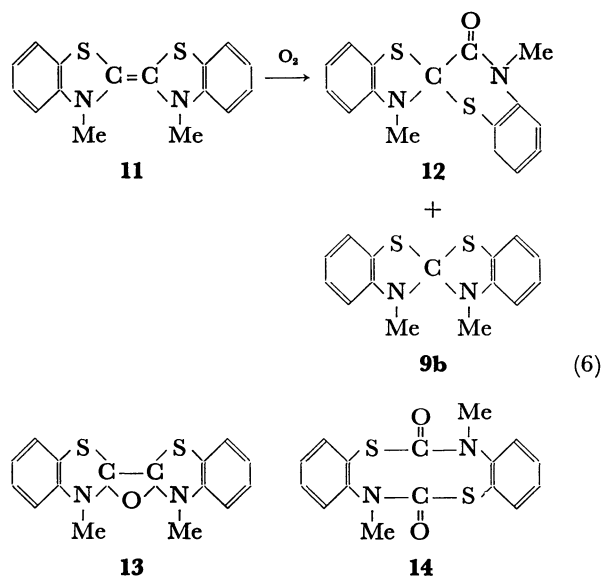
being obtained in very small amounts. The disulfide (**8a**) is a reduction product of **5a** with excess LAH, since **5a** was reduced with LAH in refluxing tetrahydrofuran (THF) to **6a** and **8a**. Formation of **9a** can be explained by means of the reaction of **1a** with *o*-anilino-benzenethiolate anion,⁸⁾ a precursor of **6**.



In order to prepare **2**, 2-hydrazono-3-phenyl-2,3-dihydrobenzothiazole (**10a**) was oxidized with mercury (II) oxide. The reaction took place very slowly at 0 °C as compared with that of benzophenone hydra-



zone, giving **4a** as the major product (*ca.* 70%). This shows that **2a** is too unstable to be isolated and gives **4a** easily. In order to study the nature of the corresponding carbene dimer, 3,3'-dimethylbi(2,3-dihydrobenzothiazolidene) (**11**) was prepared by the deoxygenation of **1** with triethyl phosphite.⁹⁾ It was found to be sensitive to air. Thus, air was bubbled into a benzene solution of **11**. Spiro-amide (**12**) was obtained as the major product (71%), which may be decomposition product of epoxide (**13**). Even if carbene dimer (**11**) were formed in the reduction reaction, **11** would be oxidized to **12** by air during the course of isolation. However, **12** could not be isolated from the reaction mixture of **1b** with LAH, indicating the absence of **11**, or fast reaction of **3** with **2**.



Wanzlick *et al.* reported that air-oxidation of **11** affords **14** in 75% yield. However, we could not substantiate the result. Our result is similar to that of the air-oxidation of naphthalene analog of **11**.^{6c)}

Reactions of 1 with Diazo Compounds. A dichloromethane solution of **1b** was refluxed for a week with diphenyldiazomethane (**15a**) and for one day with methylphenyldiazomethane (**15b**), and left to stand at

room temperature for five days with phenyldiazomethane (**15c**). In the cases of **15a** and **15c**, the isolated products were unsymmetrical azine *N*-monoxides (**16**), whereas the product was unsymmetrical azine (**17b**) in the case of **15b**. The yields of the products are summarized in Table 2.

