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1,2,4-Triazine Chemistry. 11.[1] Dihydro-1,2,4-triazines: Structural Studies on Sodium Borohydride Reduction Products from Some 3-Methylthio- and 3-Methoxy-1,2,4-triazines

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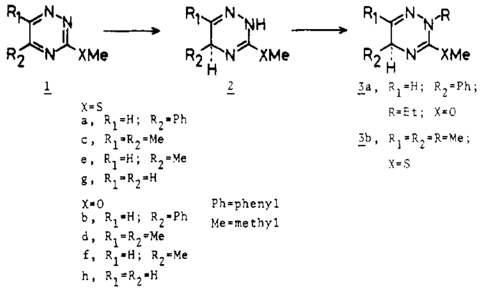
Sodium borohydride reduction of 3-(methylthio)-5-phenyl- (**1a**), 3-methoxy-5-phenyl- (**1b**), 3-(methylthio)-5,6-dimethyl- (**1c**), 3-methoxy-5,6-dimethyl- (**1d**), 3-(methylthio)-5-methyl- (**1e**), 3-methoxy-5-methyl- (**1f**), 3-(methylthio)- (**1g**), and 3-methoxy-1,2,4-triazine (**1h**) gave the corresponding 2,5-dihydro analogues (**2a–h**). The structures of **2a–h** were established by spectral comparison with the known, corresponding 4,5-dihydro tautomers. **2b** and **2c** were N_2-alkylated to 2-ethyl-3-methoxy-5-phenyl-2,5-dihydro-1,2,4-triazine (**3a**) and 2,5,6-trimethyl-3-(methylthio)-2,5-dihydro-1,2,4-triazine (**3b**), respectively. Heating **3a** with DMAD gave 2-ethyl-5-phenyl-1,2,4-triazin-3(2*H*)-one (**8**).

In the preceding paper[1] it was established that 5,6-diaryl-1,2,4-triazines with a methylthio or methoxy group at the 3-position are reduced by sodium borohydride to 2,5-dihydro-1,2,4-triazines. This paper describes spectroscopic studies on the reduction products obtained from the parent 3-methoxy- and 3-(methylthio)-1,2,4-triazines as well as derivatives substituted at the 5- and/or 6-positions.

Triazines **1a–h** were synthesized by known methods[2] (Scheme I). Reduction of **1a** with an equimolar amount of sodium borohydride gave two main products, one of which was 3-(methylthio)-5-phenyl-2,5-dihydro-1,2,4-triazine (**2a**), while similar reduction of **1b** gave 73% of 3-methoxy-5-phenyl-2,5-dihydro-1,2,4-triazine (**2b**). The melting points, ultraviolet absorptions, and ^{1}H NMR resonances of **2a,b** are given in the upper section of Tables I and II together with those reported for the tautomeric 4,5-dihydro compounds,[3] 3-(methylthio)-5-phenyl-4,5-dihydro-1,2,4-triazine (**4a**) and 3-methoxy-5-phenyl-4,5-dihydro-1,2,4-triazine (**4b**). The tautomers had been obtained by the reaction of **1g** and **1h** with phenylmagnesium bromide[3] (Scheme II). Although there are nine possible dihydro-1,2,4-triazines,[4] the areas, the chemical shifts, the presence of an imino proton, and the multiplicities (doublets) of two protons in **2a,b** limit their structures to 2,5- or 4,5-dihydrotriazines.[5] Since the 4,5-dihydro structures have been assigned to the Grignard products, our compounds are the 2,5-dihydro-1,2,4-triazines. The hypsochromic shift of the UV absorptions of **2a,b** relative to **4a,b** indicates less extensive conjugation and confirms the insulation of both double bonds. The downfield shift of the resonances of the 5-protons in **2a,b** is in accord with the presence of an adjacent double bond in these molecules.

