$Me_5Cu_3Li_2$: A Reagent for Conjugate Methylation of α,β-Unsaturated Aldehydes

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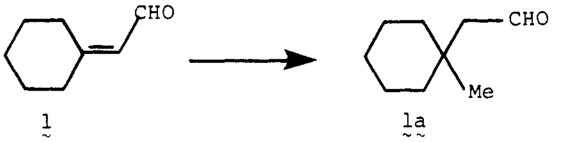
$Me_5Cu_3Li_2$, in ether or ether–pentane mixtures, converts α,β-unsaturated aldehydes efficiently into β-methyl aldehydes. In many cases of synthetic interest the amount of 1,2-methylation is negligible, and the reagent is far superior to Me_2CuLi for conjugate methylation of enals. The performance of $Me_5Cu_3Li_2$ is poor in sterically demanding situations, however. Several cuprate species were evaluated but none works as well as $Me_5Cu_3Li_2$. For example, citral undergoes conjugate methylation with $Me_5Cu_3Li_2$ in 80% yield, and the product contains less than 0.5% of 1,2-adduct. With Me_2CuLi the product contains 10% of 1,2-adduct.

Conjugate alkylation of α,β-unsaturated aldehydes as in eq 1 represents a method for preparing compounds with quaternary carbons[1] and which also contain a functional group suitable for further elaboration. In the specific case in which R = Me, decarbonylation would lead to a *gem*-dimethyl system.[2] Reactions of the type shown in eq 1, especially for R = Me, have previously been inefficient because the conventional reagent, Me_2CuLi, can give substantial amounts (ca. 5–60%) of the product arising by 1,2-addition.[3] We report here details of our experiments with $Me_5Cu_3Li_2$, a reagent that is useful for efficient conjugate methylation of enals.[4,5]



(1)

In the domain of unsaturated ketones and aldehydes only the former have been investigated in detail.[6] Apparently, the reputation[7] of enals for undergoing 1,2-addition has caused them to be neglected in this connection, but recent experiments have uncovered a few examples of efficient conjugate alkylation. The problem of the specific case of *methylation* has hitherto been difficult, a situation which is unfortunate, in view of the frequent occurrence of methyl substituents in natural products.

Prior Literature

The following examples of copper-mediated 1,4-addition to enals summarize the present situation. The generality of the conclusions is unclear, however, because of the lack of an adequate number of examples to cover all possible substitution patterns in the enal. (1) Ph_2CuLi,[8,9a] divinyl [e.g., (*Z*)-$(BuCH{=}CH)_2CuLi$],[8,10,11] and dihomoallyl[8] [e.g., $(Me_2C{=}CHCH_2CH_2)_2CuLi$] species can show exclusive or high (>90%) regioselectivity in favor of the 1,4-mode of addition. (2) The reagents $(CH_2{=}CHCH_2)_2CuLi$ and $(BuC{\equiv}C)_2CuLi$ (in THF) gave only 1,2-adducts.[8] (3) Et_2CuLi and $(n\text{-}C_8H_{17})_2CuLi$ evidently react mainly in a 1,4-fashion as the products of such a process were isolated in yields of 83%[9a] and 88%,[12] respectively. (4) Bu_2CuLi can show high regioselectivity (≥98%) in favor of 1,4-addition.[3,9a] (5) *sec*-Bu_2CuLi shows poor regioselectivity (55% of 1,2-addition product).[8] $[t\text{-}Bu(Me)CH]Cu^-MeLi^+$ gives the product of conjugate addition of the C_6 unit in 94% isolated yield.[13] (7) $[CH_2{=}C(OEt)]_2CuLi$ reacts by the 1,2-pathway.[14]

The case of conjugate methylation is dealt with in detail in the following section. Most experiments described in the literature have involved use of Me_2CuLi, on which there is a systematic study,[3] and the few publications available report regioselectivities covering the whole range from those favoring 1,2-addition to those strongly biased toward the alternative mode.[3,9,15–17]

Discussion

In selecting a reagent to evaluate for its utility in conjugate methylation of enals, we decided to make an empirical search among methyl–copper species. Extensive descriptive literature was available for guidance, and a number of such materials were known but had not been

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(2) Other approaches to *gem*-dimethyl groups exist. Use of aluminum alkyls: Jeffery, E. A.; Meisters, A.; Mole, T. *Aust. J. Chem.* **1974**, *27*, 2569. Conjugate addition to unsaturated sulfones: Posner, G. H.; Brunelle, D. J. *J. Org. Chem.* **1973**, *38*, 2747. Use of titanium reagents: Reetz, M. T.; Westermann, J.; Steinbach, R. *J. Chem. Soc., Chem Commun.* **1981**, 237. Use of acetals: Bianchetti, G. *Ann. Chim.* (Rome) **1970**, *60*, 483. Use of cyclopropanes: Yamada, K.; Kyotani, Y.; Manabe, S.; Suzuki, M. *Tetrahedron* **1979**, *35*, 293. Oppolzer, W.; Godel, T. *J. Am. Chem. Soc.* **1978**, *100*, 2583.

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(9) (a) Schwartz, M.; Wakabayashi, N.; Thing, E. G. *Org. Prep. Proced. Int.* **1979**, *11*, 97. (b) Andersen, N. H.; Ladner, D. W. *Synth. Commun.* **1978**, 8, 449.

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(15) Gustafsson, B. *Acta Chem. Scand., Ser. B* **1977**, *31B*, 382.

(16) Reference 6c, pp 24, 31.

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tested for the purpose at hand. The search *and* our evaluation of $Me_5Cu_3Li_2$, the reagent selected, was based upon a consideration of the following literature.

(1) **Me_2CuLi.** A systematic study[3] of this reagent had been made and the results serve as a standard for comparison with other reagents. Depending on the structure of the enal, the solvent,[3,18] and the temperature, the conjugate methylation is accompanied usually by about 5–60% of 1,2-addition.[3,8,9] The rate of reaction is probably also sensitive to the stereochemistry of the enal.[16]

(2) **MeLi.** Organolithium species are known to react in a 1,2-manner with α,β-unsaturated carbonyl systems,[7] and MeLi would serve, therefore, in the preparation of authentic samples of 1,2-adducts.

(3) **$MeCu{\cdot}BF_3$.** Reaction of enals with $MeCu{\cdot}BF_3$ is reported[19] to be less effective than with Me_2CuLi, but no data are available.

(4) **Me_3CuLi_2.** This substance is in equilibrium with Me_2CuLi and MeLi in diethyl ether, dimethyl ether, and THF.[20] Conjugate methylation of oct-2-enal occurs efficiently (81% yield),[21] but the equilibrium concentration of MeLi is expected to limit the general use of the reagent for efficient 1,4-addition in cases where the other mode is relatively easy. This point was verified in our experiments (see below).