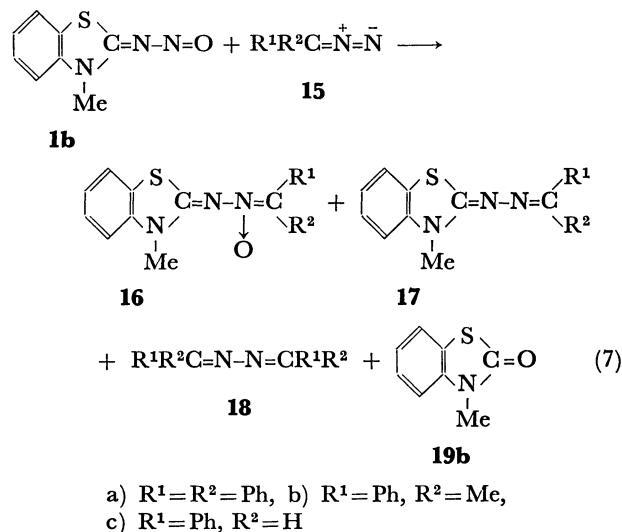


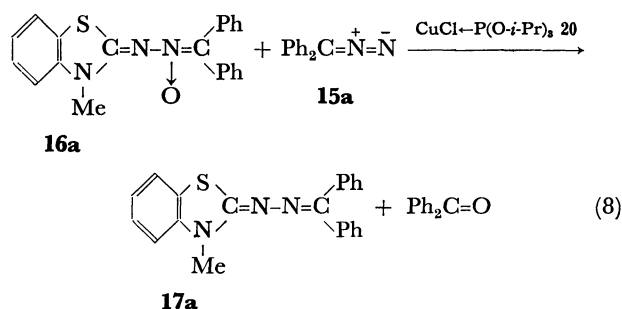
TABLE 2. REACTION OF **1b** WITH DIAZO COMPOUNDS^{a)}

15	16	17	18	19b	1b recovery
a) Ph ₂ C=N ₂	16	—	42	80	—
b) MePhC=N ₂	—	34	39	—	88
c) PhHC=N ₂	11	—	46 ^{b)}	—	90

a) The yields (mol %) of **16**, **17**, and **19b** were calculated based on the amount of **1b** consumed. The yield of **18** was calculated based on the amount of charged **15**. b) PhCOCHPhN=NCHPhCOPh (11%), probably the by-product in the preparation of **15c**, was obtained.

The reaction of **1b** with **15a** was carried out in *N,N*-dimethylformamide (DMF) in the presence of copper(I) chloride-triisopropyl phosphite complex (**20**) in order to generate carbene at low temperature (30 °C). However, the yields of **16a** and **17a** were low in spite of much effort to improve them and found to be *ca.* 7 and 4%, respectively.

The results indicate that the reactivity of **1** toward diazo compounds and carbenes is very low. This indicates that *path a* [Eq. 3] is the major route for the formation of **4**. Deoxygenation of **16a** with diphenylcarbene, generated from **15a** and **20**, gave **17a** in 75% yield under the same conditions. This shows that the primary product of the reaction of **1** with carbene is



azine *N*-monoxide (**16**) which is deoxygenated by incident carbene to give unsymmetrical azine (**17**).

Experimental

Materials. 3-Substituted 2-nitrosoimino-2,3-dihydrobenzothiazoles (**1**) were prepared by the reported methods; 3-phenyl (**1a**), mp 140 °C (dec.),¹⁰ 3-methyl (**1b**), mp 143 °C (dec.),¹¹ and 3-ethyl (**1c**), mp 143–144 °C (dec.).¹² Diphenyl-,¹³ methylphenyl-,¹³ and phenyldiazomethanes¹⁴ were prepared by the reported methods. All the reactions were carried out under nitrogen.

Reduction of 3-Methyl-2-nitrosoimino-2,3-dihydrobenzothiazole (1b) with LAH. To a stirred solution of **1b** (10.0 g 47.8 mmol) in THF (700 ml) was added LAH (1.68 g, 47.0 mmol) portionwise at –70––40 °C during the period of 1 h. Vigorous gas evolution was observed upon the addition, and stirring was continued for 10 h at room temperature. Methanol (150 ml) was added to the solution and the resulting precipitates were filtered off. The filtrate was concentrated *in vacuo* and the residue was extracted with dichloromethane. The extract was concentrated and chromatographed on silica gel.

Bis(*o*-methylaminophenyl) disulfide (**6b**, 1.36 g, 24%) was eluted with benzene as a yellow oil, which was identified by comparison of IR and NMR spectra with those of an authentic sample.^{15a} Bis[*o*-(*N*-formyl-*N*-methylamino)phenyl] disulfide (**5b**, 1.87 g, 22%) was also eluted with benzene, mp 107.0–108.5 °C (from ether) (lit.⁸) 108 °C). 3-Methyl-2,3-dihydrobenzothiazolone azine (**4b**, 2.26 g, 27%) was eluted with dichloromethane, mp 259–260.5 °C (from benzene) (lit.¹⁶) mp 260 °C).

