

Cyclic Meso-ionic Compounds. Part VIII.¹ 1,3-Dipolar Cycloaddition Reactions of Isosydnones

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1,3-Dipolar cycloadditions of isosydnones (I) (1,3,4-oxadiazolium-2-olates) with alkynes and alkenes are discussed.

ISOSYDNONES (I) have been so named to indicate their isomeric relationship with sydnones (II). Their synthesis, electric dipole moments, and spectroscopic properties are consistent with their meso-ionic formulation (I).² Their general chemistry has been investigated by Hashimoto and Ohta.³ In reactions with nucleophilic reagents such as alcohols or amines, isosydnones (I) give urethanes (VII) and semicarbazides (VIII), respectively. 1,3-Dipolar cycloaddition reactions of sydnones (II) have been extensively studied by Huisgen and his co-workers.⁴⁻⁸ The structural similarity between sydnones (II) and isosydnones (I) is such that isosydnones (I) might also be expected to participate in 1,3-dipolar cycloaddition reactions with alkynes and alkenes. Huisgen, Gotthardt, and Grashey⁶ have shown that 4,5-diphenylisosydnone (Ia) reacts with ethyl phenylpropiolate in *p*-cymene at 150° giving the pyrazole ester (III_d) (53%). Ohta and Sato⁹ have found that isosydnones (I) do not react with dialkyl acetylenedicarboxylates, phenyl isocyanate, or phenyl isothiocyanate either thermally or photochemically. Apart from these two studies, the 1,3-dipolar cycloadditions of isosydnones (I) have not been examined. We now report the reactions of isosydnones (I) with alkynes, alkenes, and carbonyl compounds.

Alkynes.—The 1,3-dipolar cycloaddition of ethyl phenylpropiolate to the three isosydnones (Ia—c) has

been investigated. In these reactions, the alkyne played the dual role of 1,3-dipolarophile and solvent, and the progress of each reaction was followed by gravimetric determination of the evolved carbon dioxide. In principle, these reactions could lead either to the pyrazole (III) or to the isomeric pyrazole (IV) *via* a bicyclic intermediate of type (V). From each of the reactions we have isolated only the pyrazole 4-esters (III; R³ = CO₂Et), identified by hydrolysis to the acids (III; R³ = CO₂H) and decarboxylation to the known pyrazoles (III; R³ = H).⁶ In each case diethyl 1-phenylnaphthalene-2,3-dicarboxylate, formed by dimerisation of ethyl phenylpropiolate,¹⁰ was also isolated.

It appears that a strong orientating influence is operating in these cycloadditions, and it was therefore of interest to make a comparative study of the reactions of isosydnones (I) with phenylacetylene. 4-Methyl-3-phenylsydnone (IIb) reacts with phenylacetylene giving a mixture of the pyrazoles (III_f) (73%) and (IV_f) (9%).⁶ 5-Methyl-4-phenylisosydnone (Ib) with phenylacetylene at 155° gave carbon dioxide (82%), 1,3-diphenyl-5-methylpyrazole (III_f) (49%), and 1,5-diphenyl-3-hydroxypyrazole (III_n) (24%). None of the isomeric pyrazole (IV_f) was observed. A speculative route to the 3-hydroxypyrazole (III_n) involves addition of the phenylacetylene to the tautomer (XIV) giving the bi-

⁵ R. Huisgen, R. Grashey, H. Gotthardt, and R. Schmidt, *Angew. Chem. Internat. Edn.*, 1962, **1**, 48.

⁶ R. Huisgen, H. Gotthardt, and R. Grashey, *Chem. Ber.*, 1968, **101**, 536.

⁷ H. Gotthardt and R. Huisgen, *Chem. Ber.*, 1968, **101**, 552.

⁸ H. Gotthardt, Dissertation, Munich, 1963.

⁹ M. Ohta and H. Kato, in 'Nonbenzenoid Aromatics,' ed. J. P. Snyder, Academic Press, New York, 1969, pp. 117—248.

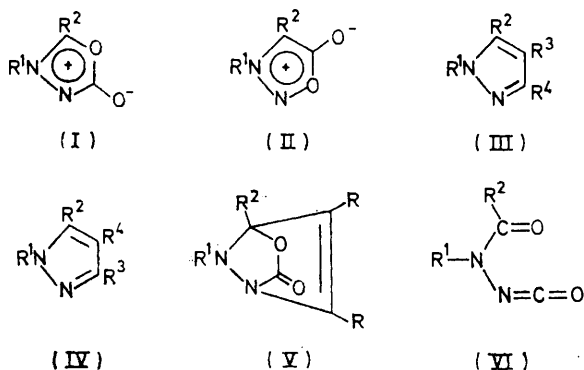
¹⁰ P. Pfeiffer and W. Möller, *Ber.*, 1907, **40**, 3839.