(5) **$Me_5Cu_3Li_2$.** This species, which can be formed in diethyl ether but not in THF,[20,22] is slightly more reactive toward enones (1,4-addition) than is Me_2CuLi.[18a] The study with enones, however, did not reveal the relative synthetic potential of the pentamethyl species because Me_2CuLi itself is usually a highly effective reagent for conjugate methylation of these substrates.[6c,18a]

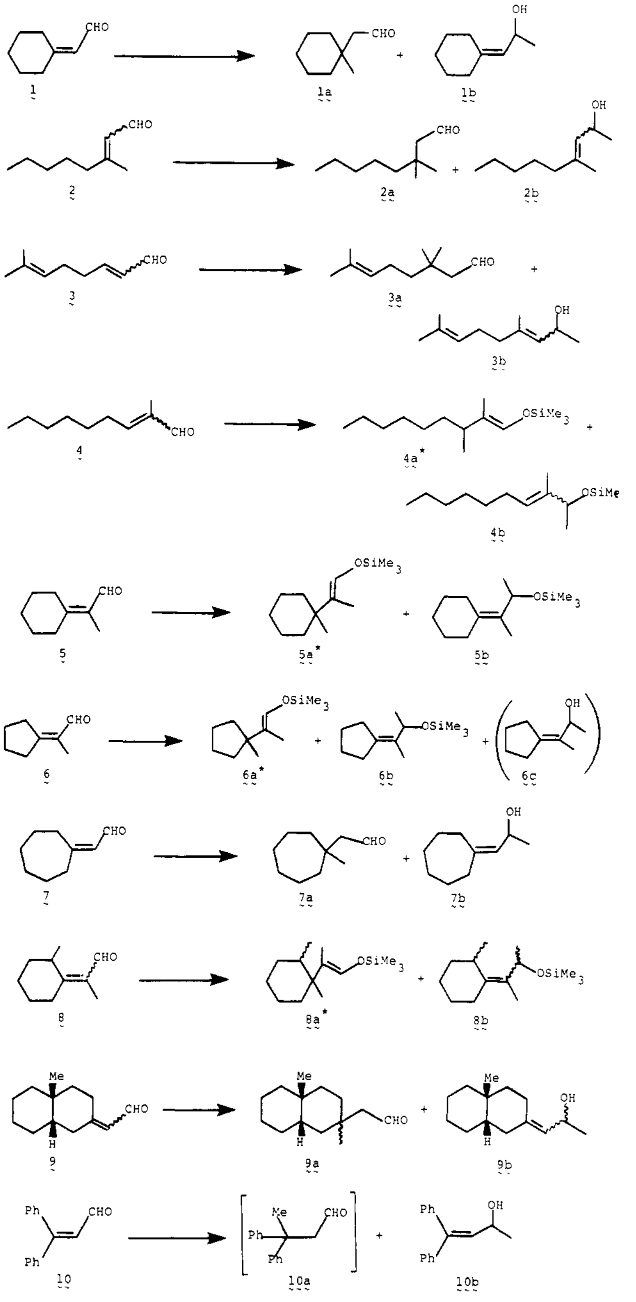
(6) **$R_4(Me)Cu_3(MgBr)_2$.** Species of the indicated stoichiometry are more reactive than R_2CuLi for 1,4-addition of group R to enones,[23] and this property made it necessary to examine material with the stoichiometry $Me_5Cu_3(MgBr)_2$ (see below).

(7) **Me_3Cu_2Li.** This compound, which is not formed in diethyl ether,[20,22] reacts (in THF) with enones in a 1,4-fashion.[18a] We examined its reaction with enals (see below).

(8) **MeCu(R)MgX.** Reaction with cinnamaldehyde [R = 2-[1-(dimethylamino)ethyl]phenyl] affords the 1,4-adduct in low yield (transfer of methyl).[24,25] In contrast, reaction with *enones* proceeds well[26] even with substrates resistant to the action of the corresponding R_2CuLi. Consequently, the reaction of Me_2CuMgX with enals merited examination (see below).

(9) **MeCu.** Salt-free MeCu does not generally behave[6c] as a reagent for conjugate addition to enones. We did, however, examine $MeCu{\cdot}LiI$ and found that it caused reduction of a test enal (see later).

Scheme I[a]



[a] An asterisk indicates that there is probably one geometric isomer only (NMR). The assignment shown here is arbitrary.

(10) **$MeCu{\cdot}MgBr_2$, $MeCu{\cdot}LiI$, $Me_2CuMgCl$, and MeMgBr + 10% CuBr.** A recent survey[8] of these four species indicated that $Me_2CuMgCl$[27] was the most highly regioselective: with (*E*)-2-methyl-2-pentenal, better than 99% of the product was that resulting from 1,4-addition. The yield (49%) was not optimized. As a consequence of this observation we have subjected $Me_2CuMgCl$ to a more demanding test (see below) and found it to be inferior to $Me_5Cu_3Li_2$.

(11) **$Me_3Cu_2MgX(LiBr)_n$ [n = 0, 2, 6 for X = Cl; n = 6 for X = Br] and $Me_3Cu_2Li(LiBr)_6$.** Reaction of these species with alkynes has been reported.[28] No information

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[18] With enones, reaction is faster in ether than in THF, and the extent of 1,4-addition is increased: (a) Ashby, E. C.; Lin, J. J.; Watkins, J. J. *J. Org. Chem.* **1977**, *42*, 1099. (b) House, H. O.; Respess, W. L.; Whitesides, G. M. *Ibid.* **1966**, *31*, 3128. (c) House, H. O.; Wilkins, J. M. *Ibid.* **1978**, *43*, 2443.

[19] Yamamoto, Y.; Muruyama, K. *J. Am. Chem. Soc.* **1978**, *100*, 3240.

[20] Ashby, E. C.; Watkins, J. J. *J. Am. Chem. Soc.* **1977**, *99*, 5312.

[21] (a) Still, W. C.; Macdonald, T. L. *Tetrahedron Lett.* **1976**, 2659. The geometry of the enal used was not specified. $Me_3Cu_2Li_2$ appears to react with ketone carbonyl groups faster than does MeLi. (b) See also: Macdonald, T. L.; Still, W. C. *J. Am. Chem. Soc.* **1975**, *97*, 5280.

[22] $Me_5Cu_3Li_2$ is reported to be *insoluble* in THF and Me_3Cu_2Li is insoluble in diethyl ether: Ashby, E. C.; Lin, J. J. *J. Org. Chem.* **1977**, *42*, 2805.

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[24] Hansson, A.-T.; Rahman, M. T.; Ullenius, C. *Acta Chem. Scand., Ser. B* **1978**, *32B*, 483.

[25] For 1,4-addition (R = Ph) to (*E*)-4-phenylbut-3-en-2-one see: Sjoholm, R.; Backlund, P. *Finn. Chem. Lett.* **1980**, 28; *Chem. Abstr.* **1980**, *93*, 168350.

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[27] Cf. comments made above under item 8.

[28] Westmijze, H.; Kleijn, H.; Meijer, J.; Vermeer, P. *Recl. Trav. Chim. Pays-Bas* **1981**, *100*, 98.

Table I. Reactions of Various Enals with $Me_5Cu_3Li_2$ and Me_2CuLi

expt	starting matl	reaction solvent; temp, °C[a] (quench)	reagent	% yield[b]	% methylation[c]	
					1,4	1,2
1	**1**	Et_2O; −40 (AcOH)	$Me_5Cu_3Li_2$	90	99.0	1.0[e]
			Me_2CuLi	71[d]	87.0	13.0
2	**2**	Et_2O; −40 (AcOH)	$Me_5Cu_3Li_2$	90	>99.5	<0.5[f]
			Me_2CuLi	90	91.5	8.5
3	**3**	Et_2O; 0 (AcOH)	$Me_5Cu_3Li_2$	80	>99.5	<0.5[f]
			Me_2CuLi	78	90.0	10.0
4	**4**	Et_2O; −20 (Me_3SiCl)	$Me_5Cu_3Li_2$	92	98.5	1.5
			Me_2CuLi	92	94.5	5.5
5	**5**	Et_2O-pentane; 0 (Me_3SiCl)	$Me_5Cu_3Li_2$	88	>99.5	<0.5[f]
			Me_2CuLi	91	80.0	20.0
6	**6**	Et_2O; 0 (Me_3SiCl)	$Me_5Cu_3Li_2$	85	77.5	22.5
			Me_2CuLi	86[g]	36[g]	64[g]
		Et_2O-pentane; 0 (Me_3SiCl)	$Me_5Cu_3Li_2$	88	85.0	15.0
7	**7**	Et_2O; −20 (AcOH)	$Me_5Cu_3Li_2$	88	94.5	5.5
			Me_2CuLi	88	83.0	17.0
		Et_2O-pentane; −10 (AcOH)	$Me_5Cu_3Li_2$	80	95.1	4.9[e]
8	**8**	Et_2O-pentane; 0 (Me_3SiCl)	$Me_5Cu_3Li_2$	88	46.0	54.0
			Me_2CuLi	87	48.5	51.5
9	**9**	Et_2O; −20 (AcOH)	$Me_5Cu_3Li_2$	86	98.0	2.0[e]
			Me_2CuLi	84	97.5	2.5[e]
10	**10**	Et_2O; 0 (AcOH)	$Me_5Cu_3Li_2$	73	0.0	100.0
			Me_2CuLi	42	0.0	100.0