Scheme I



Scheme II

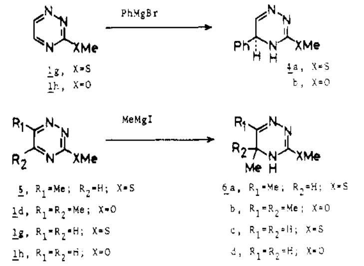


Table I. Ultraviolet Absorption of 2,5-Dihydro-1,2,4-triazines **2a–h** and 4,5-Dihydro-1,2,4-triazines **4a,b**[a] and **6a,b**[a] in 95% EtOH

compd	mp, °C	λ_{max}, nm (ϵ)
2a	103-105	240 (4800, infl)
2b	133-135	258 (1100, infl)
4a	95-96	235 (8100), 286 (6000, infl)
4b	85-86	264 (7900), 287 (5300)
2c	93-96	260 (1900, infl)
2d	77-78.5	243 (1700)
2e	80-85	270 (1100, infl)
2f	oil	247 (1400)
2g	144.5-145.5	270 (1000, infl)
2h	60-62	247 (1100)
6a	oil	216 (6300), 267 (2000)
6b	62-63	218 (4500), 255 (7800), 322 (2600)
6c	75-76	221 (5900), 265 (1500, infl), 326 (200, infl)
6d	65-66	221 (11 700), 255 (7800)

[a] Reference 3.

Similar reduction of **1c** and **1d** afforded 3-(methylthio)-5,6-dimethyl-2,5-dihydro-1,2,4-triazine (**2c**) and 3-methoxy-5,6-dimethyl-2,5-dihydro-1,2,4-triazine (**2d**) in 70 and 68% yields, respectively. The structures of **2c,d** followed from the comparison of their spectral properties with those reported[3] for 3-(methylthio)-5,6-dimethyl-4,5-dihydro-1,2,4-triazine (**6a**) and 3-methoxy-5,5,6-trimethyl-4,5-dihydro-1,2,4-triazine (**6b**). The hypsochromic shift of the UV absorptions of **2c,d** as compared with those of **6a,b** and the deshielding of the H_5 resonance of **2c** as contrasted with that of **6a** reveal the same situation as encountered in the case of **2a,b**. Although the literature

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[1] Sasaki, T.; Minamoto, K.; Harada, K. *J. Org. Chem.*, preceding paper in this issue.

[2] Paudler, W. W.; Chen, T.-K. *J. Heterocycl. Chem.* **1970**, *7*, 767.

[3] Daunis, J.; Pigiere, C. *Bull. Soc. Chim. Fr.* **1973**, 2493.

[4] 1,2-, 1,4-, 1,6-, 2,3-, 2,5-, 3,4-, 3,6-, 4,5-, and 5,6-dihydro-1,2,4-triazines.

[5] Reference 3 refers to neither coupling between H_5 and the N_4H nor the signal of the N_4H for the compounds cited here. The recording conditions (with or without D_2O addition) are also not described. At least, models of 4,5-dihydro-1,2,4-triazines indicate that H_5 and the N_4H can have a dihedral angle of ca. 90°.

Table II. ^{1}H NMR Spectra of 2,5-Dihydro-1,2,4-triazines 2a-h and the Derivatives of 4,5-Dihydro-1,2,4-triazine (4a,b[a] and 6a-d[a]) in $CDCl_3$

