Dinitrones from *C*-Benzyl Nitrones

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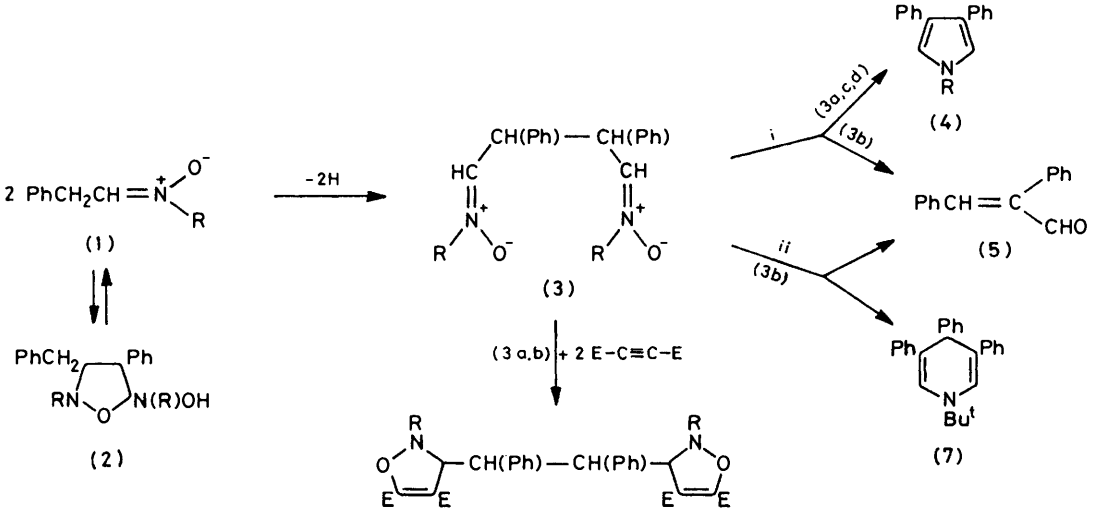
N,N'-Dialkyl- and diaryl-dinitrones of the 2,3-diphenylbutanediylidenebisamine *N,N'*-dioxide (3) are shown to be intermediates in the spontaneous conversion of C-benzyl nitrones (1) into the diphenylpyrroles (4) or 2,3-diphenylprop-2-en-1-al (5). The process therefore involves oxidative coupling at the benzylic carbon atoms. The dinitrones (3) have in fact been isolated on treatment of the nitrones (1) or their cyclic dimers (2) with oxygen. The *N,N'*-dialkyl dinitrones (3a) and (3b) gave the expected bis-cycloadducts (6) on treatment with dimethyl acetylenedicarboxylate.

C-Benzyl nitrones [*N*-(2-phenylethylidene)amine *N*-oxides], either as dimers, (2c) and (2d), or in equilibrium, (1a) and (2a), in chloroform solution, have been shown to give rise to the corresponding 3,4-diphenylpyrroles (4).[1] The nitrone (1b), prepared in a similar way to the parent compounds and obtained as an oily monomer, gave rise neither to the dimer (2b) nor the expected 1-t-butyl-3,4-diphenylpyrrole (4b). Prolonged exposure of the nitrone (1b) to the atmosphere resulted in the formation of the dinitrone (3b). Analogous dinitrones have been obtained, as well as the corresponding pyrroles (4), by storing solutions of the dimers (2) in diethyl ether [giving compound (3a)] or in methanol [giving compounds (3c) and (3d)]. The yields of the dinitrones (3) were low, but could be increased by carrying out the above reactions with an excess of oxygen.



a; R = Me
b; R = Bu^t
c; R = Ph
d; R = *p*-Tol
E = CO_2Me
i Room temperature
ii With heating

SCHEME 1

The structures ascribed to compounds (3a) and (3b) are fully supported by spectroscopic and chemical evidence. From the ^1H and ^{13}C n.m.r. spectra the symmetry of the structures is apparent, the *N*-substituents being equivalent,† and the signals ascribed to the CHCHCHCH protons are consistent with an AA'XX' spin system. Both the ^1H and ^{13}C chemical shifts of the ethylene group and the observed multiplicities agree with the illustrated structure (3). The ^1H and ^{13}C n.m.r. spectra of deuteriated dimers (3a) and (3b), prepared from the deuteriated dimers (2a) and (2b) respectively,[1] showed the simplifications expected for deuteriation of the saturated CH.

