Notes

N,N′-Methylenebis(4,5-oxazolidinedione): A Novel Route to New Copolyoxamide Precursors

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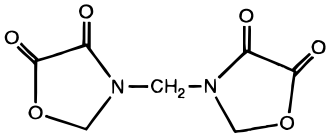
Introduction

Several works published on copolyoxamide synthesis during the recent past[1−10] showed the various difficulties encountered and asked for improvement in synthesis pathways, especially because polyoxamides have interesting industrial applications. They can be used as UV stabilizers,[11] synthetic fibers,[12] and oxygen barrier layers (useful in packaging of laminated films[13] and in desalination membrane synthesis.[14−16] They are also used as blend polymers for thermoplastic mouldings.[17] In this case, modification of their melting points,[1,12,18] via chain extensors, could improve such applications.

Our interest for copolyoxamides started during a study on the chemistry of hydrogen cyanide.[19] Our initial objective was the synthesis of ethylenediamine using waste industrial products like hydogen cyanide, i.e by methods other than those normally used industrially.[20] Thus, we imagined a catalytic process, represented in Scheme 1, in which the central compound was 4,5-oxazolidinedione (**1**). Such a catalytic process had been conceived, according to previous works.[21]

The first attempts to verify the process led us to synthesize a compound resulting from the reaction between 2 mol of **1** and 1 mol of formaldehyde. This compound, *N,N′*-methylenebis(4,5-oxazolidinedione) (**10**), already described in a short communcation,[22] was easily synthesized and appeared as an interesting potential precursor in the synthesis of polyoxamides and copolyoxamides.



(10)

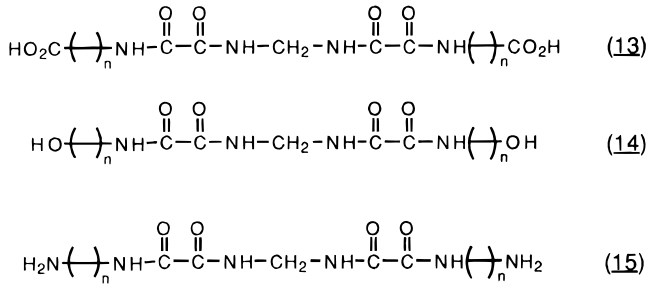
N,N'-methylenebis (4,5-oxazolidinedione)

We describe in this paper the synthesis of several new precursors of copolyoxamides derived from *N,N′*-methylenebis(4,5-oxazolidinedione).

Results

Interesting monomers for copolyoxamides could be diols, diamines, and diacids. Our target was therefore the synthesis of the following molecules:

In the first instance, we studied the reactivity of α-aminoacetonitrile on *N,N′*-methylenebis(4,5-oxazolidinedione) (**10**). The resulting product (**11**) was easily obtained in 83% yield. However, when the reaction was carried out with α-aminopropionitrile, the dinitrile was obtained in a very low yield (15%), probably because of the increasing organic character which reduces its solubility in water.



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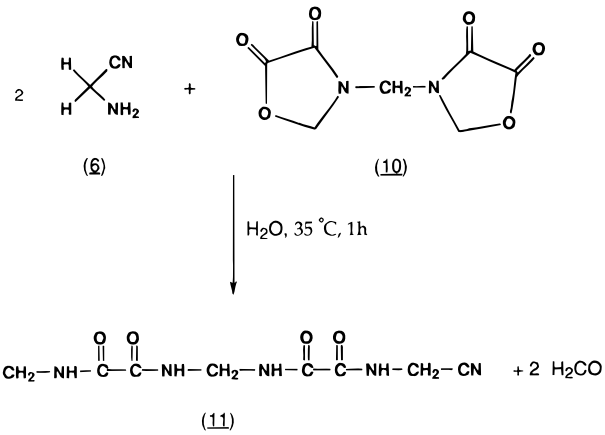
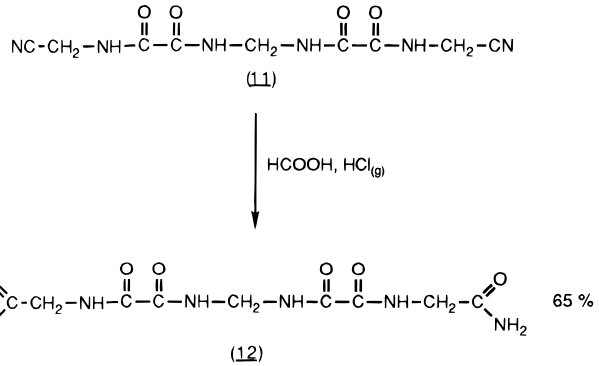


