Polyhalogeno-aromatic Compounds. Part XXVI.[1] Photochemistry of Pentachloropyridine and Some Derivatives

By **Ernest Ager, Geoffrey E. Chivers** (in part), and **Hans Suschitzky,*** Department of Chemistry and Applied Chemistry, University of Salford, Salford M5 4WT, Lanchashire

Irradiation of pentachloropyridine in cyclohexane, diethyl ether, or dioxan gave 2,3,4,6-tetrachloropyridine, whereas in benzene tetrachloro-3-phenylpyridine was obtained. Irradiation of pentachloropyridine 1-oxide in carbon tetrachloride gave pentachlorobutadienyl isocyanate. Irradiation of tetrachloro-*N*-methyl-2-pyridone gave tetrachloro-2-methyl-2-azabicyclo[2.2.0]hex-5-en-3-one. Some nucleophilic substitutions in 2,3,4,6-tetrachloropyridine are also described.

We here add further examples and details to our brief report [2] on the photochemical behaviour of pentachloropyridine and its 1-oxide. The results observed on irradiating pentachloropyridine in various solvents are given in the Table. The primary photolytic process apparently involved cleavage of the C(3)–Cl bond to give

Irradiation of pentachloropyridine with a medium pressure lamp

Solvent	Time (h)	Products (%)
Benzene	18	2,3,4,6-Tetrachloro-5-phenyl-pyridine (40)
Dioxan	90	2,3,4,6-Tetrachloropyridine (42)
		2,3,5,6-Tetrachloropyridine (trace)
Diethyl ether	24	2,3,4,6-Tetrachloropyridine (43)
		2,3,5,6-Tetrachloropyridine (2)
Cyclohexane	120	2,3,4,6-Tetrachloropyridine (14)
		2,3,5,6-Tetrachloropyridine (trace)

a 2,3,4,6-tetrachloropyridyl and a chlorine radical which may interact with the solvent. Our observations are in fact analogous to those reported for the irradiation of various substituted chlorobenzenes.[3,4] As an alternative preparation of 2,3,4,6-tetrachloropyridine (3), which is the main photolytic product, 2,3,6-trichloro-4-methyl-thiopyridine [5] was oxidised with a mixture of 85% hydrogen peroxide, acetic acid, and concentrated sulphuric acid [6] to give 2,3,6-trichloro-4-methyl-sulphonylpyridine 1-oxide. The action of phosphorus

pentachloride then gave a mixture of 2,3,4,6-tetrachloro-pyridine (37%) and 2,3,6-trichloro-4-methylsulphonyl-pyridine [5] (4) (15%).

SCHEME 1

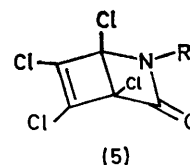
(5)
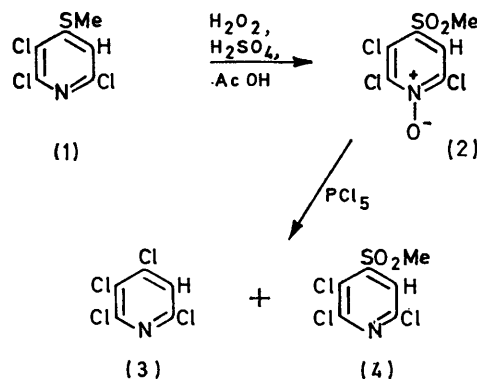
Irradiation of pentachloropyridine 1-oxide in dry carbon tetrachloride gave pentachlorobutadienyl isocyanate by a previously discussed mechanism.[2]

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[2] E. Ager, G. E. Chivers, and H. Suschitzky, *J.C.S. Chem. Comm.*, 1972, 505.

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[5] E. Ager, B. Iddon, and H. Suschitzky, *J. Chem. Soc. (C)*, 1970, 193.

