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# The Stereochemistry of the Conjugate Addition of Derivatives of *endo*-2-Norbornylcopper(I) to Mesityl Oxide[1a]

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Reaction between mesityl oxide and the ate complex formed by mixing *endo*-2-norbornyl(tri-*n*-butylphosphine)copper(I) (*endo*-**2**) and *tert*-butyllithium yields the conjugate adduct, 4-methyl-4-(*endo*-2-norbornyl)pentan-2-one (**3**), with high stereoselectivity; no detectable 4-methyl-4-(*exo*-2-norbornyl)pentan-2-one (**4**) is formed. This stereochemical outcome excludes a free norbornyl radical as an intermediate in this particular conjugate addition reaction. Similar stereochemical results are obtained using either the analogous trimethyl phosphite complex or the ate complex formed by mixing *endo*-**2** with methyllithium; the same mechanistic conclusion can be drawn concerning these reactions. The copper-catalyzed conjugate addition of *endo*-2-norbornylmagnesium bromide (*endo*-**1**) to mesityl oxide yields an 81:19 ratio of endo and exo conjugate adducts; the conjugate addition of **2** itself occurs with extensive loss of stereochemistry. Mechanistic interpretation of these latter reactions is complicated both by the formation of conjugate adduct in relatively low yields, and by the two possibilities that epimerization of the copper reagents competes with their conjugate additions and that the endo and exo organometallic reagents differ in their reactivity in these additions. A comparison of the combined yields of **3** and **4** obtained on reaction of mesityl oxide with **1** in a copper-catalyzed reaction, with **2**, and with a number of ate complexes containing **2** and primary, secondary, tertiary, and aromatic lithium reagents indicates that the mixed ate complex of **2** and *tert*-butyllithium is uniquely active in the transfer of the 2-norbornyl group in the conjugate addition.

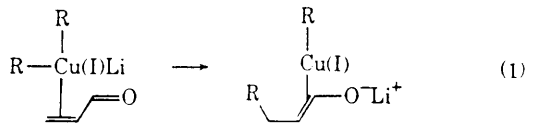
Both the copper-catalyzed conjugate addition of organomagnesium and -lithium reagents to $\alpha,\beta$-unsaturated ketones and the rapid stoichiometric conjugate addition of lithium dialkylcuprates to these substances are well established and synthetically important reactions.[2] However, the mechanism by which the copper ion encourages addition of the anionic organic moiety to the $\beta$-carbon atom of the unsaturated ketone moiety at the expense of addition to the carbonyl group is not understood.[3] Several experimental generalizations known or believed to be true for it follow.

(a) Copper(I) is the valence state that is active in the conjugate addition; further, the copper(I) is apparently not oxidized or reduced irreversibly during the course of the reaction.[4]

(b) Copper(I) alkyls add to a number of types of carbon–carbon multiple bonds in the absence of a conjugating carbonyl moiety; in particular, lithium dialkylcuprates add smoothly to $\alpha,\beta$-unsaturated epoxides[6] and ethynylcarbinyl acetates,[7] and organocopper(I) compounds themselves add to terminal acetylenes[8] and nitroaromatics.[9] Thus, the presence of a conjugating carbonyl group is not necessary for the addition of an organic moiety bonded to copper to a carbon–carbon multiple bond.

(c) Conjugate addition can occur successfully to $\alpha,\beta$-unsaturated ketones confined to a transoid configuration; a cyclic transition state for the addition, involving a cisoid conformation for the ketone, is thus not required.[3,10,11]

Four basic classes of mechanisms have been proposed to account for the influence of copper on reactions of organometallic reagents with $\alpha,\beta$-unsaturated ketones. First, the reaction has been suggested to involve as its basic step the nucleophilic addition of an anionic alkyl group to the carbon–carbon double bond. In this mechanism (represented schematically by eq 1), the copper atom might serve either to orient



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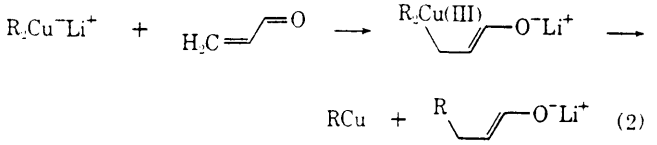


(2)

the alkyl group in a position favorable for attack on the $\beta$-carbon atom of the enone moiety by coordination with the double bond, or to activate this bond for

(1) (a) Supported by the National Science Foundation, Grants GP-28586X and GP-14247, and by the International Copper Research Association; (b) National Science Foundation Trainee, 1970–1971.

(2) For reviews and references, see (a) H. O. House, W. L. Respess, and G. M. Whitesides, *J. Org. Chem.*, **31**, 3128 (1966); (b) H. O. House and W. F. Fischer, Jr., *ibid.*, **33**, 949 (1968).

(3) The catalytic activity of copper in organic reactions has been reviewed: R. G. R. Bacon and H. A. O. Hill, *Quart. Rev., Chem. Soc.*, **19**, 95 (1965); O. A. Chaltykian, "Copper-Catalytic Reactions," A. E. Stubbs, Translator, Consultants Bureau, New York, N. Y., 1966.

(4) Alkylcopper(I) compounds frequently precipitate on reaction of the corresponding lithium dialkylcuprates with $\alpha,\beta$-unsaturated ketones.[2b,5]

(5) H. O. House and W. F. Fischer, Jr., *J. Org. Chem.*, **34**, 3615 (1969).

(6) R. W. Herr and C. R. Johnson, *J. Amer. Chem. Soc.*, **92**, 4979 (1970); R. J. Anderson, *ibid.*, **92**, 4978 (1970).

(7) P. Rona and P. Crabbé, *ibid.*, **91**, 3289 (1969).

(8) J. F. Normant and M. Bourgain, *Tetrahedron Lett.*, 2583 (1971).

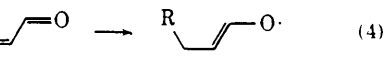
(9) M. Nilsson, C. Ullenius, and O. Wennerström, *ibid.*, 2713 (1971).

(10) H. O. House, R. A. Latham, and C. D. Slater, *J. Org. Chem.*, **31**, 2667 (1966).

(11) C. P. Casey and R. A. Boggs, *Tetrahedron Lett.*, 2455 (1971).

addition.[12] Second, the copper atom might take part directly in the reaction by an oxidative addition process yielding an intermediate copper(III) species, followed by reductive elimination of the conjugate adduct from this intermediate (eq 2).[13,14] Third, conjugate addition might take place through a free radical chain process (eq 3–5). In this reaction se-

$$R_2CuLi \xrightarrow{\text{initiation}} R\cdot \quad (3)$$



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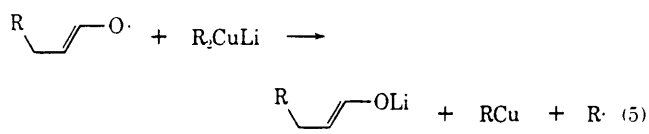
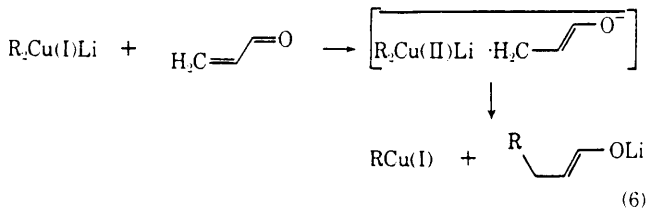


(5)

quence, the copper(I) would serve as the metallic center in a radical displacement reaction (eq 5).[17] The conjugate addition of trialkylboranes to $\alpha,\beta$-unsaturated ketones is reported to be a free-radical process, presumably taking place by a sequence of reactions analogous to those represented by eq 3–5, and provides precedent for the involvement of free radicals in conjugate additions.[18] Finally, conjugate addition has been suggested to involve electron transfer in an important step (eq 6).[2,19] The catalytic activity of cop-



(6)

(12) The structures of the ate complexes formed between organocopper(I) compounds and organolithium reagents have not been established. For simplicity, we will refer to these materials as "lithium dialkylcuprates," and represent them by formulas of the type $R_2CuLi$ or $R_2Cu^-Li^+$, with no conviction that these descriptions of the structures of the copper ate complexes necessarily bear any relationship to those actually existing.