[a] Temperature refers to the highest temperature reached by the reaction mixture before the reaction was quenched at −75 °C. [b] Yields refer to isolated and distilled materials of >97% purity (VPC). [c] Ratios determined by 200-MHz NMR, except where indicated. [d] The mixture was quenched with a saturated aqueous ammonium chloride solution. [e] Ratio determined by VPC (relative peak areas). [f] Actually, none was detected (VPC, NMR). [g] Data from ref 3.

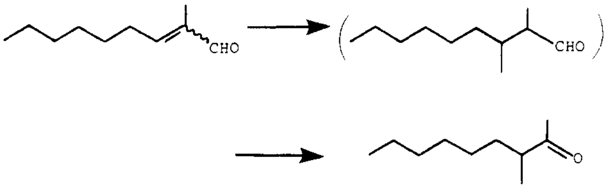
is available on their reactions with α,β-unsaturated carbonyl systems and we, too, did not study these cuprates.

On the basis of the above summary, the following were selected for examination: $MeCu{\cdot}LiI$, Me_2CuLi, $Me_5Cu_3Li_2$, Me_3CuLi_2, $Me_5Cu_3(MgBr)_2$, Me_3Cu_2Li, $Me_2CuMgCl$ (in THF). Of these, $Me_5Cu_3Li_2$ is the best and, in absolute terms it works in a synthetically efficient manner.

For the initial experiments we used the enal **1**. $Me_5Cu_3Li_2$ was prepared, following the published[20] directions, by addition of freshly titrated MeLi (containing ca. 5% LiCl) to copper(I) iodide in diethyl ether at 0 °C. The solution was cooled to −75 °C, and the enal (2 mol/mol of $Me_5Cu_3Li_2$) was introduced. No precipitation of polymeric methyl copper occurred at −75 °C, and so the temperature was raised to −40 °C, which is about 10 °C above the value at which reaction was discernible (through the formation of a precipitate). The workup after an arbitrary reaction time afforded **1a** and **1b** (Scheme I) in a ratio (VPC, relative peak areas) of 99:1 as well as cyclohexylidene ethanol. The latter comprised about 5% of the total product. To test whether this reduction product was formed by the action of methylcopper, we treated the enal **1** with methylcopper,[29] slurried in diethyl ether, at −10 °C and observed the slow production of **1a** and 2-cyclohexylideneethanol in a 2:1 ratio (VPC). No trace (VPC) of **1b** was detected. This reduction, in the case of the pentamethyl species, could be suppressed completely by using equimolar amounts of $Me_5Cu_3Li_2$ and enal.

The method of workup of reactions between enals and Me_2CuLi is an important factor in determining the yield and purity of the product,[3] and the same is true in experiments with $Me_5Cu_3Li_2$. For example, in the reaction of **1** with $Me_5Cu_3Li_2$, a workup by pouring the mixture onto an ice-cold aqueous solution of ammonium chloride gave the reaction product in 71% yield, after distillation. However, when the reaction mixture was cooled from −40 °C (at the end of the conjugate methylation) to −75 °C and quenched by rapid addition of acetic acid, the yield improved to 90%.

In the case of α-substituted enals (e.g., **4**) a different workup procedure is necessary for the following reason. The aldehydes released after conjugate methylation and protonation are unstable in the reaction medium and afford saturated ketones resulting from decarbonylation (eq 2). This reaction,[30] which was also observed in experiments with Me_2CuLi,[3,8] can be avoided by quenching the reaction with chlorotrimethylsilane in the presence of triethylamine and HMPA.[3,8,31] In such cases, of course, the products are trimethylsilyl enol ethers,[32] but these are easily convertible into the parent aldehydes in good yield.[8]



(2)

In a further experiment, compound **1** was treated with Me_2CuLi in diethyl ether in the temperature range −75 to −40 °C. Quenching with saturated aqueous ammonium chloride gave, in 71% yield, a mixture of **1a** and **1b** in the ratio 87:13.

The above two reactions of the test enal **1** with $Me_5Cu_3Li_2$ and Me_2CuLi suggested that the former species behaves in a synthetically more useful fashion toward enals, and, therefore, we made a detailed study of the response of this reagent to enals of different substitution patterns. With each one we also ran a parallel experiment using Me_2CuLi. The presence of 1,2-adducts was excluded, or confirmed, by comparison of the VPC and NMR (200 MHz) data for the total reaction product (after distillation)

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(29) Generated from CuI and MeLi; i.e., 1 mol of LiI was present. See: House, H. O.; Fischer, Jr., W. F. *J. Org. Chem.* **1968**, *33*, 949.

(30) Van Rheenan, V. *Tetrahedron Lett.* **1969**, 985. Briggs, L. H.; Bartley, J. P.; Rûtledge, P. S. *Ibid.* **1970**, 1237.

(31) Funk, R. L.; Vollhardt, K. P. C. *J. Am. Chem. Soc.* **1980**, *102*, 5253.

(32) Garst, M. E. *Synth. Commun.* **1980**, *10*, 863.

with the data obtained from authentic 1,2-adducts. These were prepared from the enals by reaction with methyllithium. The results of this comparative study are shown in Scheme I and Table I. In the experiments summarized by entries no. 1-7 (see Table I), $Me_5Cu_3Li_2$ is clearly superior to Me_2CuLi for conjugate methylation.

The reaction of citral (**3**) with Me_2CuLi had been reported[3] to give 19% (relatively) of 1,2-adduct or ca 5% (in another study).[9] Operating at a lower temperature than that which led to 19% 1,2-adduct, we obtained rather less of this unwanted product.

Compounds **8** and **9** were chosen to examine, in a qualitative way, the effect of remote substituents.[33] With **8**, the major product from experiments using either $Me_5Cu_3Li_2$ or Me_2CuLi was the 1,2-adduct. The 1,4-adduct obtained from each experiment was a 3:1 mixture of diastereoisomers.[34] With **9**, both $Me_5Cu_3Li_2$ and Me_2CuLi were almost equally effective in producing the product of 1,4-methylation (as a 95:5 mixture of epimeric aldehydes **9a**).

Compounds **5** and **6** were used to test the pentamethyl reagent with substrates rendered more resistant to conjugate addition by virtue of their substitution pattern (see later).[35] Compound **6** was already known to be a particularly difficult case: with Me_2CuLi in diethyl ether it had been found to give 64% (relatively) of 1,2-adduct.[3] When it was treated with $Me_5Cu_3Li_2$ in diethyl ether, 77.5% of the product was the result of conjugate addition. This result was improved on the basis of the fact[18c] that use of nonpolar solvents promotes copper-mediated 1,4-addition to enones relative to side reactions (that are unrelated to electron-transfer processes). In a few reactions of Me_2CuLi with enals, the use of ether–pentane mixtures instead of pure diethyl ether had increased the proportion of 1,4- relative to 1,2-addition.[3] Therefore, we tried ether–pentane (ca. 1:1)[36a] with $Me_5Cu_3Li_2$. Addition of the nonpolar solvent might, of course, alter the nature of the copper species. In the event, we observed no change of color nor any precipitation on adding three volumes of pentane to an ether solution of $Me_5Cu_3Li_2$, and introduction of **6** (in diethyl ether) gave, in 88% isolated yield, a mixture of **6a** and **6b** in the ratio of 85:15.[36b]

Similar use of the mixed solvent with **5** suppressed the 1,2-addition completely while Me_2CuLi, even in this favorable solvent system, led to 20% (relatively) of 1,2-adduct.

