(*E*)-3-hexen-1-ol with a 2-h reaction time, under conditions where the reaction time was on the order of 1 min before protonolysis. Indeed, as reference to Table I shows, the carbometalation is remarkably facile with the brief reaction time very effective at improving the yields and percent conversions.

The effect of adding a "third-component" to the basic $TiCl_4$–$Al_2Et_4Cl_2$–$HOCH_2CH_2C{\equiv}CH$ systems was also studied. The addition of organic bases (third-components) to Ziegler–Natta polymerization systems has been extensively studied with beneficial effects on poly-α-olefin formation.[11] We examined methoxide (added as CH_3OH to the organoalane) and triphenyl phosphite. Methoxide addition inhibits the primary carbometalation and subsequent secondary reactions, e.g., oligomerization. At corresponding temperatures the yields of (*E*)-3-hexen-1-ol are low (<5%) but the mass balance is improved. With the addition of triphenyl phosphite percent conversions are better at corresponding temperatures, but the overall yield of (*E*)-3-hexen-1-ol is still low (<25%). (Specific reaction data for the base effects as well as reaction data for several other similar systems is available as supplementary data—see paragraph at the end of the paper.)

The third component data above compares well with the effects of several Lewis base components added to the $TiCl_4$–$Al_2Et_4Cl_2$–$HOCH_2CH{=}CH_2$ system. The data for this system (Table II) indicate clearly that as the σ Lewis base strength increases from phosphites through amines the overall amount of 3-buten-1-ol which reacts decreases with the strongest bases, pyridine and triethylamine essentially stopping the carbometalation process. Note also that the phosphorus-containing bases enhance ethylation at the terminal carbon of 3-buten-1-ol and that they inhibit β-hydride elimination so that very little (*E* or *Z*)-3-hexen-1-ol is formed and little of the hydrogenation product, 1-butanol, is seen. Thus, the base effect is one that enhances significantly the selectivity of the carbometalation reaction; however, it is unfortunate that the factors which curtail unwanted side reactions and improve selectively also apparently are those which decrease the facility of the primary carbometalation reaction.

The ethylation of two substituted homopropargyl alcohols, 4-pentyn-2-ol and 3-pentyn-1-ol, was studied. The terminal alkynol was selectively ethylated, giving (*E*)-4-hepten-1-ol in moderate yields. Surprisingly, the internal alkynol gave none of the expected monoethylated products.

In conclusion, the titanium tetrachloride–diethylaluminum chloride system does hold promise for the ethylation of terminal homopropargyllic alcohols. At this point, however, the addition of Lewis bases to Z–N systems appears to have the major effect of curtailing the primary carbometalation of the unsaturated carbon–carbon linkage and thus does not look promising for improving the synthetic usefulness of group 4B organolane reagents.

Acknowledgment. We thank the donors of the Petroleum Research Fund, administered by the American Chemical Society, for partial support of the work. We also thank the Jeffress Memorial Trust for research support, the Ethyl Corporation for gifts of organoalanes, and E. I. duPont de Nemours and Company and the National Science Foundation for funds with which to purchase gas chromatographs. Experimental assistance by J. J. Plunkett and J. D. Maimon is gratefully acknowledged.

Registry No. 1, 111-27-3; (*E*)-2, 928-97-2; 7, 627-27-0; 14, 927-74-2; III, 24469-79-2; $AlEt_2Cl$, 96-10-6; $TiCl_4$, 7550-45-0; 4-pentyn-2-ol, 2117-11-5; 3-pentyn-1-ol, 10229-10-4.

Supplementary Material Available: Extended reaction data for attempted ethylations of 3-butyn-1-ol and 3-pentyn-1-ol (2 pages). Ordering information is given on any current masthead page.

(11) Boor, J. "Ziegler–Natta Catalysts and Polymerization"; Academic Press: New York, 1979; pp 213–243.

Organocuprate Reactions with Cyclopropanes. Evidence for Three Types of Mechanism[1]

Steven H. Bertz* and Gary Dabbagh

Bell Laboratories, Murray Hill, New Jersey 07974

James M. Cook* and Vidya Honkan

Department of Chemistry, University of Wisconsin—Milwaukee, Milwaukee, Wisconsin 53201

Received August 9, 1982

Cyclopropane ring openings by organocuprates can be classified into three distinct classes. Mechanistically, the simplest openings are the direct nucleophilic displacements with enolate leaving groups. In order to be synthetically useful, these reactions usually require activation by two groups. Substrates that contain vicinal olefin and activating groups generally are opened by S_N2'-like displacements. Finally, β-cyclopropyl-α,β-unsaturated ketones react by a mechanism intimately related to the conjugate addition reaction of α,β-unsaturated ketones.