The reactivity of the dinitrones (3a) and (3b) towards dipolarophiles appeared to be sluggish: several attempts (with phenylacetylene, styrene, and phenyl isocyanate)

† In fact, in the spectra of the dinitrone (3a), two signals for the Me protons are detected, *ca.* 0.5 Hz apart: this very narrow splitting might arise from a conformational effect. Similarly, a splitting of the aromatic ^{13}C signals, observed in the spectrum of the cycloadduct (6b), is ascribed to hindered rotation.

failed, and it was only with dimethyl acetylenedicarboxylate that these compounds gave the expected biscycloadducts (6a) and (6b).

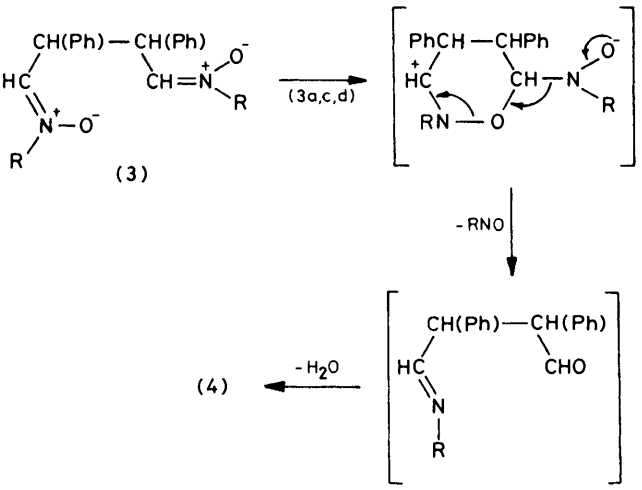
The insolubility of the *N*-aryl dinitrones (3c) and (3d) in common organic solvents was a serious obstacle to their study. They could not be recrystallised and their spectra could not be observed in solution, decomposition occurring faster than cycloaddition. However, their analogy with the parent *N*-alkyl compounds is shown not only by their formation and evolution, but also by their i.r. spectra, where all the compounds (3) exhibit bands in the regions expected for the $\nu_{C=N}$ and the ν_{NO} of nitrones,[2,3] and by a common fragmentation pattern shown in the mass spectra. With the exception of the dinitrone (3b), whose base-peak is found at *m/z* 57 ($Me_3C^{+\bullet}$), the fragment ions $[Ph_2C_3NHR]^{+\bullet}$ are, in general, the base-peaks. The other main peaks observed in the mass spectra of all the dinitrones (3a)—(3d) are ascribed to the pyrrole ions $[4]^{+\bullet}$ and to the fragment ions $[PhCH{=}CHNHR]^{+\bullet}$ and $[RN{=}CH]^{+\bullet}$; in addition, the fragment ions at *m/z* 178, 165, 91, and 77 are common to the four compounds, while those corresponding to $[0.5M]^{+\bullet}$ are given by the dinitrones (3a), (3b), and (3d).

Since the relative abundance of the ions corresponding to the pyrroles (4) is largely dependent on the sample temperature, the samples of dinitrones are probably converted in part into pyrroles on heating in the mass spectrometer. Solutions of the dinitrones (3a), (3c), and (3d) in chloroform, prepared at room temperature [with prolonged stirring for compounds (3c) and (3d)], in fact gave spontaneously the corresponding pyrroles (4).

The dinitrone (3b) is more stable, decomposing very slowly in solution at room temperature to give 2,3-diphenylprop-2-en-1-al (5), which is only a minor by-product in the conversion of compounds (2a), (2c), and (2d) into the corresponding pyrroles (4). When heated at 120 °C without solvent the decomposition of both the nitrone (1b) and the dinitrone (3b) to give 2,3-diphenylprop-2-en-1-al is much faster. Among the by-products 1-t-butyl-3,4,5-triphenyl-1,4-dihydropyridine (7) is identified on the basis of elemental analysis, mass and ^1H and ^{13}C n.m.r. spectral evidence (see Experimental section).

