butylsilane in 25 mL of dry ether. The reaction mixture was stirred and triethylamine (6.0 g, 0.059 mol) in 25 mL of dry ether added slowly via syringe. After the mixture was allowed to stir for 12 h under nitrogen, the precipitated triethylamine hydrochloride was filtered and the solvent removed under vacuum to afford a clear oil which was distilled.

**Phenyl Trimethylsilyl Sulfide (8a)**: 7.7 g (85%); bp 73–75 °C (3.0 torr) [lit.[8] 72–74 °C (3.0 torr)].

**Phenyl Dimethyl-*tert*-butylsilyl Sulfide (8b)**: 9.5 g (85%); bp 78–83 °C (4–5 torr); NMR ($CDCl_3$) δ 0.13 (s, 6 H, Me), 0.96 (s, 9 H, $CMe_3$), and 7.02 (m, 5 H). Anal. Calcd for $C_{12}H_{20}SiS$: C, 64.26; H, 8.92; S, 14.29. Found: C, 64.39; H, 8.74; S, 14.47.

**Trialkylsilyl Benzenesulfinates (12a and 12b): Oxidation of 8a and 8b. NMR-Scale Reaction.** In a dry 5-mm NMR tube was placed 0.31 mmol of the appropriate silyl sulfide (**8a** or **8b**) in 1 mL of $CDCl_3$ or $CCl_4$ followed by 0.082 g (0.31 mmol) of 2-(benzenesulfonyl)-3-phenyloxaziridine (**11**).[7] After the reaction was complete (immediately in the case of **8a** and approximately 10 min for **8b**), the NMR spectra of the reaction mixture indicated the presence of **8a** and **8b**, **12a** and **12b**, and benzenesulfonimine ($PhSO_2N{=}CHPh$) in the ratio of 1:1:1 as determined by the integrated peak areas.

**Preparative-Scale Reaction.** In a dry 50-mL single-necked flask equipped with a magnetic stirring bar, syringe cap, and nitrogen inlet was placed 10.0 mmol of the appropriate silyl sulfide (**8a** and **8b**) in 10 mL of dry $CH_2Cl_2$. Via syringe was added dropwise with stirring 5.34 g (20.4 mmol) of **11** in 10 mL of $CH_2Cl_2$. After 1 h the solvent was evaporated with a stream of dry nitrogen, affording an oily semisolid which was distilled under vacuum.

**Trimethylsilyl Benzenesulfinate (12a)**: 1.5 g (70%) of a clear oil, extremely moisture sensitive; bp 55–60 °C (0.25 torr); IR (film) 1250 (s) and 1140 (s) $cm^{-1}$ (S=O); NMR ($CDCl_3$) δ 0.38 (s, 9 H, $SiMe_3$) and 7.4–7.8 (m, 5 H).

**Phenyl Dimethyl-*tert*-butylsilyl Sulfide (12b)**: 2.0 g (80%) of a clear moisture-sensitive oil; bp 98–104 °C (0.25 torr); IR (film) 1265 (s) and 1140 (s) $cm^{-1}$ (S(O)O); NMR ($CCl_4$) δ 0.2 (s, 3 H, Me), 0.28 (s, 3 H, Me), 0.92 (s, 9 H, $Me_3C$), and 7.62 (m, 5 H).

**Synthesis of 12a and 12b from Benzenesulfinic Acid.** Benzenesulfinic acid was prepared by addition of 4.0 g of sodium benzenesulfinate (Aldrich) to 40 mL of a 7% $H_2SO_4$ solution cooled to 0 °C in an ice bath. The reaction mixture was stirred for 0.5 h and extracted with ether (3 × 50 mL) followed by water (2 × 15 mL). The ether extracts were dried over anhydrous $MgSO_4$ and the solvent was removed under vacuum to afford the solid benzenesulfinic acid (~70%) which was used without further purification.

In a dry 100-mL single-necked flask equipped with a magnetic stirring bar, nitrogen inlet, and syringe cap was placed 2.35 g (16.5 mmol) of benzenesulfinic acid and 17.0 mmol of the appropriate chlorosilane in 25 mL of dry $CH_2Cl_2$. The reaction mixture was cooled to 0 °C in an ice bath and 1.98 g (19.6 mmol) of triethylamine in 10 mL of $CH_2Cl_2$ added dropwise via syringe. The reaction mixture was stirred for 0.5 h at room temperature, the precipitated triethylamine hydrochloride filtered under nitrogen, and the solvent removed under vacuum to afford an oil. Distillation of the oil under vacuum afforded **12a** and **12b** (50–60%) whose IR and NMR spectra were identical with those of **12a** and **12b** prepared as described above.

**Acknowledgment.** We are indebted to Professor Harold Kwart, University of Delaware, for helpful discussions and acknowledge financial support from the donors of the Petroleum Research Fund, administered by the American Chemical Society, and the National Science Foundation (CHE-7819890).