(13) The activation of carbon–carbon double bonds toward nucleophilic attack by coordination with transition metals is illustrated, *inter alia*, by the Wacker process and many reactions of the type i → ii.

i ii

See, for examples, J. Halpern, *Advan. Chem. Ser.*, **70**, 1 (1968); P. M. Henry, *ibid.*, **70**, 126 (1968); M. M. Jones, "Ligand Reactivity and Catalysis," Academic Press, New York, N. Y., 1968, pp 84–85; P. M. Maitlis, "The Organic Chemistry of Palladium," Academic Press, New York, N. Y., 1971; A. Panunzi, A. De Renzi, and G. Paiaro, *J. Amer. Chem. Soc.*, **92**, 3488 (1970); G. N. Schrauzer, J. H. Weber, and T. M. Beckham, *ibid.*, **92**, 7078 (1970).

(14) Oxidative addition of carbon-containing residues to copper(I) has been discussed previously in connection with the reactions of lithium dialkylcuprates with organic halides,[15,16] and $\alpha,\beta$-unsaturated epoxides.[6] However, no firm experimental evidence bearing on the importance of this process in organocopper(I) chemistry is presently available.

(15) G. M. Whitesides, W. F. Fischer, Jr., J. San Filippo, Jr., R. W. Bashe, and H. O. House, *J. Amer. Chem. Soc.*, **91**, 4871 (1969), and references cited therein.

(16) J. R. Collman, *Accounts Chem. Res.*, **1**, 136 (1968).

(17) A rapidly increasing body of evidence indicates that radical displacements at metallic centers may be very rapid processes: P. J. Krusic and J. K. Kochi, *J. Amer. Chem. Soc.*, **91**, 3942 (1969); A. G. Davies and B. P. Roberts, *J. Organometal. Chem.*, **19**, P17 (1969); K. U. Ingold and B. P. Roberts, "Free Radical Substitution Reactions," Wiley, New York, N. Y., 1971; and references in each.

(18) H. C. Brown, *et al.*, *J. Amer. Chem. Soc.*, **92**, 710 (1970); H. C. Brown and G. W. Kabalka, *ibid.*, **92**, 712, 714 (1970).

(19) (a) I. N. Rozhkov and S. M. Makin, *Zh. Obshch. Khim.*, **34**, 59 (1964); *Chem. Abstr.*, **60**, 10576 (1964); (b) H. O. House and M. J. Umen, *J. Amer. Chem. Soc.*, **94**, 5495 (1972).

per(I) in a reaction of this type would be due to the accessibility of the copper(II) valence state, and the resulting ease of one-electron oxidation of organocopper(I) compounds. Lithium dialkylcuprates in general react readily with oxidizing agents. However the principal organic products from these reactions are the corresponding alkyl dimers,[15,20] and oxidative dimerization of alkyl groups derived from the organometallic component of a conjugate addition reaction mixture is not a common side reaction.

The work reported in this paper was designed to detect free alkyl radicals that might be present as intermediates in representative conjugate addition reactions, *viz.*, the reactions of lithium dialkylcuprates derived from *endo*-2-norbornylcopper(I) with mesityl oxide (2-methylpent-2-en-4-one). The intermediacy of free 2-norbornyl radicals (eq 3–5) in these reactions would be expected to result in the formation of conjugate adduct containing norbornyl groups epimerized at C-2;[21] nucleophilic addition of the norbornyl moiety to the carbon–carbon double bond (eq 1) or an oxidative addition–reductive elimination path (eq 2) would be expected to take place with retention of stereochemistry at C-2, by analogy with the stereochemical outcome of reactions of 2-norbornylcuprates with alkyl halides and tosylates.[15,20] The stereochemical course of an electron-transfer mechanism not involving free alkyl radicals (eq 6) is difficult to predict, but might also involve retention of configuration at C-2.

## Results

*endo*-2-Norbornylmagnesium bromide (*endo*-1) was obtained from a mixture of endo and exo epimers by preferential destruction of the exo epimer using the procedure of Jensen and Nakamaye;[22] its conversion into *endo*-2-norbornyl(tri-*n*-butylphosphine)copper(I) (*endo*-2) was accomplished by reaction with bromo(tri-*n*-butylphosphine)copper(I) in ether at −78°.[20] The diastereomeric purity of the resulting 2 was determined by glpc analysis of the mixture of *endo*- and *exo*-2-methylnorbornane formed on nitrobenzene oxidation of the solution obtained by addition of methyllithium to 2. This oxidative coupling has been demonstrated previously to take place stereospecifically with retention of configuration.[20]

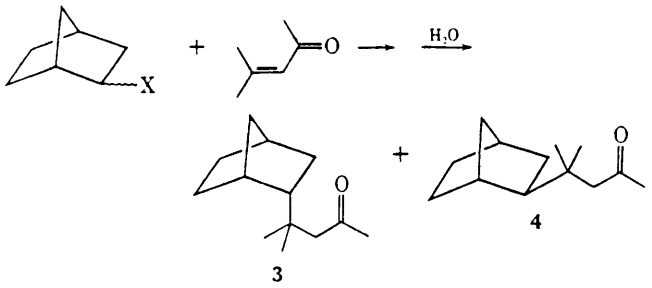
Reactions of a number of organometallic derivatives of the 2-norbornyl moiety with mesityl oxide were surveyed to find conditions that would give high conversions to the 2-norbornyl conjugate adduct. For convenience, these reactions were carried out using the epimeric mixture of alkyl metal compounds obtained from the equilibrium mixture of *exo*- and *endo*-2-norbornylmagnesium bromides (~35 exo:65 endo),[19] and

(20) G. M. Whitesides, J. San Filippo, Jr., C. P. Casey, and E. J. Panek, *J. Amer. Chem. Soc.*, **89**, 5302 (1967). These oxidative dimerizations apparently do not involve free alkyl radicals as intermediates; *cf.* G. M. Whitesides, J. San Filippo, Jr., E. R. Stedronsky, and C. P. Casey, *ibid.*, **91**, 6542 (1969).

(21) For previous studies in which a reaction involving an intermediate free 2-norbornyl radical has been characterized by loss of stereochemistry at C-2, see P. J. Kropp, *ibid.*, **91**, 5783 (1969); A. Fang, Ph.D. Thesis, Massachusetts Institute of Technology, Cambridge, Mass., 1966; P. D. Bartlett, G. N. Fickes, F. C. Haupt, and R. Helgeson, *Accounts Chem. Res.*, **3**, 177 (1970); D. I. Davies and S. J. Cristol, *Advan. Free Radical Chem.*, **1**, 155 (1965); G. M. Whitesides and J. San Filippo, Jr., *J. Amer. Chem. Soc.*, **92**, 6611 (1970).

