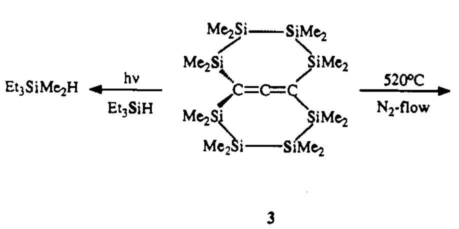
evidenced by trapping with Et_3SiH.



Acknowledgment. Ames Laboratory is operated for the U.S. Department of Energy by Iowa State University under Contract No. W-7405-ENG-82. This work was supported by the Director for Energy Research, Office of Basic Energy Sciences.

Synthesis of (*R*)-(−)-Muscone by an Asymmetrically Catalyzed Macrocyclization of an ω-Alkynal

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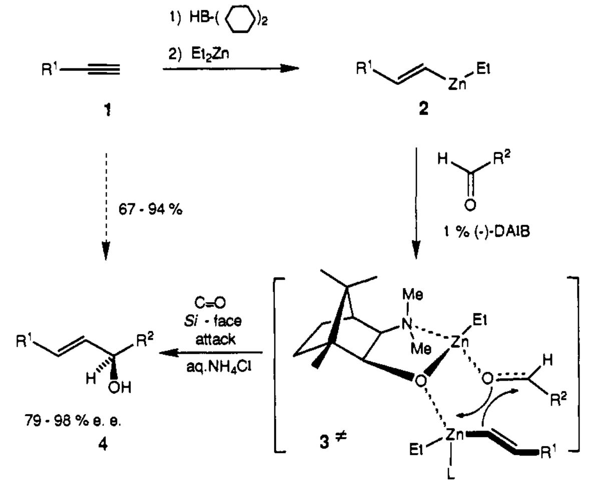
Received December 7, 1992

Recently, we reported a catalytic enantio-controlled approach to secondary (*E*)-allyl alcohols **4** (Scheme I).[1] Monohydroboration of alkynes **1** and "transmetalation" of the resulting (*E*)-(1-alkenyl)dicyclohexylboranes with diethylzinc conveniently provides (1-alkenyl)ethylzinc reagents **2**. Nonisolated reagents **2** undergo exclusively π-face selective 1-alkenyl transfer to various aldehydes in the presence of 1 mol % of (−)-3-*exo*-(dimethylamino)isoborneol (DAIB).[2] This catalyst-directed 1-alkenyl/aldehyde addition is consistent with transition state **3**‡, where the zinc–aminoalkoxide chelate coordinates with both the aldehyde and the alkenylzinc reagent.[2] Were these two reactive units to be linked by a chain, one could expect a smooth macrocyclization to occur.

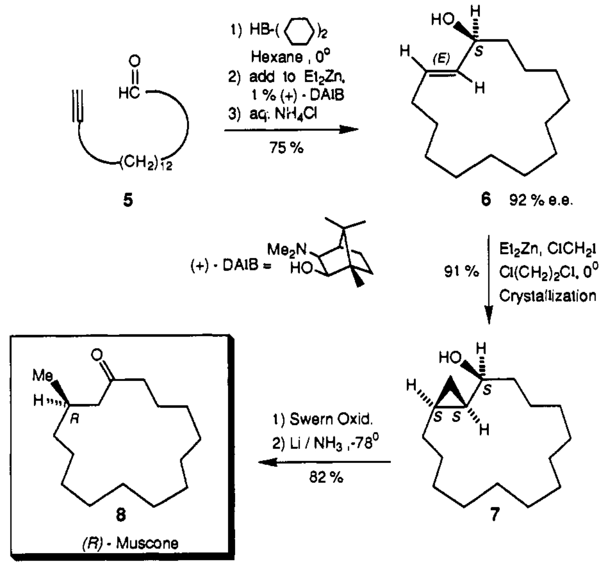
Hence, optically pure, macrocyclic (*E*)-allyl alcohols should be readily available from ω-alkynals in a single operation. This, however, requires that the dicyclohexylborane and the diethylzinc should react faster with the acetylene and alkenylborane functionalities, respectively, relative to their reaction with the aldehyde group.