Introduction

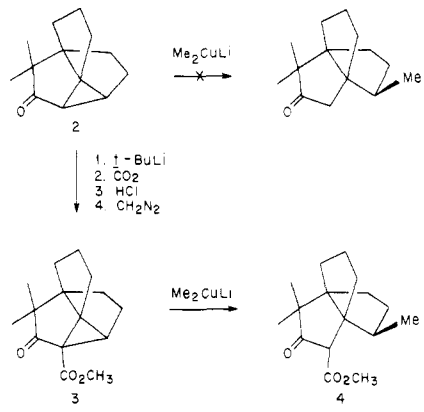
House and his co-workers have reported the results of a number of experiments supporting an electron-transfer mechanism for the conjugate addition reaction of lithium diorganocuprates to α,β-unsaturated ketones;[2-6] however, alternative explanations also have been advanced. For example, Casey and Cesa[7] have pointed out that the cis-

(1) Presented in part by S.H.B. at the Mechanisms Conference, Salt Lake City, UT, June 21, 1982. New Copper Chemistry, part VII. Part VI, see ref 36. Part V: Bertz, S. H.; Dabbagh, G.; Villacorta, G. M. *J. Am. Chem. Soc.* **1982**, *104*, 5824.

(2) House, H. O. *Acc. Chem. Res.* **1976**, *9*, 59.
(3) House, H. O.; Weeks, P. D. *J. Am. Chem. Soc.* **1975**, *97*, 2770.
(4) House, H. O.; Weeks, P. D. *J. Am. Chem. Soc.* **1975**, *97*, 2778.
(5) House, H. O.; Prabhu, A. V.; Wilkins, J. M.; Lee, L. F. *J. Org. Chem.* **1976**, *41*, 3067.
(6) House, H. O.; Snoble, K. A. J. *J. Org. Chem.* **1976**, *41*, 3076.

0022-3263/84/1949-1739$01.50/0

Scheme I



trans isomerization[3] of *cis*-2,2-dimethyl-5-phenyl-4-penten-3-one that accompanies the 1,4-addition reaction of lithium dimethylcuprate (**1**) could be a side reaction unrelated to the conjugate addition. Likewise, Posner[8] has observed that the reduction of 4-acetoxy-2-cyclohexen-1-one by **1** could occur either by electron transfer to produce an intermediate radical anion (as proposed by Ruden and Litterer[9]) or by direct nucleophilic addition of $^{-}CuMe_2$ to the 3-position followed by an E1cb-like elimination of ^{-}OAc. The focus of this controversy has recently centered on the alkylative ring opening of β-cyclopropyl-α,β-unsaturated ketones.[4-7,10] Following Marshall and Ruden,[10] House proposed a cyclopropylcarbinyl–homoallyl rearrangement of an intermediate radical anion;[2] however, Casey and Cesa showed the reaction to be stereospecific, and they proposed a direct nucleophilic attack by **1** on the cyclopropane.[7] The opening of activated cyclopropanes by organocopper reagents has been studied in many laboratories, but a comprehensive picture of the scope and limitations of these reactions has not emerged. We wish to communicate the results of several studies that help to resolve some of the mechanistic and synthetic questions regarding these reactions.

Results

Experiments initially involved the pair of cyclopropyl propellanes **2** and **3** (Scheme I), which were treated with **1** in the hope of stereospecifically introducing a methyl group as the key step in a synthesis of modhephene.[11] While **2** could not be induced to react with **1**, **3** was opened smoothly to **4** by **1**.

In order to determine whether our inability to open **2** was due to steric inhibition or the lack of a second activating group, we studied the reaction of **1** with benzoylcyclopropane (**5**), an unhindered cyclopropane with but one activating group. Table I summarizes the results of treating **5** with halide-free[7] Me_2CuLi and with Me_2CuLi–LiBr in ether and in THF. The yield of 1,2-addition product, cyclopropylmethylphenylcarbinol (**6**), is as high as 66% (**1**·LiBr; 24 h) in ether, where there is apparently a positive effect of LiBr on the reaction (cf. **1**; 24 h). In THF the yields are low (7–15%) and do not appear to be influenced by LiBr. The amount of 1,4-adduct, butyl phenyl ketone (**7**), is higher in THF than in ether, and in both solvents the final yield (24 h) is higher when LiBr is present; however, the yield is always low.