(22) F. R. Jensen and K. L. Nakamaye, *ibid.*, **88**, 3437 (1966).

in several instances, no effort was made to analyze the resulting mixtures of the adducts 4-methyl-4-(*endo*-2-norbornyl)pentan-2-one (**3**) and 4-methyl-4-(*exo*-2-norbornyl)pentan-2-one (**4**) for epimeric compositions. Instead, product mixtures were analyzed for the combined yield of **3** and **4**. Results of these experiments




are listed in Table I. In this table, the entries in the column headed "X" are not intended to imply the existence of discrete, characterized ate complexes having compositions related in some simple way to the quantities of reagents present; the entries refer simply to the components that have been added to the solution. Thus, "Cu(I)$PBu_3$ + $C_6H_5Li$" indicates a solution prepared by adding 1 equiv of phenyllithium to a solution of 2-norbornyl(tri-*n*-butylphosphine)copper(I); the name "lithium norbornylphenylcuprate" is used only for convenience in referring to this solution. Although both chemical and spectroscopic evidence suggests that solutions prepared in this manner do in fact contain organometallic clusters having more than one type of organic moiety on the cluster, such clusters have not been characterized.[23]

TABLE I

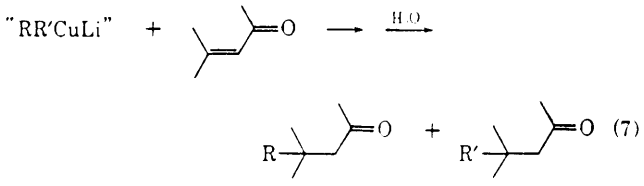
COMBINED YIELD OF THE EPIMERIC 4-METHYL-4-(2-NORBORNYL)PENTAN-2-ONES **3** AND **4** FROM CONJUGATE ADDITION OF ORGANOMETALLIC DERIVATIVES NORBORNANE-2-X TO MESITYL OXIDE[a]

| X | Yield **3** + **4**, %[b] |
|---|---|
| MgBr | 0 |
| MgBr + 5 mol % $ICuPBu_3$ | 18 |
| MgBr + 12 mol % $BrAgPBu_3$ | 3 |
| MgBr + 5 mol % $(Ph_3P)_2Ni(CH_2{=}CH_2)$ | 0 |
| MgBr + 5 mol % $(Ph_3P)_2NiBr_2$ | 0 |
| MgBr + 4 mol % $(Ph_3P)_2Pt(CH_2{=}CH_2)$ | 0 |
| MgBr + 5 mol % $(Ph_3P)_2PtCl_2$ | 0 |
| MgBr + 5 mol % $K_2PtCl_4$ | 0 |
| MgBr + 5 mol % $ClAuPEt_3$ | 0 |
| Cu(I)$PBu_3$ | 16 |
| Cu(I)$PBu_3$ + $C_6F_5Li$ | 0 |
| Cu(I)$PBu_3$ + *n*-$C_4H_9Li$ | 2 |
| Cu(I)$PBu_3$ + *n*-$C_4H_9Li$·TMEDA | 18 |
| Cu(I)$PBu_3$ + *n*-$C_4H_9Li$ | 0[c] |
| Cu(I)$PBu_3$ + *s*-$C_4H_9Li$ | 4 |
| Cu(I)$PBu_3$ + $(C_6H_5)_3CLi$ | 4 |
| Cu(I)$PBu_3$ + *c*-$C_6H_9Li$ | 5 |
| Cu(I)$PBu_3$ + $C_6H_5Li$ | 5 |
| Cu(I)$PBu_3$ + $C_6H_5(CH_3)_2CH_2Li$ | 6 |
| Cu(I)$PBu_3$ + $CH_3Li$ | 8[d] |
| Cu(I)$PBu_3$ + 3 *t*-$C_4H_9Li$ | 35[e] |
| Cu(I)$PBu_3$ + 5 *t*-$C_4H_9Li$ | 59[f] |
| Cu(I)$PBu_3$ + *t*-$C_4H_9Li$ | 66 |

[a] Reactions were carried out between 1 mmol of norbornylmetal compound and 1 mmol of mesityl oxide in 20 ml of ether at 0° for 0.5–2.0 hr, unless otherwise noted. Solutions contained 1 mmol of magnesium bromide. [b] Reproducibility in yields was ~±2%. [c] The solvent in this reaction was 50:50 ether–pyridine. [d] A 90% yield of 4,4-dimethylpentan-2-one was obtained in this reaction. [e] *Ca.* 4 mmol of mesityl oxide was used. [f] *Ca.* 6 mmol of mesityl oxide was used.

One feature of the data of Table I may have pertinence to the synthetic application of organocopper reagents in conjugate addition that extends beyond the immediate stereochemical object of this work. The high yield of **3** + **4** obtained on reaction of lithium norbornyl-*tert*-butylcuprates with mesityl oxide suggests that "mixed" copper ate complexes may have useful practical application in their own right: this yield is sufficiently higher than that obtained in the other experiments summarized in Table I that it would clearly be the method of choice in a preparative procedure.[24]

The origin of the marked superiority of the mixed ate complex, lithium *tert*-butyl-2-norbornyl(tri-*n*-butylphosphine)cuprate, in transferring the norbornyl group in conjugate addition reactions is not clear. The product distribution observed in reaction of lithium methyl-2-norbornylcuprate with mesityl oxide indicates, in this instance, that the conversion of the $\alpha,\beta$-unsaturated ketone to its conjugate adducts containing either methyl or norbornyl moieties proceeds in very high yield (Table I), and that the important factor in determining the composite yield of **3** + **4** is apparently the relative facility with which the norbornyl and methyl moieties transfer from the metal cluster to the $\alpha,\beta$-unsaturated ketone (eq 7). However, the limited



(7)

data available in Table I are not sufficient to establish whether steric bulk, alkyl group basicity, or aggregate structure determine this facility of transfer.

Taking the data of Table I as a guide in selecting reaction systems for examination, the stereochemistry of the conjugate addition of several metal derivatives of the *endo*-2-norbornyl moiety to mesityl oxide was determined. In order to prove the stereochemistry of the products, and to obtain materials for glpc calibration, an authentic sample of **4** was prepared following the reaction sequence outlined in Scheme I;[25] an anal-

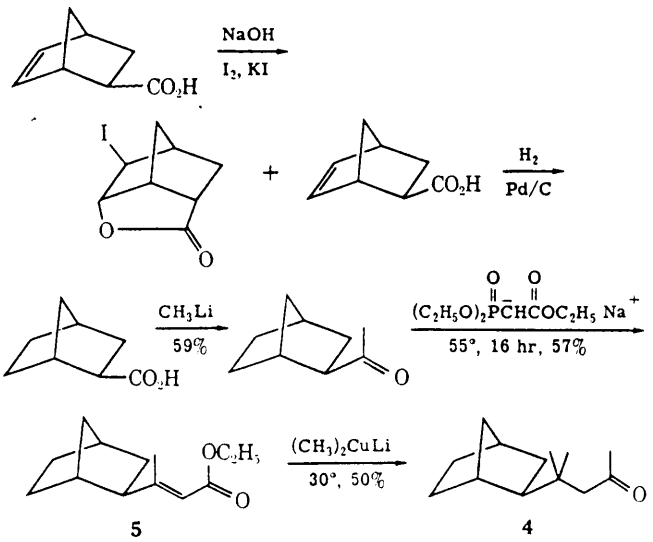
(23) J. San Filippo, Jr., Ph.D. Thesis, Massachusetts Institute of Technology, Cambridge, Mass., 1970. For structural analogies in related organometallic series, see also T. L. Brown, *Advan. Organometal. Chem.*, **3**, 365 (1966); J. P. Oliver, *ibid.*, **8**, 167 (1970); T. L. Brown, *Accounts Chem. Res.*, **1**, 23 (1968); M. Y. Darensbourg, B. Y. Kimura, G. E. Hartwell, and T. L. Brown, *J. Amer. Chem. Soc.*, **92**, 1236 (1970).

(24) We presume that lithium dinorbornylcuprate would compete in yield in these conjugate addition reactions with lithium norbornyl-*tert*-butylcuprate. However, in this system, as in many of synthetic interest, the Grignard reagent of one component can be obtained more easily and in higher purity than can the corresponding alkyllithium compound. Thus the copper ate complex obtained by mixing 1 equiv of the Grignard reagent of a component of interest and 1 equiv of *tert*-butyllithium may provide a practical alternative to the ate complex obtained from the lithium reagent of this component.

(25) Diastereomerically pure *endo*- and *exo*-norbornane-2-carboxylic acids were obtained from a mixture of *endo*- and *exo*-norborn-5-ene-2-carboxylic acids by the procedure of J. A. Berson and D. A. Ben-Efraim, *J. Amer. Chem. Soc.*, **81**, 4083 (1959), and references cited therein.

