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Photolysis of Pyridazin-3-one 1-Imides: Ring Contraction into 3-Pyrrolin-2-one Derivatives

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Irradiation of pyridazin-3-one 1-ethoxycarbonylimide (**9a**) resulted in ring contraction to give the azamaleimide (**11**), whereas the 6-methyl derivative (**9b**), upon irradiation, afforded the 3-pyrrolin-2-one (**12**). On the other hand, the photolysis of 2-methylpyridazin-3-one 1-imides (**10a**, **b**) gave both azamaleimides (**13a**, **b**) and 3-pyrrolin-2-ones (**14a**, **b**). The mechanism of this photo-induced ring contraction reaction is discussed.

Keywords——photolysis; ring contraction; pyridazin-3-one 1-imide; azamaleimide, 3-pyrrolin-2-one

We have already reported that the photolysis of pyridazine *N*-oxides (**1**),[1] pyridazine *N*-ylides (**2**),[2] pyridazine *N*-imides (**3**),[3] pyridazine-3-ones (**4**),[4] and pyridazin-3-one *N*-oxides (**5**)[5] resulted in ring contraction mainly with loss of nitrogen to give various kinds of five- and/or three-membered ring compounds, as shown in Chart 1. On the other hand, pyridine,[6] quinoline,[7] and isoquinoline *N*-imides[8] and related fused pyridine *N*-imides[9] condensed with aromatic heterocyclic rings are known to undergo photo-induced rearrangement with ring expansion to afford the corresponding seven-membered diazaheterocycles, diazepines, respectively.

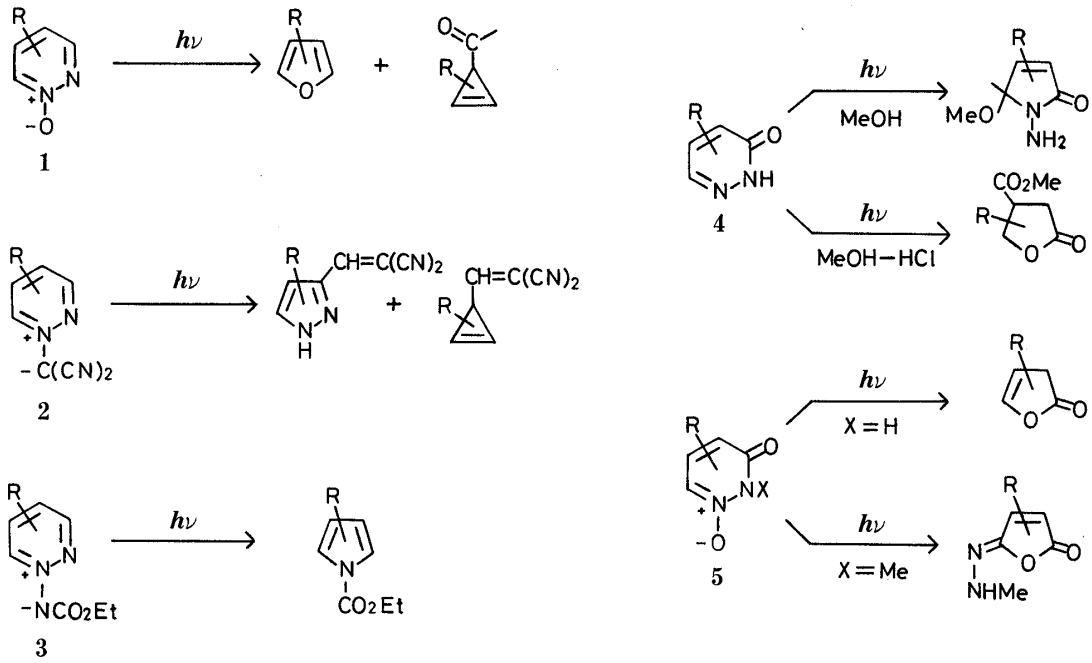

Chart 1

These results prompted us to examine the photochemical behavior of pyridazinone *N*-imides, and we report here the results of the photolysis of pyridazin-3-one 1-imides.