Table I. Reaction of Cyclopropyl Phenyl Ketone with Me_2CuLi

reagent	solvent	time, h	% 5[a,b]	% 6[a,c]	% 7[a,d]
Me_2CuLi (1)	ether	1	55	38	2
		24	25	50	3
	THF	1	88	12	7
		24	72	15	11
Me_2CuLi–LiBr (1·LiBr)	ether	1	54	42	2
		24	18	66	5
	THF	1	89	7	6
		24	67	15	16

[a] Yields determined by GLC calibrated with authentic products and internal standard. [b] Cyclopropyl phenyl ketone. [c] Cyclopropylmethylphenylcarbinol. [d] Butyl phenyl ketone.

Table II. Competition Reactions

reagent	temp, °C	time, min	% 8[a,b]	% 9[a,c]	% 10[a,d]	% 11[a,e]
Me_2CuLi (1)	−78	1	88	27	0[f]	61
		5	91	22	0[f]	67
	0	1	70	16	28	42
		5	68	6	27	32
	35	1	90	0	7	53
		5	90	0	7	52
Me_2CuLi–LiBr (1·LiBr)	−78	1	89	0	4	83
		5	86	0	6	85
	0	1	72	16	29	51
		5	62	0	33	40
	35	1	83	0	16	77
		5	82	0	16	77

[a] Yields determined by GLC calibrated with authentic products and internal standard. [b] Diethyl 1,1-cyclopropanedicarboxylate. [c] 2-Cyclohexen-1-one. [d] Diethyl propylmalonate. [e] 3-Methylcyclohexanone. [f] Limit of detection ~0.05%.

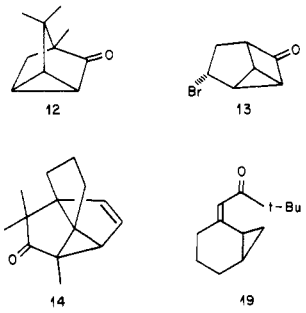
The chemoselectivity of **1** toward the ring-opening reaction of bis-activated cyclopropanes, modeled by diethyl 1,1-cyclopropanedicarboxylate (**8**), vs. the conjugate addition process of α-enones, modeled by 2-cyclohexen-1-one (**9**), was determined in competition experiments involving **8**, **9**, and **1** under various conditions. Temperature is the most important experimental variable, as proven by the data in Table II. With **1** at −78 °C, there is no competition. No diethyl propylmalonate (**10**) is observed, and all of **1** reacts with **9** to yield 3-methylcyclohexanone (**11**). (In a control experiment without **9**, **8** reacted smoothly with **1** at −78 °C.) Since the limit of detection of **10** by our GLC method is 0.05%, the ratio of conjugate addition to ring opening is *at least* 67/0.05 = 1300. At 0 °C significant ring opening occurs; nevertheless, conjugate addition is still dominant. Surprisingly, increasing the temperature to 35 °C results in a shift back toward conjugate addition. At all temperatures, the presence of LiBr increases the amounts of products.

Discussion

The set of experiments involving **2** and **3** is the first to compare singly and doubly activated cyclopropanes in which the remainder of the molecule is the same. From our results, it appeared that two activating groups were necessary for ring opening; however, the possibility remained that the additional activation of the second group was needed to overcome steric inhibition in this tetracyclic system. The results with the unhindered cyclopropane **5** removed this latter possibility. It now can be concluded that the earlier inability of Scott and Cotton[12] to open the

(7) Casey, C. P.; Cesa, M. C. *J. Am. Chem. Soc.* **1979**, *101*, 4236.
(8) Posner, G. H. "An Introduction to Synthesis Using Organocopper Reagents"; Wiley: New York, 1980; p 51.
(9) Ruden, R. A.; Litterer, W. E. *Tetrahedron Lett.* **1975**, 2043.
(10) Marshall, J. A.; Ruden, R. A. *J. Org. Chem.* **1972**, *37*, 659.
(11) Wrobel, J.; Takahashi, K.; Honkan, V.; Lannoye, G.; Cook, J. M.; Bertz, S. H. *J. Org. Chem.* **1983**, *48*, 139.