SCHEME I

SYNTHESIS OF *exo*-2-NORBORNYL-4-METHYPENTAN-2-ONE (4)




5 4

ogous procedure starting with the *endo*-2-norbornyl carboxylic acid yielded a 70:30 mixture of **3** and **4**.[26]

Table II summarizes data pertinent to the stereochemistry at C-2 of the norbornyl group of a number of

TABLE II

STEREOCHEMISTRY OF CONJUGATE ADDITION OF THE ORGANOMETALLIC DERIVATIVES NORBORNANE-2-X TO MESITYL OXIDE[a]

| X | *endo*-X:*exo*-X | **3** (endo):**4** (exo) |
|---|---|---|
| $MgBr + 5$ mol % $ICuPBu_3$ | 65:35[b] | 62:38 |
| | 99:1[c] | 81:19 |
| $CuPBu_3$ | 65:35[b] | 17:83 |
| | 99:1[c] | 47:53 |
| $CuPBu_3 + CH_3Li$ | 65:35[b] | 1:99 |
| | 99:1[c] | 94:6 |
| $CuPBu_3 + (CH_3)_3CLi$ | 65:35[b] | 40:60 |
| | 99:1[c] | 99:1[c,d] |
| $CuP(OCH_3)_3 + (CH_3)_3CLi$ | 99:1[c,e] | 99:1[c] |

[a] Reactions were carried out at 0° in diethyl ether. [b] This ratio was not measured for each experiment. These samples were derived from 2-norbornylmagnesium bromide that had been allowed to reach epimeric equilibrium, and the 65:35 ratio is the value characteristic of this equilibrium. [c] This ratio is a minimum value. [d] In a separate experiment $Mg^{2+}$ was precipitated with dioxane before addition of *tert*-butyllithium, and its concentration was reduced to 5% that of the $Cu^+$; however, ~6% epimerization was observed in the mixture of **3** and **4** obtained in this reaction, presumably due in major part to epimerization occurring during manipulation of the solution. The yield of **3** and **4** in this reaction was 57%. [e] The yield of **3** in this reaction was 40%.

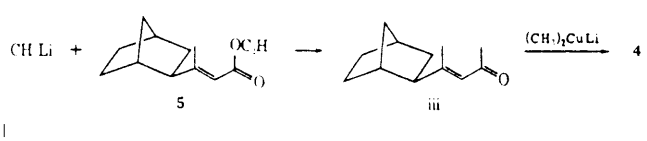
derivatives of **2** on conjugate addition to mesityl oxide. Discussion of these data is complicated by the facts that the exo epimer of each of the organometallic reagents examined appears to have greater reactivity toward $\alpha,\beta$-unsaturated ketones than the endo epimer, and that epimerization at C-2 competes in certain instances with conjugate addition. Nonetheless, the stereochemistry of several of the conjugate additions is readily interpreted.

The reactions listed in Table II can be classified into two groups on the basis of their stereoselectivity. The first, including the reactions of the phosphine and phosphite complexes of lithium *tert*-butyl-*endo*-norbornylcuprate with mesityl oxide, clearly is characterized by retention of configuration at C-2 of the norbornyl group during the step that results in carbon–carbon bond formation in the conjugate addition. The corresponding reaction of lithium methyl-*endo*-2-norbornylcuprate should probably also be included in this group. The second, including the reaction between mesityl oxide and *endo*-2-norbornyl (tri-*n*-butylphosphine)copper and possibly also the copper-catalyzed conjugate addition of *endo*-2-norbornylmagnesium bromide to this ketone, takes place with significant loss of stereochemistry.

Control experiments carried out in the first group of reactions, using cuprate solutions containing approximately 65:35 mixtures of *endo*- and *exo*-2-norbornyl moieties (Table II), establish that the high stereoselectivity observed in these reactions is not an artifact resulting either from the differences in reactivity of *endo*- and *exo*-2-norbornyl diastereomers in the conjugate addition or from isomerization of the conjugate adduct, once formed. The origin of the loss in stereochemistry observed in the second group of reactions is more difficult to identify. Attempts to determine the stereochemical stability of *endo*-2-norbornyl(tri-*n*-butylphosphine)copper(I) (**2**) under the conditions of the conjugate addition did not yield easily interpreted results.[27] Thus, a solution of **2** (99.5% endo) was allowed to react with 0.5 equiv of mesityl oxide for 15 min at 0°. Analysis of the stereochemistry of the remaining **2** by conversion to 2-methylnorbornane[20] demonstrated that it was composed of a 94:6 mixture of endo and exo diastereomers. This result could be interpreted to indicate either that epimerization of **2** is relatively slow under the conditions of the conjugate addition, or that epimerization is rapid, but that the *exo*-**2** reacts preferentially with the mesityl oxide as it is formed. However, although reaction of a 74:26 mixture of *endo*- and *exo*-**2** with limiting amounts of mesityl oxide under similar reaction conditions demonstrated enhanced reactivity for the exo epimer, the difference in reactivity between epimers appears insufficient to account for all of the loss of stereochemistry observed on reaction of *endo*-**2** with mesityl oxide (see Experimental Section). Thus it appears that some epimerization may actually take place during the conjugate addition of **2** to mesityl oxide. However, the yields of **3** and **4** obtained in this reaction were sufficiently small that this result unfortunately cannot be considered to be of great mechanistic significance (Table I).

In an effort to test the proposal of a free-radical mechanism for the conjugate addition of trialkylboranes to

(26) The conversion of the $\alpha,\beta$-unsaturated ester **5** to **4** by reaction with lithium dimethylcuprate is carried out under conditions in which the organometallic compound is decomposing thermally, and presumably proceeds by initial conversion of **5** to iii, followed by rapid subsequent conjugate addition of remaining lithium dimethylcuprate to iii.




(27) The epimerization of 2-norbornyl(tri-*n*-butylphosphine)copper(I) is known to be faster than its thermal decomposition; however, quantitative rate data are available for neither of these reactions: *cf.* C. P. Casey, Ph.D. Thesis, Massachusetts Institute of Technology, Cambridge, Mass., 1968.

α,β-unsaturated ketones, we attempted to add tri-*exo*-2-norbornylborane to mesityl oxide using reaction conditions described by Brown (see Experimental Section).[18] Essentially no conjugate addition was observed under these and a variety of other conditions, and the experiments were abandoned.

## Conclusions

The conjugate addition of norbornyl groups to mesityl oxide from a mixture of 2 and *tert*-butyllithium takes place in good yield with essentially complete retention of stereochemistry at the 2 position of the norbornyl moiety. This observation, taken together with the loss of stereochemistry at this position characteristic of reactions involving free 2-norbornyl radicals,[21] excludes the mechanism of eq 3–5 for this conjugate addition. The stereochemistry of the remaining systems summarized in Table II is less clear-cut; however, the predominant retention of stereochemistry observed in the stoichiometric reaction between mesityl oxide and lithium methyl-*endo*-2-norbornylcuprate and in its copper-catalyzed reaction with 1 suggest that the same mechanistic conclusions can be applied to these reactions. No mechanistically significant interpretation concerning the stereochemistry of the addition of 2 to mesityl oxide can be drawn at present, for reasons discussed above. Using a different stereochemical test, Casey and Boggs[11] have concluded that free vinylic radicals are not involved in the conjugate addition of lithium dipropenylcuprate to cyclohexenone.[23]

House and Umen have successfully correlated the susceptibility of a number of α,β-unsaturated ketones toward conjugate addition with their one-electron reduction potentials.[19b] Further, products easily rationalized on the basis of α,β-unsaturated ketone radical anions have been detected in certain conjugate addition reactions.[29] These observations are consistent with the hypothesis that electron transfer from the copper ate complex to the α,β-unsaturated ketone is an important part of conjugate addition (eq 6). However, neither observation necessarily establishes that free-radical anions derived from the α,β-unsaturated ketones are necessarily intermediates in the conjugate addition, since the reduction potentials may correlate with other properties of the ketones [*e.g.*, susceptibility to attack by the cuprates or ability to complex with Cu(I)], and the anion radical-derived products[29] may originate in reactions unrelated to the conjugate addition. Thus, although the data presented in this paper exclude free 2-norbornyl radicals in the conjugate addition of derivatives of 2 to mesityl oxide (and presumably exclude free radicals in other related reactions by analogy[11]), it is not yet possible to differentiate rigorously between mechanisms for conjugate addition involving electron transfer to the enone moiety (eq 6) and those requiring nucleophilic attack of an alkyl anion or metallate anion on it (eq 12).[30]

(28) Similar stereochemical results have been obtained by F. Näf and P. Degen, *Helv. Chim. Acta*, **54**, 1939 (1971); F. Näf, P. Degen, and G. Ohloff, *ibid.*, **55**, 82 (1972).

