On the Stereo- and Regioselectivity of Molybdenum-Catalyzed Allylic Alkylations. Stereocontrolled Approach to Quaternary Carbons and Tandem Alkylation–Cycloaddition

Barry M. Trost* and Mark Lautens

McElvain Laboratories of Organic Chemistry
Department of Chemistry, University of Wisconsin
Madison, Wisconsin 53706

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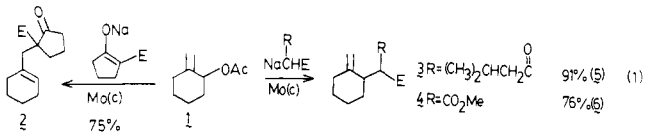
Regioselectivity in allylic alkylations of stabilized carbon nucleophiles mediated by transition metals normally is dominated by steric approach leading to attack at the less substituted carbon of a π-allyl intermediate.[1] We report that in molybdenum-catalyzed allylic alkylations[2,3] the regiochemistry depends upon the nature of the nucleophile to an unusual degree.

This unusual dependence of regioselectivity was first noted with 2-acetoxy-1-methylenecyclohexane (**1**) as shown in eq 1. Under

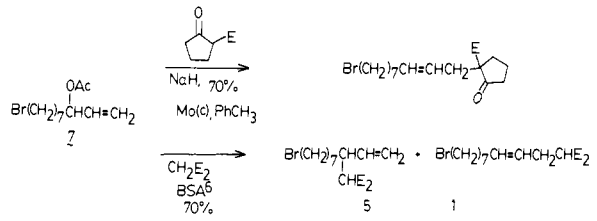


otherwise identical conditions [NaH, 5% $Mo(CO)_6$ (Mo(c)), $PhCH_3$, 110 °C], the sodium salt of 2-carbomethoxycyclopentanone gave **2** while the sodium salt of an acyclic β-keto ester **3** and of dimethyl malonate **4** gave the products **5**[4,5] and **6**,[4] respectively, of exclusive attack at the ring carbon rather than the side-chain carbon.

To explore the primary–secondary competition without complications of a ring system, the acyclic substrate **7** (Scheme I) was examined. Exactly the same trend was observed, although in this case a minor product identified as the alternative regioisomer was detected in the malonate case. This example also highlights the chemoselectivity by the reordering of the relative reactivity of the bromide and allylic acetate since in the absence of the molybdenum catalyst and in DMF solvent only bromide displacement is observed.[7]

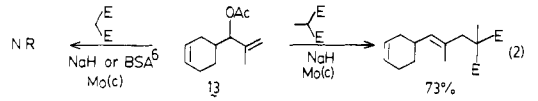
To explore this apparently contrathermodynamic result more fully, we turned our attention to the 4-*tert*-butyl-1-vinyl-1-acetoxycyclohexane case (**8** Scheme II). Even though the competition between the two termini of the allyl unit involves a primary vs. tertiary center, the anion of either dimethyl or di-*tert*-butyl malonate attacks the tertiary center exclusively to give **10**[4,8] contaminated with a small amount of its stereoisomer (ratio 6:1). On the other hand, the corresponding 1,3-diketone **11a** and β-keto ester **11b**, and the C-methylated analogues of dimethyl malonate (**11c**) and the 1,3-diketone **11d** led to exclusive terminal attack to give **12**.[4]

Scheme I

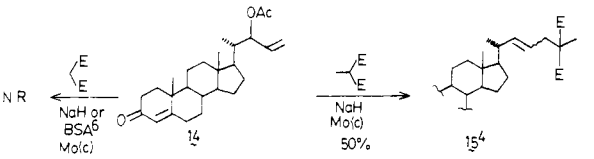


To demonstrate that the regioselectivity represented the intrinsic bias of the nucleophile and not subtle changes in catalyst, a competition between dimethyl malonate and dimethyl methylmalonate for limited amounts of **8** was conducted. Absolutely no crossover products were observed, i.e., malonate anion attacked only the tertiary position to give **10** and methylmalonate anion attacked only the primary carbon to give **12c**!