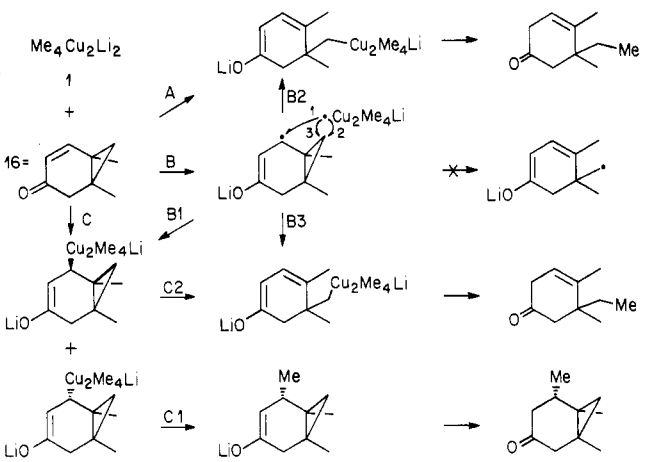
cyclopropane ring of pericyclocamphor (12) was due to insufficient activation, since, like 2, it contains but one activating group. On the other hand, 13, which is opened by cuprates,[13] can be looked upon as a special case requiring only one activating group because of the ring strain present in the tricyclo[3.2.0.0^{2,7}]heptane ring system. The



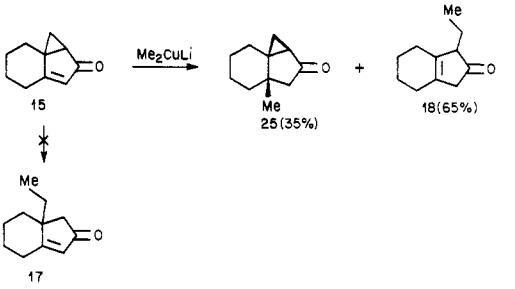
6-oxo derivatives such as 13 are known to react readily with various nucleophiles.[14] The only report of an alkylative opening of an unstrained, singly activated cyclopropane is the recent one by Johnson and Dhanoa,[15] who report a 65% yield of 1-phenyl-1-pentanone (7) from 1 and 5. In harmony with our results, House et al. had earlier reported predominately 1,2-addition with these reactants in ether and "only minor amounts (0.6–3.5%) of ring-opened products".[5,16] House has also studied the related 2,3-methanoindanone, which gives relatively more 1,4-adduct, 3-ethylindanone (13–18%), due to ring strain and favorable geometry for a direct nucleophilic displacement.[16] However, we propose an alternative mechanism for this case (vide infra). All other successful cuprate-induced cyclopropane openings[17–21] that occur *in the absence of a double bond* involve at least two activating groups on the same cyclopropyl carbon atom. We believe that these reactions (type I) proceed by direct nucleophilic displacement with β-keto ester,[17–19] cyanoacetate,[20] or malonate[19–21] enolates as leaving groups, as proposed by House and Weeks.[4]

A second class of cyclopropane openings, which often is not distinguished from those considered above, are the ones which involve a nonconjugated vinyl group as in diethyl 2-vinyl-1,1-cyclopropanedicarboxylate.[22] These ring openings are best described as S_N2' reactions (type II), such as those of cuprates with allyl acetates[23] and allyl halides.[24] Only one opening of such a substrate without allylic inversion has been discovered: Wender and Dreyer treat 14

Scheme II



Scheme III



with 1 in a key step of their modhephene synthesis.[25] This direct displacement at an allylic center belongs with the type I reactions. The reason that 14 does not undergo an S_N2' reaction was elucidated with the aid of molecular mechanics calculations.[25]

The third class of cyclopropane openings (type III) requires only one activating group–*a conjugated enone*. All of the reported cases involve fused-ring systems.[4,6] These have generally involved cyclopropanes fused to six-membered rings;[6,7,10] however, an example involving fusion to a five-membered ring has been reported (see 15, Scheme III).[26]

Casey and Cesa[7] have shown that the cyclopropane ring of 16 is opened stereospecifically by 1, thus precluding a free-radical intermediate from a cyclopropylcarbinyl–homoallyl rearrangement of a radical anion, as proposed by House[2] (Scheme II, path B). Casey and Cesa[7] suggested a direct nucleophilic displacement on the cyclopropane (path A), and, indeed, models indicate that the bond broken in 16 is oriented favorably for overlap with the π system as the reaction proceeds. However, assuming a direct nucleophilic attack with an extended enolate for a leaving group, it was disturbing to us that 2, 5, and other cyclopropanes activated by a single keto group[5,12,19,27] are not opened under conditions that suffice to open cyclopropanes activated by a conjugated enone, since the α′-hydrogens of α,β-unsaturated ketones are *kinetically* more acidic than the γ-hydrogens.[28] Thus, some 17 (enolate leaving group) should have been observed from 15 in addition to 18 (extended enolate leaving group) if a direct nucleophilic displacement were operative.

