Chemistry of Natural Compounds, Vol. 43, No. 3, 2007

ALKYLATION OF PYROCATECHOL AND RESORCINOL BY CAMPHENE

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UDC 547.565.2+547.599.2+548.737

Alkylation of pyrocatechol and resorcinol by camphene in the presence of the organoaluminum catalysts aluminum phenoxide and aluminum isopropoxide was studied.

Key words: pyrocatechol, resorcinol, camphene, organoaluminum catalysts, alkylation.

Sterically hindered dihydroxyphenols containing bulky alkyl substituents in the position *ortho* to the hydroxyls are of great interest as intermediates for synthesizing antioxidants, metal-corrosion inhibitors, medicinal preparations, and agricultural chemicals [1, 2].

Alkylation of hydroquinone by camphene in the presence of aluminum phenoxide has been studied [3]. It was found that the reaction pathway of *C*- or *O*-alkylation depended significantly on the ratio of the starting compounds.

The alkylation of polyfunctional phenols and their ethers in the presence of metal phenoxides, including aluminum phenoxide, has been little studied. The reaction of camphene with dihydroxybenzenes (resorcinol and pyrocatechol) in methylenechloride over wide-pore β-zeolite has been investigated. The products from *O*-alkylation (20-30% yield) and *C*-alkylation (20-35% yield) of the phenols were formed [4].

Herein we report results of the alkylation of pyrocatechol (**1**) and resorcinol (**9**) by camphene (**2**) in the presence of aluminum phenoxide $Al(OPh)_3$ and aluminum isopropoxide $Al(i\text{-}OPr)_3$.

Aluminum phenoxide was chosen because it is one of the most active organoaluminum catalysts [5]. However, exchange can occur if $Al(OPh)_3$ is used to alkylate difunctional phenols. This is due to reaction of the catalyst and the reagent [6] as $Al(OPh)_3 + HOC_6H_4OH \rightarrow (PhO)_2AlOC_6H_4OH + PhOH$.

The phenol produced by this reaction can undergo alkylation, thereby increasing the amount of side products. In order to avoid side reactions, $Al(i\text{-}OPr)_3$ was investigated as the catalyst.

The yields of products from alkylation of pyrocatechol (**1**) by camphene (**2**) (Scheme 1, Table 1) depended substantially on the catalyst. The yield of products was 29% if $Al(OPh)_3$ was used; 54%, $Al(i\text{-}OPr)_3$. The ratio of the starting compounds affected the selectivity of the reaction. The reaction of pyrocatechol and camphene formed the *O*- and *C*-alkylated products, the structures of which were established by IR, PMR, and ^{13}C NMR spectroscopy.

Alkylation at 160°C formed a monoether of pyrocatechol with the isobornyl structure for the terpene substituent (**3**) as the main product regardless of the catalyst used. Terpenophenols **6**, **7**, and **8** were formed through *C*-alkylation with a 2:1 ratio of **1**:**2** in the presence of $Al(i\text{-}OPr)_3$. In addition to these products, alkylation of pyrocatechol formed a mixture of isocamphyl (**4**) and isophenchyl (**5**) monoethers.

Performing the reaction at 180-200°C alkylated the aromatic ring to form monosubstituted (84%) and dialkylated (13%) pyrocatechols.

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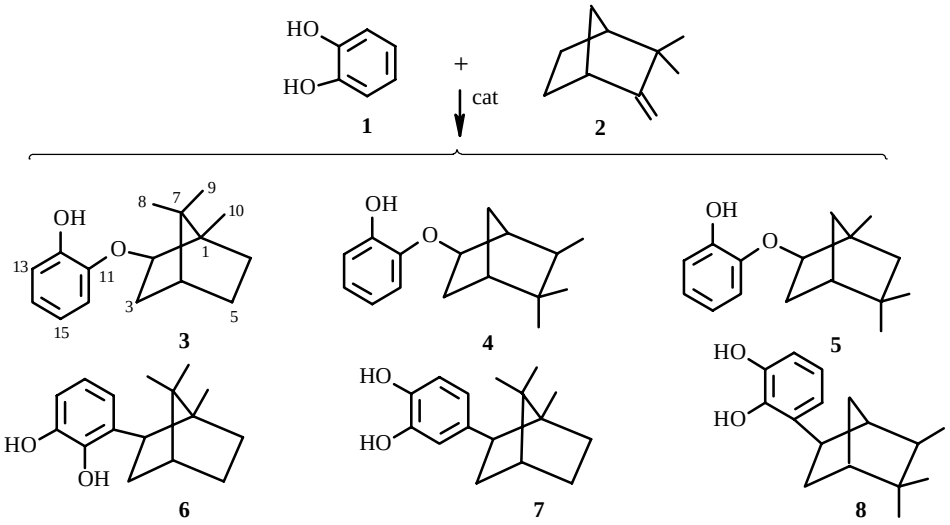
0009-3130/07/4303-0245

