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Tungsten Pentacarbonyl as a Potential Protecting Group for Soft Lewis Base Centres in Alkylation of Multifunctional Molecules.

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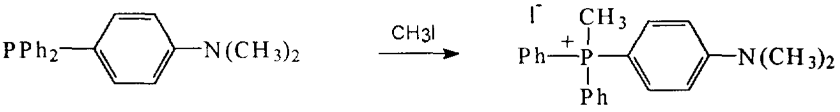
Abstract. Reaction of $W(CO)_6$ or $(PhNH_2)W(CO)_5$ with the molecules which possess both diphenylphosphanyl- and dialkylamino group or nitrogen - containing heterocyclic ring proceeds selectively through "soft" Lewis base groups and can be used for the protection of the groups from alkylation. As a rule, the diphenylphosphanyl group participates in the co-ordination, but in some cases an sp^2-hybridized nitrogen was shown to be the preferable co-ordination site. The new synthesized compounds have been characterized by NMR, IR spectroscopy, and elemental analysis.

Transition metal complexes have enjoyed the widest application in highly selective chemical transformations. As a rule, the complexes have been used as catalysts or reagents. We reported recently[1] the utilization of some complexes also as selective inhibitors of undesirable reactions. It has been shown that chemical transformations of a multifunctional molecule can proceed selectively in the presence of these complexes involving the least reactive groups while more reactive centres are protected by co-ordination with the metal ion. Selectivity of the protection can be achieved with appropriately chosen metal complexes possessing high co-ordination selectivity. Lanthanide tris-β-diketonates, as "hard" Lewis acids, turned out to be most suitable to block "hard" Lewis base functional groups allowing selective alkylation[2] or catalytic hydrogenation[3] of some difunctional molecules.

It seemed reasonable to undertake a search for "soft" metal complexes which would be capable, similarly to the lanthanide complexes, to recognize and protect "soft" Lewis base groups in a multifunctional molecule. We wish to report here the results of this search.

The necessity of "soft" functional group protection arises, for example, during the synthesis of the phosphines containing a quaternary ammonium group, because alkylation of a dialkyl(or diaryl)phosphanyl group often proceeds more rapidly then that of a dialkylamino group. Scheme (1) is a typical example from textbooks[4]:



1

Scheme (1)

Selective alkylation of the nitrogen atom in **1** requires the diphenylphosphanyl group protection, for instance, by oxidation[5]. So, **1** is a convenient model compound to evaluate the proposed approach to the "soft" functional group protection by metal complexes.

Using metal complexes for the protection, one would have to add a complex to the reaction mixture which, ideally, a) would bind reversibly with the substrate **1** through the phosphorus atom exclusively, or at least preferably; b) would remain unchanged after the isolation of the reaction end product. Our previous results with lanthanide tris-β-diketonates showed, that the complex has also to co-ordinate effectively the group to be protected in final compound so that the dialkylation of the substrate would not take place[2].

We examined first some palladium(II) complexes, but they did not meet the requirements a) or b). For example, allylpalladium chloride dimer reacts with **1** through the phosphorus atom and the complex formed can then be N-alkylated without isolation. However, the N-alkylated phosphine is a good ligand for Pd and therefore difficult to recover from the metal complex. Other complexes which have been tested -- *bis*(pentane-2,4-dionato)palladium(II) and *bis*(1,1,1-trifluoro-5,5-dimethylhexane-2,4-dionato)palladium(II) -- undergo alkylation under the reaction conditions.

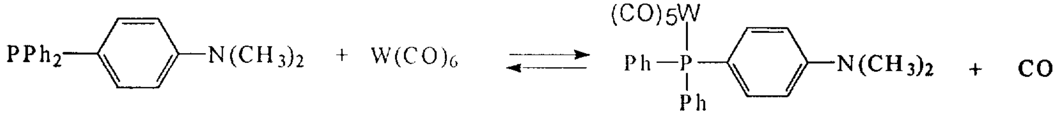
The progress was achieved with tungsten hexacarbonyl. We were led to investigate the possibility to employ metal carbonyls by the fact that they have been used for protection, for example, in peptide synthesis[6].