¹ Part VII, C. W. Atkin, A. N. M. Barnes, P. G. Edgerley, and L. E. Sutton, *J. Chem. Soc. (B)*, 1969, 1194.

² A. R. McCarthy, W. D. Ollis, A. N. M. Barnes, L. E. Sutton, and C. Ainsworth, *J. Chem. Soc. (B)*, 1969, 1185.

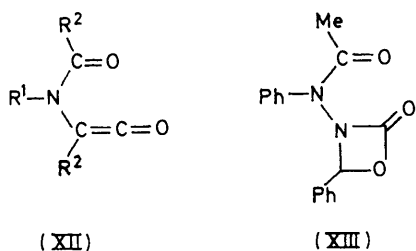
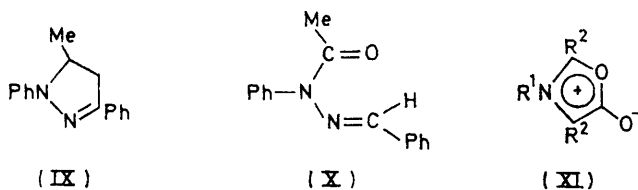
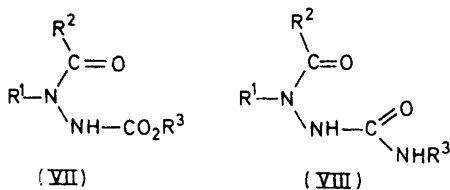
³ M. Hashimoto and M. Ohta, *Bull. Chem. Soc. Japan*, 1961, **34**, 668.

⁴ R. Huisgen, *Chem. Soc. Special Publ.*, No. 20, 1967, p. 51.



In formula (I)–(VI)

- a; $\text{R}^1 = \text{R}^2 = \text{Ph}$
 b; $\text{R}^1 = \text{Ph}, \text{R}^2 = \text{Me}$
 c; $\text{R}^1 = \text{Me}, \text{R}^2 = \text{Ph}$
 d; $\text{R}^1 = \text{R}^2 = \text{Ph}, \text{R}^3 = \text{CO}_2\text{Et}, \text{R}^4 = \text{Ph}$
 e; $\text{R}^1 = \text{Ph}, \text{R}^2 = \text{Me}, \text{R}^3 = \text{CO}_2\text{Et}, \text{R}^4 = \text{Ph}$
 f; $\text{R}^1 = \text{Ph}, \text{R}^2 = \text{Me}, \text{R}^3 = \text{H}, \text{R}^4 = \text{Ph}$
 g; $\text{R}^1 = \text{Me}, \text{R}^2 = \text{Ph}, \text{R}^3 = \text{CO}_2\text{Et}, \text{R}^4 = \text{Ph}$
 h; $\text{R}^1 = \text{Me}, \text{R}^2 = \text{Ph}, \text{R}^3 = \text{CO}_2\text{H}, \text{R}^4 = \text{Ph}$
 j; $\text{R}^1 = \text{Me}, \text{R}^2 = \text{Ph}, \text{R}^3 = \text{H}, \text{R}^4 = \text{Ph}$
 k; $\text{R}^1 = \text{Ph}, \text{R}^2 = \text{Me}, \text{R}^3 = \text{R}^4 = \text{CO}_2\text{Me}$
 m; $\text{R}^1 = \text{Me}, \text{R}^2 = \text{Ph}, \text{R}^3 = \text{R}^4 = \text{CO}_2\text{Me}$
 n; $\text{R}^1 = \text{R}^2 = \text{Ph}, \text{R}^3 = \text{H}, \text{R}^4 = \text{OH}$

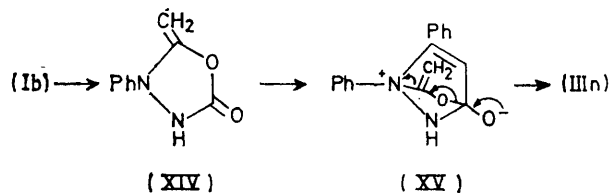


cyclic intermediate (XV),⁴ which after losing keten leads eventually to the 3-hydroxypyrazole (III_n).