TABLE 1. Reaction Conditions and Products from Alkylation of Pyrocatechol by Camphene

Ratio **1**:**2**	Catalyst, temperature, °C	Product yield, %	Monoethers, %		Monoalkylated pyrocatechol, %		
			3	mixture of ethers	**6**	**8**	**7**
1:1	$(PhO)_3Al$ 160-170	29	68.0	9.9	17.0	-	-
	$(i\text{-}PrO)_3Al$ 160-170	54	62.3	13.1	14.0	5.3	4.9
	$(i\text{-}PrO)_3Al$ 200	84	-	13*	36.5	31	19.5
1:2	$(PhO)_3Al$ 160-170	27	75.5	7.4	13.0	0.5	3.0
	$(i\text{-}PrO)_3Al$ 160-170	35	72.0	11.2	11.6	-	3.17
2:1	$(PhO)_3Al$ 160-170	22	55.5	2.0	20.6	4.0	13.3
	$(i\text{-}PrO)_3Al$ 160-170	26	12.0	-	49.0	16.0	22.0

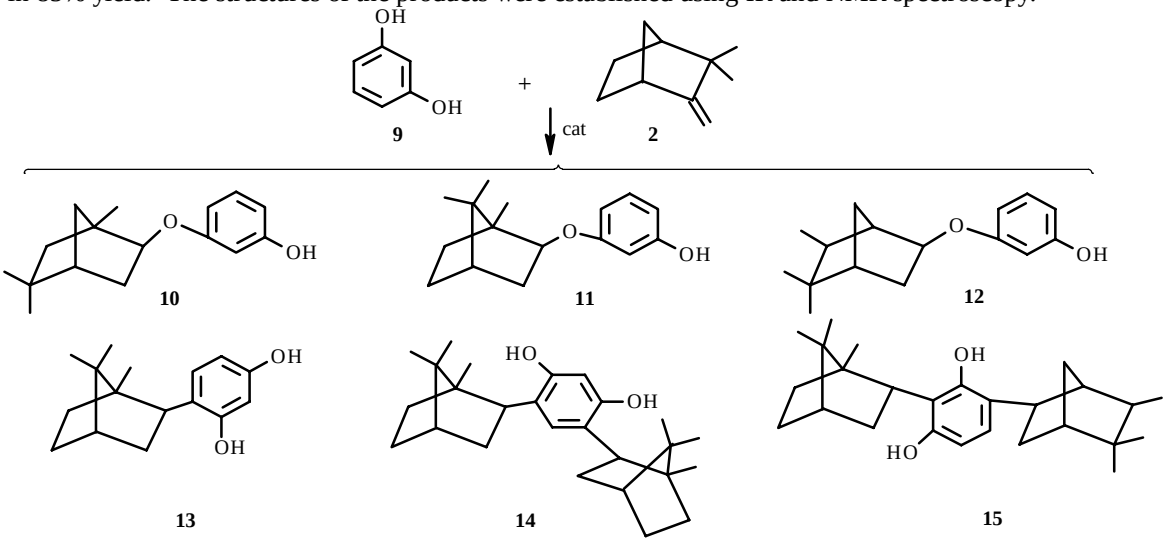
*Difficultly separated diethers and dialkylated pyrocatechols.



cat = $(PhO_3)Al$; $(i\text{-}PrO_3)Al$

Scheme 1.

Alkylation of resorcinol (**9**) by camphene (**2**) (Scheme 2, Table 2) produced a mixture of the *C*- and *O*-alkylated products in 85% yield. The structures of the products were established using IR and NMR spectroscopy.



cat = $(PhO_3)Al$; $(i\text{-}PrO_3)Al$

Scheme 2.

