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

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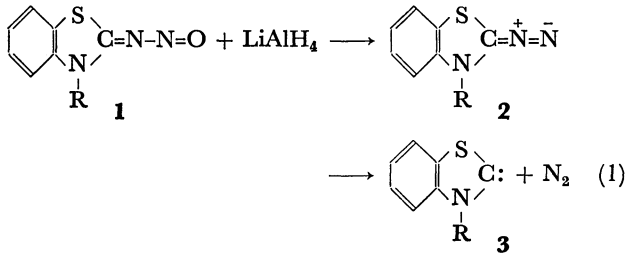
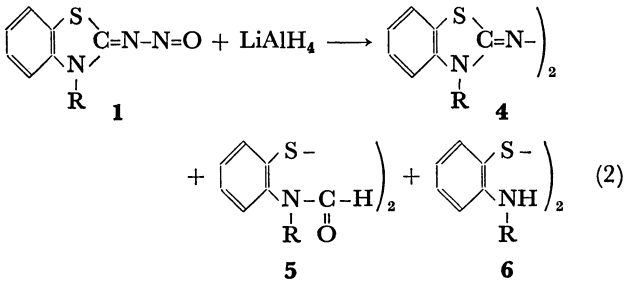
3-Substituted 2-nitrosoimino-2,3-dihydrobenzothiazoles (**1**) were reduced with lithium aluminum hydride to give the corresponding thiazolone azines and bis[*o*-(*N*-substituted *N*-formylamino)phenyl] disulfides as major products. Reactions of **1** with some substituted diazomethanes gave the corresponding 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 reagents[2] 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

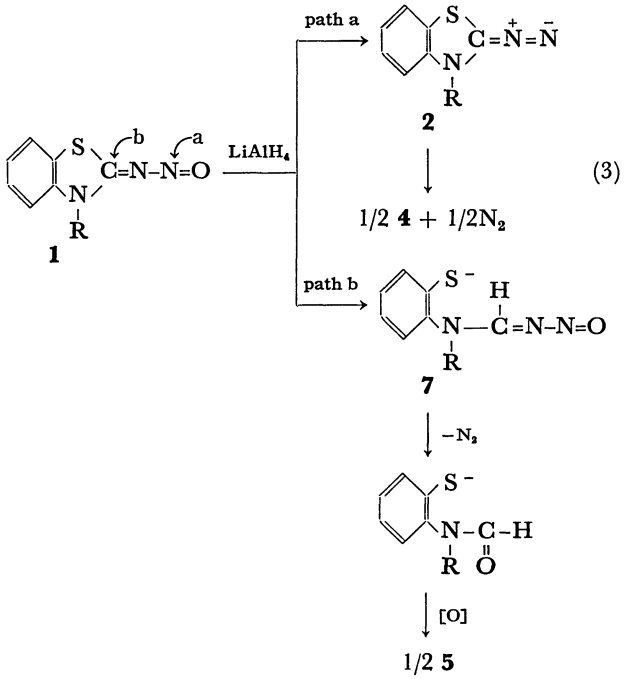
The formation of the azine (**4**) can be ascribed to the intermediacy of the diazo compound (**2**) produced by hydride attack on the nitrogen atom of the nitroso group (*path a*). On the other hand, the formation of the disulfide (**5**) can be explained by invoking the ring opened nitrosoimine (**7**) 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]

Table 1. Reduction of **1** with excess lithium aluminum hydride

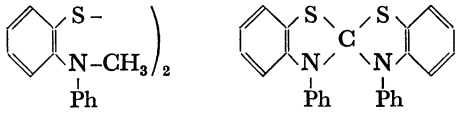
1	4	5	6
a) R=Ph	16	30	20
b) R=Me	27	22	24
c) R=Et	30	28	18

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

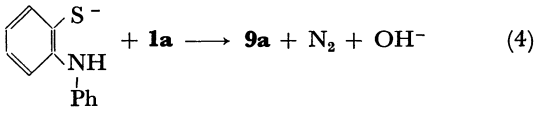
When the reaction was carried out under argon atmosphere in a closed system, the evolved gas was only nitrogen as confirmed by mass spectrometry. This supports the proposed mechanism.



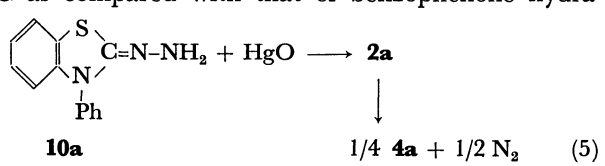
The products were scrutinized by column chromatography for the case of **1a**, two products (**8a** and **9a**)



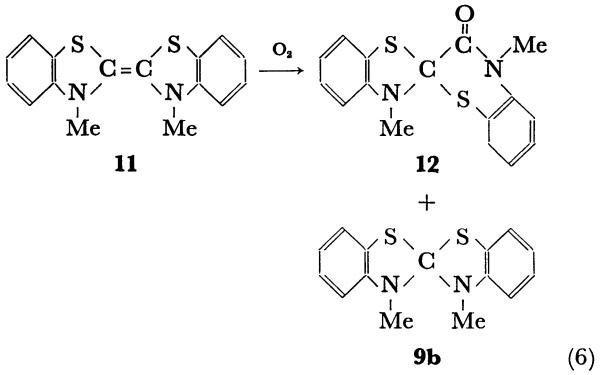
being obtained in very small amounts. The disulfide (**8a**) is a reduction product of **5a** with excess LAH, since **5a** was reduced with LAH in refluxing tetrahydrofuran (THF) to **6a** and **8a**. Formation of **9a** can be explained by means of the reaction of **1a** with *o*-anilinobenzenethiolate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