Reduction of 2-Nitrosoimino-3-phenyl-2,3-dihydrobenzothiazole (1) with LAH. LAH (2.235 g, 59.0 mmol) and **1a** (10.0 g, 39.2 mmol) were used for the reaction, the reaction mixture being treated as described for **1b**. Yellow tar (**A**, 2.16 g), eluted with benzene, was chromatographed on silica gel three times using carbon tetrachloride, carbon tetrachloride–benzene and benzene as eluents. Fractions eluted with carbon tetrachloride–benzene (2:1) were treated with preparative thin layer chromatography (TLC) to give a small amount of bis[*o*-(*N*-methyl-*N*-phenylamino)phenyl] disulfide (**8**), mp 120–123 °C (from ether); MS: *m/e* 428 (*M*⁺, 1%) and 214 (1/2 *M*⁺, 100). Yellow oil (1.6 g, 4.0 mmol, 20%), eluted with benzene, was identified as bis(*o*-anilinophenyl) disulfide (**6a**) by comparison of its IR spectrum with that of an authentic sample.^{15b}

Pale yellow tar (**B**, 2.45 g), eluted also with benzene after elution of tar **A**, was chromatographed again on silica gel to give 3-phenyl-2,3-dihydrobenzothiazolone azine (**4a**, 1.41 g, 16%), mp 274–275 °C (from benzene). IR (KBr): 1610 cm^{–1} (C=N); MS: *m/e* 450 (*M*⁺, 100%).

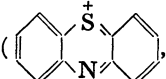
Found: C, 69.18; H, 3.96; N, 12.61; S, 14.33%. Calcd for C₂₆H₁₈N₄S₂: C, 69.32; H, 4.03; N, 12.44; S, 14.21%.

A small amount of spiro compound (**9a**, 60 mg) was also obtained from tar **B**, mp 187–189.5 °C (from ether). MS: *m/e* 410 (*M*⁺, 100%).

Found: C, 72.79; H, 4.12; N, 6.65; S, 15.16%. Calcd for C₂₅H₁₈N₂S₂: C, 73.13; H, 4.41; N, 6.82; S, 15.61%.

Bis[*o*-(*N*-formyl-*N*-phenylamino)phenyl] disulfide (**5a**, 2.68 g, 30%) was eluted with chloroform–ether (1:1), mp 161.5–162.0 °C (from ethyl acetate). IR (KBr): 1670 cm^{–1} (C=O); NMR (CDCl₃): δ 6.80–7.65 (m, 18H, Ar–H) and 9.5 (s, 2H,

2CHO); MS: *m/e* 456 (*M*⁺, ≈1%) and 198 (



100).

Found: C, 68.52; H, 4.50; N, 5.99; S, 13.96%. Calcd for C₂₆H₂₀N₂O₂S₂: C, 68.41; H, 4.42; N, 6.14; S, 14.02%.

Red-brown tar (*ca.* 1 g), eluted finally with ether–chloroform (3:1), could not be identified.

Reduction of 3-Ethyl-2-nitrosoimino-2,3-dihydrobenzothiazole (1c) with LAH. Reduction of **1c** (10 g, 44.8 mmol) with LAH

(1.94 g, 51.1 mmol) was carried out as described for **1a**, and the corresponding products were obtained as follows: bis(*o*-ethylaminophenyl) disulfide (**6c**,^{15a}) 1.25 g, 18%), bis[*o*-(*N*-ethyl-*N*-formylamino)phenyl] disulfide (**5c**, 2.43 g, 28%), mp 113–114.5 °C (from ether) (lit.⁸) 114–115 °C), and 3-ethyl-2,3-dihydrobenzothiazolone azine (**4c**, 2.59 g, 30%), mp 198.5–199.0 °C (from benzene) (lit.¹⁷) 193–202 °C).

Reduction of Bis[*o*-(*N*-formyl-*N*-phenylamino)phenyl] Disulfide (5a) with LAH. Disulfide (**5a**, 1.7 g, 3.7 mmol) and

LAH (0.442 g, 11.6 mmol) were refluxed in THF (50 ml) for 5 days. The reaction mixture was treated as above. Disulfides **6a** (0.33 g, 48%) and **8a** (0.18 g, 30%), mp 120–122.5 °C (from ether), were eluted with benzene. Unchanged **5a** (1.08 g, 63%) was recovered with chloroform–ether (2:1). Thus the yields of **6a** and **8a** were calculated on the basis of the consumed **5a**.