There are three reasons that 16 might be opened more readily than 2: (i) differences in overlap between exocyclic

(12) Scott, L. T.; Cotton, W. D. *J. Chem. Soc., Chem. Commun.* **1973**, 320.
(13) Finch, M. A. W.; Roberts, S. M.; Woolley, G. T.; Newton, R. F. *J. Chem. Soc., Perkin Trans. 1*, **1981**, 1725.
(14) Lee, T. V.; Roberts, S. M.; Newton, R. F. *J. Chem. Soc., Perkin Trans. 1* **1978**, 1179.
(15) Johnson, C. R.; Dhanoa, D. S. *J. Chem. Soc., Chem. Commun.* **1982**, 358.
(16) House, H. O.; McDaniel, W. C.; Sieloff, R. F.; Vanderveer, D. *J. Org. Chem.* **1978**, *43*, 4316.
(17) Yates, P.; Stevens, K. E. *Tetrahedron* **1981**, *37*, 4401.
(18) Trost, B. M.; Taber, D. F.; Alper, J. B. *Tetrahedron Lett.* **1976**, 3857.
(19) Clark, R. D.; Heathcock, C. H. *Tetrahedron Lett.* **1975**, 529.
(20) Corey, E. J.; Fuchs, P. L. *J. Am. Chem. Soc.* **1972**, *94*, 4014.
(21) Alexakis, A.; Cahiez, G.; Normant, J. F. *Tetrahedron* **1980**, *36*, 1961.
(22) Daviaud, G.; Miginiac, Ph. *Tetrahedron Lett.* **1972**, 997. Grieco, P. A.; Finkelhor, R. *J. Org. Chem.* **1973**, *38*, 2100. See also papers by Miyaura et al. (Miyaura, N.; Itoh, M.; Sasaki, N.; Suzuki, A. *Synthesis* **1975**, 317. Miyaura, N.; Itoh, M.; Suzuki, A. *Tetrahedron Lett.* **1976**, 255) for the corresponding reaction of 1-acyl-2-vinylcyclopropanes. For an application to natural product synthesis: Schultz, A. G.; Godfrey, J. D.; Arnold, E. V.; Clardy, J. *J. Am. Chem. Soc.* **1979**, *101*, 1276.
(23) Anderson, R. J.; Henrick, C. A.; Siddall, J. B. *J. Am. Chem. Soc.* **1970**, *92*, 735.
(24) Chapleo, C. B.; Finch, M. A. W.; Lee, T. V.; Roberts, S. M.; Newton, R. F. *J. Chem. Soc., Chem. Commun.* **1979**, 676.
(25) Wender, P. A.; Dreyer, G. B. *J. Am. Chem. Soc.* **1982**, *104*, 5805.
(26) Frejaville, C.; Jullien, R. *Tetrahedron Lett.* **1971**, 2039.
(27) Marshall, J. A.; Ruden, R. A. *Tetrahedron Lett.* **1971**, 2875.
(28) Caine, D. In "Carbon–Carbon Bond Formation"; Augustine, R. L. Ed.; Marcel Dekker: New York, 1979; Vol. 1, p 284.

and endocyclic double bonds could be important, (ii) the greater *thermodynamic* stability of the extended enolate resulting from nucleophilic opening of the cyclopropane of **16** might be the controlling factor, (iii) a mechanism other than direct nucleophilic attack on the cyclopropane might be operative in the case of **16** but not be possible for **2**.

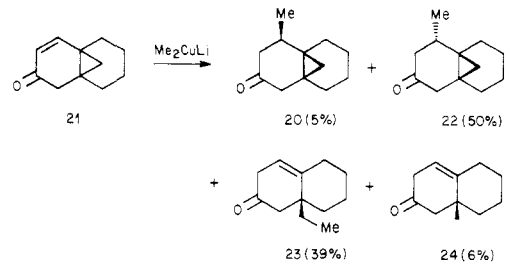
Compound **19** with its exocyclic enone is decisive in settling the first point. It readily undergoes cleavage, and, in fact, the proportion of ring-opened products to normal conjugate addition products (72:28, respectively[6]) is greater than that obtained from **16** (52:48, respectively[7]). This does not prove that the cyclopropane opening of **19** is faster than that of **16**, since the conjugate addition to **19** might well be slower; however, it does prove that the overlap with an exocyclic double bond instead of an endocyclic one is not an impediment to reaction.