Nevertheless, a different catalyst can be generated when dimethyl malonate is employed. The allylic acetate **13** shows no reaction at all with dimethyl malonate but alkylates with dimethyl methylmalonate, albeit slowly (eq 2).[4] The steroid substrate **14**

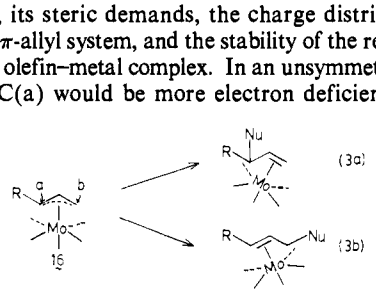


showed the same remarkable sensitivity of reactivity towards nucleophile. The source of the failure of alkylation with malonate anion and **13** or **14** appears to be due to the generation of a



different catalyst derived from the reaction of Mo(c) and dimethyl malonate such as $(CO)_{6-n}Mo[CHE_2]_n$[9] or $(CO)_5Mo[CHE_2]^-$.[10] With the slow to react substrates **13** and **14**, such catalysts appear to be of insufficient reactivity to initiate ionization. However, with the more reactive substrates, reaction proceeds normally.

The source of the unusual divergence in regioselectivity between dimethyl malonate and other nucleophiles does not appear to stem from a different catalyst as shown by the competition experiment. It would appear to stem from an intricate balance among reactivity of the anion, its steric demands, the charge distribution in the intermediate π-allyl system, and the stability of the resultant olefin as well as the olefin–metal complex. In an unsymmetrical complex such as **16**, C(a) would be more electron deficient than C(b).



Further, attack at C(a) leads to the sterically and electronically preferred olefin–Mo complex as the initial product. The higher reactivity of the malonate anion and its minimum steric requirements lead these two factors to dominate, and path 3a is traversed. On the other hand, introduction of a single alkyl substituent makes the steric demands of the nucleophile sufficiently important that path 3b totally dominates. Similarly, reducing the reactivity of the anion as in the case of a 1,3-diketone di-

(1) For reviews see: Trost, B. M.; Verhoeven, T. R. *Compr. Organomet. Chem.* **1982**, *8*, 779–938. Trost, B. M. *Pure Appl. Chem.* **1981**, *53*, 2357; *Aldrichimica Acta* **1981**, *14*, 43; *Acc. Chem. Res.* **1980**, *13*, 385.

(2) Adams, R. D.; Chodosh, D. F.; Rosan, A. M.; Faller, J. W. *J. Am. Chem. Soc.* **1979**, *101*, 2570. Faller, J. W.; Rosan, A. M. *Ann. N.Y. Acad. Sci.* **1977**, *295*, 186. Also see: Bailey, N. A.; McCleverty, J. S. *J. Chem. Soc., Chem. Commun.* **1974**, 592.

(3) (a) Trost, B. M.; Lautens, M. *J. Am. Chem. Soc.* **1982**, *104*, 5543. (b) In this paper, we reported the Mo(bpy)-catalyzed alkylation of 3-acetoxy-4-carboxaldehydocyclohex-1-ene. Subsequent control experiments reveal the reaction proceeds even in the absence of the Mo(bpy) catalyst.

(4) This compound has been fully characterized spectrally and the elemental composition determined from high-resolution mass spectroscopy and/or combustion analysis.

(5) The product is an equilibrium mixture of diastereomers, which were not separated.

(6) BSA = *O,N*-bis(trimethylsilyl)acetamide, E = CO_2CH_3.

(7) Cf.: Trost, B. M.; Verhoeven, T. R. *J. Am. Chem. Soc.* **1980**, *102*, 4730.

(8) The stereochemistry derives by comparison of the ^1H and ^{13}C NMR data to that of the ethyl ester series. See: House, H. O.; Lubinkowski, J.; Good, J. J. *J. Org. Chem.* **1975**, *40*, 86.

(9) Cf.: Dunne, T. G.; Cotton, F. A. *Inorg. Chem.* **1963**, *2*, 2633.

(10) Cf: Darensbourg, M. Y.; Conder, H. L.; Darensbourg, D. J.; Hasday, C. *J. Am. Chem. Soc.* **1973**, *95*, 5919. Darensbourg, D. J.; Darensbourg, M. Y. *Inorg. Chem.* **1970**, *9*, 1691. For pioneering work in this general field see: Fischer, E. O.; Maasbol, A. *Angew. Chem., Int. Ed. Engl.* **1964**, *3*, 580. Fischer, E. O.; Kiener, V. *J. Organomet. Chem.* **1970**, *23*, 215.

