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Reactions of Alkyllithium and Grignard Reagents with (Cyclopentadienyl)dicarbonyl(2-methylbutadiene)molybdenum: Observations of Solvent Effects on Regioselectivity

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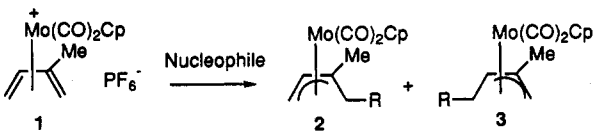
Summary: The regioselectivity that is observed during reactions of the title complex with hydride and carbon nucleophiles was found to be solvent-dependent. In diethyl ether solution, alkyllithiums and Grignard reagents add preferentially to C-1, while in THF and other solvents C-4 addition dominates. Inclusion of complexing agents (TMEDA or HMPA) in the reactions in ether leads to a reversal of selectivity. All hydride nucleophiles add selectively at C-1, irrespective of solvent. Decomplexation of the C-1 adducts, with concomitant addition of a second nucleophile, allows the completely stereoselective construction of trisubstituted carbon–carbon double bonds. The first example of osmylation of an alkene substituent in the presence of a π-allyl–Mo(CO)$_2$Cp group is described.

Several years ago, Faller and Rosan observed that reaction of the isoprene–Mo(CO)$_2$Cp complex **1** with $NaBH_3CN$ proceeded with complete regiospecificity to give the π-allyl complex **2a**.[1] More recently, we reported



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(a) R = H (d) R = Me
(b) R = CN (e) R = CH=CH$_2$
(c) R = Ph (f) R = CH$_2$CH=CH$_2$

that cyanide adds to **1** with similar regioselectivity to give a *ca.* 10:1 mixture of complexes **2b** and **3b**.[2] These reactions occur by addition of nucleophile to the sterically more hindered diene terminus, which has been attributed[1] to destabilization of π-allyl complexes of structure **3**, and the transition state preceding them, thereby leading to a kinetic preference for the formation of **2**. Electronic effects from the methyl substituent are expected to be rather weak, although in the present work we have observed that C(1) is found at slightly lower field than C(5) in the ^{13}C NMR spectrum ($\Delta\delta$ *ca.* 5 ppm), and the LUMO of **1** is expected to have its larger terminal carbon coefficient at C(1).[3] Both of these electronic effects therefore conspire to overcome steric effects when relatively small nucleophiles are added to this complex. Similarly, regioselective addition of sterically undemanding nucleophiles has been reported for analogous diene–cobalt complexes.[4] We now report an investigation of carbon nucleophile additions to complex **1** which show some unexpected solvent and temperature effects leading to potentially useful regiocontrol.

Reaction of **1** with phenyllithium in tetrahydrofuran at −78 °C, fairly standard conditions for this kind of reaction, gave a 30:70 mixture of **2c**:**3c** in 92% isolated yield (entry

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Table 1. Solvent Effects on Carbon Nucleophile Additions to Complex 1