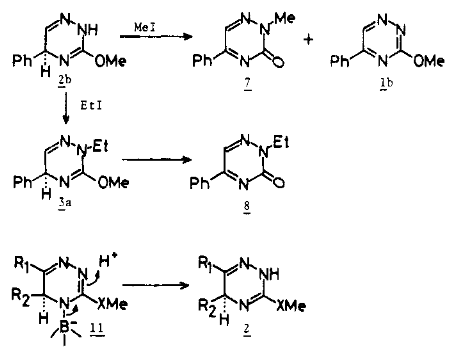
		chemical shifts, δ					
compd	coupling const, Hz	H_5	H_6	5-Me	6-Me	X-Me	NH
2a	$J_{H_5,H_6} = 2.5$	4.70 (d)	6.75 (d)			2.47 (s)[c]	8.15 (br s)
2b	$J_{H_5,H_6} = 2.5$	4.95 (d)	6.73 (d)			3.80 (s)[d]	7.70 (br s)
4a	$J_{H_5,H_6} = 2$	4.56 (d)	6.64 (d)			2.38 (s)[c]	*b*
4b	$J_{H_5,H_6} = 2$	4.52 (d)	6.62 (d)			3.72 (s)[d]	*b*
2c	$J_{H_5,Me} = 7.1$	3.90 (q)		1.26 (d)	1.97 (s)	2.44 (s)[c]	8.20 (br s)
2d	$J_{H_5,Me} = 7.4$	3.94 (q)		1.24 (d)	1.93 (s)	3.73 (s)[d]	7.37 (br s)
2e	$J_{H_5,Me} = 7.1$, $J_{H_5,H_6} = 1.9$	3.73 (dq)	6.66 (d)	1.38 (d)		2.45 (s)[c]	8.12 (br s)
2f	$J_{H_5,Me} = 7.1$, $J_{H_5,H_6} = 2.2$	3.92 (dq)	6.66 (d)	1.30 (d)		3.76 (s)[d]	8.17 (br s)
2g	$J_{H_5,H_6} = 2.5$	3.86 (d)	6.79 (t)			2.43 (s)[c]	8.25 (br s)
2h	$J_{H_5,H_6} = 2.5$	3.91 (d)	6.76 (t)			3.74 (s)[d]	7.73 (br s)
6a	$J = 6$	3.66 (q)		1.35 (d)	1.89 (s)	2.51 (s)[c]	*b*
6b				1.17 (s, 2 Me)	1.87 (s)	3.70 (s)[d]	*b*
6c	$J = 2, 8$	3.48 (m)	6.57 (d)	1.52 (d)		2.39 (s)[c]	*b*
6d	$J = 2, 8$	3.48 (m)	6.55 (d)	1.20 (d)		3.70 (s)[d]	*b*

[a] Reference 3. [b] Not described in ref 3. [c] X = S. [d] X = O.

lacks a description of 3-methoxy-5,6-dimethyl-4,5-dihydro-1,2,4-triazine for direct comparison with **2d**, the structure of **2d** is established by the similarity of its UV spectrum to that of 3-methoxy-5-methyl-1,2,4-triazine (**2f**).

Reduction of the 5-methyl compounds **1e,f**, followed by column chromatography of the rather complex reaction mixtures, led to the isolation of 3-(methylthio)-5-methyl-2,5-dihydro-1,2,4-triazine (**2e**) and its 3-methoxy analogue (**2f**) in 26 and 47% yields, respectively. The latter yield was attained by the use of $^1/_4$ equiv[6] of sodium borohydride. The ^{1}H NMR spectrum of **2e** exhibited a doublet of quartets at 3.73 ppm assignable only to H_5 coupling with H_6 and the C_5 methyl protons. The corresponding proton in the tautomer, 3-(methylthio)-5-methyl-4,5-dihydro-1,2,4-triazine (**6c**),[3] resonates at higher field (3.48 ppm) as a more complex multiplet caused by additional coupling with the adjacent N_4 H. The same changes in shift and multiplicity are observed in the spectra of the tautomeric compounds **2f** and **6d**.[3] Analogously, compound **1g** as well as **1h** afforded 3-(methylthio)-2,5-dihydro-1,2,4-triazine (**2g**, 89%) and 3-methoxy-2,5-dihydro-1,2,4-triazine (**2h**, 31%) on reduction with 0.27 and 1.05 equiv of sodium borohydride, respectively. As is seen from Table II, the doublets at 3.86 and 3.91 ppm are assignable to the magnetically equivalent 5-protons in compounds **2g,h**. The skeletal identities of **2c–h** are evident from the UV absorptions. It is interesting to note that the 6-methyl group in **2c** as well as that in **2d** affects the electronic absorption hypsochromically, probably owing to perturbation of the major conjugation system by steric repulsion between the 5- and 6-methyl groups. The general view of the ^{1}H NMR data of these reduction products discloses that (1) the replacement of the 3-methylthio by a methoxy group exerts a slight deshielding effect on H_5 in contrast to the shielding effect on H_6 within each pair of 2,5-dihydro-1,2,4-triazines, (2) the chemical shift of two protons at C_5 is nearly the same as that of one proton at C_5 which also bears a methyl group (compare **2e** with **2g**, or **2f** with **2h**),[7] and (3) H_5 and H_6 in 2,5-dihydrotriazines resonate at lower fields than those in corresponding 4,5-dihydro tautomers (compare the couples of **2a–4a**, **2b–4b**, **2c–6a**, **2g–6c**, or **2h–6d**).