TABLE 2. Reaction Conditions and Products from Alkylation of Resorcinol by Camphene*

Ratio **9**:**2**	Catalyst	Alkylated products, %			
		mixture of ethers	**13**	**14**	**15**
1:1	$(PhO)_3Al$	8	53	23	7
1:1	$(i\text{-}PrO)_3Al$	5	46	40	5
2:1	$(i\text{-}PrO)_3Al$	7	17	50	25

*Product yield 85.0%.

An interesting feature of the alkylation of resorcinol was the formation of the ether with an isophenchyl substituent (**10**) as the main monoether of resorcinol. Alkylation of other phenols produced isophenchyl ethers as side products. According to PMR spectroscopy, the ratio of ethers **10**:**11**:**12** was 9:2:1, respectively.

Because of the synergistic orientational effect of the resorcinol hydroxyls, the reaction was completed significantly faster than for pyrocatechol, had a more complicated isomeric composition, and gave a rather high yield of the disubstituted resorcinol (**14**) regardless of the reagent ratio. Furthermore, a phenol with both isobornyl and isocamphyl substituents (**15**) was isolated.

EXPERIMENTAL

IR spectra were recorded on a Specord M-80 instrument as solids in KBr disks or in a thin layer of liquid; PMR and ^{13}C NMR spectra in $CDCl_3$, on a Bruker AM spectrometer (working frequency 300 and 75 MHz, respectively) using the $CHCl_3$ signals (δ_H 7.21 and δ_C 76.90 ppm) as internal standards. The purity of starting materials and the analysis of products were performed using GC on a Kristall 2000M chromatograph with a capillary column (60 m × 0.25 mm, 0.25 μm), HP-5MS, temperature program 100-240°C at 6°C per minute, flame-ionization detector, and He carrier gas. Melting points were determined on a Kofler stage. The course of reactions was monitored by TLC on Sorbfil plates using hexane:diethylether (3:1 and 1:1). Plates were developed using $KMnO_4$ solution ($KMnO_4$, 25 g; H_2O, 300 mL; conc. H_2SO_4, 0.5 mL) and vanillin solution (vanillin, 1 g; conc. H_2SO_4, 5 mL; ethanol, 95%, 100 mL) with subsequent heating to 100-150°C. Column chromatography used silica gel L (100-200 μ).

Alkylation of Pyrocatechol by Camphene in the Presence of Organoaluminum Catalysts. A 100-mL two-necked flask equipped with a thermometer and reflux condenser was charged with phenol (0.59 g) and heated to 160°C and treated in small portions with aluminum chips (0.06 g). After the aluminum was completely dissolved, the solution was cooled to 40°C and treated with pyrocatechol (6.46 g, 57 mmol) and camphene (8 g, 59 mmol). For $Al(i\text{-}OPr)_3$, the reagents were added simultaneously. The reaction was carried out keeping the temperature at 160-170°C until camphene was completely reacted (GC and TLC monitoring). When the reaction was complete, the mixture was cooled, diluted with diethylether, treated with HCl solution (50%) to decompose the catalyst, and washed with saturated $NaHCO_3$ solution and water until the rinsings were neutral. The organic layer was dried over anhydrous Na_2SO_4. The solvent was evaporated. Unreacted pyrocatechol was separated by precipitation with hexane from diethylether.

Products were separated by column chromatography over silica gel L (100/200 μ) with elution by petroleum ether or hexane:diethylether with increasing amount of the latter. This isolated the pyrocatechol alkylation products.

2-{[Exo-1,7,7-trimethylbicyclo-[2.2.1]hept-2-yl]hydroxy}phenol (3), mp 72°C. IR spectrum (KBr, ν, cm^{-1}): 3560 (phenol –OH), 1262 and 1060 (=C–O–C), 1602, 1506 (C=C), 744 (s) and 826 (=C–H), 1372 and 1394 [$C(\underline{CH_3})_2$].

PMR spectrum (300 MHz, $CDCl_3$, δ, ppm): 1.14 (s, CH_3-10), 1.07 (s, CH_3-9), 0.95 (s, CH_3-8), 4.18-4.15 (m, H-5), 5.62 (s, OH), 6.87-6.92 (2H, m, H-13, H-15), 6.98-6.99 (m, H-14).