(29) J. A. Marshall and R. A. Ruden, *Tetrahedron Lett.*, 2875 (1971); J. Hooz and R. B. Layton, *Can. J. Chem.*, **48**, 1626 (1970).

(30) For pertinent proposals concerning the mechanism by which copper acts as a catalyst in decarboxylation of aromatic acids, see T. Cohen and R. A. Schambach, *J. Amer. Chem. Soc.*, **92**, 3189 (1970); A. Cairncross, J. R. Roland, R. M. Henderson, and W. A. Sheppard, *ibid.*, **92**, 3187 (1970). If the catalytic activity of copper(I) in conjugate addition reactions is based on its ability to coordinate with double bonds, it is curious that derivatives of a number of other transition metals, some of which are known to coordinate with double bonds more strongly than copper, show little or no catalytic activity in conjugate addition (Table I). However, many of these salts either form organometallic derivatives or are reduced in solutions containing organolithium reagents; thus, the apparent lack of catalytic activity of these ions may simply reflect their conversion to noncoordinating substances under the reaction conditions.

## Experimental Section[31]

**5-Norbornene-2-carboxylic acid** (371 g), bp 131–134° (11 Torr) [lit.[30] bp 132–134° (22 Torr)], was obtained from cyclopentadiene and acrylic acid in 87% yield following the procedure of Diels and Alder.[34]

***endo*-Norborn-5-ene-2-carboxylic Acid.**—Norborn-5-ene-2-carboxylic acid (278 g, 2.01 mol) was dissolved in a solution of 25% sodium hydroxide (80.0 g, 2.00 mol) and the solution was cooled to 0°. Sodium bicarbonate (50 g, 0.6 mol) was added, followed by a solution of iodine (570 g, 2.20 mol) dissolved in 450 ml of a saturated aqueous solution of potassium iodide. The reaction mixture was stirred for 2 hr, and the organic layer was extracted into diethyl ether. The ether phase was separated, washed with a saturated solution of sodium thiosulfate until clear, washed with water, and dried ($MgSO_4$). Ether was removed on a rotary evaporator to yield 415 g of crude iodolactone. Recrystallization of this material from a mixture of ethyl acetate and *n*-pentane (1:5) gave 316 g (63%) of pure iodolactone, mp 57.0–57.5° (lit.[35] mp 58.5°).

This iodolactone (456 g, 1.80 mol) was dissolved in 800 ml of glacial acetic acid, and the resulting solution was cooled to 15°. Zinc dust (245 g, 3.74 g-atoms) was added to the mixture over a 20-min interval. An additional 250 ml of glacial acid was added, and the reaction mixture was stirred for an additional 2 hr at 15°. The reaction mixture was warmed to 25° for 2 hr, and the remaining solids were then removed by filtration. The reaction solution was diluted with 1 l. of water and extracted with five 200-ml portions of diethyl ether. Distillation of the ether phase yielded *endo*-norborn-5-ene-2-carboxylic acid (134 g, 54%), bp 127° (12 Torr) [lit.[25] bp 134° (16 Torr)].

***endo*-2-Norbornanecarboxylic Acid.**—*endo*-Norborn-5-ene-2-carboxylic acid (95 g, 0.688 mol) was dissolved in *ca.* 100 ml of ethyl acetate, mixed with 3 wt % palladium on charcoal (10%), and charged into a Parr hydrogenation apparatus. The solution was shaken under a hydrogen atmosphere until no further hydrogen uptake was observed, and was then pressurized to 40 psi and shaken for an additional 1 hr. The catalyst was removed by filtration, and solvent was removed under vacuum to yield crude *endo*-2-norbornanecarboxylic acid. Nmr spectroscopic analysis of the resulting crude acid indicated that the starting material had been completely consumed. The acid could be recrystallized from *n*-pentane to yield pure *endo*-2-norbornanecarboxylic acid,

(31) All melting points and boiling points are uncorrected. Infrared spectra were determined with a Perkin-Elmer Model 237 grating spectrophotometer. Nmr spectra were determined with a Varian T-60 nmr spectrometer. Mass spectra were determined on a Hitachi Perkin-Elmer RMU-6 mass spectrometer. Analytical analyses were performed by Midwest Microlabs, Ltd., Indianapolis, Ind. Samples for elemental and spectral analyses were purified on a Hewlett-Packard Model 700 thermal conductivity gas chromatograph. Analytical glpc analyses were performed on F & M Model 810 flame ionization instruments. Absolute yields of products were calculated from peak areas using internal standard techniques, with response factors obtained from authentic samples. Diethyl ether and tetrahydrofuran were distilled from lithium aluminum hydride before use. Olefins were removed from hydrocarbon solvents by treatment with sulfuric acid, and the olefin-free hydrocarbons were purified by distillation from a suspension of sodium benzophenone ketyl before use. Dimethoxyethane was distilled from a solution of sodium benzophenone dianion before use. Methyl-, cyclopentyl-, *n*-butyl-, and *tert*-butyllithium reagents were supplied by Foote Mineral Corp. *sec*-Butyllithium was supplied by Alpha Inorganics, Inc. Grignard reagent solutions were analyzed following the procedure of Eastham,[31] and lithium reagents were analyzed by the Gilman double titration method.[32] All reactions involving organometallic reagents were carried out under prepurified nitrogen, using standard inert atmosphere techniques.[33]

(32) S. C. Watson and J. F. Eastham, *J. Organometal. Chem.*, **9**, 165 (1967); H. Gilman, F. K. Cartledge, and S.-Y. Sim, *ibid.*, **1**, 8 (1963); G. M. Whitesides, C. P. Casey, and J. K. Krieger, *J. Amer. Chem. Soc.*, **93**, 1379 (1971).

(33) D. F. Shriver, "The Manipulation of Air-Sensitive Compounds," McGraw-Hill, New York, N. Y., 1969, Chapter 7.

(34) O. Diels and K. Alder, *Justus Liebigs Ann. Chem.*, **460**, 117 (1928).

(35) C. D. VerNooy and C. S. Rondestvedt, *J. Amer. Chem. Soc.*, **77**, 3583 (1955).

mp 63.5–65.5° (lit.[25] mp 64–66°). The major part of the acid was not recrystallized, but was stored at −25° until use.

**Methyl Norborn-5-ene-2-carboxylate.**—Norborn-5-ene-2-carboxylic acid (370 g, 2.68 mol, a mixture of epimers) was added to 1300 g of absolute methanol containing 7 ml of concentrated sulfuric acid, and the resulting solution was refluxed for 5 hr. The solution was diluted with 1 l. of water, and the aqueous phase was extracted with four 200-ml portions of diethyl ether. The combined ether extracts were washed with 50 ml of a saturated aqueous solution of sodium bicarbonate and two 50-ml portions of water, and dried ($MgSO_4$). Distillation gave methyl norborn-5-ene-2-carboxylate (300 g, 73%): bp 70° (8 Torr) [lit.[36] bp 63.5° (5 Torr)]; nmr ($CCl_4$) δ 5.8–6.3 (2, m), 3.65 (1.1, s), 3.58 (1.9, s), 1.0–3.4 (7, various multiplets).