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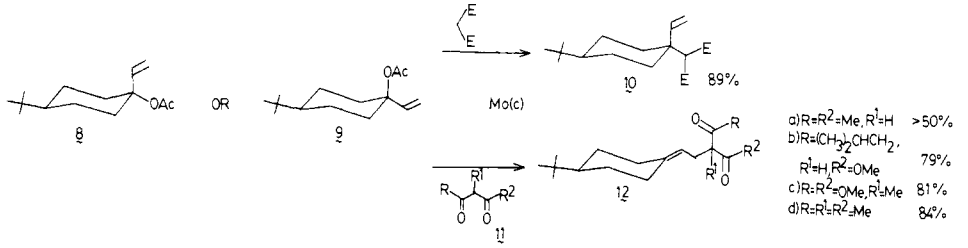
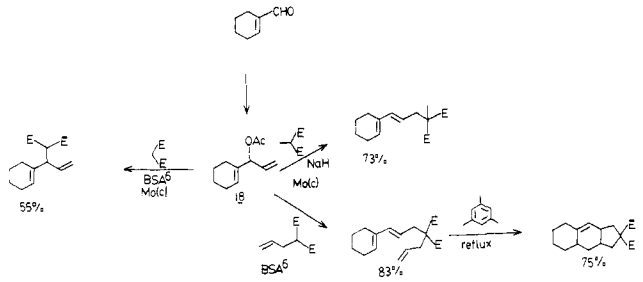
Scheme II

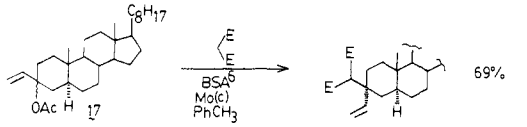


Scheme III



minishes the importance of the charge distribution in **16** and leads to preferential formation of the thermodynamically more stable olefin. Finally, a β-keto ester, intermediate in reactivity, shows intermediate behavior. When steric factors dominate as with the anion of 2-carbomethoxycyclopentanone, only path 3b is observed. On the other hand, the keto ester **11b** prefers attack at the more hindered position (i.e., formation of **5**) unless the steric requirements of the allyl system overwhelms as in the case of allyl acetate **8**.

The complementary regiochemical behavior of malonate and substituted malonates offer interesting applications. As shown in the case of **8** and the steroid substrate **17**, a high preference



for equatorial attack of malonate creates a quaternary center with high stereoselectivity[11,12] and independent of the stereochemistry of the starting allyl acetate[13]—a result that permits a single product to result from a stereoisomeric mixture of starting materials.

The failure of an additional double bond as in diallyl acetate **18**[4] to change the established trends permits a tandem alkylation–cycloaddition as shown in Scheme III.[4] The fact that **18** arises so simply by addition of a vinyl organometallic to an α,β-unsaturated carbonyl system makes this an attractive strategy for making substrates capable of an intramolecular Diels–Alder reaction.[14]

These results demonstrate that by appropriately choosing the nucleophile, great regiochemical control can be exercised in Mo(c)-catalyzed reactions. Combined with the earlier observation[3] that the choice of ligands also affects regiochemistry, molybdenum templates provide a most powerful tool for allylic alkylations.