We report here that this idea is feasible and applicable to the synthesis of enantiomerically pure (*R*)-muscone (**8**, Scheme II). This rare and valuable perfumery ingredient has been isolated from the male musk deer *Moschus moschiferus*,[3] and many syntheses of the racemate as well as of the natural antipode have appeared in the literature.[4]

Scheme I



Scheme II



ω-Alkynal **5**,[5] easily prepared by Swern oxidation[6] of 14-pentadecyn-1-ol[7] (95%), was added to a solution of freshly prepared dicyclohexylborane in hexane at 0 °C. After the reaction mixture was stirred at 0 °C for 2 h and diluted with hexane, the resulting 0.05 M solution of alkenylborane was added over 4 h to a 0.05 M solution of diethylzinc (1.5 mol equiv) in hexane containing (1*S*)-(+)-DAIB (0.01 mol equiv). Aqueous workup furnished the cyclic (*S*)-C_{15}-allyl alcohol **6**[5] in 75% yield and in 92% ee.[8] To transfer the chirality from C(1) to C(3) we envisaged a hydroxy-directed cyclopropananation[9] using the Denmark protocol.[10] Indeed, slow addition of alcohol **6** to a mixture of Et_2Zn (2 mol equiv) and $ClCH_2I$ (4 mol equiv) in 1,2-dichloroethane at 0 °C,

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[1] Oppolzer, W.; Radinov, R. N. *Helv. Chim. Acta* **1992**, *75*, 170.

[2] Reviews on asymmetric additions of organozinc reagents to aldehydes: Noyori, R.; Kitamura, M. *Angew. Chem.* **1991**, *103*, 34; *Angew. Chem., Int. Ed. Engl.* **1991**, *30*, 49. Soai, K.; Niwa, S. *Chem. Rev.* **1992**, *92*, 833.

[3] Isolation: Walbaum, H. *J. Prakt. Chem. II* **1906**, *73*, 488. Structure: Ruzicka, L. *Helv. Chim. Acta* **1926**, *9*, 715, 1008. Ställberg-Stenhagen, S. *Ark. Kemi* **1951**, *3*, 517. Olfactive comparison of (*R*)- and (*S*)-muscone: Pickenhagen, W. *Flavor Chemistry*; *Trends and Developments*; ACS Symposium Series 388; American Chemical Society: Washington, DC, 1989; p 151.

[4] Syntheses of (*R*)-muscone: (a) Branca, Q.; Fischli, A. *Helv. Chim. Acta* **1977**, *60*, 925. (b) Abad, A.; Arno, M.; Pardo, A.; Pedro, J. R.; Seoane, E. *Chem. Ind.* **1985**, *29*. (c) Nelson, K. A.; Mash, E. A. *J. Org. Chem.* **1986**, *51*, 2721. (d) Terunuma, D.; Motegi, M.; Tsuda, M.; Sawada, T.; Nozawa, H.; Nohira, H. *J. Org. Chem.* **1987**, *52*, 1630. (e) Porter, N. A.; Lacher, B.; Chang, V. H.-T.; Magnin, D. R. *J. Am. Chem. Soc.* **1989**, *111*, 8309. (f) Xie, Z.-F.; Sakai, K. *J. Org. Chem.* **1990**, *55*, 820. (g) Tanaka, K.; Ushio, H.; Kawabata, Y.; Suzuki, H. *J. Chem. Soc., Perkin Trans. 1* **1991**, 1445. (h) Ogawa, T.; Fang, C.-L.; Suemune, H.; Sakai, K. *J. Chem. Soc., Chem. Commun.* **1991**, 1438. (i) Dowd, P.; Choi, S.-C. *Tetrahedron* **1992**, *48*, 4773.