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

We have also investigated the photolysis of tetrachloro-N-methyl-2-pyridone in view of the photolytic behaviour of non-chlorinated 2-pyridones, which are reported to give Dewar-type structures [7,8] (5; H for Cl). Although previous workers have used diethyl ether [7] and methanol [8] as solvents, we found light petroleum to give the best yield of the 1,4,5,6-tetrachloro-2-azabicyclohexenone (5; R = Me). The structure follows from

(6)   (7)   (8)
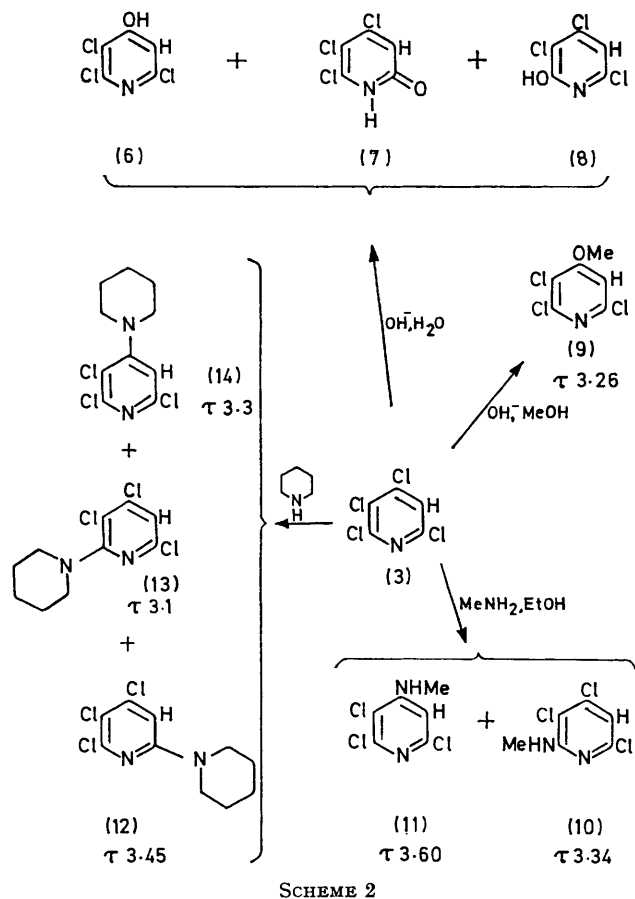
SCHEME 2

analysis and spectral observations [e.g. m/e 188 (tetrachlorocyclobutadiene, $C_4Cl_4^+$)]. Heating a solution of this lactam in petroleum (b.p. 120—160°) under reflux for 0·5 h resulted in quantitative conversion into the starting tetrachloro-N-methyl-2-pyridone, confirming the isomeric nature of the two compounds.

With 2,3,4,6-tetrachloropyridine readily available from photolysis, we studied its chemical behaviour. Metallation with n-butyl-lithium gave tetrachloro-3-pyridyl-lithium which, with an excess of dimethyl sulphate, yielded tetrachloro-3-methylpyridine (33%). This metallation route provides a potential approach to the hitherto rather inaccessible 3-substituted tetrachloropyridines.

In Scheme 2 the nucleophilic substitution reactions of

2,3,4,6-tetrachloropyridine are set out. The 4-substituted trichloropyridines shown were unambiguously prepared from 2,3,6-trichloro-4-methylsulphonylpyridine [5] (4) and sodium hydroxide, sodium methoxide, or methylamine; exclusive displacement of the labile methylsulphonyl group occurred.[9]

The structures of the 2-substituted derivatives were confirmed by n.m.r. spectroscopy. It was reasoned that the aromatic proton in 2,3,6-trichloro-4-piperidinopyridine (14) would exhibit a similar chemical shift to that in 2,3,4-trichloro-6-piperidinopyridine (12), since these protons are in similar environments. The aromatic proton in 3,4,6-trichloro-2-piperidinopyridine (13) should resonate at lower field, similar to that in 2,3,4,6-tetrachloropyridine [τ (CCl$_4$) 2·69]. As an additional proof, irradiation at the frequencies of the α-protons in the piperidine rings of compounds (12) and (13) was carried out. Only in the case of (12) was an enhancement of the aromatic proton signal observed. As the yield of 2,3,4-trichloro-6-piperidinopyridine (11) was much less than that of the isomer (13) it seems probable that the methylamino-derivative is 3,4,6-trichloro-2-methylaminopyridine (10). This is in agreement with the observation that the aromatic proton of the 4-methylamino-derivative (11) resonates at higher field than that of the 4-piperidino-compound (14), and that in 2,3,4-trichloro-6-methylaminopyridine would therefore be expected to resonate at higher field than that in the corresponding piperidino-compound (12).

