

Mechanism of Reduction of 3,4,5-Triphenylfuran-2(5*H*)-ones by Lithium Aluminium Hydride

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A detailed study of the reduction of 3,4,5-triphenylfuran-2(5*H*)-ones with lithium aluminium hydride, with deuterium as a marker, has been performed. On the basis of the results it is proposed that 1,4-hydride attack is followed by regiospecific hydridoalumination of the enolate double bond only in those cases where the resulting complex can be stabilised.

It has been reported¹ that reduction of 3,4,5-triphenylfuran-2(5*H*)-ones with lithium aluminium hydride gives a mixture of products whose relative yields are dependent on the position of substituents on the phenyl rings. We now describe a detailed investigation of the mechanism of this reduction. Attempts were made to characterize all the products, and studies were made with deuterium as a marker.

From the reduction of 3,4,5-triphenylfuran-2(5*H*)-one (1) with lithium aluminium hydride were obtained, in addition to the dihydrofuranone (3) and the diol (9) reported earlier,¹ 2,3,4,5-tetraphenylfuran (2) (1.0%), 4,5-dihydro-*r*-3,*c*-4,*c*-5-triphenylfuran-2(3*H*)-one² (6) (traces), *r*-3,*t*-4,*t*-5-triphenyltetrahydrofuran-2-ol (7),

and *rel*-(1*S*,2*S*,3*S*)-1,2,3-triphenylbutane-1,4-diol¹ (12), which were separated by column chromatography (Scheme 1). The structure of the tetraphenylfuran (2) was confirmed by unambiguous synthesis from the furanone (1) with phenylmagnesium bromide. The formation of tetraphenylfuran (2) was unexpected and no mechanism can yet be suggested for the origin of the fourth phenyl group. The cyclic hemiacetal (7) and the dihydrofuranone (3) were chemically interconvertible; therefore, positions 3, 4, and 5 in these products were assigned the same stereochemistry. On the basis of the present data it is not possible to assign the stereochemistry at C-2.

Reduction of the furanone (1) with lithium aluminium

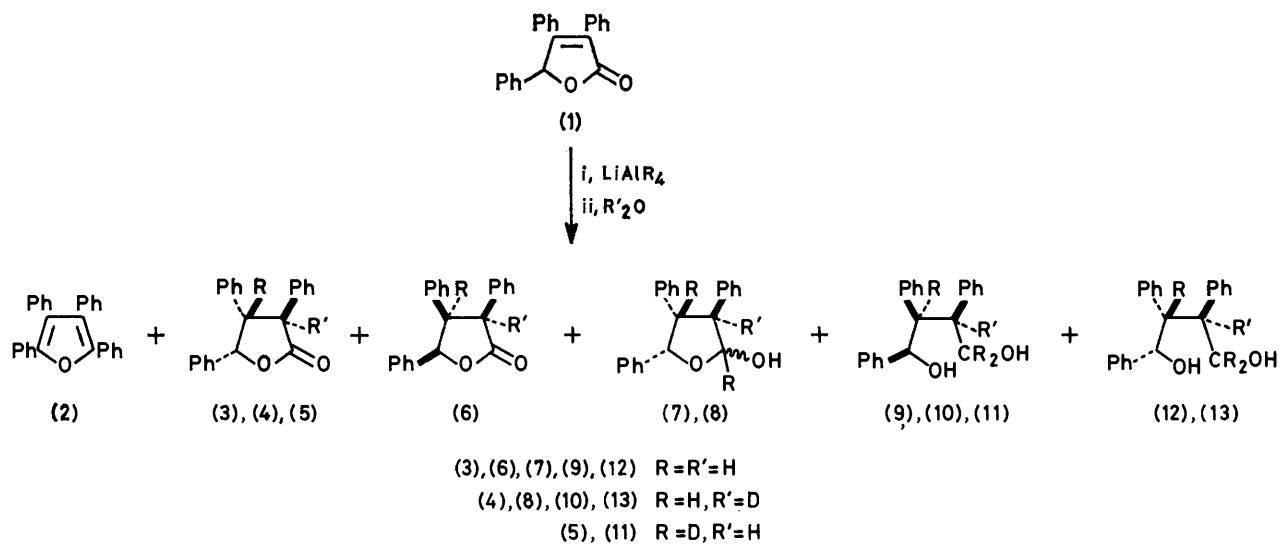
¹ K. L. Munshi, D. K. Dikshit, R. S. Kapil, and N. Anand, *Indian J. Chem.*, 1974, **12**, 336.