(6) (10)

(11)

The reaction takes place in an heterogeneous medium, with both the starting and resulting product. The latter (**11**) was clearly identified by NMR of ^{1}H (250 MHz), which confirmed the retroaddition of formaldehyde. Irradiation of the triplets at 9.53 and 9.14 ppm indicated that the NH and CH_2 groups are coupled. This dinitrile, obtained in a rather high yield, had a low solubility in ethereal solvents, which prevented its further reduction to the diamine. The only successful reaction was the hydration reaction of the dinitrile **11** to the diamide **12**.



(11)

(12)

Hydrolysis both of the dinitrile and the diamide to the diacid remained unsuccessful, mostly because of solubility problems. However, we obtained the diacid

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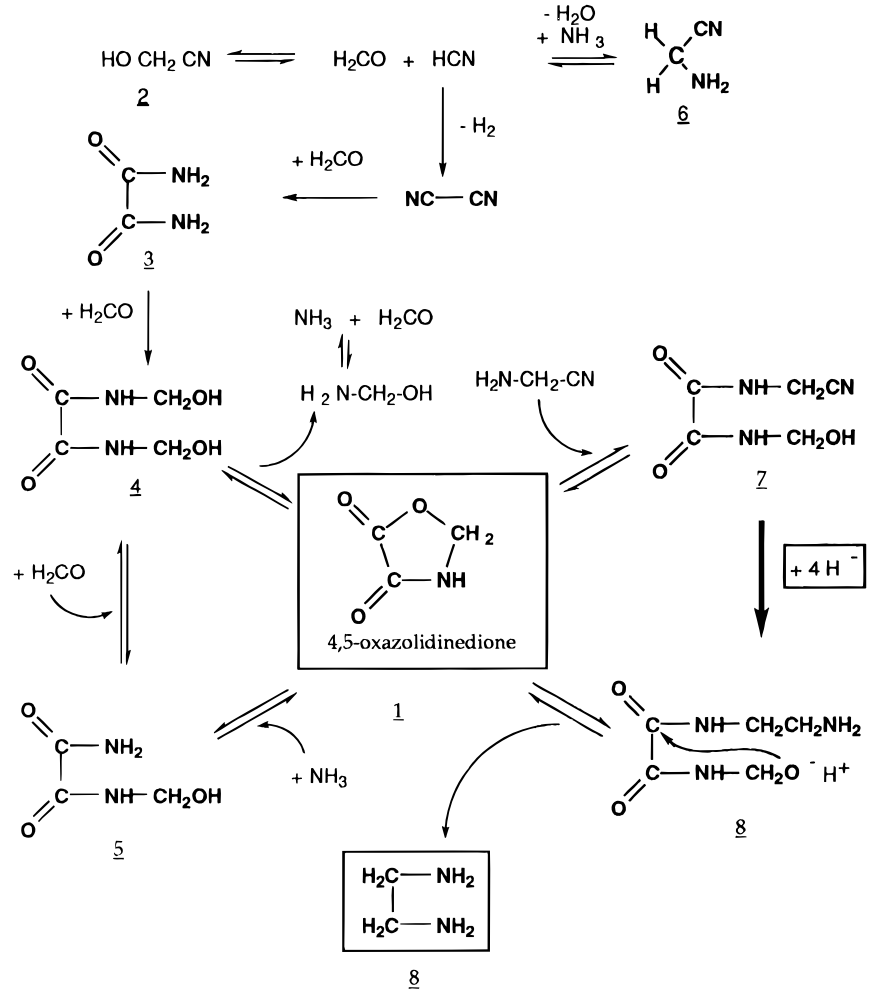
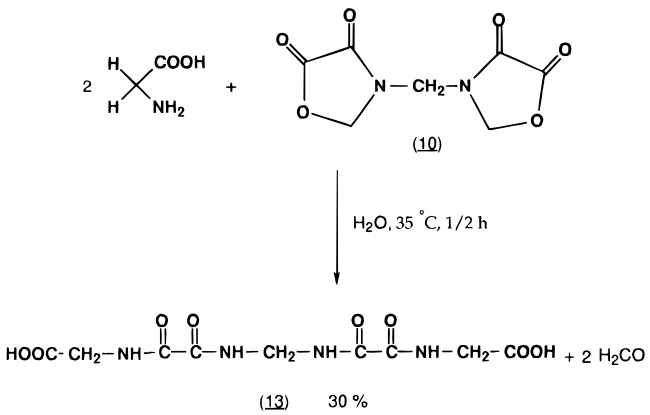
Scheme 1