Entry	nucleophile	reacn conditions[a]	yield (%)	ratio 2:3
1	PhLi	THF, −78 °C, 1 h	92	30:70
2	PhLi	THF, 0 °C to rt, 1 h	89	50:50
3	PhLi	THF, HMPA (2 equiv), 0 °C to rt, 3 h	69	15:85
4	PhLi	DME, 0 °C to rt, 3 h	62	45:55
5	PhLi	pentane, 0 °C to rt, 1 h	64	60:40
6	PhLi	CH_2Cl_2, 0 °C to rt, 1 h	78	50:50
7	PhLi	Et_2O, −78 °C, 1 h	40	55:45
8	PhLi	Et_2O, −78 °C to rt, 3 h	50	65:35
9	PhLi	Et_2O, 0 °C to rt, 1 h	74	80:20
10	PhLi	Et_2O, TMEDA (1.2 equiv), 0 °C to rt, 2 h	52	20:80
11	PhLi	Et_2O, HMPA (2 equiv), 0 °C to rt, 2 h	94	30:70
12	PhMgBr	Et_2O, 0 °C to rt, 1 h	81	70:30
13	PhMgBr	CH_2Cl_2, 0 °C to rt, 1 h	74	55:45
14	MeLi	CH_2Cl_2, 0 °C to rt, 1 h	60	50:50
15	MeLi	Et_2O, 0 °C to rt, 1 h	68	60:40
16	MeMgBr	THF, 0 °C to rt, 1 h	87	30:70
17	MeMgBr	CH_2Cl_2, 0 °C to rt, 1 h	84	20:80
18	MeMgBr	Et_2O, 0 °C to rt, 1 h	90	70:30
19	(vinyl)MgBr	CH_2Cl_2, 0 °C to rt, 2 h	94	55:45
20	(vinyl)MgBr	Et_2O, 0 °C to rt, 2 h	96	75:25
21	(allyl)MgBr	CH_2Cl_2, 0 °C to rt, 2 h	58	40:60
22	L-Selectride	THF, rt, 1.5 h	84	55:45
23	L-Selectride	CH_2Cl_2, −78 °C, 3 h	93	60:40
24	L-Selectride	Et_2O, rt, 0.5 h	83	70:30
25	$LiBH_4$	THF, rt, 1.5 h	75	60:40
26	$LiBH_4$	THF, −78 °C, 3 h	98	75:25
27	$LiBH_4$	Et_2O, 0.5 h	85	65:35
28	$NaBH_3CN$	THF, −78 °C, 3 h	76	70:30

[a] Abbreviations: THF, tetrahydrofuran; rt, room temperature; HMPA, hexamethylphosphoramide; DME, 1,2-dimethoxyethane; TMEDA, *N,N,N′,N′*-tetramethylethylenediamine.

1, Table 1).[5] Such a result was not unexpected in view of the steric bulk of PhLi as compared with hydride or cyanide. The products could be separated by preparative TLC, but during the isolation and purification procedure it was found that complexes of structure **3** are photolabile and should be handled with exclusion of light wherever possible. Furthermore, while complexes **2** show well-resolved, sharp ^1H NMR spectra, complexes **3** give very broad lines. That this effect is due to slow rotation about the π-allyl–Mo axis was demonstrated by the observation of sharp NMR signals for **3a** at elevated temperature. At low temperature, two sets of peaks are obtained, owing to the presence of *exo* and *endo* conformers.[1] These effects are considered again later. When the reaction was performed at 0 °C, with warming to room temperature, a 50:50 mixture (NMR) of regioisomers was obtained in 89% isolated yield. Inclusion of HMPA in the latter reaction led to the formation of a 15:85 mixture (entry 3). These observations prompted us to investigate the effect of solvent on the reaction, the results of which are summarized in Table 1 (entries 4–11). For the most part, the results are unspectacular, reactions in both pentane and dichloromethane giving an almost equimolar ratio of products (note that complex **1** is insoluble in THF, ether, andpentane but soluble in CH_2Cl_2). Reaction in ether, however, shows a *reversal* of selectivity, which is increased at higher temperatures (compare entries 8 and 9). Given the fact that the products are easily separated by chromatography, these results indicate that either regioisomer can be prepared fairly efficiently by a judicious choice of reaction conditions. The reactions in ether in the presence of TMEDA (entry 10) or HMPA (entry 11) are especially striking, inclusion of the complexing agents leading to a complete reversal of selectivity.

This phenomenon appears to be quite general, other alkyllithiums as well as Grignard reagents showing a dependence of regioselectivity on solvent (entries 12–20); the exception is allylmagnesium bromide, which gave no reaction in Et_2O. We also investigated reactions of hydride nucleophiles with **1** (entries 22–28). Lithium borohydride showed little or no solvent effect at room temperature but did show some temperature effects, while L-Selectride showed some solvent dependence. We were puzzled by the apparent difference between our results and those reported earlier by Faller and Rosan,[1] so we repeated their experiment (entry 28), which showed that the reaction of **1** with cyanoborohydride is not regio*specific* as originally claimed. However, we did observe that the ^1H NMR spectrum of complex **3a** is extremely broad at room temperature and that this complex is quite photolabile. Both of these effects could have originally resulted in this complex not being observed in the mixture, especially using NMR at 60 MHz, as was the case in Faller's work. We isolated **3a** and studied its NMR spectroscopic behavior in more detail. As expected, the complex shows two limiting conformations (*syn* and *anti*[1]) that interconvert slowly at room temperature; at 80 °C a single set of well-resolved NMR peaks is obtained, while at −40 °C two sets of peaks are observed. The integrated intensities of the signals corresponding to each conformer in the latter spectrum suggest a $\Delta G°$ of 2.9 kcal mol^{-1}, while a variable-temperature experiment over the range −60 to +80 °C gives a value of 16.2 kcal mol^{-1} for the energy barrier to conformational interconversion. We have not established which conformation is the more stable.