It is well-known that $W(CO)_6$ reacts readily with tertiary phosphines: the reaction (scheme (2)) is reversible, and the phosphine ligand can be recovered by CO treatment under pressure or UV-irradiation[7].

$$W(CO)_6 \quad + \quad R_3P \quad \rightleftharpoons \quad (R_3P)W(CO)_5 \quad + \quad CO \qquad \text{Scheme (2)}$$

It was of importance to investigate if $W(CO)_6$ coordinates selectively with a phosphine group in the presence of a dialkylamino group or an sp^2-hybridized nitrogen. We have established, that the co-ordination of $W(CO)_5$ is very selective and proceeds, as a rule, with the groups which normally undergo alkylation by alkyl halides or alkyl sulfates.

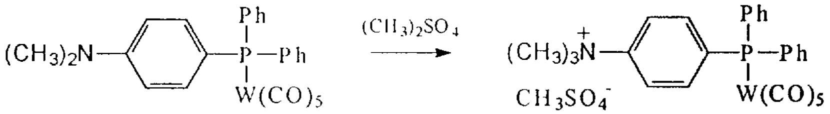
As expected, the reaction of $W(CO)_6$ with **1** leads to the complex **2**, where the "soft" tungsten atom binds the "soft" diphenylphosphanyl group (scheme (3)).



1 2

Scheme (3)

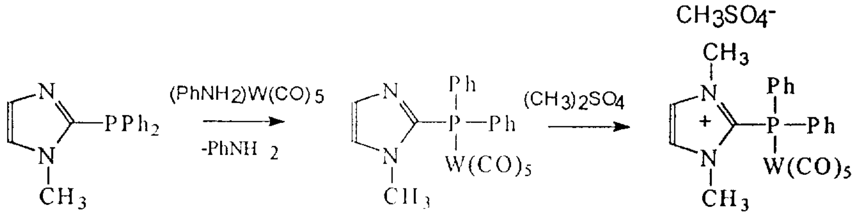
$Mo(CO)_6$ and $Cr(CO)_6$ react analogously with **1**, but tungsten complexes are preferable because of their higher thermal and atmospheric stability. As the dimethylamino group is not co-ordinated in **2**, it is accessible to alkylating reagents (scheme (4)):



2 3

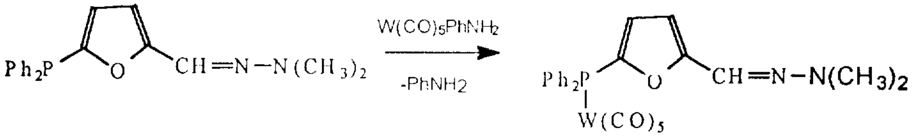
Scheme (4)

Reaction (3) was performed in boiling diglyme. These conditions turned out unacceptable in the case of phosphines containing a heterocyclic ring because of decomposition of the starting materials. The complex with the labile ligand -- pentacarbonyl(aniline)tungsten -- have been used successfully in lieu of $W(CO)_6$ (schemes (5), (6)):



4 5 6

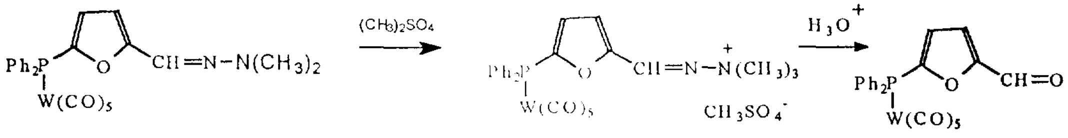
Scheme (5)



7 8

Scheme (6)

The compounds **2**, **3**, **5**, **6**, **8** with the protected diphenylphosphanyl group can be isolated by liquid chromatography. They are stable enough, so after alkylation further useful chemical transformations can be performed (scheme (7)):



8 **9** **10**

Scheme (7)

The reactions (3), (5), (6) were followed by ^{31}P-NMR spectroscopy. ^{31}P-NMR signals of the reaction end products, as a rule, are shifted downfield in comparison with those of the starting phosphines (Table 1). However, the reaction between $(PhNH_2)W(CO)_5$ and imidazo[1,2-a]pyridine derivatives **11** and **12** proceeded without considerable changes in ^{31}P-NMR spectrum of the reaction mixture, that has cast some doubt on the diphenylphosphanyl group participation in the co-ordination. The reaction could, in principle, involve aromatic π-system or sp^2-hybridized nitrogen atoms in **11**, **12**. The latter hypothesis seemed highly improbable: the known examples of the monosubstituted tungsten hexacarbonyl derivatives with the phosphines containing a donor nitrogen atom are the complexes with the W-P bond[5] The structure of one of the complexes --**13** -- has been conclusively established by X-ray analysis. The results (Fig. 1 and Table 2) unequivocally showed that the 3-nitrogen atom co-ordinates with tungsten while the diphenylphosphanyl group does not.