Air-oxidation of 3,3'-Dimethylbi(2,3-dihydrobenzothiazolidene) (11). Air was bubbled for 3 h with stirring into a

solution of **11**⁹ (5.02 g, 16.2 mmol) in benzene (70 ml). After evaporation of the solvent, the brown residue was chromatographed on silica gel. 3,3'-Dimethylbi(2,3-dihydrobenzothiazolidenyl) (0.16 g), which was an impurity contained in **11**, was eluted with benzene, mp 156.2–157.0 °C (from 2-propanol). NMR (CDCl₃): δ 3.00 (s, 6H, 2N–CH₃), 5.03 (s, 2H, 2C–H), and 6.4–7.4 (m, 8H, Ar–H); MS: *m/e* 300 (*M*⁺, 20%) and 150 (*M*⁺/2, 100). Spiro-amide (**12**, 20 mg) was eluted with dichloromethane–chloroform (1:2) and brown tar (4.78 g) was eluted with dichloromethane–chloroform (1:8). A portion of the brown tar was treated with preparative TLC (silica gel, benzene–dichloromethane (2:1)). The major fraction was extracted with dichloromethane to give spiro compound (**9b**, 100 mg), mp 200–203 °C (lit.⁸) 203.5–204 °C), *m/e* 286 (*M*⁺), and **12** (3.5 g, 71%), mp 132–133.5 °C (from methanol). IR (KBr): 1670 cm^{–1}; δ 3.10 (s, 3H, N–CH₃), 3.55 (s, 3H, CONCH₃), and 6.7–7.4 (m, 8H, Ar–H); MS: *m/e* 298 (*M*⁺–16, 10%), 165 (**19b**⁺, 72) and 136 (*o*-S=C₆H₄=N⁺CH₃, 100).

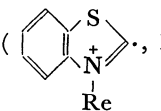
Found: C, 61.44; H, 4.43; N, 8.96; S, 20.10%. Calcd for C₁₆H₁₄N₂O₂F₂: C, 61.14; H, 4.49; N, 8.91; S, 20.36%.

Essentially the same result was obtained by keeping a chloroform solution of **11** to stand in the air with stirring.

Reaction of 1b with Diphenyldiazomethane (15a). Di-

phenyldiazomethane (5.17 g, 26.4 mmol) and **1b** (2.52 g, 13.1 mmol) in dichloromethane (150 ml) were refluxed for a week. After evaporation of the solvent, the residue was chromatographed on silica gel. Benzophenone azine (**18a**, 1.98 g, 42%) was eluted with benzene–dichloromethane (1:1), mp 158–161 °C (from ethanol) (lit.¹⁸) 162 °C). The thiazolone (**19b**, 1.73 g, 80%) was eluted with dichloromethane. Unsymmetrical azine *N*-monoxide (**16a**; 0.15 g, 16%) was eluted with dichloromethane–ether (1:1), mp 188.5–189.5 °C (from ethanol). IR (KBr): 1540, 1435, 1350, and 1225 cm^{–1}; NMR (CDCl₃): δ 3.3 (s, 3H, N–CH₃) and 7.1–8.1 (m, 14H, Ar–H); MS: *m/e* 359 (*M*⁺, 10%), 343

(*M*⁺–16, 18), and 149 (



Found: C, 70.35; H, 4.43; N, 11.50; S, 9.07%. Calcd for

$C_{21}H_{17}N_3OS$: C, 70.17; H, 4.77; N, 11.69; S, 8.92%.

Reaction of 1b with Methylphenyldiazomethane (15b).