The mixture of compounds obtained from the reaction of aqueous sodium hydroxide with 2,3,4,6-tetrachloropyridine could not be separated. However, spectroscopy (i.r.) showed that it contained both a pyridinol and a pyridone. 2,3,6-Trichloropyridin-4-ol has been reported as the product of the reaction of (15) with phosphoryl chloride.[10] However, from an unambiguous preparation of 2,3,6-trichloropyridin-4-ol (from aqueous sodium hydroxide and 2,3,6-trichloro-4-methylsulphonylpyridine) we found that its m.p. (166°) and its i.r. spectrum differed from those quoted. Thus the compound described as the ' 4-hydroxy-derivative ' (6) is probably 3,4,6-trichloropyridin-2-ol (16).

(15)   (16)

(17)   (18)
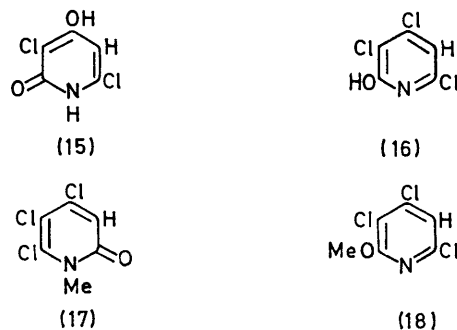
Since compound (16) is reported to exist as a pyridinol, the structure of compound (6) must be as shown. This

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[8] R. C. de Selms and W. R. Schleigh, Tetrahedron Letters, 1972, 3563; H. Furrer, Chem. Ber., 1972, 105, 2780.
[9] E. Ager, B. Iddon, and H. Suschitzky, J.C.S. Perkin I, 1972, 133.
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assignment is in contrast to the observation that the presence or absence of a halogen atom in the β-position has little effect on the tautomerism of 2-hydroxy-pyridines,[11] since the only difference between structures (6) and (16) is in the position of the β-chlorine atom. On treatment of the mixture from the reaction with aqueous sodium hydroxide with dimethyl sulphate 2,3,6-tri-chloro-4-methoxypyridine (9) (18%), 4,5,6-trichloro-N-methyl-2-pyridone (17) (18%), and 3,4,6-trichloro-2-methoxypyridine (18) (9%) could be separated.

EXPERIMENTAL

Photolysis of Pentachloropyridine.—(a) *In benzene.* A solution of pentachloropyridine (2·5 g, 10·0 mmol) in dry (P₂O₅) benzene (200 ml) was photolysed for 90 h at ambient temperature. The benzene was evaporated off and the residue was chromatographed on silica gel in light petroleum (b.p. 60—80°) to give pentachloropyridine (0·8 g, 32%). Elution with light petroleum–benzene (4 : 1) gave 2,3,4,6-tetrachloro-5-phenylpyridine (1·1 g, 40%), m.p. 98° (from ethanol–hexane) (lit.,[12] 101—103°) (Found: C, 44·6; H, 1·2; N, 4·7. Calc. for C₁₁H₅Cl₄N: C, 44·8; H, 1·7; N, 4·8%). Its i.r. spectrum is different from those of 2,3,5,6-tetrachloro-4-phenylpyridine[13] and 2,3,4,5-tetrachloro-6-phenylpyridine.[14] Elution with benzene gave 2,3,4,5-tetra-chloro-6-phenylpyridine (trace), identical with an authentic sample.[14] (b) For other solvents, see Table.

2,3,6-Trichloro-4-methylsulphonylpyridine 1-Oxide.—Hydrogen peroxide (85%; 1·5 ml) was added drop-wise to a stirred mixture of 2,3,6-trichloro-4-methyl-thiopyridine[5] (0·85 g, 3·7 mmol), acetic acid (8 ml), and concentrated sulphuric acid (8 ml) at 0°, and the resulting mixture was stirred at room temperature for a further 24 h. It was then poured into crushed ice (40 g) and the precipitate was filtered off, washed with water, and recrystallised from acetone to give 2,3,6-trichloro-4-methylsulphonylpyridine 1-oxide (0·75 g, 73%), m.p. 185—186° (Found: C, 26·5; H, 1·5; N, 5·1. C₆H₄Cl₃NO₃S requires C, 26·0; H, 1·5; N, 5·1%).