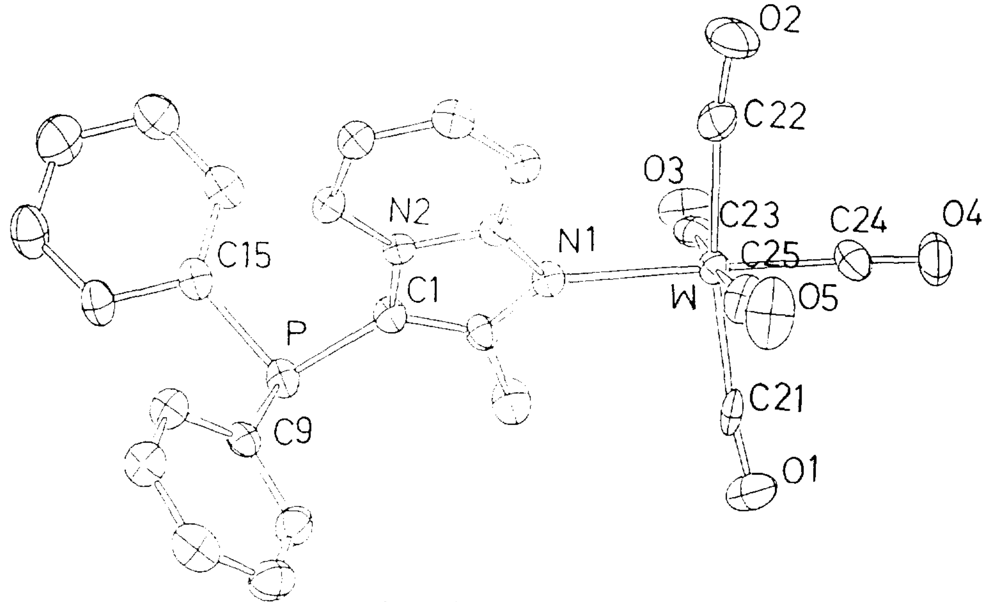
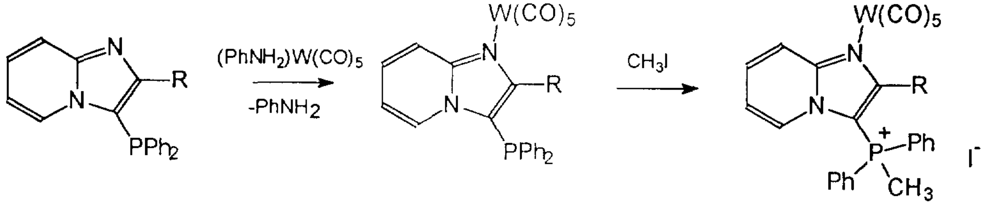


Figure 1. X-Ray structure of **13**.

It is noteworthy, that the heterocyclic compounds **11**, **12** react with alkylating reagents through the 3-nitrogen atom[8]. The tungsten co-ordination can serve in this case as a protection for the sp2-hybridized nitrogen (Scheme (8)):



11, R=CH$_3$
12, R=Ph

13, R=CH$_3$
14, R=Ph

Scheme (8)

The recovering of the modified phosphine ligand was tested with the complex **3**. Two problems have come to light. The reaction between **3** and CO requires quite vigorous conditions: UV irradiation or high pressure. We have observed that the ligand exchange with CO proceeds also in the presence of a heterogeneous catalyst - Pd/C. However, it is difficult to shift the equilibrium to obtain the phosphine with a reasonable yield. In addition, the phosphine recovered is highly susceptible to oxidation. The rearrangement which leads to P-alkylated products is also possible. One way around these problems is to use the complexes which undergo ligand exchange under milder conditions. The compounds which exhibit associative mechanisms of the ligand exchange[9] are among the possible candidates.