Methylphenyldiazomethane (45 mmol) and **1b** (4.46 g, 23.1 mmol) in dichloromethane (150 ml) were refluxed overnight. After evaporation of the solvent, the residue was chromatographed on silica gel. Acetophenone azine (**18b**, 2.06 g, 39%) was eluted with hexane–benzene (1:1), mp 118–122 °C (lit.¹⁹ 121 °C). Unsymmetrical azine (**17b**, 0.26 g, 34%) was eluted with hexane–benzene (1:1) and benzene, mp 115.0–116.0 °C (from ethanol). IR (KBr): 1610, 1575, 1550, and 1475 cm^{-1} ; NMR ($CDCl_3$): δ 2.5 (s, 3H, C–CH₃), 3.6 (s, 3H, N–CH₃), and 6.8–8.1 (m, 9H, Ar–H); MS: m/e 281 (M^+ , 100%).

Found: C, 68.13; H, 5.21; N, 15.17%. Calcd for $C_{16}H_{15}N_3S$: C, 68.30; H, 5.37; N, 14.93%.

Unchanged **1b** (3.92 g, 88% recovery) was eluted with benzene–dichloromethane (1:1) and dichloromethane.

Reaction of 1b with Phenyldiazomethane (15c).

An ethereal solution (50 ml) of phenyldiazomethane was prepared from azibenzil (11.13 g, 50.1 mmol) by treatment with methanolic sodium hydroxide.¹⁴ To the solution was added **1b** (4.83 g, 25.0 mmol) in dichloromethane (300 ml) and the mixture was stirred for 5 days at room temperature. After evaporation of the solvent, the residue was chromatographed on silica gel. Benzaldazine (**18c**, 2.35 g, 46%) was eluted with hexane–benzene (2:1), mp 91–93 °C (from ethanol) (lit.¹⁹ 93 °C). *trans*-Stilbene (0.27 g, 6%) was eluted with benzene, mp 122 °C (from ethanol). Azobis(α -benzoyl- α -phenylmethane) (0.90 g, 11%) was eluted with benzene, mp 201–202 °C (from ethanol). IR (KBr): 1680 cm^{-1} .

Found: C, 80.43; H, 5.06; N, 6.78%. Calcd for $C_{28}H_{22}N_2O_2$: C, 80.36; H, 5.30; N, 6.70%. Unsymmetrical azine *N*-monoxide (**16c**, 81 mg, 11%) was eluted with benzene, mp 178–179 °C (from ethanol). IR (KBr): 1550, 1130, and 1120 cm^{-1} ; NMR ($CDCl_3$): δ 3.6 (s, 3H, N–CH₃), 7.3 (m, 7H, Ar–H), 7.6 (s, 1H, N–C–H), and 8.2 (m, 2H, Ar–H); MS: m/e 283 (M^+ , 10%) and 90 ($PhCH^+$, 100%).

Found: C, 63.56; H, 4.87; N, 14.54; S, 11.03%. Calcd for $C_{16}H_{13}N_3OS$: C, 63.58; H, 4.62; N, 14.83; S, 11.32%.

Residual **1b** (4.36 g, 90% recovery) was eluted with benzene and dichloromethane.

Unsymmetrical azines (**17**) as authentic samples were prepared by condensation of **10b** with the corresponding carbonyl compounds: **17a**, mp 151–152 °C; **17b**, mp 115–116 °C; **17c**, mp 163–164 °C (lit.¹¹ mp 163 °C).

Reaction of 1b with 15a in the Presence of 20. Diphenyldiazomethane (**15a**, 5.17 g, 26.4 mmol) in DMF (50 ml) was added to **1b** (2.51 g, 13.0 mmol) and **20** (1.79 g, 6 mmol) in DMF (40 ml) and the mixture was left to stand overnight at 30 °C. The complex (**20**) was decomposed with a few ml of 30% aqueous hydrogen peroxide under cooling with ice–water. The solution was dried over anhydrous magnesium sulfate and filtered. After evaporation of the solvent under reduced pressure, the residue was chromatographed on silica gel. Benzophenone (3.25 g, 68%) was eluted with benzene and benzophenone azine (**18a**, 0.24 g, 10%) was eluted with benzene–dichloromethane (1:1). Elution with dichloromethane gave **16a** (mp 186–188 °C, 0.325 g, 7%), **17a** (mp 147–148.5 °C, 0.18 g, 4%) and **19b** (0.24 g, 11%).

The reaction was carried out under various conditions and **16a** and **17a** were determined by high speed liquid chromatography (HSLC) (Hitachi gel 3010: styrene–divinylbenzene copolymer) using methanol containing concd ammonia (1% v/v) as eluent. Results were essentially the same as described above.