DISCUSSION

The observed oxidative coupling of the benzylnitrones (1) to the dinitrones (3) is clearly related to the known oxidation of similarly activated benzyl compounds, with establishment of a C–C bond.[4] In the present case, however, this process is closely connected with the formation of the pyrroles (4) from the dinitrones (3); the nitroso-compounds produced in the second step (a possible mechanism is illustrated in Scheme 2) oxidize the nitrones (1) to the dinitrones (3). Although direct evidence for the suggested mechanism is lacking, this pathway allows a rationalisation of the following facts: (i) when the dimers (2a), (2c), and (2d) are allowed to decompose *without oxygen* only traces of the corresponding dinitrones (3) are obtained, the main products being the substituted pyrroles (4); large amounts of azoxy-compounds are also detected from the reactions of the *N*-aryl dimers (2c) and (2d). Since the oxidizing agent necessary for the production of the dinitrones (3) is generated in the course of their formation they cannot accumulate unless an additional oxidant is available. The azoxy-compounds are produced by condensation of the nitroso-compounds with their reduction products, *i.e.* the *N*-arylhydroxylamines.



SCHEME 2

(ii) The yields of the dinitrones (3) are increased [up to 20—25% for the compounds (2a), (2c), and (2d), and over 70% for the compound (2b)] by treatment of the dimers (2) *with oxygen*, particularly by daylight irradiation. A similar increase is observed when the dimers (2c) and (2d) are oxidised with nitrosobenzene; the reactions are much faster in this case, but the products (3c) and (3d) are less pure. t-Butyl hydroperoxide is efficient only on the dimer (2a). The larger yield of the dinitrone (3b) is ascribed to its higher stability.

(iii) The dinitrones (3a), (3c), and (3d) spontaneously give rise to the corresponding pyrroles (4), but only the *N*-methyl compound (4a) is produced in a satisfactory yield; the *N*-arylpyrroles (4c) and (4d) are obtained (without appreciable production of azoxy-compounds) in much lower yields than those obtained by direct preparation from the nitrone dimers (2c) and (2d). The *N*-arylpyrroles (4c) and (4d) possibly react with the nitroso-side-products,* while the *N*-methylpyrrole (4a) is scarcely affected by MeNO or its products. The yields of the *N*-arylpyrroles (4c) and (4d) are improved by carrying out the decomposition of the dinitrones (3c) and (3d) in the presence of the corresponding *N*-substituted hydroxylamines, thus avoiding interference by RNO.

(iv) The dinitrone (3b) is more stable than the parent compounds; it can be easily obtained in good yield and its conversion into the pyrrole (4b) has not been observed. The reported mechanism of pyrrole formation implies

* Reactions of nitroso-compounds with 1-substituted pyrroles are not known, but condensations of 1-substituted indoles with nitrosobenzene have been reported.[5]

intramolecular attack of one nitrone group on the other; since such a process is subject to severe steric requirements, it seems reasonable to ascribe to overcrowding the lack of former rearrangement observed in the dinitrone (3b). With heat a different reaction takes place leading to the aldehyde (5) by an unknown mechanism. It is not susprising that each nitrone group in the dinitrone (3b) reacts independently to give the bis-cycloadduct (6b) without difficulty.

We referred previously [1] to the mechanism reported for a similar reaction, observed for the nitrone $MeO_2CCH_2C(CO_2Me)=N(O)Ph$.[6] However, no oxidative coupling at the active methylene has been shown to occur in this case and the proposed mechanism suggests loss of *N*-phenylhydroxylamine from the nitrone dimer analogous to (2), ring opening at C3–C4, followed by a sigmatropic ' Cope-type ' rearrangement. For the benzylnitrones (1) the pathway reported in the present paper appears to be the predominant, if not the sole, mechanism for the production of the pyrroles (4).