When we repeated the reaction of **2** with Me_2CuLi, but in ether–pentane, there was no improvement in the 1,4/1,2 ratio obtained in diethyl ether. This observation suggests that addition of pentane as a cosolvent is effective only in limiting cases where the reduction potential of the enal is ca. −2.2 V (see later).[37]

Table II. Action of Various Cuprates on 2-Cyclopentylidene Propionaldehyde

conditions	% yield[a]	% addition[b] 1,4	1,2
Me_2CuLi, ether, 0 °C[c]	86	36	64
$Me_5Cu_3Li_2$, ether, −50–0 °C	85.5	77.5	22.5
$Me_5Cu_3Li_2$, ether–pentane, −50–0 °C	88	85	15
Me_3CuLi_2, ether, −50–0 °C	84.8	4	96
$Me_5Cu_3Mg_2Br_2$, ether, −40–0 °C	92.0	4	96
Me_3Cu_2Li, THF, −50–0 °C	*d*	20	80
$Me_2CuMgCl$, THF, −5–0 °C	89.6	25	75

[a] Yields refer to distilled samples that were better than 99% pure (VPC, DEGS, 100 °C) unless otherwise stated. [b] Reactions were quenched with chlorotrimethylsilane (see Experimental Section). Proportions of 1,4- and 1,2-adducts were estimated by ^1H NMR ($CDCl_3$, 200 MHz). [c] Data from ref 3. [d] The mixtures of **6a** and **6b** were contaminated by impurities (ca. 50% of the total product, estimated by VPC relative peak areas).

Our results establish that compound **6** represents a demanding test for conjugate addition to an enal, and so we have used it to evaluate other copper species that might be more highly regioselective than $Me_5Cu_3Li_2$. These experiments are shown in Table II, and the following points should be noted in connection with the data that it summarizes. (i) As stated earlier in the discussion, Me_3CuLi_2, in ethereal solution, is in equilibrium with MeLi. Some 1,2-addition should, in general, occur, particularly in difficult cases, and, in fact, with compound **6** this is the major pathway. (ii) Notwithstanding the favorable reputation of $R_4(Me)Cu_3(MgBr)_2$ for conjugate transfer of group R to enones, we found that a suspension of $Me_5Cu_3(MgBr)_2$, prepared according to directions given[23] for $R_4(Me)Cu_3(MgBr)_2$, results in 1,2-addition almost exclusively. (iii) In the initial literature survey of copper species we had found very little information to suggest the likely regiochemical behavior of Me_3Cu_2Li.[20] The substance is not formed in diethyl ether. It was, therefore, prepared[20,22] in THF, a solvent that is a poor choice for conjugate methylation with Me_2CuLi,[18,38] and on testing it we obtained mainly the 1,2-adduct (see Table II). (iv) Recently, $Me_2CuMgCl$ in THF was found[8] to hold promise for highly regioselective conjugate addition to enals: a single example gave an *unoptimized* yield of 49% of almost exclusive (>99%) 1,4-addition to (2*E*)-2-methyl-2-pentenal. In the case of compound **6**, however, 75% of the product was the result of 1,2-addition, and this performance is inferior to that of $Me_5Cu_3Li_2$ in ether–pentane at a low temperature.

Miscellaneous Experiments

Reaction of $Me_5Cu_3Li_2$ with 11 and 12. Although $Me_5Cu_3Li_2$ has been evaluated as a reagent for conjugate addition to enones,[18a] we wanted to establish if it would add in those cases where 1,4- or 1,2-addition fails to occur with Me_2CuLi. Compound **11** is such an example.[39] We find that the pentamethyl species does not react (95% recovery) with it (in ether–pentane at 0 °C).

A less demanding test, on the basis of reduction potentials (see later), is **12**. Treatment in ether–pentane with $Me_5Cu_3Li_2$ gave a reaction product (64% yield) consisting of recovered **12** (50%), the 1,4-adduct[18c] (43%), and the 1,2-adduct (7%). With Me_2CuLi the product (66%) was a mixture of **12** (66%), its 1,4-adduct[18c] (30%), and the 1,2-adduct (4%).[40]

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(33) See references cited in footnote 21 for stereochemistry of cuprate attack on cyclohexanones. Cf. also: Chérest, M.; Felkin, H. *Tetrahedron Lett.* **1971**, 383. For a theoretical treatment of the stereochemistry of nucleophilic attack on an sp^2-hybridized carbon in a cyclohexane ring system see: Cieplak, A. S. *J. Am. Chem. Soc.* **1981**, *103*, 4540.

(34) Only two Me_3Si signals occur in the 200-MHz NMR spectrum. Probably, therefore, only one double bond geometry occurs, here arbitrarily shown as *E*.

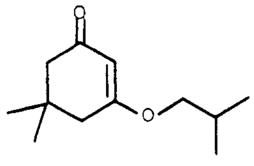
(35) A strain and the exocyclic nature of the double bond with respect to a six- or five-membered ring would influence the ease of 1,4-methylation. Methylenecyclopentane is less strained than cyclopentane while methylenecyclohexane is more strained than cyclohexane: Schleyer, P. v. R.; Williams, J. E.; Blanchard, K. R. *J. Am. Chem. Soc.* **1970**, *92*, 2377.

(36) (a) This ratio is the *final* solvent composition. (b) When the *final* solvent composition was 1:3 (diethyl ether/pentane) the ratio of **6a**/**6b** fell to 75:25.

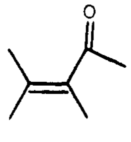
(37) A similar effect has been noted with enones (see ref 18c). Reaction of **7** with $Me_5Cu_3Li_2$ in ether–pentane changed the percent of 1,2-addition from 5.5% to 4.9%.

(38) $R_4(Me)CuMgX$ *does* react in THF (see ref 23) with enones.

(39) House, H. O.; Umen, M. J. *J. Am. Chem. Soc.* **1972**, *94*, 5495.



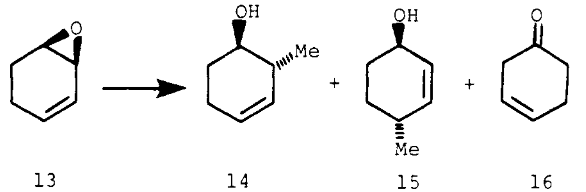
11



12

The experiments with **11** and **12**, while not being a definitive test, do not reveal any large difference in oxidation potentials of $Me_5Cu_3Li_2$ and Me_2CuLi (see later).