² D. K. Dikshit, K. L. Munshi, R. S. Kapil, and N. Anand, *Indian J. Chem.*, in the press.

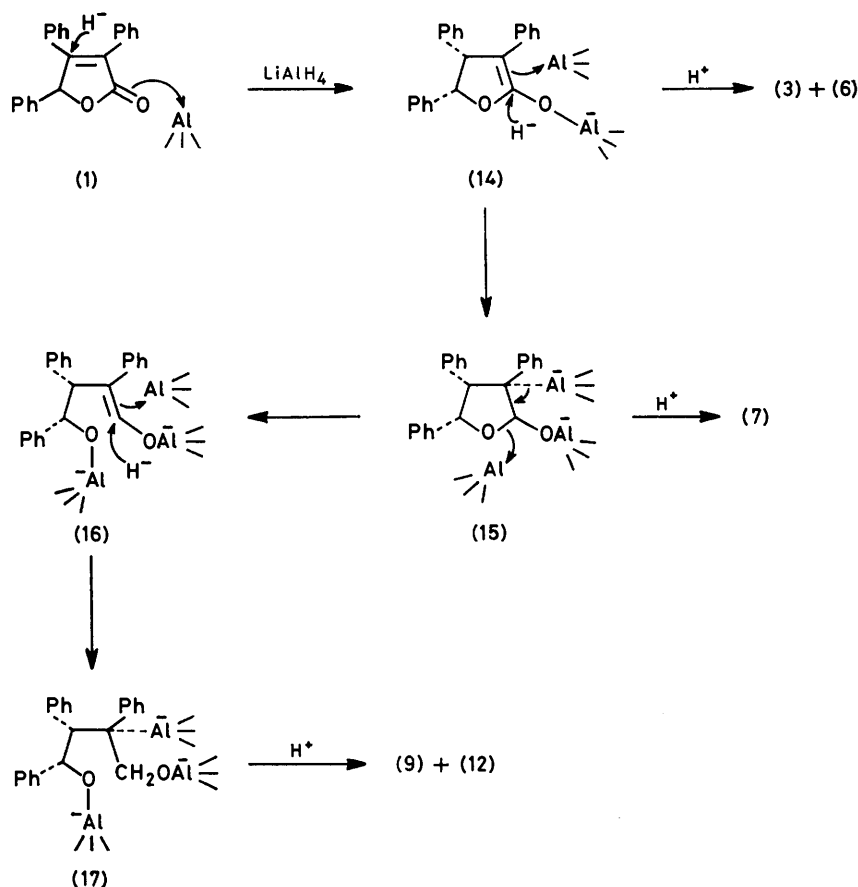
hydride followed by work-up with D_2O furnished the tetraphenylfuran (2), 3-deuterio-4,5-dihydro-*r*-3,*t*-4,*t*-5-triphenylfuran-2(3*H*)-one (4), 3-deuterio-*r*-3,*t*-4,*t*-5-triphenyltetrahydrofuran-2-ol (8), and the *rel*-(1*R*,2*R*,3*S*)- and *rel*-(1*S*,2*S*,3*S*)-3-deuterio-1,2,3-triphenylbutane-1,4-

diols (10) and (13) (Scheme 1). In compounds (4), (8), (10), and (13), only one deuterium atom was present, at position 3, as evidenced by spectral data and chemical interconversions.