EXPERIMENTAL

M.p.s were observed on a RCH Kofler apparatus. Molecular weights were measured in chloroform solution with a Hitachi–Perkin-Elmer 115 osmometer. N.m.r. spectra recorded in deuteriochloroform solution with Varian FT-80 A (^{13}C) and Perkin-Elmer R 32 (^1H) spectrometers. I.r. spectra were recorded on potassium bromide pellets using a Perkin-Elmer 283 spectrophotometer. Mass spectra were recorded on a Perkin-Elmer 270 mass spectrometer. G.l.c. analyses were carried out with a Perkin-Elmer F 30 gas-chromatograph.

C-*Benzyl nitrone Dimers* (2a), (2c), and (2d).—Prepared as previously reported.[1]

N-(2-*Phenylethylidene*)-N-*t-butylamine* N-*Oxide* (N-*t-Butyl*-C-*benzyl nitrone*) (1b).—A solution of t-butylhydroxylamine in ethanol (0.036 mol in 50 ml) was prepared from the hydrochloride [7] with cooling (ice). Phenylacetaldehyde (3.5 ml, 0.03 mol) was added to the cold solution and the mixture set aside for 1 d in the dark at room temperature. Removal of the solvent *in vacuo* afforded the *nitrone* (1b) as a crude, unstable oil which could not be distilled without decomposition (0.6 Torr); ν_{NO} 1 130 cm^{-1}; $\delta(^1H)$ 7.00 (1 H, t) and 3.81 (2 H, d).

2,3-*Diphenylbutane*-1,4-*diylidenebis*(*methylamine* N-*oxide*) (3a).—A solution of the dimer (2a) in diethyl ether (0.33%) was set aside under a stream of oxygen, the solvent volume being restored when necessary. After 2 weeks the solid dinitrone (3a) was collected (crude yield, 21%); m.p. 174—175 °C (decomp.) (from ethanol) (Found: C, 72.8; H, 6.8; N, 9.7. $C_{18}H_{20}N_2O_2$ requires C, 72.95; H, 6.8; N, 9.45%); ν 1 595 (C=N) and 1 160 (NO) cm^{-1}; $\delta(^1H)$ 3.46 (s, CH_3), 6.7 (m, =CH, s in the deuteriated compound), and 4.95 (m, sat. CH, not detected in the deuteriated compound); $\delta(^{13}C)$ 52.62 (q, CH_3, J_{CH} 132 Hz), 137.71 (d, =CH, J_{CH} 180 Hz), and 44.91 p.p.m. (d, sat. CH, J_{CH} 145 Hz, s in the deuteriated compound).

Oxidation with t-butyl hydroperoxide (in excess) in diethyl ether gave 14% of the dinitrone (3a) in 1 d. Nitrosobenzene was inefficient.

2,3-*Diphenylbutane*-1,4-*diylidenebis*(*t-butylamine* N-*oxide*) (3b).—This compound was prepared similarly from an ethereal solution of the crude nitrone (1b) and oxygen, yield 72% (with respect to phenylacetaldehyde) in 5 d, recryst. from ethanol, m.p. 169—171 °C (decomp.) (Found: C, 75.6; H, 8.4; N, 7.3. $C_{24}H_{32}N_2O_2$ requires C, 75.8; H, 8.4; N, 7.4%); ν 1 575 (C=N) and 1 140 (NO) cm^{-1}; $\delta(^1H)$ 1.25 (s, 3 × Me), 6.88 (m, =CH, s in the deuteriated compound); and 4.95 (m, sat. CH, not detected in the deuteriated compound); $\delta(^{13}C)$ 69.41 (s, N–C); 27.76 (q, 3 × Me, J_{CH} 128 Hz), 134.38 (d, =CH, J_{CH} 175 Hz), and 45.41 p.p.m. (d, sat. CH, J_{CH} 134 Hz, s in the deuteriated compound).