Reaction of $Me_5Cu_3Li_2$ with 13. The epoxy olefin **13** was treated with $Me_5Cu_3Li_2$. The corresponding reaction with Me_2CuLi has been reported,[41] and we found that the pentamethyl reagent gives virtually the same product distribution (eq 3) as Me_2CuLi.[42] The mechanism of cuprate addition to olefinic epoxides may well be entirely different from that of addition to α,β-unsaturated carbonyl systems, and so the features which make $Me_5Cu_3Li_2$ a good reagent for enals are not relevant in the case of epoxides.[43]



(3)

13 14 15 16

Decarbonylation of 1a. Treatment of **1a** with chlorotris(triphenylphosphine)rhodium(I)[44] resulted in decarbonylation to 1,1-dimethylcyclohexane, but the reaction is slow, and, even in benzonitrile at 115 °C (the boiling point of 1,1-dimethylcyclohexane), there was only 20% conversion after an overnight reaction period. The process is very clean, however, but we did not pursue studies on the decarbonylation of the hindered aldehyde.[45]

Preparation of Enals. Of various routes to enals, we considered only those that involve a two-carbon homologation of a ketone or aldehyde.[46] Quite a large variety of methods is known,[47] and the compound class is easily accessible. Of several procedures that we examined, we favor that based on (*Z*)-1-bromo-2-ethoxyethylene[47t,48] for α-unsubstituted enals and that based on *tert*-butyl imines[47f] for α-substituted cases. In our hands the latter method always gave 10–20% of unreacted starting ketone.[49]

Our experience is that α,β-unsaturated aldehydes should not be stored at room temperature. They can be kept, however, under nitrogen at −20 °C for 2–4 weeks without evidence of decomposition.

Preparation of the 1,2-Adducts from Enals. Reaction of the enals with MeLi in ether proceeded cleanly to afford the 1,2-adducts in high yield.

Mechanistic Considerations. Conjugate alkylation of *enones* has been the subject of considerable mechanistic study,[6g,18c,50] and most of the evidence has been interpreted in terms of an initial electron transfer. Irrespective of the detailed mechanism, however, a correlation exists[18c] between the reduction potential (E_{red} vs. the saturated calomel electrode in an aprotic solvent) of unsaturated carbonyl compounds and their reactivity in conjugate addition with cuprates. The reduction potential should be in the range −1.3 to −2.3 V in order to obtain high yield conjugate methylation with Me_2CuLi. The values for compounds **11** and **12**, whose reactions are described above, have been measured as −2.43[50a] and −2.35 V,[18c] respectively. Saturated ketones do not react readily[51] with Me_2CuLi but saturated aldehydes do.[52]

Unsaturated aldehydes, e.g., **1**–**10**, with reduction potentials estimated[6g,50a] to be in the above range (−1.3 to −2.3 V) do afford substantial amounts of 1,2-adduct with Me_2CuLi. It is clear, therefore, that unsaturated aldehydes are a special case within the group of substrates for cuprate addition because of their tendency to react in the 1,2-mode.

For reactions of enals with Me_2CuLi it seems, from the data obtained in this and other[3] studies, that the useful range for conjugate addition does not extend below an estimated[50a] value of $E_{red} = -2.0$ V. With $Me_5Cu_3Li_2$ a slightly wider range, down to $E_{red} = -2.1$ V, is generally available.[53]

The role of solvent in conjugate additions of Me_2CuLi has been discussed[18c] in terms that also explain the observations with $Me_5Cu_3Li_2$. The cuprate cluster possesses electrophilic (Li atoms) and nucleophilic sites. The former complex with the carbonyl oxygen in the first step of the reaction. Consequently, preferential complexation with a donor solvent (THF) shifts the equilibrium of the cuprate–substrate complex and, therefore, alters the rate of the whole reaction.

Conclusion

The comparative studies (Table I and II) show that $Me_5Cu_3Li_2$ is the most promising reagent of those we have examined for conjugate methylation of enals. It works in a highly regioselective manner with enals having partially or completely substituted double bonds provided that the substrates are not sterically hindered.[54]

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(40) Cf. the results for a similar experiment reported in ref 18c.

(41) Staroscik, J.; Rickborn, B. *J. Am. Chem. Soc.* **1971**, *93*, 3046. Wieland, D. M.; Johnson, C. R. *Ibid.* **1971**, *93*, 3047.

(42) For addition of complex cuprates to olefinic epoxides see: Marino, J. P.; Hatanaka, N. *J. Org. Chem.* **1979**, *44*, 4467. Marino, J. P.; Floyd, D. M. *Tetrahedron Lett.* **1979**, 675. Wender, P. A.; Erhardt, J. M.; Letendre, L. J. *J. Am. Chem. Soc.* **1981**, *103*, 2114.

(43) For a mechanistic study see: Johnson, C. R.; Herr, R. W.; Wieland, D. M. *J. Org. Chem.* **1973**, *38*, 4263.

(44) Osborne, J. A.; Jardine, F. H.; Young, J. F.; Wilkinson, G. *J. Chem. Soc. A* **1966**, 1711.

(45) Tsuji, J.; Ohno, K. *Synthesis* **1969**, 157.

(46) Review: Martin, S. M. *Synthesis* **1979**, 633.

(47) For example, see: (a) Trippett, S.; Walker, D. M. *Chem. Ind. (London)* **1960**, 202. (b) Mayers, A. I.; Nabeya, A.; Adickes, H. W.; Politzer, I. R.; Malone, G. R.; Kovelesky, A. C.; Nolen, R. L.; Portnoy, R. C. *J. Org. Chem.* **1973**, *38*, 36. (c) Meyers, A. I.; Munavu, R.; Durandetta, J. *Tetrahedron Lett.* **1972**, 3929. (d) Meyers, A. I.; Tomioka, K.; Fleming, M. P. *J. Org. Chem.* **1978**, *43*, 3788. (e) Brink, M. *Synthesis* **1975**, 253. (f) Corey, E. J.; Enders, D.; Bock, M. G. *Tetrahedron Lett.* **1976**, 7. (g) Dauben, W. G.; Michno, D. M. *J. Org. Chem.* **1977**, *42*, 682. (h) Babler, J. H.; Coghlan, M. J. *Synth. Commun.* **1976**, *6*, 469. (i) Corey, E. J.; Enders, D. *Chem. Ber.* **1978**, *111*, 1362. (j) Rousseau, G.; Le Perchec, P.; Conia, J.-M. *Synthesis* **1978**, 67. (k) Trost, B. M.; Stanton, J. L. *J. Am. Chem. Soc.* **1975**, *97*, 4018. (l) Cutting, I.; Parsons, P. J. *Tetrahedron Lett.* **1981**, 2021. (m) Wittig, G.; Reiff, H. *Angew. Chem., Int. Ed. Engl.* **1968**, *7*, 7. (n) Takahashi, H.; Fujiwara, K.; Ohta, M. *Bull. Chem. Soc. Jpn.* **1962**, *35*, 1498. (o) Nagata, W.; Hayase, Y. *J. Chem. Soc. C* **1969**, 460. (p) Mukaiyama, T.; Hayashi, M. *Chem. Lett.* **1974**, 15. (q) Mukaiyama, T.; Banno, K.; Narasaka, K. *J. Am. Chem. Soc.* **1974**, *96*, 7503. (r) Wollenberg, R. H.; Albizati, K. F.; Peries, R. *Ibid.* **1977**, *99*, 7365. (s) Ficini, J.; Falou, S.; Touzin, A. M.; D'Angelo, J. *Tetrahedron Lett.* **1977**, 3589. (t) Lau, K. S. Y.; Schlosser, M. *J. Org. Chem.* **1978**, *43*, 1595.

(48) Commercially available (Aldrich).

(49) For recent methods that we did not test see: Williams, D. R.; Nishitani, K. *Tetrahedron Lett.* **1980**, 4417 (this is not a 2-carbon homologation). Duhamel, L.; Tombret, F. *J. Org. Chem.* **1981**, *46*, 3741. Fishman, D.; Klug, J. T.; Shani, A. *Synthesis* **1981**, 137.

(50) (a) House, H. O.; Huber, L. E.; Umen, M. J. *J. Am. Chem. Soc.* **1972**, *94*, 8471. (b) Krauss, S. R.; Smith, S. G. *Ibid.* **1981**, *103*, 141. (c) Whitesides, G. M.; Kendall, P. E. *J. Org. Chem.* **1972**, *37*, 3718. (d) Cesa, M. C. *J. Am. Chem. Soc.* **1979**, *101*, 4236.