Reaction of 2,3,6-Trichloro-4-methylsulphonylpyridine 1-Oxide with Phosphorus Pentachloride.—An intimate mixture of the 1-oxide (5·0 g, 18·2 mmol) and phosphorus penta-chloride (15 g, 72 mmol) was heated to 90° (when it suddenly liquefied) then at 120° for 0·5 h. The mixture was cooled and chloroform (50 ml) was added followed by water (30 ml). The chloroform layer was separated, dried (MgSO₄), and evaporated. Trituration with petroleum gave 2,3,6-trichloro-4-methylsulphonylpyridine (0·7 g, 15%), identical with an authentic sample.[5] Evaporation of the petroleum solution gave 2,3,4,6-tetrachloropyridine (1·45 g, 37%), identical with an authentic sample.[15]

Irradiation of Pentachloropyridine 1-Oxide in Carbon Tetrachloride.—A solution of the 1-oxide (8·0 g, 30·0 mmol) in dry (P₂O₅ distilled) carbon tetrachloride (1 l) was irradiated for 4 h. Evaporation of the solvent left an oil which was distilled to give (i) pentachlorobutadienyl isocyanate (b.p. 55° at 0·2 mmHg; 0·5 g), identical with an authentic sample (see later), (ii) a mixture of the isocyanate with pentachloropyridine (2·5 g), and (iii) pentachloropyridine (1·5 g).

Pentachlorobutadienyl Isocyanate.—A solution of sodium azide (1·3 g) in water (4 ml) was added dropwise with stirring to a solution of pentachloropenta-2,5-dienoyl chloride[16] (4·3 g, 15 mmol) in acetone (40 ml) at 0—5°. The mixture was stirred for 15 min, then ice (50 g) was added followed by diethyl ether (50 ml). The organic layer was separated (with the temperature kept at 0—5°), washed with cold water, and dried (MgSO₄). Evaporation of the solvent at 0—5° under reduced pressure gave pentachloropenta-2,5-dienoyl azide (3·9 g, 88%), v_{max} 2130 and 2160 (N₃), and 1695 cm⁻¹ (C=O). A solution of the azide (3·3 g, 11·1 mmol) in dry benzene (40 ml) was heated under reflux for 0·5 h. Evaporation of the solvent and distillation of the residue gave pentachlorobutadienyl isocyanate (2·7 g, 90%), b.p. 55° at 0·2 mmHg, v_{max} 2260 cm⁻¹ (N=C=O). Unfortunately the high reactivity of this compound precluded a good elemental analysis and its structure follows from spectroscopic data and the following reaction.

Reaction of Pentachlorobutadienyl Isocyanate with Dry Methanol.—The isocyanate (1·0 g, 3·7 mmol) was added to dry methanol (20 ml). The solvent was evaporated off; distillation of the product at 0·15 mmHg gave *methyl N-pentachlorobutadienylcarbamate* (0·99 g, 90%), m.p. 71—73° (Found: C, 24·6; H, 1·4. C₆H₄Cl₅NO₂ requires C, 24·1; H, 1·3%).

Irradiation of Tetrachloro-N-methyl-2-pyridone.—A solution of the pyridone (2·0 g, 8·2 mmol) in light petroleum (b.p. 40—60°; 1 l) was irradiated for 4 days. Evaporation of the solvent at 10—15° (reduced pressure) gave a solid which was recrystallised (below 30°) from methanol to give 1,4,5,6-*tetrachloro-2-methyl-2-azobicyclo*[2.2.0]*hex-5-en-3-one* (1·4 g, 70%), m.p. 86·5—87·5°, v_{max} 1785 (C=O) and 1615 cm⁻¹ (C=C), τ (CCl₄) 7·03, m/e 188 (C₄Cl₄) (Found: C, 29·3; H, 1·5; N, 5·5%. C₆H₃Cl₄NO requires C, 29·2; H, 1·2; N, 5·7%).