[5] All new compounds were characterized by IR, ^1H NMR, ^{13}C NMR, and mass spectra.

[6] Mancuso, A. J.; Huang, S.-L.; Swern, D. *J. Org. Chem.* **1978**, *43*, 2480.

[7] Prepared by alkylation of bilithiated propargyl alcohol with 1-bromododecane (98%) and base-induced alkyne isomerization of resulting 2-pentadecyn-1-ol (93%): Utimoto, K.; Tanaka, M.; Kitai, M.; Nozaki, H. *Tetrahedron Lett.* **1978**, 2301. Abrams, S. R. *Can. J. Chem.* **1984**, *62*, 1333.

[8] Enantiomeric excess (ee) determined by ^{19}F NMR of the (1*S*)-α-methoxy-α-(trifluoromethyl) phenylacetate: Dale, J. A.; Dull, D. L.; Mosher, H. S. *J. Org. Chem.* **1969**, *34*, 2543. Absolute configuration of **6** assigned in analogy to the topicity of bimolecular 1-alkenylzinc/aldehyde additions[1] and confirmed by the conversion of **6** into (*R*)-muscone.

[9] Simmons–Smith reaction of (*E*)-cycloocten-3-ol: DePuy, C. H.; Marshall, J. L. *J. Org. Chem.* **1968**, *33*, 3326. Diastereoselective cyclopropanations of cyclic (*Z*)-allyl alcohols: Poulter, C. D.; Friedrich, E. C.; Winstein, S. *J. Am. Chem. Soc.* **1969**, *91*, 6892; **1970**, *92*, 4274. NOESY correlation indicates a conformation of **6** with a synperiplanar C(1)H/C(3)H orientation.

[10] Denmark, S. E.; Edwards, J. P. *J. Org. Chem.* **1991**, *56*, 6974.

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stirring the mixture at 0 °C for 0.5 h, and workup (aqueous NH_4Cl) afforded a single diastereoisomer (**7**) (NMR, GC). Flash chromatography and crystallization (pentane) gave pure (*S*,*S*,*S*)-cyclopropylcarbinol **7**[5] in 91% yield (mp 79–80 °C). Swern oxidation[6] of carbinol **7** and regioselective cyclopropane hydrogenolysis of the resulting, known ketone[4c,11] with lithium in rigorously anhydrous NH_3/Et_2O at −78 °C provided, after bulb-to-bulb distillation, pure (*R*)-muscone[12] (**8**, 82% yield).

In summary, we have synthesized pure (*R*)-muscone **8** from the commercial precursors propargyl alcohol and bromododecane in 48% overall yield, which compares very favorable with previous syntheses of **8**.[4,13] This work represents, to our knowledge, the first asymmetrically catalyzed macrocyclization;[14] moreover, it highlights the synthetic potential of the novel (1-alkenyl)ethylzinc reagents **2** and demonstrates the suitability of cyclic (*E*)-allyl alcohols for efficient chirality transfer.

Acknowledgment. Financial support of this work by the Swiss National Science Foundation, Sandoz Pharma Ltd., Basel, and Givaudan-Roure AG, Dübendorf, is gratefully acknowledged. We thank Firmenich SA, Geneva for kindly providing a sample of (*R*,*S*)-muscone.

Supplementary Material Available: Preparations and analysis data, including mp, IR, ^1H NMR, ^{13}C NMR, MS, and [α] values (4 pages). Ordering information is given on any current masthead page.

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[11] The use of rigorously dried liquid ammonia was essential to prevent the reported[4c] concomitant reduction of the carbonyl group.

[12] Identified by comparison (GC, IR, ^1H NMR, ^{13}C NMR, MS) with racemic muscone. $[\alpha]_D = -12.7°$ (c = 0.9, MeOH, 18 °C); lit.[4g] $[\alpha]_D = -12.5°$ (c = 5.0, MeOH, 18 °C).