(51) See ref 21b and references therein.

(52) Posner, G. H.; Whitten, C. E.; McFarland, P. E. *J. Am. Chem. Soc.* **1972**, *94*, 5106. Barreiro, E.; Luche, J. L.; Zweig, J.; Crabbé, P. *Tetrahedron Lett.* **1975**, 2353.

(53) The correlations with E_{red} values must be regarded as a rough guide only. See: Clark, R. D.; Heathcock, C. H. *J. Org. Chem.* **1976**, *41*, 636, footnote 20.

(54) E.g., compound **8**. The reason for the equal performance of Me_2CuLi and $Me_5Cu_3Li_2$ with **9** is not clear.

The pentamethyl reagent can be used to generate quaternary centers, and the aldehyde group is available for further manipulation leading to branched acyclic carbon structures.[55]

Experimental Section

Except where stated to the contrary, the following particulars apply. Apparatus was oven dried (130 °C). Experiments were done with magnetic stirring under a slight static pressure of nitrogen, purified by passage through a column (3.5 × 42 cm) of R-311 catalyst[56] and then through a similar column of Drierite. Solvents were distilled before use for chromatography. Dry triethylamine, diisopropylamine, pentane, chlorotrimethylsilane, and HMPA were distilled from CaH$_2$, the latter under reduced pressure (0.1 mm), and dry THF and ether from sodium (benzophenone indicator). Cuprous iodide was purified by the literature procedure[57] and stored under a nitrogen atmosphere.

The commercial (Aldrich) methyllithium used contained ca. 5% LiCl[58] and was titrated[59] periodically. Methylmagnesium bromide in ether (Aldrich) was titrated[60] with chlorodimethylphenylsilane. During product isolation, solutions were dried (where necessary) over Na$_2$SO$_4$ and evaporated under water-pump vacuum at room temperature. Isolated products were submitted directly for combustion analysis without need for additional purification. For VPC, the columns used were as follows: 6 ft, 10% DEGS, Chromosorb W, 80–100 mesh, and 6 ft, 10% FFAP, Chromosorb W, 80–100 mesh. Purities and compositions evaluated by VPC represent relative peak areas. Silica gel for flash chromatography[61] was Merck Type 60 (230–400 mesh). Commercial TLC plates (Camag DF-B or Merck 60F-254) were used. Mass spectra were run at an ionizing voltage of 70 eV. Boiling points quoted for products distilled in a Kugelrohr apparatus refer to the oven temperature.

***α,β*-Unsaturated Aldehydes.** Dienal **3** (Aldrich) was distilled before use [bp 120 °C (20 mm)]. The material was a mixture (NMR) of geometric isomers. **1**,[47f] **5**,[47f] and **10**[47b] were prepared by the literature procedures cited and the other known compounds, **2**,[47g] **4**,[62] and **6**,[3] were made by a general method[47f] that is described in detail below for the new compound **8**. The compounds are rather unstable but can be stored for short periods (2–4 weeks) at −20 °C under a nitrogen atmosphere. New aldehydes were made by general methods as follows.

Cycloheptylideneacetaldehyde (7). A general method reported in the literature[47f] was followed with some modifications. (Trimethylsilyl)acetaldehyde *tert*-butylimine (5.655 g, 33.0 mmol) in dry THF (5 mL) was added over 10 min to a stirred, cooled (−40 °C) solution of LDA [from diisopropylamine (4.2 mL, 30 mmol) and butyllithium in hexane (1.40 M, 21.4 mL, 30 mmol)] in THF (90 mL). The temperature was allowed to reach −10 °C over 1 h, and the solution was cooled to −70 °C. Then cycloheptanone (2.40 mL, 20 mmol) in THF (10 mL) was added over a 10-min period. The mixture was stirred for 3.5 h while the temperature was allowed to rise to 25 °C. Water (20 mL) was added in one portion, followed by enough oxalic acid dihydrate to bring the pH to 4.5. The mixture was stirred for 3 h and then partitioned between ether (100 mL) and water (100 mL). The organic phase was washed with saturated aqueous sodium hydrogen carbonate (2 × 50 mL) and brine (50 mL) and was dried over MgSO$_4$. Filtration and evaporation gave the crude product. Flash chromatography over silica gel (4 × 20 cm) with hexane containing 3% v/v of ethyl acetate followed by Kugelrohr distillation [90–95 °C (2 mm)] gave **7** (1.50 g, 54.3%) of better than 98% purity (VPC, DEGS, 150 °C): IR (film) 1670 cm^{-1}; NMR (CDCl$_3$, 100 MHz) δ 1.3–1.9 (m, 8 H), 2.2–2.5 (m, 2 H), 2.6–3.0 (m, 2 H), 5.88 (td, J_1 = 8 Hz, J_2 = 1 Hz, 1 H) 10.00 (d, J = 8 Hz, 1 H); exact mass 138.1046 (calcd for C$_9$H$_{14}$O 138.1045). For characterization a sample of the aldehyde was converted[63] into its 2,4-dinitrophenylhydrazone: mp 165–166.5 °C (from ethanol). Anal. Calcd for C$_{15}$H$_{18}$N$_4$O$_4$: C, 56.59; H, 5.70; N, 17.60. Found: C, 56.55; H, 5.71; N, 17.68.

2-(2-Methylcyclohexylidene)propionaldehyde (8). A literature method[47f] was followed with some modifications. 2-(Trimethylsilyl)propionaldehyde *tert*-butylimine (3.510 g, 18.94 mmol) was injected neat over 10 min to a stirred, cold (0 °C) solution of LDA [from diisopropylamine (2.5 mL, 17.71 mmol) and butyllithium in hexane (1.40 M, 12.7 mL, 17.78 mmol)] in THF (60 mL). After a further 10 min at 0 °C the mixture was cooled to −75 °C, and 2-methylcyclohexanone (1.307 g, 11.65 mmol) in THF (2 mL plus 2 × 1 mL rinse) was injected (main portion over about 3 min). The mixture was stirred overnight, during which period the cold bath attained room temperature. Water (20 mL) and enough oxalic acid dihydrate to bring the pH to 4.5 were added. The mixture was stirred for 50 min and then partitioned between ether (50 mL) and water (50 mL). The organic phase was washed with saturated aqueous sodium hydrogen carbonate (2 × 50 mL) and with brine (50 mL) and was dried over anhydrous potassium carbonate. Filtration and evaporation gave the crude product in which the major impurity (ca. 15%, VPC) was the starting ketone. Flash chromatography over silica gel (4 × 20 cm) with hexane containing increasing amounts (0.5–1% v/v) of ethyl acetate followed by Kugelrohr distillation [145 °C (10 mm)] gave **8** (892 mg, 50%) as a 1:1 mixture (NMR, 200 MHz) of *E* and *Z* isomers of better than 97% purity (VPC, DEGS, 150 °C): IR (film) 2770, 1665, 1612 cm^{-1}; NMR (CDCl$_3$, 200 MHz) δ 1.11 (d, J = 7.20 Hz, 1.5 H), 1.19 (d, J = 6.85 Hz, 1.5 H), 1.29–2.03 (m, 9 H), 2.18 (m, 1 H), 2.63 (m, 0.5 H), 3.05 (m, 0.5 H), 3.33 (m, 0.5 H), 3.79 (m, 0.5 H), 10.15 (s, 0.5 H), 10.20 (s, 0.5 H); exact mass 152.1202 (calcd for C$_{10}$H$_{16}$O 152.1201).