Deoxygenation of Azine N-Monoxide (16a) with Diphenyldiazomethane. Diphenyldiazomethane (0.997 g, 5.1 mmol) in DMF (10 ml) was added dropwise to azine *N*-monoxide (**16a**, 0.171 g, 0.48 mmol) and the complex (**20**, 0.280 g, 0.91 mmol) in DMF (10 ml). Almost quantitative formation of azine (**17a**) was shown by HSLC, **17a** (0.21 g, 75%) being isolated by column chromatography.

References

- 1) For part XIV see: K. Akiba, T. Tsuchiya, I. Fukawa, and N. Inamoto, *Bull. Chem. Soc. Jpn.*, **49**, 550 (1976).
- 2) K. Akiba, T. Kawamura, M. Hisaoka, and N. Inamoto, *Bull. Chem. Soc. Jpn.*, **48**, 3262 (1975); M. Hisaoka, K. Akiba, and N. Inamoto, *ibid.*, **48**, 3266 (1975); K. Akiba, M. Hisaoka, T. Kawamura, and N. Inamoto, *ibid.*, **48**, 3270 (1975).
- 3) M. Hisaoka, K. Akiba, and N. Inamoto, *Bull. Chem. Soc. Jpn.*, **48**, 3274 (1975).
- 4) Preliminary report: K. Akiba, T. Kawamura, M. Ochiumi, and N. Inamoto, *Heterocycles*, **1**, 35 (1973).
- 5) H. E. Zimmerman and D. H. Paskovich, *J. Am. Chem. Soc.*, **86**, 2149 (1964).
- 6) a) H. Balli, *Angew. Chem.*, **76**, 995 (1964); b) H. Quast and S. Huenig, *Chem. Ber.*, **99**, 2017 (1966); c) H. W. Wanzlick, H. J. Kleiner, I. Lasch, H. U. Fueldner, and H. Steinmaus, *Justus Liebigs Ann. Chem.*, **708**, 155 (1967).
- 7) C. J. Thoman, S. J. and I. M. Hunsberger, *J. Org. Chem.*, **33**, 2852 (1968); K. Akiba, S. Matsunami, C. Eguchi, and N. Inamoto, *Bull. Chem. Soc. Jpn.*, **47**, 935 (1974).
- 8) W. H. Mills, L. M. Clark, and J. A. Aeschlimann, *J. Chem. Soc.*, **123**, 2358 (1923).
- 9) H. J. Kleiner, *Justus Liebigs Ann. Chem.*, **724**, 221 (1969).
- 10) H. Passing, *J. Prakt. Chem.*, [2] **153**, 1 (1939).
- 11) E. Besthorn, *Ber.*, **43**, 1519 (1910).
- 12) R. F. Hunter, *J. Chem. Soc.*, **1930**, 125.
- 13) L. I. Smith and K. L. Howard, *Org. Synth.*, Coll. Vol. III, 351 (1955); H. Staudinger and A. Gaule, *Ber.*, **49**, 1907 (1916).
- 14) P. Yates and B. L. Shapiro, *J. Org. Chem.*, **23**, 759 (1958).
- 15) a) A. I. Kiprianov and Z. N. Pazenko, *J. Gen. Chem.*, **19**, 1523 (1949); *Chem. Abstr.*, **44**, 3487 (1950); b) A. I. Kiprianov and I. K. Ushenko, *ibid.*, **17**, 2201 (1947); *Chem. Abstr.*, **42**, 5016 (1948).
- 16) R. Riemschneider, *Monatsh. Chem.*, **89**, 683 (1958); S. Huenig, H. Geiger, G. Kaupp, and W. Kniese, *Justus Liebigs Ann. Chem.*, **697**, 116 (1966).
- 17) S. Huenig, H. Balli, H. Conrad, and A. Schott, *Justus Liebigs Ann. Chem.*, **676**, 36 (1964).
- 18) T. Curtius and F. Rauterberger, *J. Prakt. Chem.*, [2] **44**, 192 (1891).
- 19) T. Curtius and L. Pflug, *J. Prakt. Chem.*, [2] **44**, 535 (1891).