**Registry No.** **4a**, 52778-10-6; **4b**, 53075-89-1; **4c**, 53075-91-5; **4d**, 66883-59-8; **5a**, 73116-69-5; **5b**, 73116-70-8; **5c**, 73116-71-9; **5d**, 73116-72-0; **7a**, 49833-30-9; **7b**, 73116-73-1; **7c**, 66883-79-2; **7d**, 66883-80-5; **8a**, 4551-15-9; **8b**, 73116-74-2; **11**, 69849-45-2; **12a**, 73116-75-3; **12b**, 73116-76-4; methyl propiolate, 922-67-8; thiophenol, 108-98-5; benzenesulfinic acid, 618-41-7.

# Furazans and Furazan Oxides. 8.[1] Preparation of 2-Oxy- and 2-Aminoindazoles by Rearrangement of Benzofurazan Oxide Derivatives

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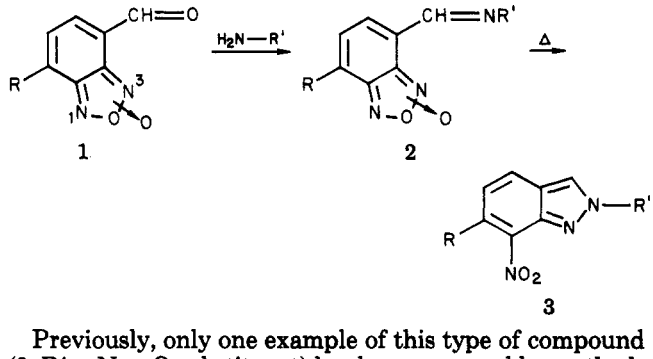
Oximes and hydrazones of 4-formylbenzofurazan oxides rearrange on heating to 2-oxy- and 2-amino-substituted indazoles. $^1H$ NMR spectral studies on the benzofurazan oxide derivatives are reported.

In an earlier paper in this series,[1] the preparation of a variety of 2-alkyl- and 2-aryl-7-nitroindazoles (**3**; R′ = alkyl, Ph) by condensation of 4-formylbenzofurazan oxides (**1**) with primary amines and rearrangement of the intermediate imines **2**, which could not be isolated, was reported. Oximes and hydrazones of the aldehydes **1** have obvious potential for conversion into 2-hydroxy-, 2-alkoxy-, 2-amino-, and 2-(substituted amino)indazoles, which are very little investigated classes of compound. We now report on the realization of this objective. At the outset, it was not obvious whether these compounds (**3**; R′ = OH, OR″, $NH_2$, $NR''_2$ etc.) would be thermodynamically more, or less, stable than the aldehyde derivatives **2**, and since our early experiments gave ambiguous results, their publication has been deferred until now, when further work has clarified the position.




Previously, only one example of this type of compound (**3**; R′ = N or O substituent) has been prepared by methods analogous to those described here; the 2-anilinoindazole

(1) Part 7: S. N. Balasubrahmanyam, A. S. Radhakrishna, A. J. Boulton, and Thoe Kan-Woon, *J. Org. Chem.*, **42**, 897 (1977).

0022-3263/80/1945-1653$01.00/0 

Table I. Preparation of Formylbenzofurazan Oxide Derivatives (2)[d]

| substituents | | reaction conditions | | | yield, | | crystal form | recryst |
|---|---|---|---|---|---|---|---|---|
| R | R′ | solvent | time, h | temp, °C | % | mp, °C[a] | and color | solvent |
| OMe | OH | MeOH | 6 | 20 | 59 | 236-240 | orange prisms | MeCN |
| Cl | OH | THF[b] | 48 | 27 | 62 | 247-250 | yellow needles | EtOAc |
| OMe | OMe | EtOH | 3 | reflux | 54 | 120-125 | orange needles | MeOH |
| Cl | OMe | MeOH | 0.75 | reflux | 66 | 113-114 | yellow plates | MeOH-$H_2O$ |
| OMe | $OCH_2Ph$ | MeOH | 3 | 20 | 43 | 123-125 | yellow plates | EtOH |
| OMe | OPh | MeOH | 2 | 20 | 73 | 127-128 | yellow needles | MeOH |
| OMe | $NMe_2$ | MeOH[c] | 5 | 20 | 58 | 121-123 | red prisms | MeOH |
| Cl | $NMe_2$ | MeOH[c] | 0.5 | reflux | 30 | 93-94 | red needles | MeOH-$H_2O$ |
| OMe | NHPh | MeOH[c] | 2.5 | 20 | 84 | 145-149 | red prisms | MeOH |
| Cl | NHPh | THF | 0.3 | reflux | 67 | 257-260 | red needles | EtOAc |

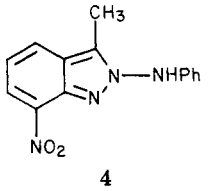
[a] With decomposition, unless range given is ≤2 °C. [b] Tetrahydrofuran, with sufficient water to dissolve salts. [c] With 1-3 drops of acetic acid. [d] Satisfactory analyses (±0.3% for C, H, N) were reported for all compounds in Tables I and II.