Syntheses of the Starting Pyridazin-3-one 1-Imides

The 3-methoxypyridazines (**6a, b**) were aminated with *O*-mesitylenesulfonylhydroxylamine (H_2NOMes)[10] to give the 1-aminopyridazinium mesitylenesulfonates (**7a, b**) in high yields. This *N*-amination of 3-methoxypyridazines proceeded preferentially at the 1-position, as does the *N*-oxidation.[11] Treatment of the salts (**7**) with ethyl chloroformate in the presence of potassium carbonate afforded the ethoxycarbonylimides (**8a**: 80% yield, **8b**: 46% yield).

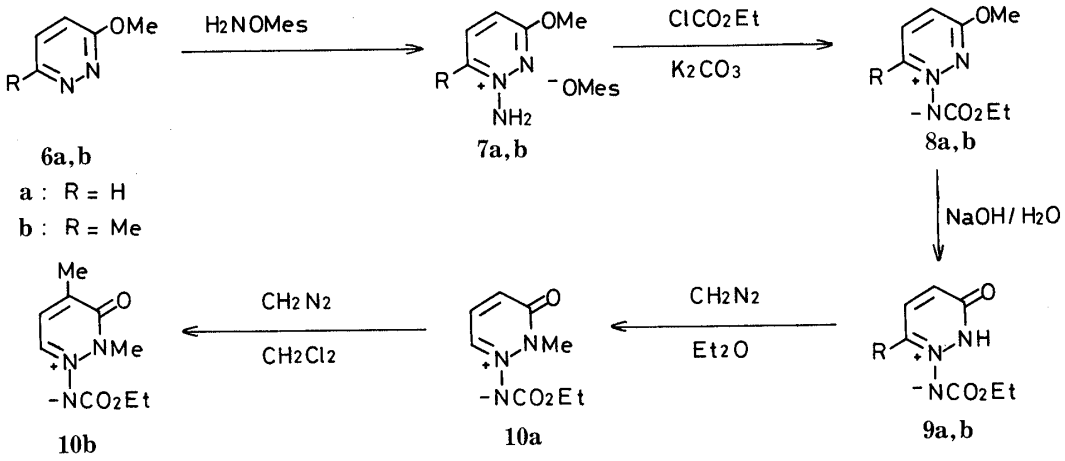

Chart 2

The pyridazin-3-one 1-imides (**9a, b**) were obtained in good yields by the hydrolysis of the 3-methoxy compounds (**8**) in aqueous sodium hydroxide solution. Treatment of **9a** with diazomethane in ether gave the *N*-methyl compound (**10a**) in 40% yield, together with the *O*-methyl compound (**8a**) in 42% yield. However, treatment of the 6-methylpyridazin-3-one 1-imide (**9b**) with diazomethane yielded only the *O*-methyl compound (**8b**) and not the desired *N*-methyl derivative. The *N*-methyl compound (**10a**) was further treated with diazomethane in methylene chloride to give the 4-methyl derivative (**10b**) in 77% yield. This *C*-methylation may proceed by addition of methylene carbene generated from diazomethane to the $C_4=C_5$ double bond, by analogy with the case of the *C*-methylation of 2-methyl-6-phenylpyridazin-3-one using ethyl chloroacetate in the presence of sodium hydride.[12] All the *N*-imides thus obtained were characterized by elemental and spectral analyses.

Photolysis of the Pyridazin-3-one 1-Imides

Irradiation of pyridazin-3-one 1-ethoxycarbonylimide (**9a**) in methanol for 2 h resulted in ring contraction without loss of nitrogen to give the azamaleimide derivative (**11**) in 98% yield, whereas the photolysis of the 6-methyl compound (**9b**) under similar conditions gave the denitrogenated product (**12**), 3-pyrrolin-2-one derivative, in 17% yield as the sole characterizable product. On the other hand, irradiation of the 2-methylpyridazinone 1-imides (**10a, b**) for 30 min resulted in the formation of both the azamaleimides (**13a, b**) and the 3-pyrrolin-2-ones (**14a, b**) in 10—15% and 15—20% yields, respectively. In any case, the expected ring expansion products, such as triazepinones, could not be obtained. The structures of the products obtained above were characterized by elemental and spectral analyses and by comparison with the spectral data for various 3-pyrrolin-2-ones already reported.[4,5,13]