For characterization a sample of the aldehyde was converted[63] into its 2,4-dinitrophenylhydrazone, mp 120 and 158–159 °C (from ethanol, double melting point). Anal. Calcd for C$_{16}$H$_{20}$N$_4$O$_4$: C, 57.82; H, 6.07; N, 16.86. Found: C, 57.67; H, 6.17; N, 16.59.

(4a*β*,8a*β*)-4a-Methyldecahydronaphth-2-ylidene)acetaldehyde (9). A general procedure[47t] was followed. *tert*-Butyllithium in pentane (1.72 M, 14 mL, 24.2 mmol) was added to THF (30 mL) at −75 °C, and the solution was kept at this temperature. (*Z*)-1-Bromo-2-ethoxyethylene[47t] (1.820 g, 12.1 mmol) was injected neat over 5 min and THF (3 × 1 mL) was used to rinse all of the bromide into the *tert*-butyllithium solution. After a further period of 30 min at −75 °C, *cis*-4a-methyloctahydro-2-naphthalenone[64] (1.677 g, 10.09 mmol) in THF (5 mL plus 2 × 1 mL rinse) was added (main portion over 10 min).

The cold bath was left in place, and after 5 h the reaction mixture had attained room temperature. The mixture was then cooled to 0 °C, aqueous hydrochloric acid (10% v/v, 15 mL) was added, the cooling bath was removed, and the two-phase system was stirred vigorously for 15 min. The organic layer was removed, the aqueous phase was extracted with ether (50 mL), and the combined organic extract was washed with water and with brine, dried (Na$_2$SO$_4$), and evaporated. Flash chromatography of the residue over silica gel (4 × 25 cm) with hexane containing increasing amounts (2–5% v/v) of ethyl acetate followed by Kugelrohr distillation [130–135 °C (0.15 mm)] afforded **9** (1.460 g, 75%) as a pure (TLC, silica, 1:20 ethyl acetate–hexane) 1:1 mixture (NMR, 200 MHz) of *E* and *Z* isomers: IR (film) 2765, 1662, 1625 cm^{-1}; NMR (CDCl$_3$, 200 MHz) δ 0.7–3.1 (m, 18 H, incorporating s at δ 1.07), 5.4–5.8 (m, 1 H), 9.85 (d, J = 3.5 Hz, 0.5 H), 9.93 (d, J = 3.5 Hz, 0.5 H); exact mass 192.1513 (calcd for C$_{13}$H$_{20}$O 192.1514).

For characterization a sample was converted[63] into its 2,4-dinitrophenylhydrazone, mp 131–134 °C (from ethanol). Anal. Calcd for C$_{19}$H$_{24}$N$_4$O$_4$: C, 61.27; H, 6.50; N, 15.04. Found: C, 61.11; H, 6.42; N, 14.83.

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(55) In principle, highly branched *α,β*-unsaturated esters can be alkylated in a conjugate fashion with MeCu·BF$_3$ and the ester group then converted into a formyl group. The conjugate alkylation is reported for only one example (with BuCu·BF$_3$, yields, using highly substituted enoates, are ~55%.) See reference 19.

(56) An American supplier of this BASF catalyst is Chemical Dynamics Corp., South Plain Field, NJ.

(57) Kauffmann, G. B.; Teter, L. A. *Inorg. Synth.* **1963**, *7*, 9.

(58) In the preliminary communication[4] it is erroneously implied that the ratio MeLi/LiCl is 1:1.

(59) Kofron, W. G.; Baclawski, L. M. *J. Org. Chem.* **1976**, *41*, 1879.

(60) House, H. O.; Respess, W. L. *J. Organomet. Chem.* **1965**, *4*, 95.

(61) Still, W. C.; Kahn, M.; Mitra, A. *J. Org. Chem.* **1978**, *43*, 2923.

(62) Honwad, V. K.; Rao, A. S. *Curr. Sci.* **1965**, *34*, 534.

(63) Vogel, A. I. "A Textbook of Practical Organic Chemistry", 3rd ed.; Longmans, Green and Co.: London, 1956; p 344.

(64) Yanagita, M.; Yamakawa, K. *J. Org. Chem.* **1957**, *22*, 291.

General Procedures[65] for Reaction of α,β-Unsaturated Aldehydes with Cuprates. (A) $Me_5Cu_3Li_2$ in Ether. Purified cuprous iodide (3 mmol) was placed in a dry 50-mL three-necked flask carrying a magnetic stirring bar. Two necks of the flask were closed by rubber septa and the other by a vacuum take-off equipped with a stopcock. The flask was alternately evacuated and filled with nitrogen (three cycles), and dry ether (10 mL) was then injected. The slurry was stirred at ca. 0 °C (ice bath), and commercial ethereal MeLi (ca. 1.8 M, 5 mmol) was injected over 2–3 min. A dark yellow precipitate of methylcopper was deposited and then dissolved. Five minutes after the end of the addition the colorless (or faintly yellow) solution was cooled to the specified temperature, and the enal (1 mmol) in ether (1 mL plus 2 × 1 mL rinse) was added over 5 min.[66] After the appropriate time the mixture was quenched as specified below.

(B) $Me_5Cu_3Li_2$ in Ether–Pentane. Cuprous iodide (3 mmol) in dry ether (5 mL) was treated at 0 °C with MeLi (5 mmol) as described in part A. Five minutes after the end of the addition of the cuprate solution was cooled to the specified temperature, and dry pentane (15 mL) was injected. The enal (1 mmol) in ether (1 mL plus 2 × 1 mL rinse) was added as described in part A, and, after the appropriate time, the reaction mixture was quenched as specified below.

(C) Me_2CuLi in Ether. Cuprous iodide (1.2 mmol) in dry ether (10 mL) was treated at 0 °C with MeLi (2.4 mmol) as described in part A. Five minutes after the end of the addition the cuprate solution was cooled to the specified temperature, the enal (1 mmol) in ether (1 mL plus 2 × 1 mL rinse) was injected as in A and, after the appropriate time, the reaction mixture was quenched as specified below.

(D) Me_2CuLi in Ether–Pentane. Cuprous iodide (1.2 mmol) in dry ether (5 mL) was treated at 0 °C with MeLi (2.4 mmol) as described in A. Five minutes after the end of the addition the cuprate solution was cooled to the specified temperature, and dry pentane (15 mL) was injected, followed by the enal (1 mmol) in ether (1 mL plus 2 × 1 mL rinse). The mixture was quenched after the appropriate time as described below.

Quenching Procedures.[65] (E) Acetic Acid. After an appropriate time, the reaction mixture was cooled to –75 °C, and acetic acid (0.2 mL/mmol of MeLi used) was injected very quickly with vigorous stirring. The cold bath was removed (gas evolution), and after ca. 5 min an excess (ca. 10 mL) of saturated aqueous ammonium chloride was added. The stirred mixture was allowed to reach room temperature (ca. 30 min), and the white precipitate was filtered off. The solid was washed with ether (30 mL) and water (30 mL), and the combined organic phases were washed with saturated aqueous sodium hydrogen carbonate (2 × 50 mL) and with brine (2 × 50 mL). The solution was dried (Na_2SO_4) and evaporated, and the product was obtained by Kugelrohr distillation.[67]

(F) Chlorotrimethylsilane. After completion of the conjugate addition the reaction mixture was cooled to –75 °C, and, for every millimole of MeLi used, chlorotrimethylsilane (0.17 mL, 1.30 mmol) was added quickly, followed by triethylamine (0.20 mL, 1.43 mmol) and HMPA (0.12 mL). The cold bath was removed, and the suspension was stirred vigorously for 40 min, during which time the mixture attained room temperature. An excess (10 mL) of saturated aqueous ammonium chloride was added cautiously, and petroleum ether (bp 30–60 °C, 30 mL) was also added. The mixture was filtered by suction through a filter paper to afford two clear phases, the aqueous one usually being blue. The organic layer was washed with saturated aqueous ammonium chloride solution (30 mL), with water (3 × 30 mL, for removal of HMPA) and, finally, with brine (2 × 50 mL). The organic solution was dried (Na_2SO_4) and evaporated, and the product was obtained by Kugelrohr distillation.