Table II. 2-Hydroxy- and 2-Aminoindazoles (3) from Benzofurazan Oxides (2)

| substituents | | reaction conditions | | | yield, | | crystal | |
|---|---|---|---|---|---|---|---|---|
| R | R′ | solvent | time, h | temp, °C | % | mp, °C | form | recryst solvent |
| OMe | OH[a] | $Me_2SO$[b] | 5 | 100 | 32 | 241-244[c] | needles | EtOH |
| Cl | OH | xylene | 2 | reflux | 71 | 242-243 | needles | EtOAc |
| OMe | OMe | toluene | 25 | reflux | 45 | 83-84 | plates | MeOH |
| Cl | OMe | $CDCl_3$ | 24 | 100[d] | 72 | 108-109 | plates | light petroleum |
| OMe | $OCH_2Ph$ | toluene | 12 | reflux | 64 | 103-105 | plates | MeOH |
| OMe | OPh | toluene | 2.5 | reflux | 12 | 217-218 | needles | EtOH-$H_2O$ |
| OMe | $NMe_2$ | toluene | 1 | reflux | 56 | 118-119 | plates | MeOH |
| Cl | $NMe_2$ | $CDCl_3$ | 37 | 100[d] | [e] | | | |
| OMe | NHPh | toluene | 11 | reflux | 8 | 181-183 | plates | EtOH-$H_2O$ |
| Cl | NPh | xylene | 1.5 | reflux | 72 | 186-187 | needles | $CHCl_3$ |

[a] See text for consideration of tautomeric structure. [b] Dimethyl sulfoxide. [c] With decomposition. [d] In sealed NMR tube. [e] Not isolated or characterized other than by $^1H$ NMR.

4 was formed (in low yield) by the thermal decomposition of 3-azido-2-nitroacetophenone phenylhydrazone; a benzofuroxan is a necessary intermediate in this reaction.[2] Other methods of preparation are summarized in the next section.

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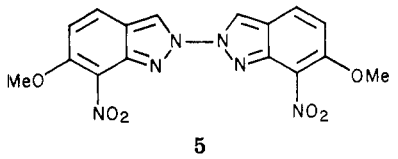


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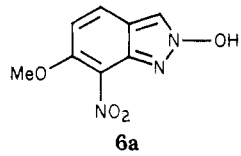
## Results and Discussion

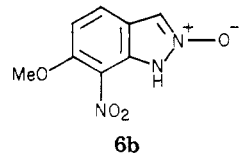
4-Formyl-7-methoxybenzofuroxan (1; R = OMe) condensed under mild conditions with hydroxylamine, *O*-methyl-, *O*-benzyl-, and *O*-phenylhydroxylamine, *N,N*-dimethylhydrazine, and phenylhydrazine. The products were the oximes and hydrazones (2; R′ = OH, OMe, $OCH_2Ph$, OPh, $NMe_2$, and NHPh, respectively), rather than the indazoles (3), as was shown by $^1H$ NMR spectroscopy: all the derivatives showed two sets of signals from the two furoxan tautomers, at and below room temperature, coalescing to a single set at higher temperatures, as the rate of the interconversion (**2a** ⇌ **2b**) increased. These spectra are discussed in detail below. The derivatives could be isolated and characterized, in contrast to the imines (2; R′ = alkyl, aryl) of ref 1. The 7-chloro compound (1; R = Cl) gave similar results. Details of these products are listed in Table I.

Further heating brought about the transformation of the benzofuroxan derivatives into the indazoles 3, which, over the range −60 to 100 °C, showed temperature-invariant $^1H$ NMR spectra. The yields were satisfactory (see Table II), except in the cases of the phenoxy and anilino compounds (3; R = OMe, R′ = OPh and NHPh). Reaction of the furoxan (1; R = OMe) with hydrazine gave the biindazole derivative 5; the intermediate azine could be isolated, but it rearranged during attempts at purification.