A reaction between isosydrones (I) and diphenyl-

acetylene was not observed, although pyrazoles were obtained by reaction with dimethyl acetylenedicarboxylate. Thus, 5-methyl-4-phenylisoydnone (Ib) in boiling dioxan gave dimethyl 5-methyl-1-phenylpyrazole-3,4-dicarboxylate (III_k) (25%) and 4-methyl-5-phenylisoydnone (Ic) gave the 1-methyl-5-phenyl isomer (III_m) (18%). Clearly the cycloaddition of alkynes to isosydrones (I) is analogous to that of sydrones (II), but the reactions proceed more slowly and the 1,3-cycloaddition is obtained in lower yield.

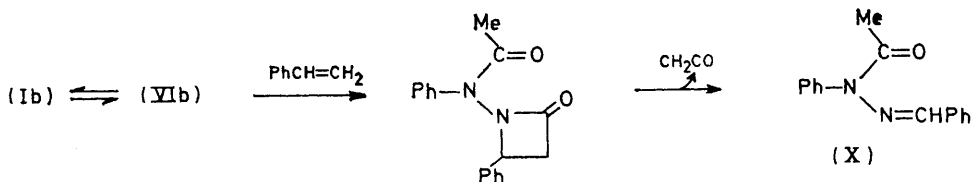
Alkenes.—The reaction between styrene and 5-methyl-4-phenylisoydnone (Ib) in ethyl benzoate at 150°



afforded a mixture of products. 1,3-Diphenyl-5-methyl- Δ^2 -pyrazoline (IX), the product expected by analogy with the corresponding sydnone reaction,⁵ was not isolated, but its oxidation product, 1,3-diphenyl-5-methylpyrazole (III_f) was obtained in low yield. The principal product was identified as benzaldehyde *N*-acetyl-*N*-phenylhydrazone (X). The formation of this compound can be accounted for by the reaction of the isosydnone (Ib) involving the tautomeric isocyanate (VI_b) (Scheme). Huisgen⁵ has provided evidence for the analogous equilibration of meso-ionic oxazolones (XI) with acylamino-ketens (XII).

Carbonyl Compounds.—5-Methyl-4-phenylisoydnone (Ib) and benzaldehyde during 42 h at 145° gave carbon dioxide (88%) and benzaldehyde *N*-acetyl-*N*-phenylhydrazone (X) (37%). Two possible routes to the phenylhydrazone (X) may be envisaged, involving either (i) a 1,3-dipolar cycloaddition followed by decarboxylation, or (ii) a [2 + 2] cycloaddition of the tautomeric isocyanate (VI_b) giving the β -lactam (XIII) as the precursor of the phenylhydrazone (X). The phenylhydrazone (X) has been previously described as the product from a 1,3-dipolar cycloaddition between 4-methyl-3-phenylsydnone (II_b) and benzaldehyde.⁸

Thermal Transformations of Isosydrones.—The possibility that some of the above products were formed directly from isosydrones was excluded by the following result. 4,5-Diphenylisoydnone (Ia), when heated (195 h) in ethyl benzoate at 150–160°, yielded carbon dioxide (55%), *NN'*-dibenzoyl-*N*-phenylhydrazine (31%), and benzanilide (5%). The isosydnone (Ia) itself on heating



SCHEME

(100 h) at 165° gave carbon dioxide (48%) and *NN'*-dibenzoyl-*N*-phenylhydrazine (44%).

EXPERIMENTAL

Unless otherwise stated, i.r. spectra were measured for solutions in chloroform, u.v. spectra in ethanol, and 60 and 100 MHz n.m.r. spectra in deuteriochloroform (tetramethylsilane as internal reference). Only significant bands from i.r. spectra are quoted.

Separations by column chromatography were carried out using Hopkins and Williams' MFC grade silica. Merck Kieselgel G was used for thick- and thin-layer chromatography (t.l.c.).

Evaporation refers to the removal of volatile materials under diminished pressure. Substances stated to be identical were so with respect to m.p.s, mixed m.p.s, and i.r. spectra.