Scheme III



Although the reaction conditions were not optimized, less substituted 1,2,4-triazines used in this work seem to give better yields when less than equimolar amounts of sodium borohydride are used, suggesting overreduction with an excess of the reagent. Some of the isolated 2,5-dihydro-1,2,4-triazines of lower molecular weight are unstable since they gradually became colored on standing at room temperature, in contrast to the stable 5,6-diaryl-2,5-dihydro-1,2,4-triazines.[1]

Methylation of selected dihydrotriazines, **2b** and **2c**, was attempted. Curiously, the reaction of **2b** with CH_3I/NaH under argon at 0 °C gave 2-methyl-5-phenyl-1,2,4-triazin-3(2*H*)-one (**7**)[9] as the only isolable product, while the same reaction at 35 °C afforded **7** and **1b** in 28 and 27% yields, respectively (Scheme III). However, alkylation of **2b** with ethyl iodide yielded the normal product, 2-ethyl-3-methoxy-5-phenyl-2,5-dihydro-1,2,4-triazine (**3a**) as an oil in a satisfactory yield. Although its rigorous purification for analysis was abandoned (see Experimental Section), the chemical shift (4.9 ppm) and coupling pattern of the ^{1}H NMR signal of H_5 (d, $J_{5,6}$ = 2.7 Hz) confirmed its structure. On the other hand, methylation of **2c** occurred normally to give 2,5,6-trimethyl-3-(methylthio)-2,5-dihydro-1,2,4-triazine (**3b**). At present, the origin of the 2-methyl group in **7** (from methyl iodide or the 3-methoxy group) or the reason for the demethylation is not clear.

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[6] In this paper "equimolar" or "1 equiv" means an "equivalent mole"; i.e., $^1/_4$ equiv means $^1/_4$-fold mole.

[7] It is probable that the 2,5-dihydrotriazines can be in the chair conformation, and conformational inversion at C_5 in **2e,f** would be limited relative to that in **2g,h**; i.e., H_5 in **2e** or **2f** is likely to take mainly an axial conformation. Axial protons in a six-membered ring are known to resonate upfield from their equatorial counterparts.[8] The methylene protons in **2g,h** can be considered to give rise to the average chemical shifts of both conformations at ambient temperature. The overall results seem to have given the relatively shielded chemical shifts of the methine protons.

[8] Jackman, L. M., Sternhell, S., Eds. "Applications of Nuclear Magnetic Resonance Spectroscopy in Organic Chemistry", 2nd ed.; Pergamon Press: New York, 1969; pp 163, 238.

[9] Paudler, W. W.; Lee, J. *J. Org. Chem.* **1971**, *36*, 3921.

During a study of the reaction of dimethyl acetylenedicarboxylate with 2-alkyl-2,5-dihydrotriazines, this reaction was also carried out with **3a**. Instead of the expected product, a 71% yield of 2-ethyl-5-phenyl-1,2,4-triazin-3-(2*H*)-one (**8**) was obtained. The structure of **8** was established by its elemental analysis, its ^1H NMR spectrum, and the identity of its UV spectrum with that of the 2-methyl compound **7**. Compound **2b** appears to be extremely unstable. The generally observed 1,4-addition of hydrogen seems to be explainable by the initial attack of BH_4^- at the 4,5-position[10] (**11**, Scheme III) followed by the uptake of a proton at N_2 from the environment. These results are in contrast with those of the Grignard reaction[3] which involves protonation at N_4 of the intermediates. The reason for these contrasting results are not clear at present. Although another mechanism involving 1,4-addition of hydrogen followed by tautomerization to give 4,5-dihydro-1,2,4-triazines had been suggested for the Grignard reaction with some 1,2,4-triazines bearing bulky groups at the 5- and 6-positions,[3] we have never observed such tautomerization through the workup procedures.

Thus, $NaBH_4$ reduction of 3-(methylthio)- and 3-methoxy-1,2,4-triazines and their 5- or 5,6-substituted derivatives gives their 2,5-dihydro derivatives. The spectral data given here and in the preceding paper[1] plus those given by Daunis et al.[3] for 4,5-dihydro-1,2,4-triazines would serve to discriminate between the nine[4] possible tautomeric forms of the dihydro-1,2,4-triazines.

Experimental Section

Melting points were obtained on a Yanagimoto micro melting point apparatus and are not corrected. A Büchi Kugelrohr distillator was used for dry distillation.