The UV spectrum of the hydroxy compound (3; R = OMe, R′ = OH) was very similar to that of the 2-methoxy analogue (3; R = R′ = OMe) [both with $\lambda_{max}$ 306 nm (ε ca. 4000), with inflection at 350 nm (ε ca. 3000)], but with an extra weak inflection at ca. 280 nm. In aqueous solution (pH 2) the spectrum was quite different, with two peaks at $\lambda_{max}$ 270 and 338 nm. It is therefore likely that the OH formula **6a**, rather than the 1(N)*H* 2-oxide structure **6b**,




6a



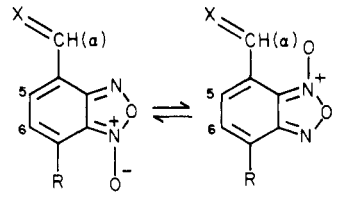

6b

correctly represents the structure of the main tautomer of this compound in ethanol, and that **6b** prevails in water, but a more positive statement cannot be made since the *N*-methyl model compound is not available (and steric effects would in any case be likely to upset the chromophore). Compound 6 was acidic, with p$K$ = 4.0 (spectrophotometric determination, in aqueous buffers[3]). The IR spectrum of a saturated $CHCl_3$ solution was taken, in an attempt to detect $\nu_{OH/NH}$ bands, but even at a 0.3-cm path length no solute absorption could be detected because of its extreme insolubility. The solid-phase spectrum (KBr

(2) A. J. Boulton, P. B. Ghosh, and A. R. Katritzky, *J. Chem. Soc. B*, 1011 (1966).

(3) Determined by K. Takada (U.E.A). The UV spectrum of the chloro analogue (3, R = Cl; R′ = OH), in ethanol and in water, suggests that the same (OH) form prevails in both solvents. As the 6-methoxy group would strengthen the basicity of N-1, and the 6-chloro would weaken it, this result is not unexpected.

Table III. $^1$H NMR Spectra of Furazan Oxides[a]



a b

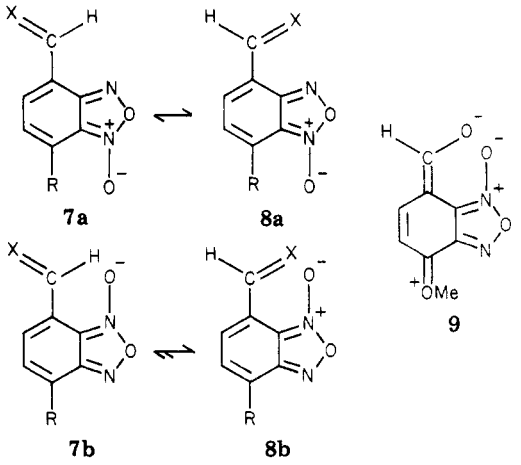
| R | X | chemical shifts (δ values) of protons 5a[b] | 5b[b] | 6a[b] | 6b[b] | αa | αb | R(a) | R(b) | X(a),X(b) | T, °C | ΔG at T,[c] kJ mol$^{-1}$ | $T_c$ (Hα), °C | ΔG‡ at $T_c$,[d] kJ mol$^{-1}$ |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| OMe | O | 7.97 | 8.02 | 6.58 | 6.74 | 10.12 | 10.47 | 4.15 | 4.20 | | −20 | 2.3 | 51 | 68 ± 4 |
| Cl | O | 7.93 | 7.90 | 7.50 | 7.72 | 10.31 | 10.56 | | | | 0 | 0.5 | 52[e] | 69 ± 5[e] |
| OMe | NOH[f] | 7.58 | 7.69 | 6.72 | 6.91 | 8.31 | 8.48 | 4.00 | 4.07 | 11.72[g] | +15 | 1.3 | 38 | 67 ± 7 |
| Cl | NOH[e] | 7.69 | 7.78 | 7.52 | 7.72 | 8.47 | 8.64 | | | 11.85, 11.98 (OH) | −50 | −2.2 | 49 | 69 ± 5 |
| OMe | NOMe | 7.30 | 7.60 | 6.30 | 6.46 | 8.16 | 8.53 | 3.92[i] | 3.95[h] | 3.98, 4.00[h] (OMe) | −21 | 1.7 | 50 | 67 ± 5 |
| Cl | NOMe | 7.48 | 7.71 | 7.24 | 7.43 | 8.34 | 8.63 | | | 4.12, 4.05 (OMe) | −20 | −1.1 | 36 | 65 ± 5 |
| OMe | $NOCH_2Ph$ | 7.35 | 7.68 | 6.36 | 6.53 | 8.31 | 8.71 | 4.02 | 4.07 | 5.30, 5.23 ($CH_2$) | −25 | 0.7 | 46 | 66 ± 5 |
| | | | | | | | | | | 7.35-7.55[g] (Ph) | | | | |
| OMe | NOPh | 7.44 | 7.78 | 6.32 | 6.52 | 8.51 | 8.90 | 3.96 | 4.03 | 6.92-7.36 (Ph) | −17 | 0.7 | 50 | 67 ± 5 |
| OMe | $NNMe_2$ | 7.32 | 7.55 | 6.37 | 6.53 | 7.44 | 7.70 | 4.00 | 4.04 | 3.10, 3.06 ($NMe_2$) | −20 | −1.1 | 26 | 63 ± 6 |
| OMe | NNHPh | 7.48 | 7.72 | 6.62 | 6.84 | 8.03 | 8.37 | 3.90 | 3.98 | 6.56-7.30[i] (Ph) | −15 | −0.6 | 34 | 64 ± 5 |
| Cl | NNHPh[e] | 7.65 | 7.93 | 7.46 | 7.69 | 8.18 | 8.43 | | | 10.71, 10.75 (NH) | −50 | −0.9 | 40 | 66 ± 5 |
| | | | | | | | | | | 6.92-7.36[g] (Ph) | | | | |