Reaction of 4,5-Diphenylisosydnone (Ia) with Ethyl Phenylpropionate.—A solution of 4,5-diphenylisosydnone (Ia) (0.50 g) in ethyl phenylpropionate (2 ml) was heated at 160° (48 h) and then at 180° (24 h). Carbon dioxide (0.09 g, 99%) was evolved. The excess of ethyl phenylpropionate was removed by distillation under diminished pressure and the residual gum was fractionated by t.l.c. (silica gel; chloroform–2% ethanol) giving (a) ethyl 1,3,5-triphenylpyrazole-4-carboxylate (III d) (0.13 g, 17%), needles, m.p. 145–147° (lit.,⁸ 146–147°) (Found: C, 78.5; H, 5.5; N, 7.75. Calc. for C₂₄H₂₀N₂O₂: C, 78.2; H, 5.5; N, 7.6%); λ_{\max} 206 and 242 nm (ϵ 37,800 and 34,000); ν_{\max} 1710 cm⁻¹; τ 2.0–3.0 (m, 15 aromatic H), 5.92 (q, O·CH₂·CH₃), and 9.03 (t, O·CH₂·CH₃); and (b) diethyl 1-phenyl-naphthalene-2,3-dicarboxylate (0.19 g), prisms, m.p. 129.5–131° (lit.,¹⁰ 129–130°) (Found: C, 76.3; H, 5.7. Calc. for C₂₂H₂₀O₄: C, 76.1; H, 5.8%); ν_{\max} 1720 cm⁻¹.

Reaction of 5-Methyl-4-phenylisosydnone (Ib) with Ethyl Phenylpropionate.—5-Methyl-4-phenylisosydnone (Ib) (0.5 g) and ethyl phenylpropionate (2 ml) were heated (70 h) at 160°. Carbon dioxide (0.12 g, 92%) was evolved. After the excess of ethyl phenylpropionate had been removed by distillation (b.p. 120–180° at 0.3 mmHg), the residue was distilled (0.02 mmHg) giving a dark yellow liquid (1.03 g). Fractional crystallisation from methanol afforded (a) ethyl 1,3-diphenyl-5-methylpyrazole-4-carboxylate (III e) (0.32 g, 37%), prisms, m.p. 105–106° (lit.,⁸ 105–106°) (Found: C, 74.4; H, 5.6; N, 9.5. Calc. for C₁₉H₁₈N₂O₂: C, 74.5; H, 5.9; N, 9.15%); λ_{\max} 208 and 226 nm (ϵ 32,200 and 23,600); ν_{\max} 1710 cm⁻¹; τ 2.15–2.73 (m, 10 aromatic H), 5.77 (q, *J* 7 Hz, O·CH₂·CH₃), 7.46 (s, CH₃), and τ 8.82 (t, *J* 7 Hz, O·CH₂·CH₃); and (b) diethyl 1-phenyl-naphthalene-2,3-dicarboxylate (0.26 g), prisms, m.p. 126–130° (lit.,¹⁰ 129–130°), identical with an authentic sample (see above).

Reaction of 4-Methyl-5-phenylisosydnone (Ic) with Ethyl Phenylpropionate.—4-Methyl-5-phenylisosydnone (Ic) (0.50 g) and ethyl phenylpropionate (1.5 ml) were heated (111 h) at 135–140°; carbon dioxide (0.07 g, 58%) was evolved. The excess of ethyl phenylpropionate was removed by distillation and the residue was distilled (b.p. 230–245° at 0.02 mmHg) giving a yellow oil (0.60 g), which was fractionally crystallised from methanol yielding (a) ethyl 1-methyl-3,5-diphenylpyrazole-4-carboxylate (III g) (0.17 g, 19%), flakes, m.p. 96–98° (Found: C, 74.7; H, 6.0; N, 9.4. C₁₉H₁₈N₂O₂ requires C, 74.5; H, 5.9; N, 9.15%); λ_{\max} 228 nm (ϵ 25,500); ν_{\max} 1700 cm⁻¹; τ 2.10–2.90 (m, 10 aromatic H),

6.30 (s, N·CH₃), 6.00 (q, *J* 7 Hz, O·CH₂·CH₃), and 9.10 (t, *J* 7 Hz, O·CH₂·CH₃); and (b) diethyl 1-phenyl-naphthalene-2,3-dicarboxylate (0.07 g), prisms, m.p. 129–130° (lit.,¹⁰ 129–130°), identical with an authentic sample (see above).

Hydrolysis of Ethyl 1-Methyl-3,5-diphenylpyrazole-4-carboxylate (III g).—The ester (III g) (50 mg) was heated under reflux (5 h) with methanolic 30% potassium hydroxide (2 ml). After cooling and dilution with water (10 ml), the solution was acidified with concentrated hydrochloric acid, giving 1-methyl-3,5-diphenylpyrazole-4-carboxylic acid (III h) (40 mg, 92%), prisms, m.p. 246–247° (decomp.) (Found: C, 73.2; H, 4.9; N, 10.1. C₁₇H₁₄N₂O₂ requires C, 73.4; H, 5.1; N, 10.1%).