13 by reaction of an α-amino acid with *N*,*N*′-methylenebis(4,5-oxazolidinedione).

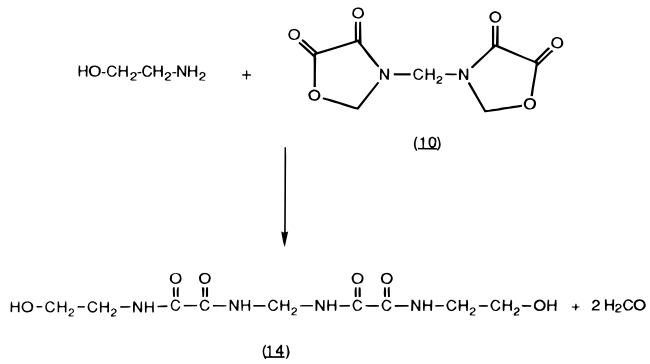


In this case, the resulting product is soluble in water and is isolated by passing through a sulfonic ion exchange resin.

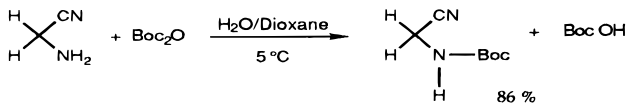
The diol **14** was obtained by reaction of ethanolamine with *N*,*N*′-methylenebis(4,5-oxazolidinedione) (**10**).

Ethanolamine contains two nucleophilic groups, namely OH and NH_2, liable to generate two possibilities of reaction. However, since the reactivity of NH_2 is greater, only the formation of the diol is observed.

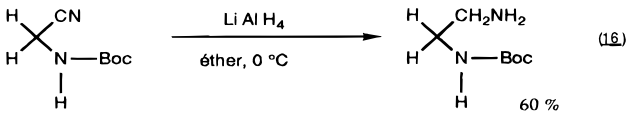
The most important bifunctional compound, the diamine **15**, could not be obtained by this one-step synthesis. A different strategy was developed, which allowed the synthesis of the hydrogen chloride salt of the diamine in a four-step synthesis.



(1) Protection of the amine group of α-aminoacetonitrile by the *tert*-butyloxycarbonyl group (Boc):

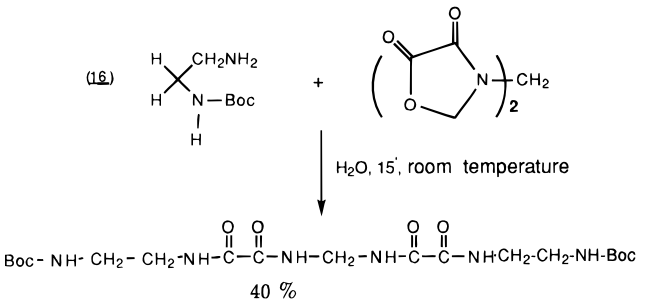


(2) Reduction of the nitrile group:

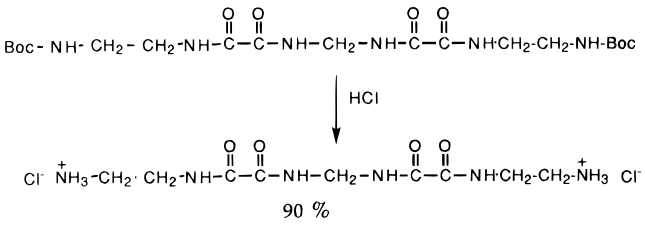


This reduction was performed in ether at 0 °C using $LiAlH_4$.