To test hypothesis (ii) we conducted the competition experiments between 2-cyclohexen-1-one and diethyl 1,1-cyclopropanedicarboxylate (**8**) for a limited amount of **1**. Cyclopropane **8** was chosen for study because it is not sterically hindered and the malonate leaving group is ca. 1000000 times more thermodynamically stable than a vinylogous enolate based upon pK_a considerations.[28] The ratio of conjugate addition to ring opening under the conditions used by Casey and Cesa[7] (halide-free **1** in ether at −78 °C) was >1000. Since in all observed type III reactions ring opening is competitive with conjugate addition, the results of our competition experiments rule out (ii) and make it appear unlikely that the ring opening involves a straightforward nucleophilic attack. Therefore, we believe (iii) to be correct.

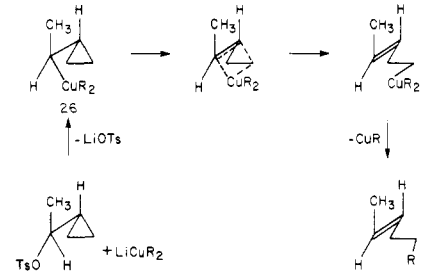
Considering the fact that ring opening and conjugate addition are always competitive in rigidly fused β-cyclopropyl enones[6,7,10,26] such as **16** and **19**, we believe that the two processes are intimately related and represent either the partitioning of a common intermediate (such as the radical anion) between conjugate addition (Scheme II, path B1) and *Cu-assisted* ring opening (path B2 or B3) or the competition between endo and exo versions of the same initial reaction (path C). In path C nucleophilic (Michael-like) addition of Cu on the face trans to the cyclopropane would be expected to proceed via reductive elimination[29] to the normal conjugate addition product (path C1). In contrast, addition of Cu to the face of the enone cis to the cyclopropane followed by insertion[29] into the vicinal cyclopropane bond (path C2) and subsequent reductive elimination would give the ring-opened product. An alternative to the Michael-like addition to yield the Cu(III) intermediate involves electron transfer (path B) followed by combination of the geminate pair (path B1).

This insertion mechanism accounts for the observation that when the cyclopropyl group is free to rotate (i.e., when it is not part of a fused system), ring opening is not observed, since in such cases the rate of insertion would be decreased whereas the rate of reductive elimination to the normal conjugate addition product would be unaffected. Further, if the rate of insertion in fused systems is not considerably faster than that of reductive elimination, some of the conjugate addition product with the β-methyl cis to cyclopropyl should be observed. In fact, such a minor product, **20** (Scheme IV), was isolated by Marshall and Ruden[10] from a closely related system, **21**, along with the usual products (**22** and **23**) and a small amount of reduction product (**24**). In the five-membered ring system **15**,

Scheme IV



Scheme V



all of the conjugate addition occurs on the same (convex) face, syn to the cyclopropane, and reductive elimination to the normal product (**25**) is more competitive with insertion than in **21**.

Our insertion mechanism also provides an alternative explanation for House's cyclopropylindanone results[16] (vide supra first paragraph of discussion): attack by the Cu of **1** at the carbonyl on the same face as the cyclopropane followed by insertion in the vicinal cyclopropyl bond would give the minor product, 3-ethylindanone (13–18%), upon reductive elimination. The major product (1,2-adduct with Me trans to cyclopropyl, 39–80%) would result from attack at the carbonyl on the face opposite the cyclopropane. Evidence was presented against electron transfer in this system.[16]

Such a cuprate-mediated cyclopropylcarbinyl–homoallyl rearrangement may be involved in the reaction of lithium dibutylcuprate with cyclopropylmethylcarbinyl tosylate to afford (*E*)-2-nonene.[30] The requirement that the C–Cu bond eclipse the vicinal cyclopropyl C–C bond in the more-stable conformation (Me eclipsing H) accounts for the fact that only the trans-olefin is observed (Scheme V). The stereoelectronic requirements for the transition state are the same as those for the β-hydride elimination reaction of cuprates and other transition metals.[29] Johnson and Dutra[31] have presented evidence that tosylates react with cuprates via Cu(III) intermediates analogous to those in Schemes II and V (**26**). An allenic Cu(III) intermediate is stable enough in solution to be trapped chemically.[32] Furthermore, there is substantial evidence that Cu(II) oxidizes alkyl radicals via Cu(III) intermediates.[33]

Ni(II) is isoelectronic with Cu(III), and an insertion analogous to the one we propose for Cu(III) has been proposed for one step in the conversion of methylenecyclopropane to butadiene mediated by the reagent prepared from bis(tributylphosphine)nickel(II) bromide and butyllithium.[34]

(29) Collman, J. P.; Hegedus, L. S. "Principles and Applications of Organotransition Metal Chemistry"; University Science Books: Mill Valley, Ca, 1980.