A possible mechanism for the photo-induced ring contraction is shown in Chart 4. This reaction might involve the initial formation of two kinds of diaziridine intermediates (**15** and

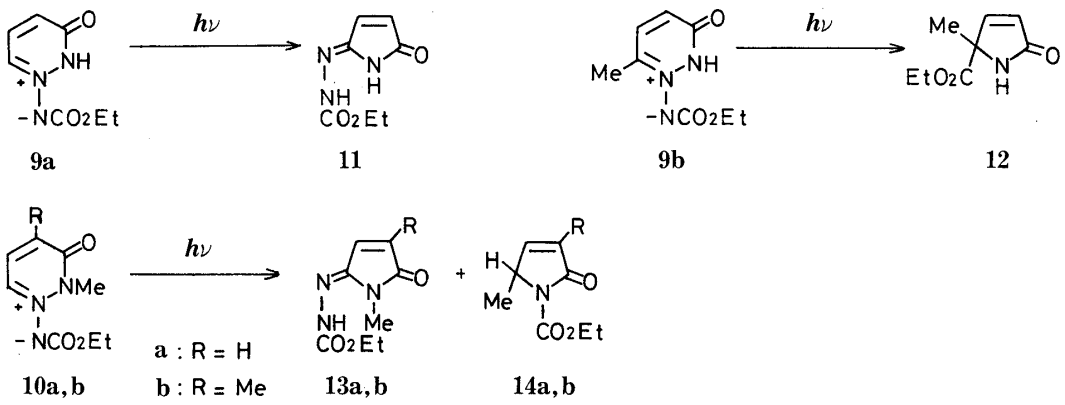

Chart 3

17). The diaziridine (**15**) may then undergo N–N bond fission to give the ring-opened intermediate (**16**), which gives the azamaleimides (**11**, **13**) by 1,3-hydrogen shift in the case of R = H, whereas in the case of R = Me, elimination of nitrogen occurs to give the pyrrolinones (**12**). Similar diaziridine or aziridine formation has been observed in the photolysis of pyridazinium-3-oleates[14] and pyridinium-3-oleates.[15]

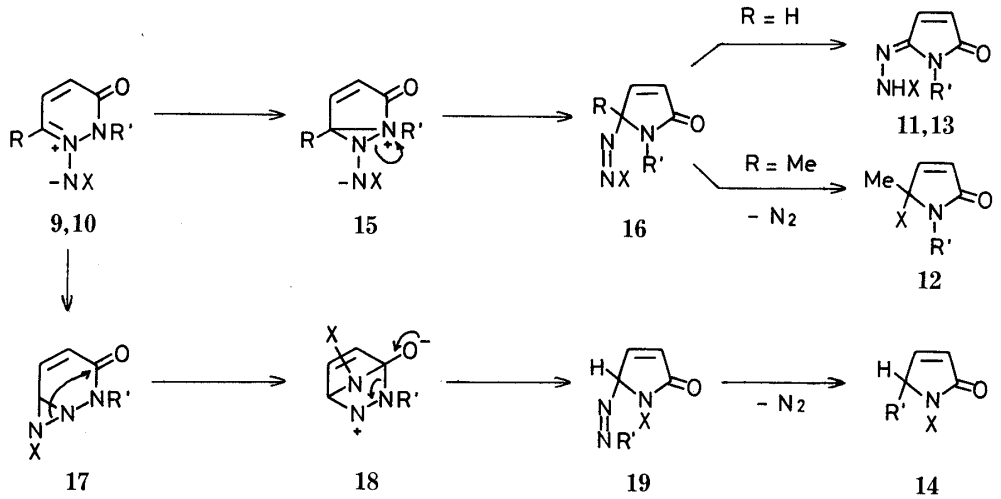

Chart 4

On the other hand, the pyrrolinones (**14**) may be derived from another diaziridine intermediate (**17**). The formation of **17** from the *N*-imides (**10**) is analogous to that observed in the photolysis of pyridine and benzopyridine *N*-imides,[6-9] in which similar diaziridine intermediates are assumed to undergo ring expansion to give the corresponding diazepines and/or N–N bond fission to give 2-amino derivatives. However, in the present case, the diaziridine (**17**) may be coverted into the ring contraction intermediate (**19**) *via* **18**, and does not undergo ring expansion. The intermediate (**19**) gives the product (**14**) by elimination of nitrogen because it cannot undergo 1,3-hydrogen shift, as in the case of **16** (R = Me).