(3) Reaction of **16** with *N*,*N*′-methylenebis(4,5-oxazolidinedione):



(4) Deprotection: finally, through deprotection in concentrated acidic medium, the diamine (**15**) is obtained as diammonium chloride.



Discussion

It is obvious, regarding the above results, that complementary studies should be carried out to improve the knowledge of such syntheses. The major problem remains the solubility of the different compounds. The most interesting aspect remains the facile ring opening of the *N*,*N*′-methylenebis(4,5-oxazolidinedione) in "chimie douce" conditions. We showed that this compound **10** leads to bifunctional dioxamide compounds bearing functionnal groups such as nitriles, amide, acid, hydroxyl, and amine groups in α and *ω* positions. These groups react with bifunctional monomers to form various macromolecules which have oxamide groups in their chains.

Experimental Section

General. NMR spectra were recorded on a Bruker AC 250 (250 MHz); chemical shifts reported as δ are relative to tetramethylsilane as an internal standard. The melting points were recorded on a Büchi 510 apparatus and are not corrected.

Materials. All solvents and reagents were obtained from commercial sources of guaranteed grade and used without further purification.

Glycolonitrile (2). Anhydrous HCN (4.35 mol) (generated by reaction of a solution of NaCN on sulfuric acid, dried on $CaCl_2$, and condensed at −10 °C) was slowly added to paraformaldehyde (4.7 moles) in suspension in 240 mL of dichloromethane, together with KCN (2 g) used as catalyst. The initial temperature was set to 22 °C and stabilized to 25−30 °C, since the reaction is exothermic. At the end of the reaction (the reaction mixture is colorless), the temperature was set back to 22 °C. Water (400 mL) was added to the medium, since the partition cofficient of glycolonitrile is more favorable to water than dichloromethane. The product was then stabilized by adding phosphoric acid until pH ≤ 3. Pure glycolonitrile was obtained, in 85% yield, by evaporating the solvent and distilling: $Eb_{0,4}$ = 86 °C; NMR (250 MHz, DMSO-d_6) δ_H 4.32 (d, 2H, C*H*$_2$), 6.08 (t, 1H, O*H*); IR ν ($CHCl_3$)/cm^{-1} 3200−3600, 2250.

α-Aminoacetonitrile (6). An aqueous ammonia solution (32 wt%) was added dropwise to pure glycolonitrile, in molar proportions 9 to 1. The reaction was followed in TLC (eluting solvent: propan-2-ol/ammonia, 70/30). The product was extracted from the aqueous phase by continuous extraction from ether during 16 h. The solvent was evaporated under reduced pressure and pure α-aminoacetonitrile obtained by distillation in 40% yield: $Eb_{0,5}$ = (50−52) °C; IR ν ($CHCl_3$)/cm^{-1} 2100, 1615; NMR (250 MHz, $CDCl_3$) δ_H 2.07 (s (broad), 2H, N*H*$_2$), 3.52 (s, 2H, C*H*$_2$); NMR (50.3 MHz, NH_3 1 M/D_2O (30%) buffer solution at pH 9) δ_C 146.1, 121.3, 29.7.

***N*,*N*′-Methylenebis(4,5-oxazolidinedione) (10).** Oxamide (9 g) **3** was dissolved with stirring in 50 mL of 95% H_2SO_4 at room temperature in an open flask. Pure paraformaldehyde (6.3 g, 0.21 mol) was added and the solution was heated with stirring for 1 h at 70 °C. After being cooled to room temperature, the solution was poured with stirring into 200 mL of ice water. The precipitate formed was filtered, washed thoroughly with distilled water, and dried at 50 °C under vacuum. The pure product is obtained by recrystallization in DMF, in 40% yield: T_f = 291 °C; IR ν (KBr)/cm^{-1} 1800, 1725, 1450; NMR (250 MHz, DMSO-d_6, TMS) δ_H 5.13 (s, 2H, NC*H*$_2$N), 5.48 (s, 2H, OC*H*$_2$N). *Anal.* Calcd for $C_7H_6N_2O_6$: C, 39.27; H, 2.8; N, 13.08; O, 44.84. Found: C, 39.52, H, 2.83; N, 13.22; O, 44.90.