[a] In $CDCl_3$, unless otherwise stated. [b] $J_{5,6}$ = 8 ± 0.5 Hz, throughout. [c] $RT$ ln [a]/[b], ± 0.4 kJ mol$^{-1}$. [d] See ref 14. [e] Measured in acetone-$d_6$. [f] Measured in $Me_2SO$-$d_6$. [g] Signal(s) from both tautomers. [h] The assignment of these pairs may be interchanged; the former of each pair is due to tautomer a. [i] NH signal(s) not found.

pellet) showed a very broad band at 2800–2000 cm$^{-1}$, due to H-bond association.

The 2-hydroxy- and 2-alkoxyindazoles reported here are stable crystalline solids with well-defined melting points. Earlier reports on this class of compound are quite restricted. There are two examples of 3-unsubstituted 2-hydroxy derivatives;[2,4] both are thermally quite stable, although with indications that the parent compound[4] does decompose at about its melting point. Five 3-aryl-2-hydroxyindazoles have been reported by Auwers[5,6] and others;[7,8] all are very unstable compounds. This contrast in properties led us to reinvestigate the structures of the 3-aryl compounds, and this work revealed that they are in fact 3-aryl-3-hydroxy-3*H*-indazoles; details are to be published separately.[9] 2-Aminoindazoles have been prepared before, as mixtures with the 1-amino compounds, by direct amination of the indazoles,[10] and also by thermal decomposition of *o*-azidobenzaldehyde hydrazones.[2,11] Other 2-(substituted amino)indazoles have been made from azido-[2,11] and nitrobenzaldehyde[12] hydrazone derivatives, and (compound 4)[2] by rearrangement. 2,2′-Biindazole[11,12] and its 7,7′-dinitro derivative[1] have also been reported.

**$^1$H NMR Spectra.** The furoxan derivatives in the present study all showed the dynamic NMR effects characteristic of these compounds.[13] Table III lists the chemical shifts observed at lower temperatures. These spectra revealed the signals from the two furoxan tautomers, and 1- and 3-oxides. Previous experience with this class of compound has shown that a 6-proton (position conjugated with the *N*-oxide group at the 1-position) appears upfield of the same proton in the isomeric 3-oxide molecule by ca. 0.17 ppm.[14] The 5- and 6-protons in the compounds of Table III would therefore be expected to suffer approximately equal and opposite shifts of this magnitude, when the oxygen atom is moved from the 1- to the 3-position. However, in practically all of the compounds of Table III, the 1- and 3-oxide shift (a → b) produces a downfield shift of *both* of the ring protons. We believe that this anomaly is the result of conformational effects. In the 1-oxides (form a) the aldehyde (or aldoxime or phenylhydrazone) substituent may exist in either the *E*- or *Z*-rotamer orientation (**7a** or **8a**), but in the 3-oxides



**7a** **8a** **9**

**7b** **8b**

dipolar repulsions (in the methoxy aldehyde) or steric effects (in the derivatives) reduce the population of the

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(14) A. J. Boulton, A. R. Katritzky, M. J. Sewell, and B. Wallis, *J. Chem. Soc. B*, 914 (1967).

Table IV. $^1$H NMR Spectra of Indazoles (3)