When the furanone (1) was reduced with lithium alu-



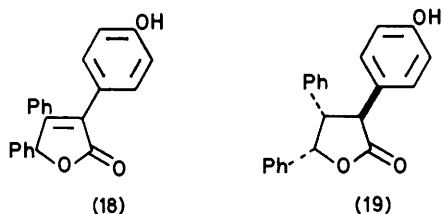
SCHEME 1



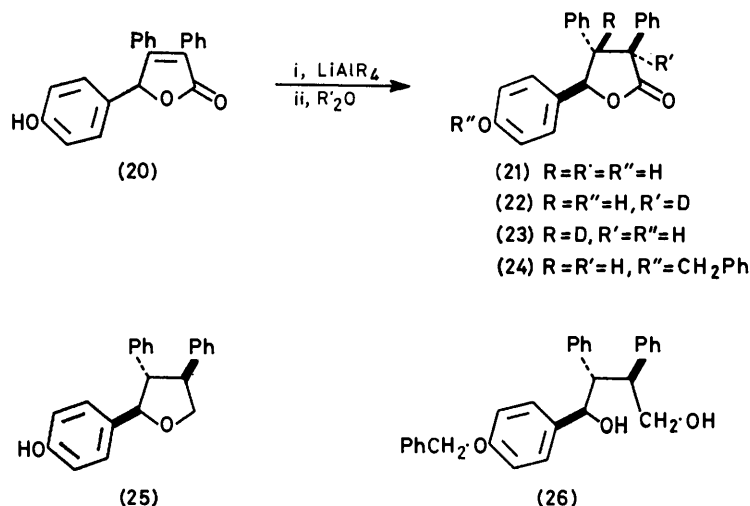
SCHEME 2

minium deuteride and the mixture was worked up with water, the 4,5-dihydro-*r*-3,*t*-4,*t*-5-triphenylfuran-2(3*H*)-one (5) and the *rel*-(1*R*,2*R*,3*S*)-1,2,3-triphenylbutane-1,4-diol (11) were obtained; owing to the use of small quantities of reactants, other products were present in amounts, too small to be isolated and identified (Scheme 1). Comparison of the n.m.r. spectra of compounds (5) and (11) with those of the corresponding undeuteriated compounds (3) and (9) showed that in the dihydrofuranone (5) deuterium had been introduced at C-4 and in the diol (11), C-2 and C-4 were fully deuteriated.

In view of the mode of hydride attack shown by the deuteration experiments, the mechanism shown in



Scheme 2 is proposed. Initial 1,4-hydride attack takes place from the less hindered side of the double bond, *i.e.* opposite to the phenyl group at C-5, thus making the



SCHEME 3

phenyl groups at C-4 and -5 *cis* to each other. Hydride attack in this manner would give rise to the enolate intermediate (14) which, on treatment with water, would pick up a proton predominantly from the α -face of the molecule to produce the more stable dihydrofuranone (3), having minimal steric interaction between the 3- and 4-phenyl groups. Further reduction of the enolate intermediate (14) would proceed by hydridoalumination of the double bond³ to give the intermediate (15). Whether or not this intermediate is formed would be greatly dependent on the degree of stabilisation of the resulting charge at C-3. In those cases where the phenyl group at C-3 is electron-rich, as in the 3-(*p*-hydroxyphenyl)furanone¹

(18), reduction of the intermediate of type (14) would not be favoured. This would explain the predominant formation of the dihydrofuranone (19) in the reduction of (18).¹ Protonation of the intermediate (15) would give the 3,4-*trans*-hemiacetal (7). An elimination reaction of (15) as shown in Scheme 2, would give the intermediate (16), which by further reduction *via* hydridoalumination would afford the diols (9) and (12).

Reduction of 5-(*p*-hydroxyphenyl)-3,4-diphenylfuran-2(5*H*)-one (20) with lithium aluminium hydride, however, gives the *r*-3,*t*-4,*c*-5-triphenyldihydrofuranone¹ (21). In reductions of the furanone (20) with $\text{LiAlH}_4\text{-D}_2\text{O}$ and with $\text{LiAlD}_4\text{-H}_2\text{O}$, the deuteriated products (22) and (23) respectively, were formed (Scheme 3). This indicates that a mechanism involving initial 1,4-hydride attack essentially similar to that proposed above for the reduction of the furanone (1) is operative. It was reported earlier¹ that reduction of the dihydrofuranone (21) with lithium aluminium hydride gives the tetrahydrofuran (25) instead of the corresponding diol, whereas the benzylated dihydrofuranone (24) on similar reduction gives only the diol (26); participation of the *p*-hydroxyphenyl group thus appears to be implicated in the formation of the dihydrofuranone (21). It appears that in the reduction of the furanone

(20) with lithium aluminium hydride the intermediate (27) is formed initially, and is subsequently epimerised to (21). The mechanism shown in Scheme 4 seems to explain this epimerisation.