**Epimerization of Methyl Norborn-5-ene-2-carboxylate.**—Methyl norborn-5-ene-2-carboxylate (330 g, 2.31 mol, predominantly the endo epimer) was added to a solution of sodium methoxide (185 g, 3.43 mol) in *ca.* 800 ml of methanol, and the mixture was refluxed for *ca.* 50 hr, at which time it appeared to have partially polymerized to a thick gel. Solvent was removed by distillation, and 500 ml of water was added to the resulting solids. Distillation of residual methanol, with periodic addition of water, was carried out until the boiling point of the distillate reached 95°. The distillation residue was then cooled, its acidity was adjusted to pH 3 with hydrochloric acid, and it was extracted with three 50-ml portions of diethyl ether. The combined ether portions were washed with 100 ml of water, dried ($MgSO_4$), and distilled to give 159 g of norborn-5-ene-2-carboxylic acid. The acid was shown to contain *ca.* 60% of the exo epimer by nmr spectroscopy. An additional 100 g of methyl norborn-5-ene-2-carboxylate, shown to be *ca.* 70% exo epimer by nmr spectroscopy, was recovered from the initial water and methanol distillate.

***exo*-2-Norbornylcarboxylic Acid.**—Norborn-5-ene-2-carboxylic acid (obtained from epimerization of methyl norborn-5-ene-2-carboxylate, *ca.* 60% exo, 157 g, 1.10 mol) was dissolved in 1 equiv of 30% aqueous sodium hydroxide solution. Sodium bicarbonate (5.0 g, 0.04 mol) was added, followed by a solution of iodine (132 g, 0.52 mol) in *ca.* 500 ml of a saturated solution of aqueous potassium iodide.[37] The mixture was shaken for 15 min, and the resulting heterogeneous mixture was extracted with four 250-ml portions of diethyl ether. The combined ether fractions were worked up as described above to obtain the iodolactone. The aqueous phase was treated with sodium thiosulfate until colorless, made acidic (pH 3) with hydrochloric acid, and extracted with three 250-ml portions of diethyl ether. The combined ether extracts were washed with 100 ml of water, dried ($MgSO_4$), and distilled, yielding norborn-5-ene-*exo*-2-carboxylic acid (88 g, *ca.* 96%), bp 85° (0.05 Torr) [lit.[25] bp 134° (16 Torr)]. The distilled acid was washed with 5 ml of a saturated solution of sodium thiosulfate and with 5 ml of water, and dried ($MgSO_4$). Recrystallization from *n*-hexane gave pure norborn-5-ene-*exo*-2-carboxylic acid, mp 43.0–44.5° (lit.[25] mp 44.0–45.0°). Norborn-5-ene-*exo*-2-carboxylic acid (12.2 g, 0.0885 mol) was dissolved in 10 ml of ethyl acetate, and the solution was mixed with palladium on charcoal (10%, 0.5 g, 4 wt %). The mixture was charged into a Parr hydrogenation apparatus, and was hydrogenated at 40 psi until no pressure drop was observed for 1.5 hr. The resulting solution was filtered to remove the catalyst, and solvent was removed using a rotary evaporator to give crude *exo*-2-norbornylcarboxylic acid (12.2 g, 99%). Recrystallization from *n*-hexane gave pure *exo*-2-norbornylcarboxylic acid: mp 57–58° (lit.[25] mp 57–58.5°); nmr ($CCl_4$) δ 12.2 (s, 1), 2.57 (m, 1), 2.29 (m, 2), 1.20–2.00 (m, 8).

***endo*-2-Norbornyl Methyl Ketone.**—*endo*-2-Norbornylcarboxylic acid (17.1 g, 0.124 mol) was dissolved in 150 ml of dimethoxyethane, and the solution was transferred to a three-necked 500-ml flask fitted with a reflux condenser and mechanical stirrer. Methyllithium (1.68 *N*, 148 ml, 0.248 mol) was added dropwise through a cannula at a rate that maintained the solution at gentle reflux. The mixture was refluxed with external heating for 18 hr after the addition was completed, and was then transferred cautiously into 500 ml of a stirred solution of saturated aqueous ammonium chloride. The water and ether layers were separated, and the aqueous phase was extracted with three 100-ml portions of diethyl ether. The combined organic fractions were washed with 25 ml of water and dried ($Na_2SO_4$). Distillation gave *endo*-2-norbornyl methyl ketone (10.1 g, 60%), bp 53° (2.5 Torr) [lit.[38] bp 91° (30 Torr)]. Glpc analysis showed the ketone to be *ca.* 90% pure, and samples were collected by glpc for spectral and elemental analyses. Pure samples had nmr ($CCl_4$) δ 2.65–2.97 (m, 2), 2.23 (m, 1), 2.03 (s, 3), 1.10–1.70 (m, 8); ir ($CCl_4$) 2940, 2860, 1705, 1450, 1350, 1305, 1190, 1176, 1166, 1110, 947 $cm^{-1}$; mass spectrum *m/e* (rel intensity): 138 (5), 120 (8), 105 (8), 95 (53), 80 (51), 71 (74), 67 (57), 43 (100).

*Anal.* Calcd for $C_9H_{14}O$: C, 78.21; H, 10.21. Found: C, 78.50; H, 10.46.

***exo*-2-Norbornyl Methyl Ketone.**—*exo*-2-Norbornylcarboxylic acid (12.0 g, 85.7 mmol) was dissolved in 20 ml of DME and dried over molecular sieves for 10 hr. The solution of the acid was transferred to a three-necked, 1-l., round-bottomed flask fitted with a dropping funnel, condenser, and mechanical stirrer, and was diluted with an additional 80 ml of DME. Methyllithium (1.68 *N*, 102 ml, 171 mmol) was transferred into the addition funnel, and added to the acid solution at a rate sufficient to maintain gentle reflux. The reaction mixture was heated to reflux for 15 hr after addition had been completed, and was then transferred rapidly through a cannula into 300 ml of a stirred saturated aqueous solution of ammonium chloride. The resulting aqueous and organic phases were separated, and the aqueous phase was extracted with two 100-ml portions of diethyl ether. The combined ether fractions were washed with 25 ml of water and dried ($Na_2SO_4$). Distillation gave *exo*-2-norbornyl methyl ketone (7.0 g, 59%), bp 56° (3.0 mm) [lit.[38] bp 91° (30 mm)]. Samples were collected by glpc for analyses: nmr ($CCl_4$) δ 2.25–2.39 (m, 3), 2.08 (s, 3), 1.03–1.90 (m, 8); ir ($CCl_4$) 2940, 2860, 1710, 1450, 1355, 1310, 1175, 1060 $cm^{-1}$; mass spectrum *m/e* (rel intensity) 138 (4), 95 (100), 80 (13), 71 (33), 67 (55), 43 (84).

*Anal.* Calcd for $C_9H_{14}O$: C, 78.21; H, 10.21. Found: C, 78.12; H, 10.35.

**Ethyl 3-(*exo*-2-Norbornyl)but-2-enoate (5).**—Triethyl phosphonoacetate[39] (5.55 g, 25.0 mmol) was added slowly to a slurry of sodium hydride (0.600 g, 25.0 mmol) in 50 ml of DME, and the mixture was heated to 50° until the sodium hydride had reacted. *exo*-2-Norbornyl methyl ketone (3.5 g, 25.3 mmol) was added to the solution, and the reaction mixture was stirred at 55° for 16 hr. The reaction mixture was poured into 300 ml of water, and the resulting aqueous phase was extracted with two 50-ml portions of diethyl ether. The combined ether fractions were washed with 20 ml of water, dried ($Na_2SO_4$), and distilled to yield ethyl 3-(*exo*-2-norbornyl)but-2-enoate (3.0 g, 57%): bp 70° (0.06 Torr); nmr ($CCl_4$) δ 5.51 (m, 1), 4.04 (q, 2), 1.98–2.35 (m, 3), 2.08 (d, 3), 1.25 (t, 3), 1.02–1.80 (m, 8); ir ($CCl_4$) 2935, 2860, 1720, 1645, 1450, 1370, 1325, 1265, 1170, 1150, 1050 $cm^{-1}$.