[13] Using the same protocol but employing 1 mol % of (−)-DAIB as a macrocyclization "catalyst" gave unnatural (*S*)-muscone.

[14] For the asymmetric macrocyclization of a chiral α-alkoxyallylstannane aldehyde, see: Marshall, J. A.; Gung, W. Y. *Tetrahedron Lett.* **1988**, *29*, 1657.

[3 + 2] and [4 + 2] Cycloadditions of C_{60}

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Received October 19, 1992

The unique structure and properties of C_{60} (buckminsterfullerene)[1-5] have resulted in an outburst of scientific investigation. During a systematic study of the reactivity of C_{60} with substituted diazomethanes,[6] we obtained experimental evidence of the dipolarophilic character and hence of the high reactivity of C_{60} in cycloadditions.[5]

Table I. Cyclic Voltammetry of C_{60}, **2**, **3**, **5**, and $C_{61}Ph_2$ Fulleroid[a]

	peak position (mV)			
compd	E1	E2	E3	E4
C_{60}	−238	−838	−1418	−1921
2	−406	−979	−1585	−2042
3	−362	−930	−1578	−2002
5	−366	−930	−1536	−1992
Ph_2C_{61}	−346	−924	−1476	−1953

[a] Conditions: Pt working and counter electrodes; scan rate, 1000 mV/s; Ag/AgCl/3 M NaCl, reference electrode; ferrocene internal reference (+620 mV); 0.1 M $TBABF_4$ in THF in a drybox.

In this communication we report the behavior of C_{60} toward trimethylenemethane (TMM, [3 + 2] cycloaddition) and isobenzofuran ([4 + 2] cycloaddition).[7]

There are at least two types of TMM intermediates which could be employed, "nonpolar" (diradicaloid) and "polar" (dipolar). A nonpolar TMM would be one generated from a 7-alkylidene-2,3-diazabicycloheptene,[8-10] whereas a polar TMM would be generated by thermolysis of methylenecyclopropanes.[11] The former and the latter have provided simple access to five-membered ring compounds, e.g., cyclopentanes[8,11] and tetrahydrofurans.[10,12] The TMM precursor which gave the best results in terms of isolation and characterization,[13] in the present work, was the methylenecyclopropanone ketal **1**,[11,12] which was heated overnight in 1,2-dichlorobenzene at 70 °C in the presence of equimolar C_{60}. Purification through column chromatography

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[†] On leave from CMRO-CNR and Department of Organic Chemistry, University of Padova, Italy.

[1] Krätschmer, W.; Lamb, L. D.; Fostiropoulos, K.; Huffman, D. R. *Nature* **1990**, *347*, 354.

[2] See the entire issue: *Acc. Chem. Res.* **1992**, *25* (3).

[3] Haufler, R. E.; Conceicao, J.; Chibante, L. P. F.; Chai, Y.; Byrne, N. E.; Flanagan, S.; Haley, M. M.; O'Brien, S. C.; Pan, C.; Xiao, Z.; Billups, W. E.; Ciufolini, M. A.; Hauge, R. H.; Margrave, J. L.; Wilson, L. J.; Curl, R. F.; Smalley, R. E. *J. Phys. Chem.* **1990**, *94*, 8634. Allemand, P.-M.; Koch, A.; Wudl, F.; Rubin, Y.; Diederich, F.; Alvarez, M. M.; Anz, S. J.; Whetten, R. L. *J. Am. Chem. Soc.* **1991**, *113*, 1050. Dubois, D.; Kadish, K. M.; Flanagan, S.; Wilson, L. J. *J. Am. Chem. Soc.* **1991**, *113*, 7773.

[4] *Fullerenes Synthesis, Properties, and Chemistry of Large Carbon Clusters*; Hammond, G., and Kuck, V. J., Eds.; ACS Symposium Series 481; American Chemical Society: Washington, DC, 1992.