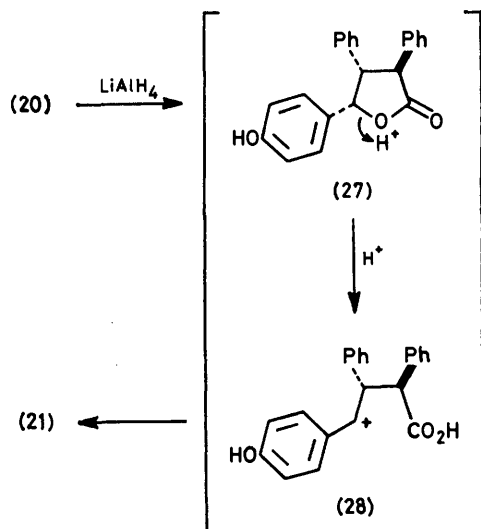
EXPERIMENTAL

N.m.r. spectra were recorded with a Varian A-60D spectrometer (Me_4Si as internal reference).

Reduction of 3,4,5-Triphenylfuran-2(5H)-one (1) with Lithium Aluminium Hydride; Decomposition of the Complex with Water.—A solution of the furanone (1) (30.0 g) in dry tetrahydrofuran (THF) (300 ml) was added dropwise to a stirred suspension of LiAlH_4 (24.0 g) in THF (500 ml). The

³ Cf. P. Pino and G. P. Lorenzi, *J. Org. Chem.*, 1966, **31**, 329.

mixture was then refluxed for 4 h, cooled, and decomposed by cautious addition of water. The solvent was then distilled off and the residue extracted with dichloromethane (4 × 250 ml). The combined extract was washed with water, dried (Na₂SO₄), and concentrated. The residue was chromatographed on a column of silica gel (1.5 kg) in n-hexane containing increasing proportions of benzene to give



SCHEME 4

2,3,4,5-tetraphenylfuran (2) (0.3 g); m.p. 165°; $\lambda_{\text{max.}}$ (EtOH) 233, 260, and 227 nm; τ (CDCl₃) 2.23–2.83 (1 H, m, ArH); m/e 372 (M^+) (Found: C, 90.0; H, 5.45. C₂₈H₂₀O requires C, 90.3; H, 5.35%); 4,5-dihydro-*r*-3,*t*-4,*t*-5-triphenylfuran-2(3H)-one (3) (7.0 g); m.p. 151°; $\nu_{\text{max.}}$ (KBr) 1770 cm⁻¹ (CO); τ (MeCN) 2.44–4.17 (15 H, m, ArH), 3.02 (1 H, four lines, 5-H), and 5.52 (2 H, three lines, 3- and 4-H); τ (CDCl₃) 2.42–3.20 (15 H, m, ArH), 4.04 (1 H, three lines, 5-H), and 5.71 (2 H, two lines, 3- and 4-H); m/e 314 (M^+) (Found: C, 84.25; H, 6.05. C₂₂H₁₈O₂ requires C, 84.05; H, 5.75%); and *rel*-(1*R*,2*R*,3*S*)-1,2,3-triphenylbutane-1,4-diol (9) (4.1 g); m.p. 160°; $\nu_{\text{max.}}$ (KBr) 3 500 cm⁻¹ (OH); τ (CDCl₃) 2.23–3.27 (15 H, m, ArH), 5.23 (1 H, d, *J* 3.0 Hz, 1-H), 6.33 (3 H, m, 4-H₂ and 3-H), 6.85 (1 H, m, 2-H), and 8.00–9.05br (2 H, two OH) (Found: C, 82.7; H, 7.15. C₂₂H₂₂O₂ requires C, 83.0; H, 6.9%). In the mother liquor left after several crystallisations of compound (3), the presence of the *r*-3,*c*-4,*c*-5-triphenyldihydrofuranone (6) was shown by n.m.r. spectroscopy.