**Ethyl 3-(*endo*-2-Norbornyl)but-2-enoate.**—Triethyl phosphonoacetate (10.6 g, 47.1 mmol) was added dropwise to a stirred slurry of sodium hydride (1.10 g, 45.8 mmol) in 100 ml of DME at 25°. The mixture was heated to 60° for 3 hr, and the remaining sodium hydride was allowed to settle. The supernatant solution was transferred to a clean, dry 250-ml round-bottomed flask, and was cooled to 10° in a water bath. *endo*-2-Norbornyl methyl ketone (6.50 g, 47.1 mmol) was added, and the resulting solution was stirred for 14 days at 10°. (A higher reaction temperature resulted in unacceptable epimerization of the starting ketone.) The reaction mixture was poured into 500 ml of water, and the resulting aqueous phase was extracted with two 100-ml portions of diethyl ether. The combined ether fractions were washed with 10 ml of water, dried ($Na_2SO_4$), and distilled to give ethyl 3-(*endo*-2-norbornyl)but-2-enoate (3.6 g, 27%), bp 85° (0.3 mm). Nmr spectroscopy indicated that the material was *ca.* 85% endo epimer and 15% exo epimer. Samples for analyses were collected by glpc: nmr ($CCl_4$) δ 5.63 (m, 1), 4.06 (q, 2), 2.22–2.67 (m, 3), 2.20 (d, 3), 1.25 (t, 3), 1.20–1.40 (m, 8); ir ($CCl_4$) 2945, 2860, 1710, 1638, 1450, 1360, 1310, 1260, 1210, 1145, 1070, 1035 $cm^{-1}$; mass spectrum *m/e* (rel intensity) 208 (15), 193 (6), 163 (14), 145 (23), 95 (44), 79 (46), 67 (92), 59 (80), 43 (68), 41 (100).

*Anal.* Calcd for $C_{13}H_{20}O_2$: C, 74.96; H, 9.68. Found: C, 74.68; H, 9.66.

**4-Methyl-4-(*endo*-2-norbornyl)pentan-2-one (3).**—Methyllithium (1.68 *N*, 35.4 ml, 60.0 mmol) was added to cuprous iodide

(36) J. D. Roberts, *et al.*, *J. Amer. Chem. Soc.*, **72**, 3116 (1950).

(37) It is important to have only a slight excess of iodine, relative to the amount of endo epimer believed to be present, in order to avoid reactions involving the exo epimer.

(38) J. G. Dinwiddie, Jr., and S. P. McManus, *J. Org. Chem.*, **30**, 766 (1965).

(39) Triethyl phosphonoacetate was obtained commercially from Aldrich Chemical Co., and was used without further purification.

(6.05 g, 30.3 mmol) at −30° in a 100-ml round-bottomed flask, and the mixture was warmed to room temperature after the cuprous iodide had dissolved. Ethyl 3-(*endo*-2-norbornyl)but-2-enoate (*ca.* 85% endo, 0.9174 g, 4.58 mmol) was added slowly, and the reaction was stirred for 36 hr at 25°. The reaction was quenched in 500 ml of a saturated aqueous solution of ammonium chloride, and the aqueous and ether phases were separated. The aqueous phase was extracted with three 50-ml portions of diethyl ether, and the combined ether fractions were washed with 20 ml of water, dried ($Na_2SO_4$), and distilled to give a mixture of **4** and **3** (0.405 g, *ca.* 45%), bp 60° (0.05 mm). The nmr spectrum indicated that the material was *ca.* 70% endo epimer and 30% exo epimer, and this conclusion was verified by glpc analysis. Samples of **3** were purified by glpc for analyses: nmr ($CCl_4$) $\delta$ 2.28 (s, 2), 2.22 (m, 2), 2.03 (s, 3), 1.08–2.00 (m, 9), 1.04 (s, 3), 0.98 (s, 3); ir ($CCl_4$) 2940, 2860, 1715, 1460, 1380, 1350, 1300, 1200, 1150 $cm^{-1}$; mass spectrum *m/e* (rel intensity) 194 (1), 136 (21), 107 (20), 95 (35), 67 (26), 43 (100).

*Anal.* Calcd for $C_{13}H_{22}O$: C, 80.46; H, 11.33. Found: C, 80.44; H, 11.18.

**4-Methyl-4-(*exo*-2-norbornyl)pentan-2-one (4).**—Methyllithium (1.68 *N*, 47.7 ml, 80.6 mmol) was added to cuprous iodide (9.01 g, 47.3 mmol) at 0° in a 100-ml flask fitted with a magnetic stirring bar, and the mixture was stirred at 0° until solution of this cuprous iodide was completed. The resulting lithium dimethylcuprate was warmed to 25°, and ethyl 3-(*exo*-2-norbornyl)but-2-enoate (*ca.* 2.0 g, 9.7 mmol) was added by syringe. The solution was stirred for 24 hr at 25°, and was then poured into 300 ml of a saturated aqueous solution of ammonium chloride. The aqueous and ether phases were separated, and the aqueous phase was extracted with two 50-ml portions of diethyl ether. The combined ether fractions were washed with 20 ml of water, dried ($MgSO_4$), and distilled to give 4-(*exo*-2-norbornyl)-4-methyl-2-pentanone (0.90 g, *ca.* 50%), bp 60° (0.05 Torr). Samples were collected by glpc for analyses: nmr ($CCl_4$) $\delta$ 2.21 (s, 2), 2.08 (m, 2), 2.06 (s, 3), 1.00–1.52 (m, 9), 0.93 (s, 3), 0.87 (s, 3); ir ($CCl_4$) 2950, 2870, 1715, 1460, 1380, 1360, 1350, 1295, 1205, 1140, 1020 $cm^{-1}$; mass spectrum *m/e* (rel intensity) 136 (18), 121 (5), 107 (16), 95 (49), 67 (28), 43 (100).

*Anal.* Calcd for $C_{13}H_{22}O$: C, 80.46; H, 11.33. Found: C, 80.62; H, 11.14.

***endo*-2-Norbornylmagnesium bromide (*endo*-1)** was prepared following the description of Jensen and Nakamaye.[32] An equilibrium mixture of diastereomers of 2-norbornylmagnesium bromide (20 ml, 1.175 *N*, 23.5 mmol) was cooled to −70° in a 40-ml centrifuge tube capped with a No-air stopper and containing a magnetic stirring bar. The tube containing the Grignard reagent solution was removed from the cold bath and was stirred vigorously as a solution of benzophenone in ether (7.40 ml, 1.91 *N*, 14.1 mmol) was injected into it using a syringe. The reaction mixture was stirred at ambient temperature for *ca.* 1 min, the tube was transferred to a centrifuge, and the precipitated solids were compacted by centrifugation. The clear, deep red solution of *endo*-2-norbornylmagnesium bromide was transferred to a clean, dry centrifuge tube by cannula, cooled to −78°, and titrated.[31] The Grignard reagent solution was stored at −78° until used. Analysis of the diastereomeric composition of the solution by conversion first to **2** and then to 2-methylnorbornane (*vide infra*) indicated that it contained >99.5% endo diastereomer.

**Copper-Catalyzed Conjugate Addition of 1 to Mesityl Oxide.**—Bromo(tri-*n*-butylphosphine)copper(I) (0.0186 g, 0.0538 mmol) and *n*-heptadecane (0.0770 g, 0.321 mmol, an internal glpc standard) were weighed into a 40-ml centrifuge tube and dissolved in 20 ml of diethyl ether. The solution was cooled to −78°, and 2-norbornylmagnesium bromide (1.175 *N*, 0.853 ml, 1.00 mmol) was added by syringe. The resulting solution was warmed to 0°, and mesityl oxide (0.098 g, 1.00 mmol) was added by syringe. The reaction was stirred for 2 hr at 0°, and then poured into 100 ml of a saturated aqueous solution of ammonium chloride. The aqueous and ether layers were separated, and the aqueous phase was extracted with two 20-ml portions of diethyl ether. The combined ether fractions were washed with 10 ml of water and dried ($MgSO_4$). Analyses for total yields of **3** and **4** were carried out on a 6 ft × 0.125 in. 10% UC-W98 on Chromosorb P column at 140°. For analyses of relative yields of **3** and **4**, the unresolved peak corresponding to these materials was collected from an 8 ft × 0.25 in. UC-W98 column at 180° and reanalyzed on a 48 ft × 0.125 in. 1% SE-30 column. Results of these experiments are summarized in Tables I and II.