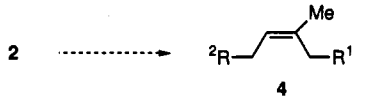
An explanation of the princely position occupied by diethyl ether as a solvent for these reactions is, to say the least, difficult. It is well-known that aggregation of alkyllithiums occurs in organic solvents and that the degree of aggregation is dependent on temperature, concentration, and solvent.[6] The nature of the aggregates affects the

(5) Regioisomeric mixtures were separated by chromatography on silica gel, and individual compounds were characterized by using ^1H and ^{13}C NMR, IR, and high-resolution mass spectrometry. Ratios of isomers were determined by ^1H NMR spectroscopy of the mixtures prior to separation. Selected analytical data are as follows for compounds not previously reported. Complex **2c**: R_f 0.53 (EtOAc/hexanes, 1:9); IR (ν_{max}, $CHCl_3$) 1943, 1856 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.2 (5H, m), 5.28 (5H, s), 4.08 (1H, dd, J = 11, 7.5 Hz), 2.99 (1H, d, J = 14.2 Hz), 2.80 (1H, dd, J = 7.5, 3.3 Hz), 1.66 (3H, s), 1.54 (1H, d, J = 14.2 Hz), 1.36 (1H, dd, J = 11, 3.3 Hz); ^{13}C NMR ($CDCl_3$) δ 242.2, 235.8, 141.1, 128.8, 128.1, 126.1, 92.0, 84.1, 68.1, 41.7, 31.7, 27.2; HRMS calcd (^{98}Mo) 364.0362, found 364.0351. Complex **3c**: R_f 0.64 (EtOAc/hexanes, 1:9); IR (ν_{max}, $CHCl_3$) 1938, 1863 cm^{-1}; ^1H NMR shows Cp at δ 5.2 and Ph at δ 7.2, but the remaining peaks are broad due to slow conformational interconversions; HRMS calcd (^{98}Mo) 364.0362, found 364.0375. Complex **2d**: R_f 0.34 (hexanes); IR (ν_{max}, $CHCl_3$) 1936, 1852 cm^{-1}; ^1H NMR ($CDCl_3$) δ 5.4 (5H, s), 4.2 (1H, dd, J = 10.6, 7.5 Hz), 2.66 (1H, dd, J = 7.5, 2.6 Hz), 1.79 (3H, s), 1.72 (1H, m), 0.96 (1H, dd, J = 10.6, 2.6 Hz), 0.84 (3H, t, J = 5.4 Hz), 0.10 (1H, m); ^{13}C NMR ($CDCl_3$) δ 242.4, 236.4, 91.8, 87.1, 67.8, 31.0, 29.3, 26.7, 16.4; HRMS calcd (^{98}Mo) 302.0205, found 302.0194. Complex **3d**: R_f 0.50 (hexanes); IR (ν_{max}, $CHCl_3$) 1935, 1858 cm^{-1}; ^1H NMR ($CDCl_3$) δ 5.16 (5H, s, Cp), other peaks broadened due to slow conformational interconversion; HRMS calcd (^{98}Mo) 302.0205, found 302.0218. Complex **2e**: R_f 0.53 (EtOAc/hexanes, 2:8); IR (ν_{max}, $CHCl_3$) 1937, 1854, 1636 cm^{-1}; ^1H NMR ($CDCl_3$) δ 5.4–5.6 (1H, m, vinyl), 5.25 (5H, s), 5.0–4.9 (2H, m, vinyl), 4.5 (1H, dd, J = 10.5, 7.4 Hz), 2.66 (1H, dd, J = 7.4, 3.3 Hz), 2.5 (1H, dd, J = 15, 8.3 Hz), 1.77 (3H, s), 1.14 (1H, dd, J = 10.5, 3.2 Hz), 0.97 (1H, dd, J = 15, 4.0 Hz); ^{13}C NMR ($CDCl_3$) δ 241.9, 236.0, 138.8, 115.7, 91.9, 82.0, 68.0, 40.6, 31.5, 27.2; HRMS calcd (^{98}Mo) 314.0205, found 314.0189.