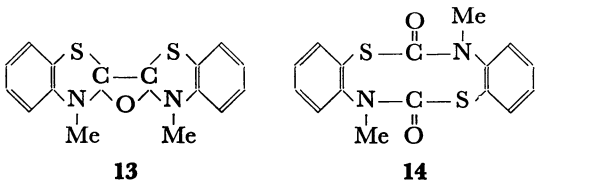
In order to prepare **2**, 2-hydrazono-3-phenyl-2,3-dihydrobenzothiazole (**10a**) was oxidized with mercury (II) oxide. The reaction took place very slowly at 0 °C as compared with that of benzophenone hydrazone, giving **4a** as the major product (*ca.* 70%). This shows that **2a** is too unstable 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**.



10a 1/4 **4a** + 1/2 N_2 (5)



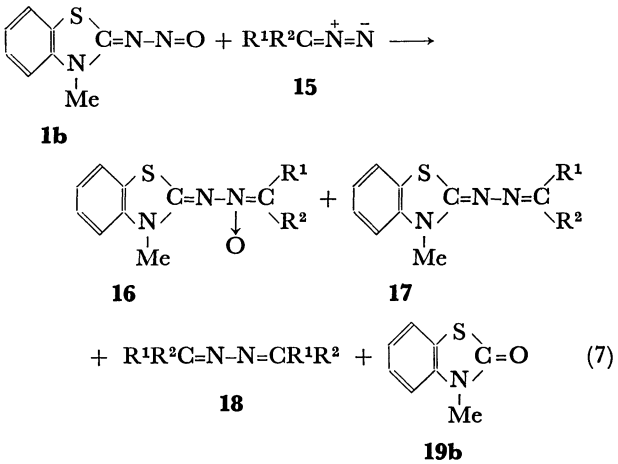
11 **12** **9b** (6)



13 **14**

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.



1b **15** **16** **17** **18** **19b** (7)

a) $R^1=R^2=Ph$, b) $R^1=Ph$, $R^2=Me$, c) $R^1=Ph$, $R^2=H$

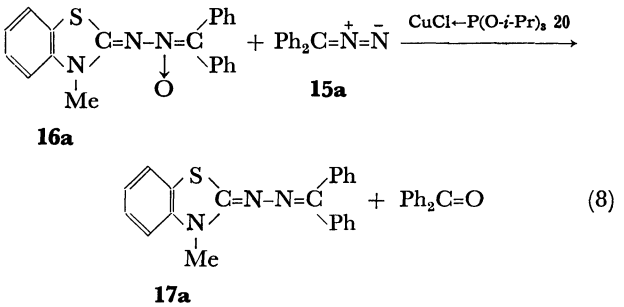
Table 2. Reaction of **1b** with diazo compounds[a]

15	16	17	18	19b	1b recovery
a) $Ph_2C=N_2$	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



16a **15a** **17a** (8)

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 phenyldiazomethanes[14] 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).

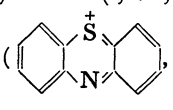
Reduction of 2-Nitrosoimino-3-phenyl-2,3-dihydrobenzothiazole (1) with LAH. LAH (2.235 g, 59.0 mmol) and **1a** (10.0 g, 39.2 mmol) were used for the reaction, the reaction mixture being treated as described for **1b**. Yellow tar (*A*, 2.16 g), eluted with benzene, was chromatographed on silica gel 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 $C_{26}H_{18}N_4S_2$: 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 $C_{25}H_{18}N_2S_2$: 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 ($CDCl_3$): 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 $C_{26}H_{20}N_2O_2S_2$; 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.

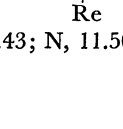
Reduction of 3-Ethyl-2-nitrosoimino-2,3-dihydrobenzothiazole (1c) with LAH. Reduction of **1c** (10 g, 44.8 mmol) with LAH (1.94 g, 51.1 mmol) was carried out as described for **1a**, and the corresponding products were obtained as follows: bis(*o*-ethylaminophenyl) disulfide (**6c**,[15a] 1.25 g, 18%), 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-dihydrobenzothiazolinyl) (0.16 g), which was an impurity contained in **11**, was eluted with benzene, mp 156.2—157.0 °C (from 2-propanol). NMR ($CDCl_3$): δ 3.00 (s, 6H, 2N–CH_3), 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–CH_3), 3.55 (s, 3H, CONCH_3), and 6.7—7.4 (m, 8H, Ar–H); MS: *m/e* 298 (M^+−16, 10%), 165 (**19b**$^+$, 72) and 136 (*o*-S=C_6H_4=$\overset{+}{N}$=CH_2, 100).

Found: C, 61.44; H, 4.43; N, 8.96; S, 20.10%. Calcd for $C_{16}H_{14}N_2OF_2$: 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). Diphenyldiazomethane (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 ($CDCl_3$): δ 3.3 (s, 3H, N–CH_3) and 7.1—8.1 (m, 14H, Ar–H); MS: *m/e* 359 (M^+, 10%), 343 (M^+−16, 18), and 149 ( , 100).

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–CH_3), 3.6 (s, 3H, N–CH_3), 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–CH_3), 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 $C_{15}H_{13}N_3OS$: 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 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 Diphenylcarbene.* 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.

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