Decarboxylation of the Acid (III h).—A mixture of the carboxylic acid (III h) (0.03 g) and barium hydroxide (50 mg) was strongly heated at 15 mmHg giving 1-methyl-3,5-diphenylpyrazole (III j) (0.02 g, 95%) (lit.,¹¹ m.p. 69°); λ_{\max} 252 nm (ϵ 29,000); τ 2.0–2.8 (m, 10 aromatic H), 3.40 (s, pyrazole 4-H), and 6.10 (s, N·CH₃); *M*⁺ 234.

Reaction of 5-Methyl-4-phenylisosydnone (Ib) with Phenylacetylene.—5-Methyl-4-phenylisosydnone (Ib) (0.50 g) and phenylacetylene (3.0 ml) were heated (74 h) at 155°. Carbon dioxide (0.10 g, 82%) was evolved. The excess of phenylacetylene was removed and the residue was distilled (0.01 mmHg) giving a pale yellow, viscous liquid (0.78 g). T.l.c. (silica gel; chloroform–light petroleum) gave (a) 5-methyl-1,3-diphenylpyrazole (III f) (0.32 g, 49%), which was distilled (b.p. 100° at 0.02 mmHg) and crystallised from ether–light petroleum (b.p. 40–60°) as flakes, m.p. 44–46° (lit.,¹² 47°; lit.,¹³ 77–77.5°) (Found: C, 82.2; H, 5.9; N, 11.8. Calc. for C₁₆H₁₄N₂: C, 82.0; H, 6.0; N, 11.8%); λ_{\max} 267 nm (ϵ 22,000); ν_{\max} 1610, 1560, 1510, 1465, and 1370 cm⁻¹; τ 2.0–2.8 (m, 10 aromatic H), 3.55 (s, pyrazole 4-H), and 7.73 (s, CH₃); (b) 1,5-diphenylpyrazol-3-ol (III n) (0.16 g, 24%), needles, m.p. 243–250° (subl., decomp.) (lit.,¹⁴ 251°); λ_{\max} 238 and 260 nm (ϵ 10,400 and 8900); ν_{\max} 3500–2500 (OH), 1560, and 1500 cm⁻¹; *M*⁺ 236; and (c) 1-phenyl-naphthalene (0.19 g) as a yellow oil (lit.,¹⁵ m.p. 45°) (Found: C, 94.7; H, 5.7. Calc. for C₁₆H₁₂: C, 94.1; H, 5.9%); λ_{\max} 226 and 288 nm (ϵ 58,100 and 9620); τ 2.00–2.90 (m, aromatic H).

Reaction of 5-Methyl-4-phenylisosydnone (Ib) with Dimethyl Acetylenedicarboxylate.—5-Methyl-4-phenylisosydnone (Ib) (1.0 g) and dimethyl acetylenedicarboxylate (2 ml) were heated (38 h) in dioxan (5 ml) at 110–120°. Carbon dioxide (0.25 g, 100%) was evolved. Volatile materials were removed by distillation (b.p. 90° at 18 mmHg) and the residue was distilled (b.p. 190–210° at 0.1 mmHg) giving a pale yellow oil. T.l.c. (silica gel; chloroform) gave dimethyl 5-methyl-1-phenylpyrazole-3,4-dicarboxylate (III k) (0.63 g, 25%) (lit.,⁶ m.p. 57–59°) (Found: C, 61.0; H, 5.4; N, 10.2. Calc. for C₁₄H₁₄N₂O₄: C, 61.3; H, 5.15; N, 10.2%); ν_{\max} 1720 and 1735 cm⁻¹; τ 2.60 (s, C₆H₅), 6.17 (s, O·CH₃), 6.24 (s, O·CH₃), and 7.57 (s, CH₃).

Reaction of 4-Methyl-5-phenylisosydnone (Ic) with Dimethyl Acetylenedicarboxylate.—4-Methyl-5-phenylisosydnone (Ic) (0.50 g) and dimethyl acetylenedicarboxylate (1.00 g) were heated (120 h) at 130° and then (78 h) at 140°. Carbon dioxide was evolved. The excess of ester was removed (b.p. 120° at 1 mmHg) and the residue was distilled (0.04 mmHg) giving a yellow oil (0.51 g). T.l.c.

¹³ K. v. Auwers and H. Mauss, *Ber.*, 1926, **59**, 611.