EXPERIMENTAL

General Procedures. All the NMR spectra were measured with a Bruker NMR spectrometer at 100.13 MHz for protons. Tetramethylsilane was used as an internal standard for ^{1}H-NMR spectra, 20% H_3PO_4 in D_2O was an external standard for ^{31}P-NMR measurements. IR spectra were taken on SP3-300 Pye Unicam infrared spectrophotometer. Melting points were measured on a hot stage and are uncorrected. Physical properties, spectral parameters, the data of elemental analysis, and yields of the new synthesized compounds are listed in Table 1. (Aniline)pentacarbonyltungsten was obtained from $W(CO)_6$ and excess of aniline in tetrahydrofurane under UV irradiation.The synthesis of the starting heterocycles was performed using the reported procedures[8,10,11].

X-Ray determinations. Crystal data for 13: $C_{25}H_{17}N_2O_5PW$, M=640.25, monoclinic, a=9.620(2), b=12.009(2), c=20.856(5) A, β=92.30(2)°, V=2407.4 A^3, z=4, d_{calc}=1.77 g/cm^3, space group P2$_1$/c (N14),

$\mu=50.0\ cm^{-1}$, F(000)=1240.

Crystallographic measurements were made at 20°C using the Enraf-Nonius CAD-4 diffractometer operating in the ω-2θ scan mode (the ratio of the scanning rates $\omega/\theta=1.2$). The intensity data were collected within the range $1<\theta<28°$ using graphite monochromated Mo-K_α radiation ($\lambda=0.71073$ A). Intensities of 4583 unique reflections were measured. The structure was solved by direct methods and refined by full-matrix least-squares with the weighting scheme $\omega=1/\sigma^2(F_0)$. In the refinement, 3190 reflections with $I>3\sigma$ were used. About 75% of the hydrogen atoms were located in the difference Fourier maps, the position of the remaining atoms were calculated. All the hydrogen atoms were included in the final refinement with the fixed positional and thermal ($B_{iso}=4\ A^2$) parameters. Convergence was obtained at R=0.031 and $R_W=0.037$, GOF=1.24. The calculations were performed using the SDP-PLUS program. The atomic co-ordinates and bond lengths and angles have been deposited at the Cambridge Crystallographic Data Center.

Crystals of **13** suitable for X-ray analysis were obtained by slow (4 days) crystallization of the compound (150 mg) from a hot cyclohexane-hexane mixture (1:3, 8 ml) in an argon atmosphere. Rapid crystallization may lead to formation of a solvate - two molecules of cyclohexane per a molecule of **13**.

Pentacarbonyl[(4-diphenylphosphanylphenyl)-dimethylamine-κP]tungsten (2) $W(CO)_6$ (898.7 mg, 2.55mmol) and **1** (692.1 mg, 2.27 mmol) were refluxed in dry diglyme (30 ml) under an argon atmosphere for 3 h. Argon was passed through the hot reaction mixture to remove the unreacted $W(CO)_6$. The solution was filtered and evaporated in vacuum to 2-3 ml, then diluted with hexane (20 ml). The solid was recrystallized twice from a chloroform-hexane mixture (1:2) to obtain **2** (890 mg, 55.5 % yield).

Pentacarbonyl[(4-diphenylphosphanylphenyl)-trimethylaminium–κP]tungsten methylsulfate (3). The mixture of **2** (293.2 mg, 0.47 mmol), $(CH_3)_2SO_4$ (0.132 ml, 1.39 mmol) and benzene (10 ml) were refluxed under an argon atmosphere for 20h. The solution was cooled to room temperature and the crystalline product was filtered, washed with benzene, dissolved in methanol (1.5 ml). The methanol solution was then filtered, and pure **3** (228.8 mg, 65%yield) was obtained by precipitation with benzene (20 ml).

Pentacarbonyl(2-diphenylphosphanyl-1-methyl-1H-imidazole–κP)tungsten (5), pentacarbonyl[N'-(5-diphe-nylphosphanylfuran-2-ylmethylene)-N,N-dimethylhydrazine–κP]tungsten, (8) pentacarbonyl(3-diphenyl-phosphanyl-2-methylimidazo-κN^1-[1,2-a]pyridine)tungsten (13) and pentacarbonyl(3-diphenylphosphanyl-2-phenylimidazo-κN^1-[1,2-a]pyridine)tungsten (14) were obtained by the following common procedure.