3-(Methylthio)-5-phenyl-2,5-dihydro-1,2,4-triazine (2a). To a solution of **1a** (1.015 g, 5.0 mmol) in THF/MeOH (4:1, 20 mL) was added sodium borohydride (190 mg, 5.0 mmol), and the mixture was stirred under argon for 14 h. TLC (alumina, 3:1 $CHCl_3$/EtOAc) indicated two slower moving products, the less polar of which was expected to be a dihydrotriazine according to our former experience with the 5,6-diaryldihydro-1,2,4-triazines.[1] After being neutralized with AcOH/MeOH (1:5), the mixture was evaporated, and the residue was partitioned between ethyl acetate (50 mL) and water (10 mL). The separated EtOAc layer was dried over sodium sulfate and evaporated, and the residue was applied to an alumina column (2.5 × 15 cm). Elution with $CHCl_3$/EtOAc (3:1) gave from the earlier fractions 250 mg (24%) of **2a** after recrystallization from methanol. Later fractions contained another noncrystalline product which was not further investigated. Anal. Calcd for $C_{10}H_{11}N_3S$: C, 58.51; H, 5.40; N, 20.47. Found: C, 58.59; H, 5.61; N, 20.41.

3-Methoxy-5-phenyl-2,5-dihydro-1,2,4-triazine (2b). A solution of **1b** (936 g, 5.0 mmol) in THF/MeOH (5:1, 30 mL) was treated with $NaBH_4$ (210 mg, 5.5 mmol) under argon as above for 17 h. The mixture was neutralized with AcOH/MeOH (1:5) and evaporated, and the residue was partitioned between EtOAc and water. The obtained EtOAc-soluble material was recrystallized from methanol to give 595 mg of **2b**. A further 100 mg of **2b** was obtained by preparative TLC (alumina, 5:1 $CHCl_3$/EtOAc) of the filtrate (total yield 73%). Anal. Calcd for $C_{10}H_{11}N_3O$: C, 63.48; H, 5.86; N, 22.21. Found: C, 63.46; H, 6.12; N, 22.25.

3-(Methylthio)-5,6-dimethyl-2,5-dihydro-1,2,4-triazine (2c). A solution of **1c** (1.29 g, 8.31 mmol) in THF/MeOH (4:1, 23 mL) was treated with $NaBH_4$ (325 mg, 8.59 mmol) under argon for 20 h. The mixture was worked up as for **2b** and the crude product recrystallized from ethyl acetate to give 720 mg of **2c** as colorless crystals. Preparative TLC (silica gel, 10 × 20 cm; $CHCl_3$/acetone, 1:1) of the mother liquor gave an additional crop (130 mg, total 70%). Anal. Calcd for $C_6H_{11}N_3S$: C, 45.83; H, 7.05; N, 26.72. Found: C, 45.77; H, 6.85; N, 26.86.

3-Methoxy-5,6-dimethyl-2,5-dihydro-1,2,4-triazine (2d). A solution of **1d** (1.0 g, 7.18 mmol) in THF/MeOH (4:1, 20 mL) was treated with $NaBH_4$ (300 mg, 7.9 mmol) under argon for 18 h. The mixture was worked up as above and the product mixture applied to an alumina column (2.5 × 20 cm). Elution with $CHCl_3$/EtOAc (3:1) and recrystallization of the main fraction gave 685 mg (68%) of **2d** as colorless crystals. Anal. Calcd for $C_6H_{11}N_3O$: C, 51.05; H, 7.86; N, 29.76. Found: C, 51.34; H, 7.57; N, 29.46.

3-(Methylthio)-5-methyl-2,5-dihydro-1,2,4-triazine (2e). To a stirred, ice-cooled solution of **1e** (500 mg, 3.56 mmol) in THF/MeOH (3:1) was added $NaBH_4$ (147 mg, 3.85 mmol) under argon bubbling. After being stirred under cooling for 2 h, the mixture was worked up as above and the product mixture put on an alumina column (2.5 × 13 cm). Elution with $CHCl_3$/EtOAc (3:1) gave a crystalline fraction which was recrystallized from ether/petroleum ether to give 130 mg (26%) of **2e** as colorless crystals. Anal. Calcd for $C_5H_9N_3S$: C, 41.94; H, 6.33; N, 29.34. Found: C, 42.19; H, 6.20; N, 29.44.