Dinitrile 11. α-Aminoacetonitrile (1.904 g, 0.034 mol) was dissolved in 25 mL of water. Finely ground **10** (1 g, 0.005 mol) was then added. The heteregeneous medium was stirred for 2 h at 35 °C. After filtration, the solid was washed with water and dried under vacuum at 50 °C. After recrystallization in DMF, **11** was obtained in 80% yield: T_f = (280−285) °C; IR ν (KBr)/cm^{-1} 2250; NMR (250 MHz, DMSO-d_6, TMS) δ_H 4.30 (d, 4H, C*H*$_2$CN), 4.65 (t, 2H, NHC*H*$_2$CN), 9.14 (t, 2H, N*H*CH$_2$N*H*), 9.53 (t, 2H, CON*H*CH$_2$). *Anal.* Calcd for $C_9H_{10}N_6O_4$: C, 40.61; H, 3.79; N, 31.57; O, 24.04. Found: C, 40.93; H, 4.21; N, 31.54; O, 24.18.

Diamide 12. Gaseous HCl was bubbled in a suspension containing **11** (0.5 g, 1.88×10^{-3} mol) in 15 mL of formic acid. The medium became completely homogeneous after 1 h. After an additional $^1/_2$ h of bubbling, the solvent was evaporated under reduced pressure, and the residual solid was dried at 50 °C under vacuum. After recrystallization in DMF, pure **12** was obtained in 85% yield: T_f = 310−315 °C; NMR (250 MHz, DMSO-d_6, TMS) δ_H 4.46 (d, 4H, C*H*$_2$CONH$_2$), 5.13 (t, 2H, NHC*H*$_2$NH), 7.65 (d (broad), 4H, CON*H*$_2$), 9.00 (t, 2H, N*H*CH$_2$N*H*), 9.20 (t, 2H, CON*H*CH$_2$). *Anal.* Calcd for $C_9H_{14}N_6O_6$: C, 35.76; H, 4.67; N, 27.80; O, 31.76. Found: C, 35.20; H, 4.95; N, 26.45; O, 32.31.

Diacid 13. In a 25 mL flask containing glycine (0.263 g, 0.0035 mol) dissolved in 10 mL of water and adjusted to pH 10 with 0.1 N NaOH was added **10** (0.250 g, 0.0012 mol). After 2 h of stirring at 35−40 °C, the medium became completely homogeneous. The solution was then acidified to pH 6.5 with 0.1 N HCl and passed through an ion exchange sulfonic resin (C_6H_5-SO_3H). The unreacted glycine and the Na^+ ions remained attached to the resin (C_6H_5-$SO_3^{-+}NH_3CH_2COOH$ and C_6H_5-SO_3^- Na^+). The remaining solution was lyophilized and dried at 50 °C under vacuum to yield 30% of **13**: T_f = (285−290) °C; NMR (250 MHz, DMSO-d_6, TMS) δ_H 3.80 (d, 4H, C*H*$_2$-COOH), 4.63 (t, 2H, N*H*CH$_2$N*H*), 9.00 (m 4H, N*H*), 12.80 (s (broad), 2H, O*H*). *Anal.* Calcd for $C_9H_{12}N_4O_8$: C, 35.53; H, 3.98; N, 18.42; O, 42.06. Found: C, 34.24; H, 5.05; N, 16.45; O, 41.03.

Diol 14. In a 50 mL flask containing a suspension of **10** (1 g, 0.005 mol) in 25 mL of water, ethanolamine (0.856 g, 0.014 mol) dissolved in 10 mL of water in 1 h. The reaction was carried out at 40 °C, and stirring continued for an additionnal hour after complete addition. The solid obtained after filtration was washed with water and dried under vacuum at 50 °C. The pure compound was obtained in 35% yield after recrystallization in DMF: T_f = (27−277) °C; NMR (250 MHz, DMSO-d_6, TMS) δ_H 3.30 (q, 4H, C*H*$_2$CH$_2$OH), 3.54 (t, 4H, CH$_2$C*H*$_2$OH), 4.40 (s, 2H, NHC*H*$_2$NH), 4.70 (t, 2H, O*H*), 8.22 (s (broad), 2H, N*H*CH$_2$N*H*), 8.64 (s (large), 2H, N*H*CH$_2$CH$_2$).