$(PhNH_2)W(CO)_5$ (417 mg, 1 mmol) and a corresponding heterocyclic compound (0.95 mmol) were dissolved in benzene (10 ml) under an inert atmosphere. The reaction was monitored by ^{31}P-NMR and TLC (Silufol UV-250, benzene as an eluent). After the reaction was complete (8-24 h), the solvent was evaporated in vacuum and the remained solid was applied to a chromatography column (25x1 cm, Silicagel Merck 60, benzene as an eluent) to give the reaction end product

Pentacarbonyl[N'-(5-diphenylphosphanylfuran-2-ylmethylene)-N,N,N-trimethylhydrazinium–κP]tungsten methylsulfate, (9). The starting complex, pentacarbonyl[N'-(5-diphenylphosphanylfuran-2-ylmethylene)-,N,N-dimethylhydrazine–κ-P]tungsten **8** (100 mg, 0.15 mmol) was dissolved in benzene (10 ml) and $(CH_3)_2SO_4$ (0.073 ml, 0.77 mmol) was added. The solution was brought to reflux for 24 h. The alkylated complex **9** was crystallized from the reaction mixture at room temperature. The crystals (82.2 mg, 71%) were filtered, and washed with benzene. The complex **5** was alkylated analogously to obtain **6** in 77% yield.

Pentacarbonyl(5-diphenylphosphanylfuran-2-carbaldehyde)tungsten (10). The complex **9** (50 mg, 0.06 mmol) was boiled in 1M HCl (2 ml) for about a minute. The starting compound was dissolved first, then the formation of the insoluble **10** was observed. After cooling to room temperature the product was filtered, washed with water, and dried in vacuum over P_4O_{10} (30.2 mg, 83.3% yield).

Table 1. Physical Properties, Spectral Parameters, the Data of Elemental Analysis, and Yields of the New Synthesized Compounds

Comp N°	**Color**	**Melting point, °C**	**Spectral data**	**Data of elemental analysis**	**Yield %**
2	light-green	166-168	^{1}H-NMR (CDCl$_3$, δ): 7.30-7.50 (m, 12H); 6.69 (dd, ^3J=8.5 Hz, ^4J=1.5 Hz, 2H); 3.00 (s, 6H); ^{31}P-NMR (CDCl$_3$, δ): 17 ($^1J_{W\text{-}P}$=260 Hz); IR (KBr, cm^{-1}): $\nu_{C=O}$ 1940, 2080.	Calcd. for $C_{25}H_{20}NO_5PW$: C, 47.72; H, 3.20; N, 2.23. Found: C, 47.81; H, 3.25; N, 2.54.	55.5
3	white	198-200	^{1}H-NMR (CD$_3$OD, δ): 8.08 (d, ^3J=8.8 Hz, 2H); 7.30-7.80 (m, 12H); 3.69 (s, 9H), 3.65 (s, 3H); ^{31}P-NMR (CD$_3$OD, δ): 22 ($^1J_{W\text{-}P}$=260 Hz); IR (KBr, cm^{-1}): $\nu_{C=O}$ 1950, 2090	Calcd. for $C_{27}H_{26}NO_9PSW$: C, 42.93; H, 3.47; N, 1.85. Found: C, 43.02; H, 3.50; N, 1.91	65
6	white	164-166	^{1}H-NMR (CD$_3$OD, δ): 7.35-8.00 (m, 12H); 3.67 (s, 9H); ^{31}P-NMR (CD$_3$OD, δ): 17 (s)	Calcd. for $C_{23}H_{21}N_2O_9PSW$: C, 38.56; H, 2.96; N, 3.91. Found: C, 38.55; H, 2.99; N, 3.87	77

Table 1 (continued).