Experimental

Melting points were measured on a Yamato MP-21 apparatus and are uncorrected. Infrared (IR) spectra were determined with a JASCO IRA-2 spectrometer and mass spectra (MS) were recorded on a JEOL DX-300 instrument. Proton nuclear magnetic resonance spectra (^{1}H-NMR) were recorded on a JEOL JNM-MH100 spectrometer in

$CDCl_3$ using tetramethylsilane as an internal standard unless otherwise stated; spectral assignments were confirmed by spin-decoupling experiments and, in the case of NH protons, by exchange with D_2O. Microanalyses were performed in the Microanalytical Laboratory of this school by Mrs. R. Igarashi. Photolyses were carried out in an immersion apparatus equipped with a 400 W high-pressure Hg lamp and a Pyrex filter, which was cooled internally with running water.

1-Amino-3-methoxypyridazinium Mesitylenesulfonates (7a, b)——A solution of *O*-mesitylenesulfonylhydroxylamine (1.1 mol eq) in CH_2Cl_2 (200 ml) was added dropwise to a solution of a 3-methoxypyridazine (**6**: 0.1 mol) in CH_2Cl_2 (50 ml) with stirring in an ice bath. The reaction mixture was stirred for an additional 20 min at room temperature. After addition of ethyl acetate (400 ml) to the reaction mixture, the resulting crystalline precipitates were collected by filtration and recrystallized from ethanol–ethyl acetate to give the salts (**7**).

7a: 85% yield, mp 138—140 °C, colorless needles.[3)]

7b: 90% yield, mp 122—124 °C, colorless needles. *Anal.* Calcd for $C_{15}H_{21}N_3O_4S$: C, 53.08; H, 6.24; N, 12.38. Found: C, 52.81; H, 6.31; N, 12.44.

3-Methoxypyridazine 1-Ethoxycarbonylimides (8a, b)——Solid anhydrous potassium carbonate (1.5 mol eq) and ethyl chloroformate (1.1 mol eq) were added to a solution of a salt (**7**: 15—20 g) in anhydrous ethanol (150 ml) with stirring. The mixture was stirred for a further 20 h at room temperature and then the resulting inorganic precipitates were filtered off. The filtrate was concentrated *in vacuo* and the residue was extracted with CH_2Cl_2. The extract was dried over $MgSO_4$ and concentrated *in vacuo*. The residue was chromatographed on silica gel using CH_2Cl_2–methanol as an eluent to give the imides (**8**).

8a: 80% yield, mp 147—149 °C, yellow needles.[3)]

8b: 46% yield, pale yellow oil. IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1635 (C=O). MS *m/e*: 211 (M^+). NMR δ: 1.33 and 4.18 (3H, t, and 2H, q, CO_2Et), 2.65 (3H, s, 6-Me), 4.04 (3H, s, 3-OMe), 7.18 (1H, d, 5-H), 7.83 (1H, d, 4-H), $J_{4,5}=9$ Hz. *Anal.* Calcd for $C_9H_{13}N_3O_3$: C, 51.17; H, 6.20; N, 19.90. Found: C, 51.11; H, 6.15; N, 19.78.

Pyridazin-3-one 1-Ethoxycarbonylimides (9a, b)——A solution of a 3-methoxypyridazine 1-imide (**8**: *ca.* 3 g) in aq. 10% NaOH was heated at 70—75 °C with stirring. After cooling, the reaction solution was neutralized with aq. 10% HCl and then evaporated to dryness *in vacuo*. The residue was extracted with hot ethanol and the extract was evaporated to dryness *in vacuo*. The resulting crystalline residue was recrystallized from ethanol to give **9**.