¹⁴ L. Knorr, *Ber.*, 1887, **20**, 1107.

¹⁵ F. D. Chattaway, *J. Chem. Soc.*, 1893, **63**, 1185.

¹¹ K. v. Auwers and W. Ernst, *Z. phys. Chem. (Leipzig)*, 1926, **122**, 244.

¹² L. Knorr and A. Blank, *Ber.*, 1885, **18**, 931.

(silica gel; chloroform) gave dimethyl 1-methyl-5-phenylpyrazole-3,4-dicarboxylate (III_m) (0.28 g, 18%); ν_{\max} 1730 cm^{-1} ; τ 2.60 (m, C_6H_5), 6.17 (s, $\text{O}\cdot\text{CH}_3$), 6.31 (s, $\text{O}\cdot\text{CH}_3$), and 6.40 (s, $\text{N}\cdot\text{CH}_3$).

Reaction of 5-Methyl-4-phenylisosydnone (Ib) with Styrene.—Styrene (1.2 g), stabilised with hydroquinone (0.06 g), and 5-methyl-4-phenylisosydnone (Ib) (0.5 g) were heated (117 h) in ethyl benzoate (2 ml) at 150°. Concentration left a residue which was distilled (0.05 mmHg) and fractionated by t.l.c. (silica gel; acetone–light petroleum), giving (a) benzaldehyde *N*-acetyl-*N*-phenylhydrazone (X) (0.15 g, 23%), pale yellow needles, m.p. 120–122° (from methanol) (lit.,¹⁶ 119–120°) (Found: C, 75.7; H, 5.9; N, 12.0. Calc. for $\text{C}_{15}\text{H}_{14}\text{N}_2\text{O}$: C, 75.6; H, 5.9; N, 11.8%); ν_{\max} 1675 cm^{-1} ; λ_{\max} 284, 289sh, and 300 nm (ϵ 24,400, 23,500, and 17,100); τ 2.3–3.0 (m, aromatic H + CH) and 7.40 (s, CH_3); and (b) 5-methyl-1,3-diphenylpyrazole (III_f) (0.05 g), identical with an authentic sample (see above).

Reaction of 5-Methyl-4-phenylisosydnone (Ib) with Benzaldehyde.—A mixture of 5-methyl-4-phenylisosydnone (Ib) (0.55 g), benzaldehyde (2 ml), and hydroquinone (0.01 g) evolved carbon dioxide (0.12 g, 88%) when heated (42 h) at 145°. The excess of benzaldehyde was removed under diminished pressure, and the residue was distilled (0.02 mmHg) giving a viscous, yellow oil (0.66 g). T.l.c. (silica gel; chloroform), followed by sublimation (100° at 0.2 mmHg) and crystallisation from ethanol, gave benzaldehyde

N-acetyl-*N*-phenylhydrazone (X), m.p. 120–122° (0.27 g, 37%).

Pyrolysis of 4,5-Diphenylisosydnone (Ia).—(a) 4,5-Diphenylisosydnone (Ia) (1.0 g) evolved carbon dioxide (0.1 g, 55%) when heated in ethyl benzoate (3 ml) at 150–160° (195 h). The mixture was evaporated and the residual oil was separated by t.l.c. (silica gel; chloroform–ethyl acetate). Two major fractions were isolated: *NN'*-dibenzoyl-*N*-phenylhydrazine (0.2 g, 31%), pale yellow needles (from acetone), m.p. 172–177° (lit.,¹⁷ 177–178°) (Found: C, 75.2; H, 5.0; N, 8.9. Calc. for $\text{C}_{20}\text{H}_{16}\text{N}_2\text{O}_2$: C, 75.9; H, 5.1; N, 8.9%); ν_{\max} 3400, 1705, and 1665 cm^{-1} ; and benzanilide (0.02 g), flakes (from ethanol), m.p. 161–163°, identical with an authentic sample.

(b) 4,5-Diphenylisosydnone (Ia) (0.5 g) evolved carbon dioxide (0.04 g, 48%) when heated at 165° (100 h). The brown residue was separated by t.l.c. (silica gel; chloroform–methanol) and the major product was identified as *NN'*-dibenzoyl-*N*-phenylhydrazine (0.15 g, 44%), needles, m.p. 178–180°, identical with an authentic sample (see above).

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¹⁶ V. Schroeder, *Ber.*, 1884, **17**, 2096.

¹⁷ H. Franzen, *Ber.*, 1909, **42**, 2465.