3-Methoxy-5-methyl-2,5-dihydro-1,2,4-triazine (2f). An ice-cooled solution of **1f** (500 mg, 4.0 mmol) in THF/MeOH (4:1, 10 mL) was treated with $NaBH_4$ (1 mmol, $^1/_4$ equiv) under argon for 24 h as in the case of **2e**. The mixture was worked up as usual and subjected to column chromatography (alumina, 2.5 × 15 cm; $CHCl_3$/EtOAc, 3:1) to give from the main fraction 240 mg (47%) of **2f** as a colorless oil. A 135-mg (25%) quantity of starting material was recovered. For analysis, a part of the oily product was dried at 30–35 °C under vacuum. Anal. Calcd for $C_5H_9N_3O$: C, 47.23; H, 7.13; N, 33.05. Found: C, 46.98; H, 6.93; N, 33.15.

3-(Methylthio)-2,5-dihydro-1,2,4-triazine (2g). A solution of **1g** (500 mg, 3.95 mmol) in THF/MeOH (4:1, 10 mL) was treated with $NaBH_4$ (1.05 mmol, 0.27 equiv) for 1 h with ice cooling and argon bubbling. The mixture was worked up as usual, and the crude product was sublimed (0.1 torr, 60 °C) to give 452 mg (89%) of pale yellow crystals. Anal. Calcd for $C_4H_7N_3S$: C, 37.19; H, 5.46; N, 32.53. Found: C, 37.47; H, 5.36; N, 32.47.

3-Methoxy-2,5-dihydro-1,2,4-triazine (2h). A solution of **1h** (2.0 g, 18.0 mmol) in THF/MeOH (5:1) was treated with $NaBH_4$ (715 mg, 19.0 mmol) for 1 h under the same conditions as for **2g**. The mixture was worked up as above, and the crude product was sublimed (0.1 torr, 40–50 °C) to afford 622 mg (31%) of **2h**. Anal. Calcd for $C_4H_7N_3O$: C, 42.47; H, 6.24; N, 37.14. Found: C, 42.67; H, 6.18; N, 37.01.

Reaction of 3-Methoxy-5-phenyl-2,5-dihydro-1,2,4-triazine (2b) with Methyl Iodide. To an ice-cooled, stirred solution of **2b** (400 mg, 2.07 mmol) in DMF (12 mL) under argon was added 50% oil-immersed sodium hydride (109 mg, 2.27 mmol). After 30 min, methyl iodide (0.14 mL, 2.25 mmol) was added and the mixture stirred with ice cooling for 1 h. The mixture was evaporated and the residue subjected to EtOAc extraction and preparative TLC (silica gel, 20 × 20 cm; $CHCl_3$/EtOAc, 5:1) to give 235 mg (60%) of **7** as colorless crystals: mp 159–161 °C (lit.[9] mp 158.5 °C); λ_{max} (MeOH) 215 nm (ϵ 14100, sh), 293 (13500). This product had IR and UV spectra identical with those of an authentic sample.

2-Ethyl-3-methoxy-5-phenyl-2,5-dihydro-1,2,4-triazine (3a). To a stirred, ice-cold solution of **2b** (500 mg, 2.64 mmol) in DMF (10 mL) was added 50% oil-immersed sodium hydride (132 mg, 2.64 mmol) under argon. After 40 min, ethyl iodide (0.22 mL, 2.64 mmol) was added and the mixture stirred at room temperature for 1.5 h. The solvent was evaporated, the residue partitioned between EtOAc and water, and the EtOAc soluble material subjected to preparative TLC (silica gel, 20 × 20 cm; $CHCl_3$/EtOAc, 5:1) to give from the main band 393 mg of TLC-pure yellowish oil after prolonged drying at room temperature under high vacuum. Distillation was not attempted in order to avoid thermal transformation: ^1H NMR ($CDCl_3$) δ 1.20 (3 H, t, J = 7 Hz, CH_3), 3.62 (2 H, q, J = 7 Hz, CH_2), 3.78 (3 H, s, OMe), 4.90 (1 H, d, J_{H_5,H_6} = 2.7 Hz, H_5), 6.64 (1 H, d, J_{H_6,H_5} = 2.7 Hz, H_6), 7.30 (5 H, s, phenyl).