| R | R′ | solvent | chemical shifts, δ | | | | |
|---|---|---|---|---|---|---|---|
| | | | H(3) | H(4)[a] | H(5)[a] | R | R′ |
| OMe | OH | $Me_2SO$-$d_6$ | 8.29 | 7.86 | 7.12 | 3.88 | 3.26, br (OH) |
| Cl | OH | $Me_2SO$-$d_6$ | 8.54 | 8.11 | 7.40 | | b (OH) |
| OMe | OMe | $CDCl_3$ | 8.00 | 7.85 | 7.07 | 4.00 | 4.30 (OMe) |
| Cl | OMe | $CDCl_3$ | 8.06 | 7.25 | 7.17 | | 4.32 (OMe) |
| OMe | $OCH_2Ph$ | $CDCl_3$ | 7.55 | 7.66 | 6.97 | 4.00 | 5.51 ($CH_2$)<br>7.30 (Ph) |
| OMe | OPh | $Me_2SO$-$d_6$ | 9.04 | 8.06 | 7.22 | 3.98 | 7.7, dd[c] (o-Ph)<br>7.1, m (m,p-Ph) |
| OMe | $NMe_2$ | $CDCl_3$ | 8.01 | 7.78 | 7.00 | 3.98 | 3.00 ($NMe_2$) |
| Cl | $NMe_2$ | $CDCl_3$ | 8.07 | 7.72 | 7.12 | | 3.03 ($NMe_2$) |
| OMe | NHPh | acetone-$d_6$ | 8.50 | 8.00 | 7.22 | 3.98 | 6.54, d (o-Ph)[d]<br>6.86, t (p-Ph)<br>7.17, t (m-Ph) |
| Cl | NHPh | $CDCl_3$ | 8.34 | 7.84 | 7.22 | | 6.46, d (o-Ph)[d]<br>6.86, t (p-Ph)<br>7.10, t (m-Ph) |

[a] $J_{4,5}$ = 9 ± 0.5 Hz, throughout. [b] Exchanged with $D_2O$ in solvent. [c] Double doublet, $J$ = 7, 2 Hz. [d] NH signal not found.

*Z* rotamer (**8b**); these isomers therefore exist predominantly in the *E* form (**7b**). Since the *E* conformers (**7a**, **7b**) are responsible for the majority of the deshielding experienced by the neighboring ring proton, this proton appears at an unexpectedly low field in the 3-oxide isomers (b). It should be noted that this anomaly was not found in 7-chloro-4-formylbenzofuroxan; both in acetone[15] and in chloroform-$d$[16] the two ring protons moved in the expected (i.e., opposite) directions. Possibly conjugation with the methoxy group (**9**) is required to make the repulsion in **8b** effective.

At the highest temperatures available, with $CDCl_3$ or acetone-$d_6$ as solvent and tetramethylsilane as spectrometer lock signal, the majority of the spectra showed broad bands, although the coalescence temperatures had been exceeded in all cases. Rearrangement to the indazole was observed in the course of running some of the high-temperature spectra, and one compound (**2**; R = Cl, R′ = $NMe_2$) was inadvertently completely rearranged before its spectra were recorded; this is therefore missing from Table III. Approximate values for the energy of activation of the furoxan (1 ⇌ 3-oxide) isomerization reaction were obtained from the coalescence temperatures of the NMR signals of the formyl protons.[13] The equilibrium constants derived from the low-temperature spectra were converted into free-energy differences, $\Delta G$. These values are listed in Table III.

The indazole spectra are reported in Table IV. They show no dynamic effects at the temperatures of measurement. The position of absorption of the 3-proton was rather variable (δ 7.55–9.04), depending on the 2-substituent.

## Experimental Section

Spectrometric instrumentation was as described in earlier parts of this series;[1] in addition, some $^1$H NMR spectra were obtained in Bangalore on a Bruker WH-270 spectrometer. IR spectra were of samples in KBr disks. Preparative-layer chromatography (PLC) was performed as outlined earlier.[1] Melting points were measured on a Reichert hot-stage microscope.

**6-Methoxyanthranil.** Bartulin's method for the reduction of 2-nitroanisaldehyde was carried out as described in the preparation of the chloroanthranil.[1] The oily product could be distilled (0.2 torr) to give the solid methoxy compound, mp ca. 30 °C, which was not characterized further.

**4-Formyl-7-methoxybenzofurazan oxide** (1; R = OMe) and **7-chloro-4-formylbenzofurazan oxide** (1; R = Cl) were prepared by nitration, followed by rearrangement, of the 6-R-substituted anthranils, as described earlier.[1]

**Preparation of Oxime and Hydrazone Derivatives 2.** Standard methods were applied to the preparation of these derivatives from the aldehydes **1**. Thus, for the methoxy imine **2** (R = R′ = OMe), methoxylamine hydrochloride (0.13 g, 1.5 mmol) and sodium acetate hydrate (0.1 g, 0.8 mmol) in water (2 mL) were added to 4-formyl-7-methoxybenzofuroxan (0.29 g, 1.5 mmol) in ethanol (20 mL). The mixture was refluxed for 3 h, cooled, and poured onto ice (50 g). Filtration yielded the methoxy imine, which was recrystallized from methanol. Yields, melting points, and other details on the preparation of these compounds are listed in Table I.

**Rearrangement of Formylfurazan Oxide Derivatives 2 to Nitroindazoles 3.** The derivatives **2** were heated in the solvents, at the temperatures and for the times indicated in Table II. Progress of the reactions was monitored by TLC. The yellow products were isolated by solvent evaporation, or by dilution with water when the rearrangement solvent was dimethyl sulfoxide, by using PLC ($SiO_2$, eluant toluene/EtOH 15:1) for the separation of the phenoxy derivative (**3**; R = OMe, R′ = OPh). Rearrangement of two of the derivatives (with R = Cl; see Table II) was performed in $CDCl_3$, and proceeded apparently quantitatively.