2,3-*Diphenylbutane*-1,4-*diylidenebis*(*aniline* N-*oxide*) (3c) *and* 2,3-*Diphenylbutane*-1,4-*diylidenebis*(p-*tolylamine* N-*oxide*) (3d).—These compounds were obtained from solutions of the dimers (2c) and (2d) in methanol (0.55% and 1% respectively) by treatment with oxygen for 10 d. The crude products were collected and washed thoroughly with chloroform and with methanol. Compound (3c), yield 19.5%, m.p. 172—173 °C (decomp.) (Found: C, 79.5; H, 5.9; N, 7.5. $C_{28}H_{24}N_2O_2$ requires C, 80.0; H, 5.75; N, 6.7%); ν 1 565 (C=N) and 1 115 (NO) cm^{-1}; compound (3d), yield 24.5%, m.p. 164—165 °C (decomp.) (Found: C, 79.5; H, 6.35; N, 6.3. $C_{30}H_{28}N_2O_2$ requires C, 80.3; H, 6.3; N, 6.25%); ν 1 560 (C=N) and 1 115 (NO) cm^{-1}. The mother liquors contained considerable amounts of the corresponding pyrroles (4c) and (4d). t-Butyl hydroperoxide was inefficient in this case, whereas oxidation with nitrosobenzene (2 equiv.) afforded the dinitrones (3c) and (3d) in yields of 18 and 11% respectively in 1 d.

Neither the dinitrone (3c) nor (3d) could be recrystallised or examined in solution because of its insolubility in common organic solvents.

Cycloaddition of the Dinitrone (3a) *to Dimethyl Acetylenedicarboxylate*; 3,3′-(1,2-*Diphenylethylene*)*bis*(4,5-*bismethoxycarbonyl*-2-*methyl*-4-*isoxazoline*) (6a).—The dinitrone (3a) (150 mg) was added to a large excess of the acetylenic ester (2 ml) and the mixture stirred at 80 °C for 1 h. The excess of ester was removed *in vacuo* from the clear solution, ethanol (15 ml) was added to the residue, and the solution stored in a refrigerator. The *adduct* (6a) was collected (55%) and recrystallised several times from ethanol, m.p. 144—145 °C (decomp.) (Found: C, 62.0; H, 5.5; N, 5.1. $C_{30}H_{32}N_2O_{10}$ requires C, 62.1; H, 5.6; N, 4.8%); *m/z* 391 (5%), 298 (4), 233 (100), 220 (10), 219 (6), 218 (7), 101 (43), 100 (19), 69 (10), 59 (14), and 56 (14); $\delta(^1H)$ 2.72 (s, NMe), 3.52 and 3.70 (s, OMe), 3.88 and 4.32 (m, methine H), and 7.2 to 7.35 (m, aromatic H); $\delta(^{13}C)$ 46.9 (q, NMe), 51.6 (q, OMe), 52.6 (q, OMe), 51.95 and 75.65 (both d, methine C), 109.85 (s, isoxazoline C-4), 149.7 and 159.0 and 163.2 (all s, isoxazoline C-5 and O=CO), 139.0 (s, Ar-C), 127.1 and 127.9 and 130.1br p.p.m. (all d, aromatic C).

Cycloaddition of the Dinitrone (3b) *to Dimethyl Acetylenedicarboxylate:* 3,3′-(1,2-*Diphenylethylene*)*bis*(4,5-*bismethoxycarbonyl*-2-*t-butyl*-4-*isoxazoline*) (6b).—The dinitrone (3b) (300 mg) was added to a solution of the acetylenic ester (0.3 ml, slight excess) in anhydrous ethanol (10 ml), and the mixture maintained at 60 °C until it became clear (0.5 h). The *adduct* (6b) was collected after cooling, m.p. 168—169 °C (decomp.) (65%). After 1 week more precipitate was collected and the overall yield increased to 90%, recryst. from ethanol, m.p. 170 °C (decomp.) (Found: C, 65.3; H, 6.5; N, 4.5%; *M*, 656. $C_{36}H_{44}N_2O_{10}$ requires C, 65.05; H, 6.7; N, 4.2%; *M*, 664.8); *m/z* (main fragments) 664 (M^+, 2%), 379 (10), 242 (40), 187 (100), 115 (12), and 57 (30); $\delta(^1H)$ 0.90 (s, 18 H), 3.65 (s with shoulder,* 6 H +

* Absent from the spectrum of the deuteriated compound.