[5] (a) Suzuki, T.; Li, Q.; Khemani, K. C.; Wudl, F.; Almarsson, Ö. *Science* **1991**, *254*, 1186. (b) Wudl, F. *Acc. Chem. Res.* **1992**, *25*, 157.

[6] The process was named fullerene inflation, with formation of "fulleroids C_{61}–C_{66}.

[7] In a preliminary work we observed that excess cyclopentadiene and excess anthracene react with C_{60}, giving products of multiple addition (Wudl, F.; Hirsch, A.; Khemani, K. C.; Suzuki, T.; Allemand, P.-M.; Koch, A.; Eckert, H.; Srdanov, G.; Webb, H. In ref 4, p 161).

[8] (a) Berson, J. A. *Acc. Chem. Res.* **1978**, *11*, 446. (b) Dowd, P. *Acc. Chem. Res.* **1972**, *5*, 242. (c) Noyori, R.; Hayashi, N.; Kato, M. *Tetrahedron Lett.* **1973**, 2938. (d) Noyori, R.; Hayashi, N.; Kato, M. *J. Am. Chem. Soc.* **1971**, *93*, 4948.

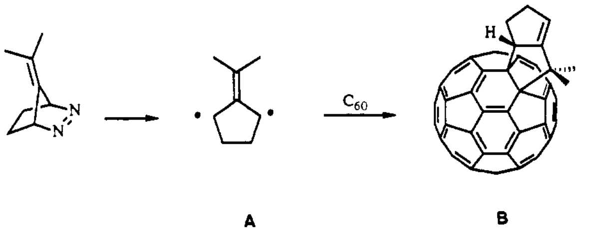
[9] Little, R. D.; Masjedizadeh, M. R.; Moeller, K. D.; Dannecker-Doerig, I. *Synlett* **1992**, 107. Moeller, K. D.; Little, R. D. *Tetrahedron Lett.* **1985**, *26*, 3417.

[10] Inter alia: McLoughlin, J. I.; Brahma, R.; Campopiano, O.; Little, R. D. *Tetrahedron Lett.* **1990**, *31*, 1377. Little, R. D.; Bode, H.; Stone, K. J.; Wallquist, O.; Dennecker, R. *J. Org. Chem.* **1985**, *50*, 2400.

[11] Yamago, S.; Nakamura, E. *J. Am. Chem. Soc.* **1989**, *111*, 7285.

[12] Yamago, S.; Nakamura, E. *J. Org. Chem.* **1990**, *55*, 5553.

[13] We have also examined the diradical addition of 2-isopropylidenecyclopentane-1,3-diyl[8-10] (A) to C_{60}. The diazene precursor of A was heated with a slight excess of C_{60} in refluxing toluene under argon atmosphere to give unreacted C_{60} and a monoadduct whose structure was determined as B on the basis of ^1H NMR spectroscopy [(500 MHz, $CS_2/CDCl_3$, δ) 5.99 (dd, *J* = 2.0, 1 H, bridgehead), 5.20 (m, 1 H, vinyl), 3.04–2.90 (m, 2 H), 2.80–2.71 (m, 1 H), 2.70–2.63 (m, 1 H), 2.12 (s, 3 H, CH_3), 2.00 (s, 3 H, CH_3)]. Unfortunately, we were unable to chromatographically separate C_{60} and this adduct because of their similar polarities. Any dimer expected to be produced by the combination of triplet diradicals was not detected by TLC (Berson, J. A.; Bushby, R. J.; McBride, J. M.; Tremelling, M. *J. Am. Chem. Soc.* **1971**, *93*, 1544). An excess of the reagent A led to multiple additions, and up to six substituents were observed by FAB mass spectrometry (m/z 1368, 1260, 1152, 1044, 936, and 720 amu).



A B

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