(30) Posner, G. H.; Ting, J.-S.; Lentz, C. M. *Tetrahedron* **1976**, *32*, 2281.

(31) Johnson, C. R.; Dutra, G. A. *J. Am. Chem. Soc.* **1973**, *95*, 7783.

(32) Dollat, J.-M.; Luche, J.-L.; Crabbé, P. *J. Chem. Soc., Chem. Commun.* **1977**, 761.

(33) Kochi, J. K.; Bemis, A.; Jenkins, C. L. *J. Am. Chem. Soc.* **1968**, *90*, 4616.

(34) Takaya, H.; Hayashi, N.; Ishigami, T.; Noyori, R. *Chem. Lett.* **1973**, 813.

Conclusions

Cyclopropane openings by organocuprates can be classified into three categories: (I) direct nucleophilic displacements which generally require activation by two groups, (II) S_N2'-like displacements, and (III) β-cyclopropyl-α,β-unsaturated ketone reactions closely related to conjugate additions to these substrates. The determination that the type III reaction is stereospecific seemed at first to rule out the intermediacy of radical anions produced by electron transfer.[7] We have reinstated the electron-transfer hypothesis as a reasonable mechanism by proposing an alternative explanation for the stereospecificity, viz., insertion of a Cu(III) intermediate into a cyclopropyl C–C bond. Since the stereochemistry of this process (retention) is opposite that of an S_N2 reaction (inversion), it should be possible to differentiate them experimentally.[35] In the meantime, our evidence against a direct nucleophilic displacement (S_N2-like) mechanism is threefold: (i) the fact that in the absence of additional strain, keto-activated cyclopropanes are not opened by organocuprates; (ii) the observation that under the conditions of the type III reaction, the type I reaction is not competitive with conjugate addition, even with a much superior leaving group; and (iii) the fact that in a system (**15**) in which two equally favorable type I reactions could occur, only one product—the one predicted by the insertion mechanism—is observed. By bringing the mechanistic issues associated with the type III reaction into clearer focus, it may be hoped that this study has advanced efforts to understand the exceedingly important conjugate addition reaction of organocuprates.

Experimental Section

General aspects have been described in detail and will not be repeated here.[36]

Methyl 2,2,6-Trimethyl-3-oxotricyclo[3.3.3.0^{1,5}]undecane-4-carboxylate (4). Methyl lithium–lithium bromide complex (5.3 mL, 1.2 M, 6.4 mmol, Aldrich) was added to 0.60 g (3.2 mmol) of CuI (Aldrich) suspended in 10 mL of ether (freshly distilled from sodium benzophenone ketyl) in a septum-sealed 25-mL round-bottom flask at −70 °C. The suspension was warmed to 0 °C and stirred magnetically until a clear, nearly colorless solution was obtained. This solution was transferred by cannula to a solution of 0.60 g (2.4 mmol) of methyl 4,4-dimethyl-3-oxotetracyclo[3.3.3.0^{1,5}.0^{2,8}]undecane-2-carboxylate (**3**)[11] in 30 mL of ether at −70 °C. The reaction mixture was allowed to warm to −10 °C (50 min) and maintained at that temperature for 1 h. It was then quenched with aqueous ammonium chloride, and the layers were separated. The aqueous layer was extracted with three 100-mL portions of ether, and the combined organic layers were back-extracted with aqueous sodium chloride, dried over anhydrous sodium sulfate, and evaporated at reduced pressure. The greenish residue was chromatographed on silica gel, eluted with benzene, to yield 0.575 g (90%). Subjecting **2**[11] to the same conditions resulted only in recovered starting material and a small amount (<10%) of 1,2-adduct after 24 h.