**4-Formyl-7-methoxybenzofurazan Oxide Azine (2; R = OMe, R′ = dimer).** The formylfuroxan (1; R = OMe) (0.155 g, 0.8 mmol) and hydrazine hydrate (0.023 g, 0.4 mmol) were stirred for 4 h at 20 °C in methanol (50 mL) containing acetic acid (3 drops). Addition of ice–water (20 g) gave an orange precipitate of the azine; $\nu_{max}$ 3100 (w), 1630 (s), 1620 (s), 1590 (m), 1560 (s), 1510 (s), 1440 (s), 1390 (m), 1300 (s), 1250 (s), 1185 (m), 1090 (s), 1070 (m) $cm^{-1}$. Attempts at recrystallization led to partial rearrangement.

**6,6′-Dimethoxy-7,7′-dinitro-2,2′-biindazole (5).** The above azine (0.15 g) was refluxed for 24 h in acetic acid (20 mL). The reaction mixture was then cooled and poured into water, and the yellow product was crystallized from dimethylformamide as needles: mp 330–335 °C dec.; $\nu_{max}$ 3155 (m), 3120 (m), 3080 (w), 1630 (s), 1550 (m), 1495 (s), 1485 (s), 1450 (m), 1375 (s), 1360 (m), 1340 (s), 1320 (s), 1285 (s), 1250 (vs), 1180 (s), 1160 (m), 1090 (s), 1025 (s), 910 (m), 820 (s) $cm^{-1}$.

All the new compounds described in this work gave mass spectra which were in agreement with the structures assigned. Parent ions ($M^+$) were prominent, usually being the base peaks of the spectra.

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(15) A. J. Boulton and R. C. Brown, *J. Org. Chem.*, **35**, 1662 (1970).
(16) This work.

Saunders, H. S. Tyagaraj, and B. S. Ramaprasad for microanalysis.

**Registry No.** 1 (R = OMe) 1-oxide, 61063-01-2; 1 (R = Cl) 1-oxide, 30080-04-7; 1 (R = OMe) 3-oxide, 61063-02-3; 1 (R = OMe) 3-oxide, 61063-00-1; 2 (R = OMe, R′ = OH) 1-oxide, 72916-82-6; 2 (R = Cl, R′ = OH) 1-oxide, 72916-83-7; 2 (R = OMe, R′ = OMe) 1-oxide, 72916-84-8; 2 (R = Cl, R′ = OMe) 1-oxide, 72916-85-9; 2 (R = OMe, R′ = $OCH_2Ph$) 1-oxide, 72925-72-5; 2 (R = OMe, R′ = OPh) 1-oxide, 72916-86-0; 2 (R = OMe, R′ = $NMe_2$) 1-oxide, 72916-87-1; 2 (R = Cl, R′ = $NMe_2$) 1-oxide, 72916-88-2; 2 (R = OMe, R′ = NHPh) 1-oxide, 72916-89-3; 2 (R = Cl, R′ = NHPh) 1-oxide, 72916-90-6; 2 (R = OMe, R′ = OH) 3-oxide, 72916-91-7; 2 (R = Cl, R′ = OH) 3-oxide, 72916-92-8; 2 (R = OMe, R′ = OMe) 3-oxide, 72916-93-9; 2 (R = Cl, R′ = OMe) 3-oxide, 72916-94-0; 2 (R = OMe, R′ = $OCH_2Ph$) 3-oxide, 72916-95-1; 2 (R = OMe, R′ = OPh) 3-oxide, 72916-96-2; 2 (R = OMe, R′ = $NMe_2$) 3-oxide, 72916-97-3; 2 (R = Cl, R′ = $NMe_2$) 3-oxide, 72916-98-4; 2 (R = OMe, R′ = NHPh) 3-oxide, 72916-99-5; 2 (R = Cl, R′ = NHPh) 3-oxide, 72917-00-1; 2 (R = OMe, R′ = dimer) 1,1′-dioxide, 72917-01-2; 3 (R = OMe, R′ = OH), 72917-02-3; 3 (R = Cl, R′ = OH), 72917-03-4; 3 (R = OMe, R′ = OMe), 72917-04-5; 3 (R = Cl, R′ = OMe), 72917-05-6; 3 (R = OMe, R′ = $OCH_2Ph$), 72917-06-7; 3 (R = OMe, R′ = OPh), 72917-07-8; 3 (R = OMe, R′ = $NMe_2$), 72917-08-9; 3 (R = Cl, R′ = $NMe_2$), 72917-09-0; 3 (R = OMe, R′ = NHPh), 72917-10-3; 3 (R = Cl, R′ = NHPh), 72917-11-4; 5, 72917-12-5; 6-methoxyanthranil, 61063-15-8.