^{13}C NMR spectrum (75 MHz, $CDCl_3$, δ, ppm): 20.25 (C-10), 20.13 (C-9), 11.87 (C-8), 47.0 (C-7), 39.48 (C-6), 27.16 (C-5), 45.12 (C-4), 34.08 (C-3), 85.57 (C-2), 49.21 (C-1), 146 (C-11), 144 (C-12), 114 (C-13), 120.85 (C-14), 119.88 (C-15), 112.16 (C-16).

Mixture of monoethers (4) and (5). IR spectrum (KBr, ν, cm^{-1}): 3556 (–OH), 1262 (m) and 1032 (ν_s =C–O–C), 1602 and 1506 (C=C), 3064, 742, and 828 (=C–H), 1392 and 1368 [$C(\underline{CH_3})_2$].

PMR spectrum (300 MHz, $CDCl_3$, δ, ppm) (**4**): 0.95, 0.96, 0.98 (s, CH_3-10, CH_3-9, CH_3-8), 4.24-4.3 (m, H-5), 5.68 (1H, s, OH).

^{13}C NMR spectrum (75 MHz, $CDCl_3$, δ, ppm): 15.7 (C-10), 27.17 (C-9), 24.34 (C-8), 32.58 (C-7), 34.74 (C-6), 81.02 (C-5), 50.89 (C-4), 43.21 (C-3), 38.85 (C-2), 48.23 (C-1), 146.12 (C-11), 144.07 (C-12), 114.38 (C-13), 121.02 (C-14), 119.9 (C-15), 112.07 (C-16).

PMR spectrum (300 MHz, $CDCl_3$, δ, ppm) (**5**): 0.86, 0.93, 1.03 (s, CH_3-10, CH_3-9, CH_3-8), 4.55-4.58 (m, H-5), 5.70 (1H, s, OH).

^{13}C NMR spectrum (75 MHz, $CDCl_3$, δ, ppm): 11.09 (C-10), 14.09 (C-9), 21.17 (C-8), 30.29 (C-7), 34.11 (C-6), 75.3 (C-5), 36.23 (C-4), 31.88 (C-3), 36.22 (C-2), 48.23 (C-1), 146.07 (C-11), 144.7 (C-12), 114.38 (C-13), 120.89 (C-14), 119.32 (C-15), 112.28 (C-16).

3-[Exo-1,7,7-trimethylbicyclo-[2.2.1]hept-2-yl]benzen-1,2-diol (6), mp 112°C. IR spectrum (KBr, ν, cm^{-1}): 3528 and 3444 (–OH), 1288 and 1182 (=C–O), 1626 and 1594 (C=C), 3040, 738, and 780 (=C–H), 1392 and 1378 [$C(\underline{CH_3})_2$].

PMR spectrum (300 MHz, $CDCl_3$, δ, ppm): 0.82, 0.87, 0.92 (s, CH_3-10), CH_3-9, CH_3-8), 1.33-1.53 (m, 2H-6), 1.60-1.72 (m, 2H-5), 1.87-1.93 (m, 2H-3), 2.16-2.25 (m, H-4), 3.14 (t, H-2), 5.3 and 5.16 (1H each, s, 2OH), 6.71-6.8 (s, H-16), 6.93-6.95 (m, 2H-14,15).

^{13}C NMR spectrum (75 MHz, $CDCl_3$, δ, ppm): 12.38 (C-10), 20.27 (C-9), 21.37 (C-8), 47.94 (C-7), 34.1 (C-6), 27.5 (C-5), 45.55 (C-4), 39.97 (C-3), 45.63 (C-2), 49.91 (C-1), 130.49 (C-11), 142.63 (C-12), 143.15 (C-13), 112.5 (C-14), 120.47 (C-15), 119.32 (C-16).

3-[Exo-2,2,3-trimethylbicyclo-[2.2.1]hept-2-yl]benzen-1,2-diol (8), mp 120°C.

PMR spectrum (300 MHz, $CDCl_3$, δ, ppm): 0.92, 0.94, 1.08 (s, CH_3-10, CH_3-9, CH_3-8), 2.91 (t, H-5), 5.24 and 5.18 (1H each, s, 2OH), 1.35-1.49 (3H, m, H-6, H-7), 1.63-1.88 (3H, m, H-7, H-1, H-4), 2.17-2.34 (m, H-3, H-2), 6.71-6.95 (m, 3H, arom.).