9a: 88% yield, mp 184—186 °C, colorless needles. MS *m/e*: 183 (M^+). IR ν_{max}^{KBr} cm^{-1}: 3400 (NH), 1725 and 1610 (C=O). NMR δ (CD_3OD): 1.32 and 4.36 (3H, t, and 2H, q, CO_2Et), 7.09 (1H, d, 4-H), 7.70 (1H, dd, 5-H), 8.45 (1H, d, 6-H), $J_{4,5}=9$, $J_{5,6}=5$ Hz. *Anal.* Calcd for $C_7H_9N_3O_3$: C, 45.90; H, 4.95; N, 22.94. Found: C, 46.08; H, 4.91; N, 22.76.

9b: 76% yield, mp 122—125 °C, colorless prisms. MS *m/e*: 197 (M^+). IR ν_{max}^{KBr} cm^{-1}: 3400 (NH), 1720 and 1610 (C=O). NMR δ (CD_3OD): 1.33 and 4.32 (3H, t, and 2H, q, CO_2Et), 2.78 (3H, s, 6-Me), 7.72 (1H, d, 4-H), 8.28 (1H, d, 5-H), $J_{4,5}=9$ Hz. *Anal.* Calcd for $C_8H_{11}N_3O_3$: C, 48.72; H, 5.62; N, 21.31. Found: C, 48.55; H, 5.59; N, 21.46.

2-Methylpyridazin-3-one 1-Ethoxycarbonylimide (10a)——A solution of diazomethane (*ca.* 4 mmol) in ether (18 ml) was added dropwise to a solution of **9a** (625 mg, 3.4 mmol) in ether (20 ml) with stirring. After being stirred for an additional 1 h at room temperature, the reaction solution was concentrated *in vacuo*. The residue was chromatographed on silica gel using CH_2Cl_2–methanol as an eluent to give **8a** (281 mg, 42% yield) and **10a** successively. **10a**: 255 mg, 38% yield, red oil. MS *m/e*: 197 (M^+). IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1740 and 1630 (C=O). NMR δ: 1.28 and 4.26 (3H, t, and 2H, q, CO_2Et), 3.49 (3H, s, N-Me), 7.08 (1H, d, 4-H), 7.42 (1H, dd, 5-H), 7.98 (1H, d, 6-H), $J_{4,5}=9$, $J_{5,6}=5$ Hz. *Anal.* Calcd for $C_8H_{11}N_3O_3$: C, 48.72; H, 5.62; N, 21.31. Found: C, 48.63; H, 5.75; N, 21.29.

2,4-Dimethylpyridazin-3-one 1-Ethoxycarbonylimide (10b)——A solution of diazomethane (*ca.* 0.4 mmol) in ether (9 ml) was added dropwise to a solution of **10a** (202 mg) in CH_2Cl_2 (10 ml) with stirring at room temperature. The reaction solution was stirred for an additional 1 h and then concentrated *in vacuo*. The residue was chromatographed on silica gel using CH_2Cl_2–MeOH as an eluent to give **10b**: 166 mg, 77% yield, red oil. MS *m/e*: 211 (M^+). IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1740 and 1610 (C=O). NMR δ: 1.25 and 4.20 (3H, t, and 2H, q, CO_2Et), 2.30 (3H, br s, 4-Me), 3.45 (3H, s, N-Me), 7.43 (1H, m, 5-H), 8.15 (1H, d, 6-H), $J_{5,6}=5$ Hz. *Anal.* Calcd for $C_9H_{13}N_3O_3$: C, 51.17; H, 6.20; N, 19.90. Found: C, 51.39; H, 6.17; N, 19.71.

Photolysis of the *N*-Imide (9a)——A solution of **9a** (1.0 g) in methanol (400 ml) was irradiated for 2 h. After removal of the solvent *in vacuo*, the resulting solid residue was recrystallized from methanol to give the 3-pyrrolin-2-one derivative (**11**): 977 mg, 98% yield, mp 176—179 °C, colorless prisms. MS *m/e*: 183 (M^+). IR ν_{max}^{KBr} cm^{-1}: 3300 (NH), 1750 and 1690 (C=O). NMR δ: 1.37 and 4.34 (3H, t, and 2H, q, CO_2Et), 6.29 (1H, d, 3-H), 7.10 (1H, d, 4-H), 9.8 (1H, br, NH), 9.9 (1H, br, NH), $J_{3,4}=6$ Hz. *Anal.* Calcd for $C_7H_9N_3O_3$: C, 45.90; H, 4.95; N, 22.94. Found: C, 45.59; H, 5.00; N, 22.71.