# Cycloaddition Reactions of *N*-Methyl-1,2-dihydropyridine

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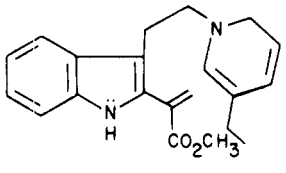
The reactions of *N*-methyl-1,2-dihydropyridine (**2**) with electron deficient $\pi$ systems have been studied. This compound is considered as a model for reactive 1,2-dihydropyridines that are not stabilized by electron-withdrawing groups on the ring. Dihydropyridine **2** behaves as an enamine rather than a diene in its primary cycloaddition reactions with methyl acrylate, dimethyl acetylenedicarboxylate, and methyl vinyl ketone. At high temperature the primary [2 + 2] cycloadduct between methyl acrylate and 1,2-dihydropyridine **2** is unstable, and the more thermodynamically stable endo and exo Diels–Alder adducts **4** and **5** are formed. From a comparison of the reactivity and photoelectron spectrum of **2** with an acyclic analogue, it is concluded that the two double bonds of the cyclic dienamine **2** are not in the same plane. *N*-Methyl-1,2-dihydropyridine behaves as both a diene and a dienophile with respect to $\alpha$-(*N*-methylindol-2-yl)acrylate **13**, giving a 2.3:1 mixture of the aspidosperma and iboga analogues **14** and **15**.

There has been recent interest in the chemistry of dihydropyridines because of their postulation as intermediates in alkaloid biosynthesis.[1] For example, the intramolecular cycloaddition reactions of dihydropyridine **1**

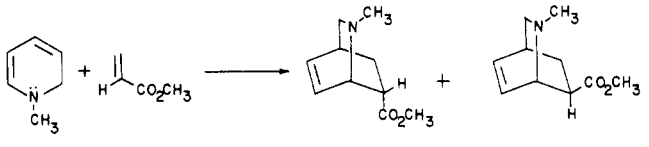


**1**

have been proposed to play an important role in the biosynthesis of the indole alkaloids.[1a-c] Although dihydropyridine **1** has been frequently discussed in the literature, it has neither been isolated nor synthesized. In spite of the extensive literature on 1,2-dihydropyridine chemistry,[2] the vast majority of 1,2-dihydropyridines known contain an electron-withdrawing group on the ring in conjugation with the nitrogen lone pair of electrons. These substituents have a perturbation on the $\pi$ system and significantly affect the chemistry of 1,2-dihydropyridines.[3] There are only a few 1,2-dihydropyridines known that could serve as a model for the 1,2-dihydropyridine ring in **1**, and there are no authenticated cycloaddition reactions of unstabilized dihydropyridines with electron-deficient alkenes.

## Results

The simplest 1,2-dihydropyridine, unencumbered by perturbing substituents and suitable for study as a model for **1**, is *N*-methyl-1,2-dihydropyridine (**2**). We have re-



**2** **3** **4** **5**

investigated the reaction of *N*-methyl-1,2-dihydropyridine and methyl acrylate and observed that the treatment of *N*-methyl-1,2-dihydropyridine with methyl acrylate (**3**) in refluxing benzene gave a 3.2:1 mixture of Diels–Alder adducts **4** and **5**.[4] These stereoisomers were separated by gas chromatography, and their stereochemistry was assigned on the basis of double-resonance $^1H$ NMR experiments and by a comparison to suitable model systems.[5] The $^1H$ NMR spectra of these compounds with proton assignments are shown in Figure 1. The major difference is the chemical shift of the proton at C-7. In the exo isomer **5** this proton occurs at high field due to the shielding effect

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(2) (a) Eisner, U.; Kuthan, J.; *Chem. Rev.* **1972**, *72*, 1. (b) Lyle, R. E. "The Chemistry of Heterocyclic Compounds, Pyridine and Its Derivatives"; Abramovitch, R. A., Ed.; Wiley: New York, 1974; Vol. 14, Part 1.

(3) Dihydropyridines without electron-withdrawing groups on the ring are relatively unstable with respect to dimerization and oxidation. Care must be exercised when handling these compounds in the laboratory.

(4) The Diels–Alder reaction of methyl acrylate with *N*-methyl-1,2-dihydropyridine has been reported previously (Wiley, R. A.; Faraj, B. A.; Jantz, A. *J. Med. Chem.* **1972**, *15*, 374). However, our results differ substantially from theirs. Professor Wiley kindly supplied us with his NMR spectra, and we conclude that the data reported are probably due to impurities, such as the 1,2-dihydropyridine dimer.

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