^{13}C NMR spectrum (75 MHz, $CDCl_3$, δ, ppm): 16.2 (C-10), 27.6 (C-9), 24.8 (C-8), 33.5 (C-7), 40.7 (C-6), 32.6 (C-5), 50.9 (C-4), 39.6 (C-3), 48.8 (C-2), 49.7 (C-1), 134 (C-11), 141.4 (C-12), 143.1 (C-13), 112 (C-14), 120 (C-15), 118 (C-16).

4-[Exo-1,7,7-trimethylbicyclo-[2.2.1]hept-2-yl]benzen-1,2-diol (7), mp 116°C. IR spectrum (KBr, ν, cm^{-1}): 3452 (–OH), 1260 (=C–O), 1608 and 1528 (C=C), 816, 884 (=C–H).

Alkylation of resorcinol with camphene in the presence of organoaluminum catalysts was carried out analogously to the method described above to afford the following compounds.

Mixture of monoethers (10), (11), and (12). IR spectrum (KBr, ν, cm^{-1}): 3412 (–OH), 1152 (=C–O–C), 1600-1506 (C=C), 1384-1390 [$C(\underline{CH_3})_2$], 784 (=C–H).

PMR spectrum (300 MHz, $CDCl_3$, δ, ppm) (**10**): 0.93, 0.91, 0.89 (s, CH_3-10, CH_3-9, CH_3-8), 3.06-3.1 (t, H-2), 4.99 (s, 1OH), 6.32-6.37 (H-14,16), 6.43-6.46 (H-12,15).

^{13}C NMR spectrum (75 MHz, $CDCl_3$, δ, ppm): 49.33 (C-1), 84.5 (C-2), 35.19 (C-3), 29.68 (C-4,5), 33.86 (C-6), 29.68 (C-7), 27.34 (C-8), 24.99 (C-9), 15.13 (C-10), 156.6 (C-11), 108.73 (C-12), 154.64 (C-13), 126.48 (C-14), 118.93 (C-15), 130.37 (C-16).

PMR spectrum (300 MHz, $CDCl_3$, δ, ppm) (**11**): 1.09, 1.07, 1.05 (s, CH_3-10, CH_3-9, CH_3-8), 4.01-3.99 (t, H-2), 5.01 (s, OH), 6.85-6.89 (H-14,16).

^{13}C NMR spectrum (75 MHz, $CDCl_3$, δ, ppm): 45.25 (C-1), 84.5 (C-2), 35.19 (C-3), 29.68 (C-4,5), 39.49 (C-6), 37.64 (C-7), 20.30 (C-8), 20.08 (C-9), 11.76 (C-10), 156.6 (C-11), 108.73 (C-12), 154.64 (C-13), 126.5 (C-14), 118.93 (C-15), 130.37 (C-16).

PMR spectrum (300 MHz, $CDCl_3$, δ, ppm) (**12**): 0.99, 0.98, 0.97 (s, CH_3-10, CH_3-9, CH_3-8), 3.35-3.39 (t, H-2), 4.01 (s OH), 7.07-7.12 (H-14,16).

^{13}C NMR spectrum (75 MHz, $CDCl_3$, δ, ppm): 40.09 (C-1), 84.5 (C-2), 48.65 (C-3), 39.49 (C-4), 49.33 (C-5), 50.6 (C-6), 33.63 (C-7), 27.85 (C-8), 24.99 (C-9), 16.43 (C-10), 156.6 (C-11), 109.15 (C-12), 154.64 (C-13), 126.5 (C-14), 118.93 (C-15), 130.37 (C-16).

4-[Exo-1,7,7-trimethylbicyclo-[2.2.1]hept-2-yl]benzen-1,3-diol (13). IR spectrum (KBr, ν, cm^{-1}): 3356 (–OH), 1286 (=C–OH), 1624 and 1524 (C=C), 936 and 846 (=C–H), 1390 and 1360 [$C(\underline{CH_3})_2$].