**Conjugate Addition of 2-Norbornyl(tri-*n*-butylphosphine)copper(I) (2) to Mesityl Oxide.**—Bromo(tri-*n*-butylphosphine)copper(I) (0.345 g, 1.00 mmol), tri-*n*-butylphosphine (0.404 g, 2.00 mmol), and *n*-heptadecane (0.0859 g, 0.358 mmol) were weighed into a 40-ml centrifuge tube capped with a No-air stopper, and dissolved in 20 ml of diethyl ether. The solution was cooled to −78°, and 2-norbornylmagnesium bromide (1.175 *N*, 0.853 ml, 1.00 mmol) was added by syringe. The resulting solution was warmed to 0°, and mesityl oxide (0.098 g, 1.00 mmol) was added by syringe. The reaction was stirred for 2 hr at 0° and then poured into 100 ml of a saturated aqueous solution of ammonium chloride. The aqueous and ether layers were separated, and the aqueous phase was extracted with two 20-ml portions of diethyl ether. The combined ether fractions were washed with 10 ml of water and dried ($MgSO_4$). Analyses were carried out as described previously.

**Conjugate Addition of Lithium Alkyl(2-norbornyl)cuprates to Mesityl Oxide.**—Iodo(tri-*n*-butylphosphine)copper(I) (0.396 g, 1.01 mmol) and *n*-heptadecane (0.0816 g, 0.340 mmol) were weighed into a 40-ml centrifuge tube capped with a No-air stopper and dissolved in 20 ml of diethyl ether. The solution was cooled to −78°, and 2-norbornylmagnesium bromide (1.175 *N*, 0.853 ml, 1.00 mmol) was added. The solution was mixed, and the appropriate alkyllithium reagent (1.05 mmol) was added by syringe. The resulting solution was warmed to 0° with stirring, and mesityl oxide (0.103 g, 1.05 mmol) was added by syringe. The reaction mixture was stirred at 0° for 2 hr and then poured into 100 ml of a saturated aqueous solution of ammonium chloride. The aqueous and ether layers were separated, and the aqueous phase was extracted with two 20-ml portions of diethyl ether. The combined ether fractions were washed with 10 ml of water and dried ($MgSO_4$). Analyses were carried out as described above.

**Attempted conjugate additions of tri-*exo*-2-norbornylborane to mesityl oxide**, carried out using *ca.* 8 mmol of borane, 10–20 mmol of mesityl oxide, and 10–20 mmol of water, with oxygen or irradiation (3000- and 3500-Å lamps in a Rayonet photochemical reactor) for initiation failed over reaction times of up to 48 hr.

**Bis(triphenylphosphine)(ethylene)platinum(0)** (72.0 mg, 50%), mp 121–124° (lit.[36] mp 122–125°), was obtained from ethylene and bis(triphenylphosphine)platinum(II) oxide following the procedure of Cook.[40]

**Bis(triphenylphosphine)(ethylene)nickel(0)** (2.34 g, 73%) was obtained from bis(acetylacetonato)nickel(II), ethylene, and triphenylphosphine following the procedure of Wilke.[41]

**Attempts of catalyze the conjugate addition of 1 to mesityl oxide** using catalysts other than copper were carried out using the same procedure as described above; the results of these experiments are summarized in Table I.

**Bromobis(trimethyl phosphite)copper(I).**—Trimethyl phosphite (46.7 g, 0.376 mol) was mixed with a slurry of cuprous bromide (27.0 g, 0.187 mol) in 200 ml of diethyl ether. The ether solution was refluxed for 30 min and filtered while hot. The resulting solution was cooled to 0°, at which temperature bromobis(trimethyl phosphite)copper(I) precipitated. The crude complex was recrystallized from 400 ml of diethyl ether to give 49.7 g (68%) of bromobis(trimethyl phosphite)copper(I), mp 61.0–62.5°, nmr ($CCl_4$) $\delta$ 3.68 (d, $J$ = 10.6 Hz).

*Anal.* Calcd for $C_6H_{18}BrCuO_6P_2$: C, 18.40; H, 4.63; Br, 20.40. Found: C, 18.98; H, 4.86; Br, 19.68.

**Analysis of the Diastereomeric Composition of Mixtures of *endo*- and *exo*-2.**—Samples of **2** in an ethereal solvent containing *ca.* 0.25 mmol of organocopper reagent were transferred through a cannula into a clean 40-ml centrifuge tube held immersed in a Dry Ice–acetone bath. Methyllithium (*ca.* 5 equiv, in ether) and nitrobenzene (*ca.* 1 ml) were added in succession to the tube by syringe. The oxidation reaction appeared to be complete on mixing. Samples of the reaction mixture were injected directly onto an 8 ft × 0.25 in. 20% UC-W98 on Chromosorb P column at 110°, and the unresolved peaks due to the diastereomeric 2-methylnorbornanes were collected. This mixture of diastereomers was diluted in *ca.* 250 μl of solvent, and analyzed for diastereomeric composition by glpc on a 48 ft × 0.25 in. 1% SE-30 column at 65°. Under these conditions, the *endo*-2-methylnorbornane has the longer retention time.

**Epimerization of *endo*-2-Norbornyl(tri-*n*-butylphosphine)copper(I) (2).**—A solution of *endo*-**2** was prepared and shown to con-

(40) C. D. Cook and G. S. Jauhal, *J. Amer. Chem. Soc.*, **90**, 1464 (1968).
(41) G. Wilke and G. Herrmann, *Angew. Chem.*, **74**, 693 (1962).

tain >99.5% endo diastereomer. Equal portions of this solution were transferred into two 40-ml centrifuge tubes containing magnetic stirring bars immersed in a Dry Ice–acetone bath. The tubes were warmed to 0° with stirring. Mesityl oxide (0.5 equiv) was added to one tube. Aliquots from both solutions were taken periodically by transferring into 40-ml centrifuge tubes held at Dry Ice temperatures. These aliquots were analyzed for the diastereomeric content of the remaining **2**. Immediately after warming to 0°, the diastereomeric purity of the **2** in the solution not containing mesityl oxide was 98.5%; after standing for 5 min at 0°, it was 97.1%. The sample containing mesityl oxide contained **2** that was 98.6% endo immediately after warming to 0°, 99.5% after 1 min at 0°, and 93.7% after 15 min.

**Competition of a Mixture of *endo*- and *exo*-2 for Limiting Quantities of Mesityl Oxide.**—An epimeric mixture of **2** was prepared at −78° and was shown to be 74% endo and 26% exo. Aliquots calculated to contain 1.19 mmol of **2** were transferred to 40-ml centrifuge tubes and warmed to 0°. Calculated amounts of mesityl oxide were added, and the reaction mixtures were stirred at 0° for *ca.* 2 min. The reaction mixtures were then cooled to −78°, and the remaining **2** was analyzed for epimeric composition by treatment with methyllithium and oxidation with nitrobenzene. The conjugate additions of **2** and of lithium methyl-2-norbornylcuprate to mesityl oxide at −78° are very slow. The results of these experiments are as follows: for 0.250 equiv of mesityl oxide/equiv of **2**, the epimeric composition of the **2** remaining after quenching was 67.8% endo; for 0.336 equiv, 69.6% endo; for 0.505 equiv, 74.8% endo; for 0.675 equiv, 77.6% endo.

**Registry No.**—*endo*-**1**, 13058-87-2; *endo*-**2**, 24473-67-4; *exo*-**2**, 35616-99-0; **3**, 35623-77-9; **4**, 35623-78-0; *exo*-**5**, 35623-75-7; *endo*-**5**, 35623-79-1; mesityl oxide, 141-79-7; *endo*-2-norbornyl methyl ketone, 824-58-8; *exo*-2-norbornyl methyl ketone, 824-59-9; bromobis(trimethyl phosphite)copper(I), 35617-00-6.

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