2,5,6-Trimethyl-3-(methylthio)-2,5-dihydro-1,2,4-triazine (3b). A solution of **2c** (1.53 g, 9.73 mmol) in DMF (20 mL) was treated with 50% oil-immersed sodium hydride (245 mg, 10.22

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[10] The reactions of metal hydrides are often viewed as concerted ones in which the hydride anion attacks carbon as the oxygen or nitrogen is complexing with the released MH_3 via a square, cyclic transition state. See for example: Hendrickson, J. B.; Cram, D. J.; Hammond, G. S. "Organic Chemistry"; McGraw-Hill: New York, 1970; pp 458.

mmol) for 30 min, followed by addition of methyl iodide (0.72 mL, 9.95 mmol). After 3 h, the solvent was evaporated and the residue partitioned between EtOAc (40 mL) and water (7 mL). The EtOAc layer was worked up as usual and subjected to preparative TLC (silica gel, 20 × 20 cm; $CHCl_3$/MeOH, 9:1) to give from the main band on oily mixture, which was further purified by dry distillation (5 torr, 120 °C) to afford 1.13 g (72%) of **3b** as an oil: λ_{max} (95% EtOH) 225 nm (ϵ 7600, infl), 256 (2600, sh); ^{1}H NMR ($CDCl_3$) δ 1.22 (3 H, d, $J_{5\text{-Me},H_5}$ = 6.8 Hz, 5-Me), 1.96 (3 H, s, 6-Me), 2.39 (3 H, s, SMe), 3.32 (3 H, s, N-Me), 3.82 (1 H, q, $J_{H_5,5\text{-Me}}$ = 6.8 Hz, H_5). Anal. Calcd for $C_7H_{13}N_3S$: C, 49.09; H, 7.65; N, 24.54. Found: C, 48.82; H, 7.56; N, 24.84.

2-Ethyl-5-phenyl-1,2,4-triazin-3(2*H*)-one (8). Compound **3a** (825 mg, 3.80 mmol) and DMAD (1.08 g, 7.6 mmol) were combined in toluene (10 mL) in a pressure tube, and the mixture was heated at 110 °C under argon for 15 h. After the mixture cooled, the volatiles were evaporated, and the residue was subjected to preparative TLC (silica gel, 20 × 20 cm; $CHCl_3$/EtOAc, 5:1). The main band was eluted with acetone and the obtained solid distilled (0.1 torr, 140–160 °C) to give 543 mg (71%) of **8**: mp 65–67 °C; λ_{max} (MeOH) 215 nm (ϵ 12 900, sh), 293 (13 700); ^{1}H NMR ($CDCl_3$) δ 1.40 (3 H, t, J = 7.5 Hz, CH_3 of the ethyl group), 4.20 (2 H, q, J = 7.5 Hz, CH_2), 7.3–8.3 (5 H, m, phenyl), 8.34 (1 H, s, H_6). Anal. Calcd for $C_{11}H_{11}N_3O$: C, 65.66; H, 5.51; N, 20.88. Found: C, 65.68; H, 5.70; N, 21.16.

Registry No. **1a**, 28735-27-5; **1b**, 28735-28-6; **1c**, 7275-70-9; **1d**, 28735-31-1; **1e**, 28735-24-2; **1f**, 28735-25-3; **1g**, 28735-21-9; **1h**, 28735-22-0; **2a**, 49597-36-6; **2b**, 49597-47-9; **2c**, 49597-40-2; **2d**, 74930-65-7; **2e**, 49597-35-5; **2f**, 49597-46-8; **2g**, 74930-66-8; **2h**, 74930-67-9; **3a**, 74930-68-0; **3b**, 74930-34-0; **7**, 31947-28-1; **8**, 74930-69-1; methyl iodide, 74-88-4; DMAD, 762-42-5.