Partially separated fractions were mixed and rechromatographed on a column of silica gel (400 g) in benzene containing increasing proportions of chloroform to furnish compounds: *r*-3,*t*-4,*t*-5-triphenyltetrahydrofuran-2-ol (7) (0.8 g); m.p. 166°; $\nu_{\text{max.}}$ (KBr) 3 550–3 600 cm⁻¹ (OH); τ (MeCN) 2.54–3.17 (15 H, m, ArH), 4.10–4.55 (2 H, m, 2- and 5-H), and 5.17–6.50 (2 H, m, 3- and 4-H); τ (CDCl₃) 2.50–3.23 (15 H, m, ArH), 3.93–4.50 (2 H, m, 2- and 5-H), and 5.20–6.50 (2 H, m, 3- and 4-H); m/e 316 (M^+); and *rel*-(1*S*,2*S*,3*S*)-1,2,3-triphenylbutane-1,4-diol (12) (1.2 g); m.p. 128°; $\nu_{\text{max.}}$ (KBr) 3 480 cm⁻¹ (OH); τ (CDCl₃) 2.52–3.17 (15 H, m, ArH), 4.79 (1 H, d, *J* 5.0 Hz, 4-H), 6.10 (2 H, d, *J* 4.5 Hz, 1-H), 6.63 (2 H, m, 2- and 3-H), and 7.72br (2 H, two OH) (Found: C, 83.35; H, 7.25. C₂₂H₂₂O₂ requires C, 83.0; H, 6.9%).

2,3,4,5-Tetraphenylfuran (2).—A solution of the furanone (1) (3.0 g) in dry ether (100 ml) was added dropwise to a suspension of phenylmagnesium bromide [from magnesium (2.0 g) and bromobenzene (12.0 g)] in dry ether (250 ml) with stirring. The mixture was then refluxed for 15 h, cooled, decomposed with 0.1*N*-hydrochloric acid and extracted with ether (2 × 100 ml). The combined extract was washed with water, dried (Na₂SO₄), and concentrated. The crude product was chromatographed on a column of silica gel in n-hexane to furnish the furan (2) (0.4 g), m.p. 165°.

Jones Oxidation of the Tetrahydrofuranol (7).—A solution of Jones reagent (4.0 ml) was added to the cyclic hemiacetal (7) (0.1 g) in acetone (10 ml) at 0 °C. The mixture was kept at this temperature for 1 h. A few drops of sodium hydrogen sulphite solution were added, and the precipitate was filtered off and washed with acetone. The filtrate was concentrated, diluted with water, and extracted with ether (2 × 25 ml). The combined ethereal layer was washed with water, dried (Na₂SO₄), and concentrated. The residue was chromatographed on a column of silica gel (5 g) with n-hexane–benzene as eluant to give the dihydrofuranone (3) (0.06 g), m.p. 150°.

Reduction of the Dihydrofuranone (3) with Di-isobutylaluminium Hydride.—A solution of di-isobutylaluminium hydride (2.0 ml) in the THF (freshly distilled over LiAlH₄; 10 ml) was added dropwise to a stirred solution of the dihydrofuranone (3) (2.0 g) in THF (25 ml) at –50 °C under nitrogen. The mixture was stirred at this temperature for a further 3 h, decomposed with water, and evaporated. The residue acidified with 0.1*N*-hydrochloric acid and extracted with ether (2 × 50 ml). The combined extract was washed with water, dried (Na₂SO₄), and concentrated to give the crude product, which was chromatographed on a column of silica gel in benzene to furnish the cyclic hemiacetal (7) (0.8 g), m.p. 165°.

Reduction of the Furanone (1) with Lithium Aluminium Hydride; Decomposition of the Complex with Deuterium Oxide.—A solution of the furanone (1) (30.0 g) in dry THF (500 ml) was reduced with LiAlH₄ (24.0 g) as described earlier. The complex was decomposed with D₂O and worked up as usual. Careful chromatography over a column of silica gel (1.5 kg) with n-hexane–benzene–ethyl acetate as eluant furnished 2,3,4,5-tetraphenylfuran (2) (0.2 g); m.p. 166°; 3-deuterio-4,5-dihydro-*r*-3,*t*-4,*t*-5-triphenylfuran-2(3H)-one (4) (6.8 g); m.p. 150°; τ (MeCN) 2.05–3.28 (15 H, m, ArH), 4.08 (1 H, d, *J* 8.5 Hz, 5-H), and 5.55 (1 H, d, *J* 8.5 Hz, 4-H); *rel*-(1*R*,2*R*,3*S*)-3-deuterio-1,2,3-triphenylbutane-1,4-diol (10) (3.8 g); m.p. 162°; τ (CDCl₃) 2.43–3.33 (15 H, m, ArH), 5.27 (1 H, d, *J* 3.0 Hz, 1-H), 6.24br (2 H, s, 4-H), 6.85 (1 H, m, 2-H), and 8.33br (2 H, two OH); 3-deuterio-*r*-3,*t*-4,*t*-5-triphenyltetrahydrofuran-2-ol (8) (0.5 g); m.p. 163°; τ (CDCl₃) 2.63–3.33 (15 H, m, ArH), 4.03 (2 H, m, 2- and 5-H), and 5.43–5.72 (1 H, dd, *J* 8.0 Hz, 4-H); m/e 317 (M^+); and *rel*-(1*S*,2*S*,3*S*)-3-deuterio-1,2,3-triphenylbutane-1,4-diol (13) (1.3 g); m.p. 128°; τ (CDCl₃) 2.28–3.43 (15 H, m, ArH), 4.76 (1 H, d, *J* 5.5 Hz, 1-H), 6.05 (2 H, s, 4-H), 6.58 (1 H, d, *J* 5.5 Hz, 2-H), and 7.90br (2 H, two OH).