Photolysis of the *N*-Imide (9b)——A solution of **9b** (1.5 g) in methanol (400 ml) was irradiated for 2 h and the reaction solution was concentrated *in vacuo*. The residue was chromatographed on silica gel using CH_2Cl_2–acetone as an eluent to give the 3-pyrrolin-2-one derivative (**12**): 220 mg, 17% yield, colorless oil. MS *m/e*: 169 (M^+). IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3450 (NH), 1735 and 1700 (C=O). NMR δ: 1.29 and 4.19 (3H, t, and 2H, q, CO_2Et), 1.64 (3H, s, 5-Me), 6.07 (1H, d, 3-H), 7.08 (1H, d, 4-H), 7.5 (1H, br, NH), $J_{3,4}=5$ Hz. *Anal.* Calcd for $C_8H_{11}NO_3$: C, 56.79; H, 6.55; N, 8.28. Found: C, 56.56; H, 6.61; N, 8.34.

Photolysis of the Imides (10a, b)——A solution of **10** (**a**: 290 mg, **b**: 180 mg) in CH_2Cl_2 (200 ml) was irradiated for 30 min and then concentrated *in vacuo*. The residue was chromatographed on silica gel using CH_2Cl_2 as an eluent to give the 3-pyrrolin-2-ones (**14** and **13**) successively.

13a: 26 mg, 9% yield, mp 121—124 °C, colorless prisms (from benzene–isopropyl ether). MS *m/e*: 197 (M^+). IR ν_{max}^{KBr} cm^{-1}: 3450 (NH), 1740 and 1690 (C=O). NMR δ: 1.28 and 4.21 (3H, t, and 2H, q, CO_2Et), 3.29 (3H, s, N-Me), 6.36 (1H, d, 3-H), 7.05 (1H, d, 4-H), 8.8 (1H, br, NH), $J_{3,4}=6$ Hz. *Anal.* Calcd for $C_8H_{11}N_3O_3$: C, 48.72; H, 5.62; N, 21.31. Found: C, 48.89; H, 5.65; N, 21.06.

13b: 25 mg, 14% yield, mp 99—101 °C, colorless prisms (from benzene–isopropyl ether). MS *m/e*: 211 (M^+). IR ν_{max}^{KBr} cm^{-1}: 3450 (NH), 1735 and 1700 (C=O). NMR δ: 1.29 and 4.20 (3H, t, and 2H, q, CO_2Et), 2.02 (3H, br, 3-Me), 3.23 (3H, s, N-Me), 6.68 (1H, m, 4-H), 8.3 (1H, br, NH). *Anal.* Calcd for $C_9H_{13}N_3O_3$: C, 51.17; H, 6.20; N, 19.90. Found: C, 51.12; H, 6.39; N, 19.68.

14a: 25 mg, 10% yield, colorless oil. MS *m/e*: 169 (M^+). IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1780 and 1720 (C=O). NMR δ: 1.40 and 4.36 (3H, t, and 2H, q, CO_2Et), 1.44 (3H, d, $J=7$ Hz, 5-Me), 4.68 (1H, m, 5-H), 6.08 (1H, dd, 3-H), 7.14 (1H, dd, 4-H), $J_{3,4}=6$, $J_{3,5}=J_{4,5}=1.5$ Hz. *Anal.* Calcd for $C_8H_{11}NO_3$: C, 56.79; H, 6.55; N, 8.28. Found: C, 56.57; H, 6.53; N, 8.02.

14b: 28 mg, 18% yield, colorless oil. MS *m/e*: 183 (M^+). IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1770 and 1720 (C=O). NMR δ: 1.38 and 4.34 (3H, t, and 2H, q, CO_2Et), 1.42 (3H, d, $J=7$ Hz, 5-Me), 1.88 (3H, br, 3-Me), 4.52 (1H, m, 5-H), 6.75 (1H, m, 4-H). *Anal.* Calcd for $C_9H_{13}NO_3$: C, 59.00; H, 7.15; N, 7.65. Found: C, 59.08; H, 6.87; N, 7.52.

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