Reactions of 2,3,4,6-Tetrachloropyridine.—(a) *With potassium hydroxide.* A mixture of 2,3,4,6-tetrachloropyridine (0·75 g, 3·5 mmol), potassium hydroxide (0·39 g, 7·0 mmol), and water (15 ml) was heated under reflux for 48 h. Acidification gave a precipitate (0·45 g) which was shown by t.l.c. to be a chromatographically inseparable mixture of at least two components. The i.r. spectrum showed both OH and C=O absorptions.

The product mixture (0·4 g), dimethyl sulphate (0·28 g), potassium carbonate (0·58 g; anhydrous), and acetone (13 ml) were heated under reflux for 2 h; the solvent was evaporated off, water (30 ml) was added, and the pre-cipitate (0·3 g) was filtered off. Column chromatography on silica in light petroleum–benzene (30 : 70) gave (i) 3,4,6-*trichloro-2-methoxypyridine* (0·052 g, 7%), m.p. 62—64°, τ (CCl₄) 2·98 (5-H) (Found: C, 33·9; H, 2·3. C₆H₄Cl₃NO requires C, 33·9; H, 1·9%); (ii) 2,3,6-trichloro-4-methoxypyridine (0·1 g, 14%), m.p. 132—134° (from methanol) (lit.,[17] 136·5—137·5); and (iii) 4,5,6-*trichloro-N-methyl-2-pyridone* (0·1 g, 14%), m.p. 148—150° [from light petroleum–carbon tetrachloride (1 : 1)] (Found: C, 33·8; H, 2·0; N, 6·6. C₆H₄Cl₃NO requires C, 33·9; H, 1·9; N, 6·6%).

(b) *With methanolic sodium hydroxide.* A mixture of the chloropyridine (0·5 g, 2·3 mmol), sodium hydroxide (0·01 g,

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[12] C. H. Chase and J. Walker, *J. Chem. Soc.*, 1953, 3548.
[13] J. D. Cook and B. J. Wakefield, *J. Chem. Soc. (C)*, 1969, 2376.
[14] F. Binns and H. Suschitzky, *J. Chem. Soc. (C)*, 1971, 1223.
[15] W. J. Sell and F. W. Dootson, *J. Chem. Soc.*, 1898, 440; 1900, 1.
[16] A. Roedig and G. Märkl, *Annalen*, 1960, **636**, 1.
[17] R. A. Fernandez, H. Heaney, J. M. Jablonski, K. G. Mason, and T. J. Ward, *J. Chem. Soc. (C)*, 1969, 1908.

2·5 mmol), and methanol (30 ml) was heated under reflux for 18 h. Evaporation of the solvent and addition of water (10 ml) gave a precipitate of 2,3,6-trichloro-4-methoxy-pyridine (0·3 g, 61%), m.p. 132—134° (from methanol).

(c) *With aqueous ethanolic methylamine.* A mixture of the chloropyridine (0·4 g, 1·9 mmol), methylamine (25% aqueous solution; 0·5 ml), and ethanol (30 ml) was heated under reflux for 18 h. The mixture was cooled, the solvent was evaporated off, water (10 ml) was added, and the precipitate (0·35 g) was filtered off. Column chromatography on silica in benzene gave (i) 3,4,6-*trichloro-2-methyl-aminopyridine* (0·1 g, 75%), m.p. 97—98° (from benzene–light petroleum), τ (CCl$_4$) 3·34 (5-H) (Found: C, 33·6; H, 2·65. C$_6$H$_5$Cl$_3$N$_2$ requires C, 34·1; H, 2·4%); and (ii) 2,3,6-trichloro-4-methylaminopyridine (0·2 g, 50%), m.p. 138—140° (from benzene–light petroleum), τ (CCl$_4$) 3·60 (5-H) (Found: C, 33·9; H, 2·4; N, 13·1. C$_6$H$_5$Cl$_3$N$_2$ requires C, 34·1; H, 2·4; N, 13·1%).