PMR spectrum (300 MHz, $CDCl_3$, δ, ppm): 0.77, 0.82, 0.86 (s, CH_3-10, CH_3-9, CH_3-8), 1.22-1.4 (m, 2H-6), 1.56-1.6 (m, 2H-5), 1.81-1.84 (m, 2H-3), 2.11-2.14 (m, H-4), 2.9-3.0 (t, H-2), 5.0-5.3 (1H each, s, 2OH), 6.3-6.38 (m, H-13), 7.1-7.25 (m, 2H-11,12).

^{13}C NMR spectrum (75 MHz, $CDCl_3$, δ, ppm): 49.51 (C-1), 45.52 (C-2), 39.81 (C-3), 45.01 (C-4), 27.47 (C-5), 33.38 (C-6), 47.92 (C-7), 21.42 (C-8), 20.18 (C-9), 12.33 (C-10), 155.59 (C-11), 122.02 (C-12), 106.96 (C-13), 128.9 (C-14), 154.02 (C-15), 102.68 (C-16).

4,6-Di-[exo-1,7,7-trimethylbicyclo-[2.2.1]hept-2-yl]benzen-1,3-diol (14). IR spectrum (KBr, ν, cm $^{-1}$): 3532 and 3352 (–OH), 1286 (=C–OH), 1390 and 1380 [$C(\underline{CH_3})_2$], 1622 and 1524 (C=C), 852 (=C–H).

PMR spectrum (300 MHz, $CDCl_3$, δ, ppm): 0.76, 0.81, 0.82 (s, CH_3-10, CH_3-9, CH_3-8), 1.28-1.39 (m, 2H-6), 1.57-1.62 (m, 2H-5), 1.82-1.84 (m, 2H-3), 2.12-2.13 (m, H-4), 2.96-3.0 (t, H-2), 4.6 (1H each, s, 2OH), 6.27 (m, H-12), 7.19 (m, 2H-15).

^{13}C NMR spectrum (75 MHz, $CDCl_3$, δ, ppm): 49.5 (C-1), 45.39 (C-2), 40.01 (C-3), 45.55 (C-4), 27.54 (C-5), 34.23 (C-6), 47.86 (C-7), 21.48 (C-8), 20.22 (C-9), 12.44 (C-10), 152.86 (C-11,13), 102.47 (C-12), 120.36 (C-14,16), 127.92 (C-15).

2,4-Di-[exo-1,7,7-trimethylbicyclo-[2.2.1]hept-2-yl]benzen-1,3-diol (15). PMR spectrum (300 MHz, $CDCl_3$, δ, ppm): 0.76, 0.83, 0.86 (s, CH_3-10′, CH_3-9′, CH_3-8′), 1.04-1.03 (m, 2H-6′), 1.33-1.41 (m, 2H-5′), 1.79-1.88 (m, 2H-3′), 2.26-2.32 (m, H-4′), 2.89-2.94 (t, H-2′), 0.89, 0.9, 0.92 (s, CH_3-10, CH_3-9, CH_3-8), 1.19-1.26 (m, 2H-7), 0.96-0.99 (m, H-6), 2.13-2.2 (m, 2H-4), 1.56-1.65 (m, 2H-3), 3.02-3.08 (t, H-2), 4.72 (1H each, s, 2OH), 6.26-6.29 (m, H-14), 6.93-6.95 (m, 2H-15).

^{13}C NMR spectrum (75 MHz, $CDCl_3$, δ, ppm): 50.52 (C-1), 49.33 (C-2), 35.39 (C-3), 50.58 (C-4), 34.2 (C-5), 41.09 (C-6), 50.58 (C-7), 27.87 (C-8), 24.98 (C-9), 16.45 (C-10), 34.25 (C-1′), 27.82 (C-2′), 45.46 (C-3′), 40.03 (C-4′), 45.78 (C-5′), 49.31 (C-6′), 40.03 (C-7′), 21.43 (C-8′), 20.15 (C-9′), 12.33 (C-10′), 151.9 (C-11), 136.94 (C-12), 150.5 (C-13), 125.17 (C-14), 107.59 (C-15), 128.8 (C-16).

ACKNOWLEDGMENT

The work was supported by the Russian Foundation for Basic Research (Grant No. 06-03-08168) and the RF President (Program for Support of Leading Scientific Schools, Grant NSh 1206.2006.3).

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