Diamine 15. The diamine was obtained in a four-step synthesis:

(1) Protection of the Amine Group of α-Aminoacetonitrile. α-Aminoacetonitrile (5.6 g, 0.1 mol) was dissolved in

30 mL of water. After the pH was adjusted to 9−10 with 1 N NaOH, 90 mL of dioxane was added to the solution. The mixture was cooled to 5 °C. *tert*-Butyloxycarbonyl anhydride (Boc_2O) (21.8 g, 0.01 mol), dissolved in the minimum of dioxane, was then added dropwise. After the end of the addition the reaction was left for 18 h at 5 °C (followed in TLC, eluting solvent: propan-2-ol/$NH_{3(aq)}$ 32%, 70/30). The mixture water/dioxane was evaporated under reduced pressure, and the residue was dissolved in ether. After drying on anhydrous Na_2SO_4, the solution was filtered and ether evaporated under reduced pressure. The oily product obtained was recrystallized, and the pure product was obtained in 86% yield: NMR (250 MHz, DMSO-d_6, TMS) δ_H 1.43 (s, 9H, CH_3), 3.93 (d, 2H, CH_2), 7.46 (s (broad), 1H, N*H*).

(2) Reduction of the Nitrile Group. $LiAlH_4$ (2 g, 0.05 mol) and anhydrous ether (200 mL) are introduced in a three-necked flask cooled to 5 °C. A solution of (*tert*-butyloxycarbonyl)aminonitrile (4.5 g, 0.029 mol) was then added drop by drop. After complete addition, the solution was stirred for 18 h at 0 °C and then refluxed for 1 h. The excess hydride was destroyed by adding $Na_2SO_4 \cdot 10H_2O$. The insoluble salts were filtered. Ether and water were evaporated under reduced pressure, and the residue was dissolved in dichloromethane. After filtration, the organic phase was dried with anhydrous Na_2SO_4 and filtered again and the solvent eliminated under reduced pressure. The pure product (**16**) was obtained, after recrystallization, in chloroform in 60% yield: NMR (250 MHz, DMSO-d_6, TMS) δ_H 1.43 (s, 9H, CH_3), 1.50 (s, 2H, NH_2), 2.92 (m, 4H, CH_2CH_2), 5.67 (s (broad), 1H, N*H*).

(3) Reaction of 16 with *N,N′*-Methylenebis(4,5-oxazolidinedione) (10). Finely ground **10** (1.25 g, 0.006 mol) was added to a solution of (*tert*-butyloxycarbonyl)ethylenediamine (**16**) (2.7 g, 0.017 mol) in water. After 15 min of stirring at room temperature, the solution was filtered. The solid obtained was washed with ether, acetone, and finally water to get rid of the excess (*tert*-butyloxycarbonyl)ethylenediamine (**16**). The residue (**17**), dried at 40 °C under reduced pressure, is obtained in 40% yield: NMR (250 MHz, DMSO-d_6, TMS) δ_H 1.37 (s, 18H, CH_3), 1.50 (s, 2H, NH_2), 3.03 (quad, 4H, CONHCH_2CH$_2$NHCOOC(CH$_3$)$_3$), 3.18 (quad, 4H, CONHCH$_2$CH_2NHCOOC(CH$_3$)$_3$), 4.63 (t, 2H, NHCH_2NH), 6.90 (t, 2H, N*H*COOC(CH$_3$)$_3$), 8.81 (t, 2H, N*H*CH$_2$N*H*), 8.90 (t, 2H, COCON*H*CH$_2$CH$_2$).

(4) Regeneration of the Amine Group. (1 g) was added to a solution of hydrochloric acid (10 mL, 3 N). The solution was heterogeneous. After $^1/_2$ h of stirring at room temperature, the solid was filtered and washed thoroughly with distilled water. It was dried at 50 °C under reduced pressure, leading to the hydrochloride in 90% yield: NMR (250 MHz, DMSO-d_6, TMS) δ_H 2.96 (quad, 4H, CH_2CH$_2$NH$_3$), 3.43 (quad, 4H, CH$_2$CH_2NH$_3$), 4.67 (t, 2H, NHCH_2NH), 7.81 (s (broad), 6H, NH$_3$), 8.96 (m, 4H, N*H*).

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