(6) For some representative studies, and other literature, see the following. (a) Alkyllithiums: Bauer, W.; Winchester, W. R.; Schleyer, P. v. R. *Organometallics* **1987**, *6*, 2371. Hope, H.; Power, P. *J. Am. Chem. Soc.* **1983**, *105*, 5320. Fraenkel, G.; Adams, D. G.; Dean, R. R. *J. Phys. Chem.* **1968**, *72*, 944. Fraenkel, G.; Henrichs, M.; Hewitt, J. M.; Su, B. M.; Geckle, M. J. *J. Am. Chem. Soc.* **1980**, *102*, 3345. Fraenkel, G.; Henrichs, M.; Hewitt, J. M.; Su, B. M. *J. Am. Chem. Soc.* **1984**, *106*, 255. Fraenkel, A. M.; Geckle, M. J.; Schloss, F. *J. Am. Chem. Soc.* **1979**, *101*, 4745. Waack, R.; West, P.; Doran, M. A. *Chem. Ind. (London)* **1966**,

steric bulk as well as the reactivity of the organolithium species. On this basis, one might have expected that reactions in THF, a coordinating solvent, would be very different from reactions in noncoordinating hydrocarbon solvents, such as pentane, but similar to diethyl ether. Such is not the case. Moreover, the inclusion of HMPA in the THF reaction (Table 1, entry 3) results in a shift toward the product of phenyllithium addition at the sterically more accessible diene terminus. Reich and coworkers[7] have recently shown that PhLi exists largely as dimeric species in THF, and addition of HMPA results in the formation of monomeric PhLi. Characterization of ether solutions of PhLi has been somewhat inconsistent, but most studies suggest the presence of a tetramer in concentrated solution.[6,8] Similarly, in noncoordinating hydrocarbon solvents, most organolithiums exist as tetramers or even hexamers. Our results suggest that aggregation is not the sole determining factor in these reactions, since the results with pentane and THF lie in the same direction, while ether and THF are opposite. Addition of complexing agents to both the ether and THF reaction systems leads to the formation of similar mixtures in favor of **3c**. Clearly, the factors that control regiochemistry during these reactions are very complex, and one must take into consideration not only the degree of aggregation of the nucleophile but also the nature of its solvation, both of which will affect its steric bulk. Undoubtedly, steric control is very important, and presumably the relatively weak coordination afforded by diethyl ether leads to an optimum size of the nucleophile that results from both of these effects.

Controlled alkylation of complex **1** allows an approach to trisubstituted alkenes having defined stereochemistry, via activation of complexes of structure **2** according to the established protocol,[9] followed by nucleophile addition and decomplexation to afford alkenes of structure **4**. It



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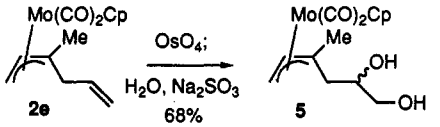
is also possible to capitalize on the ability of the $Mo(CO)_2Cp$ moiety to protect an unsaturated carbon ligand during reactions with electrophiles.[10] The vinyl-substituted complex **2e** serves to illustrate such tactics. Treatment of this complex with osmium tetraoxide, followed by standard workup, afforded the diol **5** as a 2.5:1 mixture of diastereomers. *This is the first observation of osmylation of a C=C double bond in the presence of a π-allyl–molybdenum group*, although similar reactions have been recorded for diene–$Fe(CO)_2L$ complexes.[11] The stereocontrol imposed by the neighboring metal system is rather poor in this case, but it indicates that useful results might be obtainable when the alkene and π-allyl–MoL_n groups are less distant, a proposition which will be investigated in our laboratories in the near future.



2e **5**

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