Reduction of the Deuteriodihydrofuranone (4) with Lithium Aluminium Hydride.—A solution of the dihydrofuranone (4) (0.5 g) in dry THF (15 ml) was added dropwise to a stirred suspension of LiAlH₄ (0.4 g) in dry ether (20 ml). The mixture was refluxed for 4 h and worked up as described for (1), to furnish the diol (13) (0.4 g), m.p. 128°.

Jones Oxidation of the Deuteriotetrahydrofuranol (8).—

The cyclic hemiacetal (8) (0.1 g) was oxidized with Jones reagent as described for (7). The crude product was crystallised from benzene-n-hexane to furnish the dihydrofuranone (4) (0.07 g), m.p. 149°.

Reduction of the Furanone (1) with Lithium Aluminium Deuteride; Decomposition of the Complex with Water.—A suspension of the furanone (1) (2.0 g), LiAlD_4 (1.7 g), and dry THF (60 ml) was stirred for 4 h. The complex was decomposed with H_2O and worked up as described for (1). The crude product was chromatographed over a column of silica gel in n-hexane, with n-hexane containing increasing proportions of benzene as eluant to furnish 4-deuterio-4,5-dihydro-*r*-3,*t*-4,*t*-5-triphenylfuran-2(3*H*)-one (5) (0.6 g); m.p. 148°; τ (MeCN) 2.55—3.30 (15 H, m, ArH), 4.10 (1 H, s, 5-H), and 5.61 (1 H, s, 3-H); and *rel*-(1*R*,2*R*,3*S*)-2,4,4-tri-deuterio-1,2,3-triphenylbutane-1,4-diol (11) (0.5 g), m.p. 165—166°; τ (CDCl_3): 2.45—3.25 (15 H, m, ArH), 5.25 (1 H, s, 1-H), 6.39 (1 H, s, 3-H), and 8.33br (2 H, two OH).

3-Deuterio-4,5-dihydro-c-5-(p-hydroxyphenyl)-r-3,t-4-diphenylfuran-2(3H)-one (22).—This was prepared from the furanone (20) (0.5 g) as described for the furanone (1) by using LiAlH_4 (0.23 g) and decomposing the complex with D_2O . The crude product was crystallised from benzene to furnish the dihydrofuranone (22) (0.22 g); m.p. 187°; ν_{max} (KBr) 3 450 (OH) and 1 740 cm^{-1} (CO); τ (MeCN) 2.53—3.33 (14 H, m, ArH), 4.54 (1 H, d, J 10.5 Hz, 5-H), and 6.22 (1 H, d, J 10.5 Hz, 4-H).

4-Deuterio-4,5-dihydro-c-5-(p-hydroxyphenyl)-r-3,t-4-diphenylfuran-2(3H)-one (23).—This was prepared from the furanone (20) (0.5 g) as for the furanone (1), by using LiAlD_4 (0.23 g) and decomposing the complex with H_2O . The residue was crystallised from benzene to afford the dihydrofuranone (23) (0.18 g); m.p. 187°; τ (MeCN) 2.53—3.33 (14 H, m, ArH), 4.54 (1 H, s, 5-H), and 5.66 (1 H, s, 3-H).

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