Reaction of Cyclopropyl Phenyl Ketone (5) with Lithium Dimethylcuprate (1). Halide-free MeCu was prepared at 0 °C (ice bath) by adding 0.70 mL of 1.49 M (1.04 mmol) MeLi (Aldrich, low halide, 0.18 M residual base) to 216 mg (1.05 mmol) of copper(I) bromide–dimethyl sulfide complex (Aldrich, stored in a drybox) suspended (magnetic stirring) in 5 mL of ether (freshly distilled from sodium benzophenone ketyl) in a septum-sealed 25-mL recovery flask. After the mixture was stirred for 10 min, the yellow MeCu was allowed to settle (5 min) and the supernatant liquid was withdrawn by syringe. Fresh ether (5 mL) was added, the mixture was stirred for 10 min, and the ether was removed as before. After one additional rinse, the reaction solvent (10 mL of ether or THF) was added followed by 0.67 mL (1.00 mmol) of 1.49 M MeLi. After the mixture was stirred for 5 min, a small amount of yellow solid remained (indicating that no excess MeLi and thus no Me_3CuLi_2 was present), and 146 mg (1.00 mmol) of cyclopropyl phenyl ketone (Aldrich) was added along with ~37 mg (50 μL, weighed to the nearest 0.1 mg) of dodecane (internal standard) in 3 mL of ether or THF. The reaction mixture was sampled after 1.0 and 24 h at 0 °C, and the 2-mL samples were quenched with deoxygenated 3 M aqueous ammonium chloride (1 mL/2 dram vial). The organic layers were separated, dried over anhydrous sodium sulfate, and analyzed for butyl phenyl ketone (**7**) and cyclopropylmethylphenylcarbinol (**6**) by calibrated GLC.

The above experiment was repeated with Me_2CuLi–LiBr prepared at 0 °C by adding 1.34 mL (2.00 mmol) of 1.49 M low-halide MeLi to 206 mg (1.00 mmol) of CuBr·SMe_2 suspended in 10 mL of solvent (ether or THF).

As a control experiment for the identification of **6** (the 1,2-addition product), an analogous procedure was carried out in which 1.00 mmol of MeLi was used instead of the cuprate.

Competition Experiments.[37] A suspension of 206 mg (1.00 mmol) of copper(I) bromide–dimethyl sulfide complex (Aldrich) in 10 mL of ether in a septum-sealed 25-mL recovery flask at 0 °C was treated with 0.65 mL (1.02 mmol) of 1.55 M MeLi (Aldrich, low halide, 0.08 M residual base). The resulting yellow suspension was treated with 0.64 mL (0.99 mmol) of 1.55 M MeLi. The colorless solution, which still contained a trace of yellow MeCu, was cooled to −75 °C (dry ice/2-propanol) and a cold (−75 °C) solution of diethyl 1,1-cyclopropanedicarboxylate (187 mg, 1.00 mmol, Aldrich), 2-cyclohexen-1-one (96.0 mg, 1.00 mmol, Aldrich), and *n*-decane (54.1 mg, Chemical Sample Co., internal standard) in 5 mL of ether was added to it with a cooled syringe. A flocculent yellow precipitate formed immediately. At reaction times of 1, 5, and 30 min, a 2-mL aliquot was removed with a cooled syringe and quenched by injecting it into a 2-dram vial containing 2 mL of deoxygenated (nitrogen) 3 M aqueous ammonium chloride. The organic phase was withdrawn with a disposable glass pipet and dried over anhydrous sodium sulfate in a 2-dram vial with a polyethylene seal. The amounts of **8** and **10** were measured by calibrated GLC, using a 3 m × 3 mm 5% OV-101 column (Alltech) and **9** and **11** on a 3 m × 3 mm 5% Carbowax 20M column (Alltech).

This experiment was repeated with halide-free **1** prepared as in the previous procedure. It was also repeated with both **1** containing LiBr and halide-free **1** at 0 and 35 °C.

The limits of detection of **10** were determined to be 0.05% by serial dilution of the calibration mixture.

Acknowledgment. J.M.C. and V.H. thank the National Science Foundation and the Petroleum Research Fund, administered by the American Chemical Society, for generous financial support. S.H.B. thanks Professors C. P. Casey and G. H. Posner for helpful discussions.

Registry No. **1**, 15681-48-8; **1**·LiBr, 89578-86-9; **3**, 89578-87-0; **5**, 3481-02-5; **8**, 1559-02-0; **9**, 930-68-7; **19**, 83467-87-2; CuBr·SMe_2, 54678-23-8; LiBr, 7550-35-8; CuI, 7681-65-4; MeLi, 917-54-4.

(35) Labeling studies are in progress in several laboratories.
(36) Bertz, S. H.; Dabbagh, G. *J. Org. Chem.* **1984**, *49*, 1119.
(37) Competition experiments with **1** have also been carried out by House et al.; see ref 5.