Cyclic Azo Dioxides. Synthesis and Properties of Bis(*o*-nitrosobenzyl) Derivatives[1]

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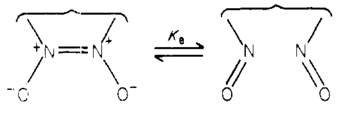
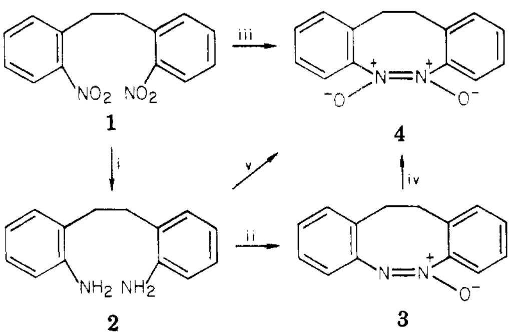
Several cyclic azo dioxides have been prepared by oxidation of the corresponding diamines with sodium tungstate–hydrogen peroxide in ethanol–water: **4** (related to *o,o′*-dinitrosobibenzyl), **8** (related to bis (*o*-nitrosobenzyl) ether), **14** (related to bis(*o*-nitrosobenzyl)amine), **13** (the trifluoroacetate salt of **14**), **12a** and **12b** (the *N*-carbomethoxy and *N*-carbo-*tert*-butoxy derivatives of **14**. In solution the azo dioxides are in equilibrium (K_e) with the corresponding dinitroso forms: K_e increases with decreasing polarity of solvent and with increasing temperature. For azo dioxide **4** in dioxane at 25 °C K_e = 0.18, $\Delta H°$ = 7.09 ± 0.47 kcal mol^{-1}, and $\Delta S°$ = 20.4 cal mol^{-1} deg^{-1}. The azo dioxides decompose at elevated temperatures (>100 °C); azo dioxide **14** is converted to 2-(*o*-nitrosobenzyl)indazole (**15**) in refluxing methylene chloride.

The equilibrium[2,3] between azo dioxides and nitroso species is of much interest: a simple, often facile, electron reorganization interconverts two species of markedly different properties—azo dioxides, which are moderately polar, colorless, and chemically unreactive, and nitroso species which are less polar, colored, and chemically reactive in a variety of ways.[4] For some uses of these substances, control of the equilibrium is complicated by the concentration dependence associated with the dimer ⇄ monomer situation (eq 1). Consequently, we have investigated a number of cyclic azo dioxides. In general, the azo dioxide is the more stable form in aliphatic systems.[2,3] Arylnitroso species are largely dissociated in solution[4,5] although they often exist in the azo dioxide form in the solid state. In this paper, we report the synthesis and properties of some cyclic azo dioxides in the aryl series.



(1)

Scheme I[a]



[a] (i) Pd/C–H_2NNH_2. (ii) *m*-$ClC_6H_4CO_3H$. (iii) (a) Zn, NH_4Cl; (b) CrO_4^{2-}, H^+. (iv) CF_3CO_3H. (v) WO_4^{2-}–H_2O_2, EtOH–H_2O.

Results

Syntheses. Our initial objective was the synthesis of cyclic azo dioxide **4** (5,6-dihydrodibenzo[*c,g*]-1,2-diazocine *N,N′*-dioxide.) The corresponding azo and azo *N*-oxide were both known,[6] as well as the related diamino and

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[1] (1) This investigation was supported by Grant No. CA 23550, awarded by the National Cancer Institute, DHEW.

[2] (2) See: Wajer, A. J. W.; deBoer, T. J. *Recl. Trav. Chim. Pays-Bas* **1972**, *91*, 565 and references cited.

[3] (3) Greene, F. D.; Gilbert, K. E. *J. Org. Chem.* **1975**, *40*, 1409.

[4] (4) (a) Smith, P. A. S. "Open-Chain Nitrogen Compounds", W. A. Benjamin, New York, 1966; Vol. II, Chapter 13. (b) Metzger, H.; Meier, H. "Methoden der Organischen Chemie (Houben-Weyl)"; Muller, E., Ed.; Georg Thieme Verlag: Stuttgart, **1971**; Band 10/1, Chapter 3; Seidenfaden, W. *Ibid.*, Chapter 4. (c) Feuer, H., Ed. "The Chemistry of the Nitro and Nitroso Groups"; Interscience: New York, **1969**, Parts I and II; Boyer, J. H. *Ibid.*, Part I, Chapter 5.

[5] (5) (a) Keussler, V.; Luttke, W. *Z. Electrochem.* **1959**, *63*, 614. (b) Cox, R. H.; Hamada, M. *Org. Magn. Reson.* **1979**, *12*, 322.

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