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Registry No. 1, 53723-50-5; **2**, 82352-45-2; **3**, 85390-61-0; **4**, 18424-76-5; **5**, 85390-62-1; **6**, 67428-13-1; **7**, 85390-63-2; **8**, 85390-64-3; **9**, 85390-65-4; **10**, 85390-66-5; **11a**, 123-54-6; **11b**, 30414-55-2; **11c**, 609-02-9; **11d**, 815-57-6; **12a**, 85390-67-6; **12b**, 85405-71-6; **12c**, 85390-68-7; **12d**, 85390-69-8; **13**, 85390-70-1; **14**, 85390-71-2; **15**, 85390-72-3; **17**, 85390-73-4; **18**, 7014-63-3; $Mo(CO)_6$, 13939-06-5; methyl 2-hydroxy-1-cyclopentene-1-carboxylate-Na, 63178-03-0; methyl 1-(10-bromodec-2-enyl)-2-oxo-1-cyclopentanecarboxylate, 85390-74-5; methyl 10-bromo-3-ethenyl-2-methoxycarbonyldecanoate, 85390-75-6; methyl 12-bromo-2-methoxycarbonyldodec-4-enoate, 85390-76-7; methyl 2-oxocyclopentanecarboxylate, 10472-24-9; methyl 5-(cyclohex-3-en-1-yl)-2,4-dimethyl-2-methoxycarbonylpent-4-enoate, 85390-77-8; 3α-ethenyl-3β-[bis(methoxycarbonyl)methyl]-5α-cholestane, 85390-78-9; methyl β-ethenyl-α-methoxycarbonyl-1-cyclohexene-1-propanoate, 85390-79-0; methyl 5-(cyclohex-1-en-1-yl)-2-methyl-2-methoxycarbonyl-4-pentenoate, 85390-80-3; 7-(cyclohex-1-en-1-yl)-4,4-bis(methoxycarbonyl)-1,6-heptadiene, 85390-81-4; 2,2-bis(methoxycarbonyl)-2,3,3a,6,7,8,9,9a,10,10a-decahydro-1*H*-benz[*f*]indene, 85390-82-5.

(11) For an excellent review see: Martin, S. F.; *Tetrahedron* **1980**, *36*, 419. For a case using Grignard reagents and allyl alcohols with nickel catalysts see: Buckwalter, B. L.; Burfitt, I. R.; Felkin, H.; Joly-Gondket, M.; Naemura, K.; Salomon, M. F.; Wenkert, E.; Wovkulich, P. M. *J. Am. Chem. Soc.* **1978**, *100*, 6445.

(12) The stereochemistry of the alkylation product of **17** is assigned by analogy to **10**.

(13) As in the case of **8**, **10** is by far the major product, but the alternative stereoisomer is also observed.

(14) Cf.: Brieger, G. *J. Am. Chem. Soc.* **1963**, *85*, 3783. Corey, E. J.; Glass, R. S. *J. Am. Chem. Soc.* **1967**, *89*, 260. Frater, G. *Helv. Chim. Acta* **1974**, *57*, 172. Bajorek, J. J. S.; Sutherland, J. K. *J. Chem. Soc., Perkin Trans. 1* **1975**, 1559. Oppolzer, W.; Snowden, R. L. *Tetrahedron Lett.* **1976**, 4187.

Lewis Acid Catalysis of Coumarin Photodimerization

Frederick D. Lewis,* Daniel K. Howard, and Joe D. Oxman

Department of Chemistry, Northwestern University Evanston, Illinois 60201

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Lewis acids have been widely employed as catalysts for thermal Diels–Alder and ene reactions, especially those involving α,β-unsaturated esters.[1,2] The enhanced reactivity and stereoselectivity observed in many such reactions have been attributed to changes in frontier orbital energies and C=C double bond polarity upon complexation of the carbonyl oxygen.[2] We recently reported that the spectroscopic properties and unimolecular photoisomerization reactions of several α,β-unsaturated esters are profoundly changed by complexation with Lewis acids such as BF_3, $EtAlCl_2$, and $SnCl_4$.[3] The possibility that Lewis acids might also serve as catalysts for photochemical [2 + 2] cycloaddition reactions was suggested many years ago by reports concerning the photodimerization of dibenzylideneacetone in the presence of UO_2^+ and $SnCl_4$[4] and is borne out by investigations currently in progress in our laboratory. We report here on the pronounced effects of the Lewis acid BF_3 on the efficiency and regiochemistry of coumarin photodimerization.

The photodimerization of coumarin has been the subject of numerous preparative and mechanistic investigations.[5] The

(1) Flemming, I. "Frontier Orbitals and Organic Chemical Reactions"; Wiley: New York, 1976,; pp 214–223.

(2) Houk, K. N.; Strozier, R. W. *J. Am. Chem. Soc.* **1973**, *95*, 4094–4096.

(3) Lewis, F. D.; Oxman, J. D. *J. Am. Chem. Soc.* **1981**, *103*, 7345–7347.

(4) (a) Stobbe, H.; Farber, E. *Chem. Ber.* **1925**, *58*, 1548–1553. (b) Alcock, N. W.; Herron, N.; Kemp. T. J.; Shoppee, C. W. *J. Chem. Soc., Chem. Commun.* **1975**, 785–786.

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