2 H), 3.74 (s, 6 H), 4.43 (br s, 2 H), 7.0 to 7.6 (m, 10 H); δ(^{13}C) 24.9 (q, Me_3), 51.8 (q, OMe), 52.55 (q, OMe), 54.3* (d, chain CH), 61.7 (s, CN), 66.2 (d, isoxazoline C-3), 108.5 (s, isoxazoline C-4), 153.2 and 158.9 and 163.7 (all s, isoxazoline C-5 and O=CO), 137.6 (s, Ar-C) and 126.7, 127.0, 127.8, 128.0, and 133.6 (all d, Ar-C).

Evolution of the Dinitrones (3) *in Solution.*—The dinitrones (3a), (3c), and (3d) were stirred in chloroform (20 ml for each 100 mg) until they dissolved; several days were necessary for the *N*-aryl compounds (3c) and (3d). The solutions were set aside and, after two weeks, the solvent was removed and a little hot ethanol (3 ml) added to the residue. The pyrrole (4a) was collected in 46% yield, while small amounts of impure pyrroles (4c) and (4d) slowly precipitated. Higher yields of the arylpyrroles (4c) (30%) and (4d) (60%) were obtained when the decomposition was carried out in the presence of the corresponding *N*-arylhydroxylamines (equiv. amounts).

A solution of the dinitrone (3b) in chloroform (300 mg in 20 ml) was set aside. T.l.c. controls (silica gel Merck F_{254}, eluting with toluene–chloroform–methanol 10 : 10 : 1) showed that, after two weeks, most of the starting material was unaffected and 2,3-diphenylprop-2-en-1-al was the only product detected.

Thermal Decomposition of the Dinitrone (3b): *2,3-Diphenylprop-2-en-1-al* (5) *and 1-t-Butyl-3,4,5-triphenyl-1,4-dihydropyridine* (7).—The dinitrone (3b) was heated 2 h at 120 °C and the residue extracted with methylene chloride and analysed by g.l.c. (2-M column packed with 3% OV1, oven temperature 150—250 °C, 10 °C min^{-1}) and by t.l.c. (silica gel, with methylene chloride as eluant): the solution showed one main component (R_F 0.50) and several side products. One of these (R_F 0.75) became predominant after more than 18 h of heating, while the amounts of both the starting material and the aldehyde (5) decreased. The two main products were separated with a silica gel column (eluant as above). The component with R_F 0.50 was identified as 2,3-diphenylprop-2-en-1-al (5), m.p. 93—96 °C [from light petroleum (b.p. 40—70 °C) or ethanol]; *m/z* 209 (17%), 208 ($M^{+\cdot}$, 100), 207 (55), 179 (71), 178 (67), 165 (22), 152 (13), 103 (10), and 102 (33); δ(^{1}H) 7.13 to 7.5 (aromatic m and ethylenic CH), and 9.76 (s, aldehydic CH). The other product (R_F 0.75), m.p. 166—167 °C [from light petroleum (b.p. 40—70 °C) or ethanol], corresponds to 1-t-butyl-3,4,5-triphenyl-1,4-dihydropyridine (7) (Found: C, 88.3; H, 7.6; N, 3.8. $C_{27}H_{27}N$ requires C, 88.7; H, 7.45; N, 3.8%); *m/z* 365 (M^+, 15%), 308 (M^+ − Bu^t, 7), 289 (11), 288 (M^+ − Ph, 44), 233 (20), and 232 (M^+ − Bu^t − Ph, 100); δ(^{1}H) 1.45 (s, 9 H), 5.05 (s, 1 H) 6.88 (s, 2 H), and 7.05 to 7.45 (m, 15 H); δ(^{13}C) 29.5 (q, Bu^t) and 55.9 (s, Bu^t), 44.6 (d, γ-CH), 113.3 (s, β-C), 123.6 (d, α-CH), 125.2, 126.0, 127.4 and 128.2 (all d, aromatic), and 140.7 and 146.8 (both s, aromatic).

Deuteriated Compounds.—Deuterium exchange of the benzylic protons was achieved by stirring chloroform solutions of *nitrone* (1b), and *nitrone dimers* (2a), (2c), and (2d) for several days with deuterium oxide.[1] Deuteriated dinitrones (3a) and (3b) and the deuteriated cycloadduct (6b) were prepared as reported above, using the appropriate deuteriated starting materials.

[1/803 *Received*, 19*th May*, 1981]

* Absent from the spectrum of the deuteriated compound.

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