(d) *With ethanolic piperidine.* A mixture of the chloropyridine (1·0 g, 4·7 mmol), piperidine (0·8 g, 9·4 mmol), and ethanol (30 ml) was heated under reflux for 18 h. The solvent was evaporated off, water (20 ml) was added, and the oil was extracted with chloroform. Column chromatography on silica in light petroleum–chloroform (10 : 1) gave (i) an oil, 3,4,6-*trichloro-2-piperidinopyridine* (0·1 g, 8%), τ (CCl$_4$) 3·1 (5-H) (Found: C, 45·1; H, 4·0; N, 10·4. C$_{10}$H$_{11}$Cl$_3$N$_2$ requires C, 45·1; H, 4·2; N, 10·5%); (ii) 2,3,4-trichloro-6-piperidinopyridine (0·02 g, 2%) identical with the sample described later; and (iii) 2,3,6-trichloro-6-piperidinopyridine (0·65 g, 53%), identical with an authentic sample.[18]

(e) *With piperidine in benzene.* A mixture of the chloropyridine (2·3 g, 11·0 mmol), piperidine (1·85 g, 22·0 mmol), and benzene (70 ml) was heated under reflux for 24 h; the solvent was evaporated off and column chromatography on silica in light petroleum–chloroform (10 : 1) gave (i) 3,4,6-trichloro-2-piperidinopyridine (1·85 g, 60%); (ii) 2,3,4-*trichloro-6-piperidinopyridine* (0·42 g, 14%), τ (CCl$_4$) 3·45 (5-H) (Found: C, 45·0; H, 4·1; N 10·6. C$_{10}$H$_{11}$Cl$_3$N$_2$ requires C, 45·1; H, 4·2; N, 10·5%); and (iii) 2,3,6-tri-chloro-4-piperidinopyridine (0·65 g, 23%).

(f) *With n-butyl-lithium.* A solution of n-butyl-lithium (2·7 mmol) in hexane was added to a stirred solution of 2,3,4,6-tetrachloropyridine (0·57 g, 2·67 mmol) in diethyl ether (30 ml) at −70°; the resulting mixture was kept at −35° for 0·5 h, then cooled to −65°, and dimethyl sulphate (1·5 g, 11·9 mmol) was added. The mixture was allowed to warm to room temperature, then heated under reflux for 5 min. Water (20 ml) was then added, followed by aqueous ammonia (3 ml; *d* 0·88). The mixture was stirred for 10 min and the organic layer was separated, washed with water, dried (MgSO$_4$), and evaporated to give tetrachloro-3-methylpyridine (0·2 g, 33%), m.p. 90—92° [from light petroleum (b.p. 60—80°)] (lit.,[19] 96—97·5°), τ (CCl$_4$) 7·5 (Me).

Reactions of 2,3,6-Trichloro-4-methylsulphonylpyridine with Nucleophiles.—(a) *With aqueous sodium hydroxide.* A mixture of the sulphone (0·28 g, 1·1 mmol), sodium hydroxide (0·09 g, 2·3 mmol), and water (20 ml) was heated under reflux for 16 h. Acidification with concentrated hydrochloric acid gave 2,3,6-*trichloropyridin-4-ol* (0·18 g, 84%), m.p. 166—167° (from CCl$_4$), τ [(CD$_3$)$_2$CO] 2·92 (5-H) (Found: C, 30·1; H, 1·1; N, 7·2. C$_5$H$_2$Cl$_3$NO requires C, 30·3; H, 1·0; N, 7·0%).

(b) *With methanolic sodium hydroxide.* A mixture of the sulphone (0·28 g, 1·1 mmol), sodium hydroxide (0·046 g, 1·1 mmol), and methanol (30 ml) was heated under reflux for 10 min. Evaporation of the solvent and addition of water (20 ml) gave a precipitate of 2,3,6-trichloro-4-methoxypyridine (0·15 g, 66%), m.p. 132—134° (MeOH) (lit.,[17] m.p. 136·5—137·5).

(c) *With ethanolic methylamine.* A mixture of the sulphone (0·2 g, 0·77 mmol), methylamine (0·050 g, 1·6 mmol), and ethanol (30 ml) was heated under reflux for 5 h. Evaporation of the solvent and addition of water (20 ml) gave 2,3,6-trichloro-4-methylaminopyridine (0·14 g, 65%), m.p. 138—140° [light petroleum (b.p. 60—80°)–benzene].

We thank the S.R.C. for a Fellowship (to E. A.)

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