8	green-yellow	106-108	^{1}H-NMR (C_6D_6, δ): 7.35-7.50 (m, 4H); 7.15 (s, 1H); 6.7-7.00 (m, 6H), 6.38-6.50 (m, 2H); 2.33 (s, 6H); ^{31}P-NMR (C_6D_6, δ): 4.6; IR (KBr, cm^{-1}): $\nu_{C=O}$ 1950, 2090; $\nu_{C=N}$ 1565	Calcd. for $C_{24}H_{19}N_2O_6PW$: C, 44.6; H, 2.96; N, 4.35. Found: C, 44.0; H, 2.83; N, 4.30	78
9	white	154-156 decomp.	^{1}H-NMR (CD_3OD, δ): 8.94 (s, 1H); 7.30-7.85 (m, 11H); 6.74 (d, 1H); 3.66 (s, 3H); 3.52 (s, 9H). ^{31}P-NMR (CD_3OD, δ): 6.0. IR (KBr, cm^{-1}): $\nu_{C=O}$ 1910, 1980, 2050; $\nu_{C=N}$ 1630.	Calcd. for $C_{26}H_{25}N_2O_{10}PSW$: C, 40.43; H, 3.26; N, 3.63. Found: C, 40.48; H, 3.29; N, 3.55	71
10	white	114-116	^{1}H-NMR ($CDCl_3$, δ): 9.75 (s, 1H); 7.35-7.68 (m, 11H); 6.61 (d, 1H). ^{31}P-NMR ($CDCl_3$, δ): 8.0. IR (KBr, cm^{-1}) : $\nu_{C=O}$ 1980; 2060; $\nu_{CH=O}$ 1680.	Calcd. for $C_{22}H_{13}O_7PW$: C, 43.73; H, 2.17. Found: C, 43.64; H, 2.15	83.3
13	yellow	142-144	^{1}H-NMR (C_6D_6, δ): 7.96 (dt, ^3J=10 Hz, ^4J=^5J=1.5 Hz, 1H); 7.96 (dt, ^3J=7Hz, ^4J=^5J=1.5Hz, 1H); 6.80-7.20 (m, 10H); 6.47 (ddd, ^3J=10 Hz, 7 Hz, ^4J=1.5Hz, 1H); 5.79 (td, ^3J=7Hz, ^4J=1.5Hz, 1H); 2.75 (s, 3H); ^{31}P-NMR (C_6D_6, δ): -31; IR (KBr, cm^{-1}): $\nu_{C=O}$ 1900, 2050.	Calcd. for $C_{25}H_{17}N_2O_5PW$: C, 46.90; H, 2.68; N, 4.38. Found: C, 46.93; H, 2.71; N, 4.34	64
14	yellow	144-146	^{1}H-NMR (C_6D_6, δ): 8.20 (d, ^3J=10 Hz, 1H); 7.71(d, ^3J=8.3 Hz, 1H); 6.85-7.50 (m, 15 H); 6.56 (t, ^3J=10 Hz, 1H); 5.86 (t, ^3J=8.3 Hz, 1H); ^{31}P-NMR ($CDCl_3$, δ): -35 (s). IR (KBr, cm^{-1}): $\nu_{C=O}$ 1900; 2070	Calcd. for $C_{30}H_{19}N_2O_5PW$: C,51.31; H, 2.73; N, 3.99. Found: C, 51.29; H, 2.76; N, 4.15	69

Table 2. Selected Bond Distances in Angstroms and Bond Angles in Degrees for **13**

Bond Distances		**Bond Angles**	
W-N(1)	2.304(4)	N(1)-W-C(21)	95.2(2)
W-C(21)	2.028(6)	N(1)-W-C(22)	93.3(3)
W-C(22)	2.046(6)	N(1)-W-C(23)	91.8(2)
W-C(23)	2.040(7)	N(1)-W-C(24)	178.7(2)
W-C(24)	1.969(7)	N(1)-W-C(25)	92.6(2)
W-C(25)	2.030(8)	C(1)-P-C(9)	100.2(2)
P-C(1)	1.803(5)	C(1)-P-C(15)	104.3(2)
P-C(9)	1.857(6)	W-C(21)-O(1)	172.7(5)
P-C(15)	1.824(6)	W-C(22)-O(2)	170.1(6)
O(1)-C(21)	1.149(7)	W-C(23)-O(3)	177.2(6)
O(2)-C(22)	1.140(7)	W-C(24)-O(4)	178.2(7)
O(3)-C(23)	1.141(7)	W-C(25)-O(5)	173.1(6)
O(4)-C(24)	1.144(7)		
O(5)-C(25)	1.142(9)		

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