Reactions with $Me_5Cu_3Li_2$. (1-Methylcyclohexyl)acetaldehyde (1a). Procedure A was followed with cyclohexylideneacetaldehyde (1; 427.9 mg, 3.445 mmol). The enal was added at –75 °C to the solution of $Me_5Cu_3Li_2$, and the reaction mixture was stirred at this temperature for 2 h. The temperature was then allowed to rise to –40 °C over 1.5 h, and the mixture was recooled to –75 °C and quenched with acetic acid. The workup and Kugelrohr distillation [125–130 °C (10 mm)] gave **1a**[68] (435.9 mg, 90%) of better than 97% purity (VPC, DEGS, 120 °C). The material contained 1% (VPC) of the 1,2-addition product, 1-cyclohexylidene-2-propanol (**1b**).[69]

1a had the following: IR (film) 2715, 1710 cm^{-1}; NMR ($CDCl_3$, 200 MHz) δ 1.08 (s, 3 H), 1.1–1.7 (m, 10 H), 2.32 (d, J = 3.4 Hz, 2 H), 9.83 (t, J = 3.4 Hz, 1 H); exact mass 139.1122 [calcd for $C_9H_{15}O$ (M – H) 139.1122].

3,3-Dimethyloctanal (2a). The procedure for **1a** was followed with 3-methyl-2-octenal (mixture of isomers, 143.1 mg, 1.02 mmol). The workup and Kugelrohr distillation [115 °C (10 mm)] gave **2a** (144.1 mg, 90.4%) of better than 99% purity (VPC, DEGS, 130 °C). The 1,2-addition product was not detected (VPC). **2a** had the following: IR (film) 2720, 1720 cm^{-1}; NMR ($CDCl_3$, 200 MHz) δ 0.89 (br t, J = 7.8 Hz, 3 H), 1.04 (s, 6 H), 1.1–1.5 (m, 8 H), 2.27 (d, J = 3.25 Hz, 2 H), 9.85 (t, J = 3.25 Hz, 1 H); exact mass 155.1435 [calcd for $C_{10}H_{19}O$ (M – H) 155.1436]. For characterization a sample of **2a** was converted[63] into the 2,4-dinitrophenylhydrazone, mp 96 °C (from ethanol). Anal. Calcd for $C_{16}H_{24}N_4O_4$: C, 57.13; H, 7.19; N, 16.66. Found: C, 57.14; H, 7.21, N, 16.52.

3,3,7-Trimethyl-6-octenal (3a). Procedure A was followed with 3,7-dimethyl-2,6-octadienal (**3**; mixture of isomers, 186.3 mg, 1.224 mmol). The enal was added at –75 °C to the solution of $Me_5Cu_3Li_2$, and the reaction mixture was immediately allowed to warm to 0 °C over 4 h. The mixture was then recooled to –75 °C and quenched with acetic acid. The workup and Kugelrohr distillation [70–80 °C (0.5 mm)] gave **3a**[9] (165.6 mg, 80.4%) of better than 98% purity (VPC, DEGS, 140 °C). The 1,2-addition product was not detected (VPC, NMR). **3a** had the following: IR (film) 2715, 1710 cm^{-1}; NMR ($CDCl_3$, 200 MHz) δ 1.07 (s, 6 H), 1.25–1.45 (m, 2 H), 1.59 (s, 3 H), 1.68 (s, 3 H), 1.96 (m, 2 H), 2.27 (d, J = 3.5 Hz, 2 H), 5.07 (m, 1 H), 9.82 (t, J = 3.50 Hz, 1 H); exact mass 168.1508 (calcd for $C_{11}H_{20}O$ 168.1514).

[(2,3-Dimethyl-1-nonen-1-yl)oxy]trimethylsilane (4a). Procedure A was followed with 2-methyl-2-nonenal (**4**; mixture of *E* and *Z* isomers, 126.1 mg, 0.818 mmol). The enal was added at –75 °C to the solution of $Me_5Cu_3Li_2$, and the mixture was stirred at this temperature for 2 h. The temperature was then allowed to rise to –20 °C over 2 h, and the mixture was recooled to –75 °C and quenched by general procedure F with chlorotrimethylsilane. The workup and Kugelrohr distillation [150 °C (10 mm)] gave **4a** (183.6 mg, 92.6%) of better than 98% purity[70] (VPC, DEGS, 95 °C). The material contained 1.5% of the 1,2-addition product, [(3-methyl-2-decen-yl)oxy]trimethylsilane (**4b**), as judged by comparison (NMR, 200 MHz) with an authentic sample.[69] **4a** had the following: IR (film) 1673, 1166 cm^{-1}; NMR ($CDCl_3$, 200 MHz) δ 0.16 (s, 9 H), 0.86 (t, J = 7.5 Hz, 3 H), 0.96 (d, J = 7.6 Hz, 3 H), 1.05–1.5 (m, 10 H), 1.50 (d, J = 1.5 Hz, 3 H), 2.01 (m, 1 H), 6.05 (m, 1 H); exact mass 242.2068 (calcd for $C_{14}H_{30}OSi$ 242.2066). Anal. Calcd for $C_{14}H_{30}OSi$: C, 69.35; H, 12.47. Found: C, 69.61; H, 12.57.

[[2-(1-Methylcyclohexyl)-1-propenyl]oxy]trimethylsilane (5a). Procedure B for reactions in ether–pentane was followed with 2-(cyclohexylidene)propionaldehyde (**5**; 140.3 mg, 1.015 mmol). The enal was added at –50 °C to the solution of $Me_5Cu_3Li_2$, and the reaction mixture was immediately allowed to warm to 0 °C over 2 h. The mixture was kept at this temperature for a further 30 min, cooled to –75 °C, and quenched by general method F with chlorotrimethylsilane. The workup and Kugelrohr distillation [140 °C (10 mm)] gave **5a**[70] (202.2 mg, 88.0%) of better than 99% purity (VPC, DEGS, 115 °C). The 1,2-adduct **5b** was not detected (VPC). **5a** had the following: IR (film) 1675, 1252 cm^{-1}; NMR ($CDCl_3$, 200 MHz) δ 0.16 (s, 9 H), 0.94 (s, 3 H, 1.1–1.7 (m, 13 H, incorporating d, J = 1.5 Hz at δ 1.54, 3 H), 6.11 (q, J = 1.5 Hz, 1 H); exact mass 226.1751 (calcd for $C_{13}H_{26}OSi$ 226.1753). Anal. Calcd for $C_{13}H_{26}OSi$: C, 68.96;

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[65] In reactions done on a scale different from that given in the general procedure, all solvent volumes were adjusted accordingly. Addition times, however, were essentially unchanged.

[66] This is the addition time for the main (1 mL) solution. The rinses were also added slowly.

[67] All yields are for distilled products.

[68] Burgstahler, A. W.; Nordin, I. C. *J. Am. Chem. Soc.* **1961**, *83*, 198.

[69] For preparation of 1,2-adducts see later.

[70] Probably one geometrical isomer only is present (NMR), here arbitrarily shown as *E*.

H, 11.58. Found: C, 69.21; H, 11.65.

(1-Methylcycloheptyl)acetaldehyde (7a). Procedure A was followed with cycloheptylideneacetaldehyde (**7**; 60.7 mg, 0.439 mmol). The enal was added at −75 °C to the solution of $Me_5Cu_3Li_2$, and the mixture was stirred at this temperature for 2 h. The temperature was then allowed to rise to −20 °C over 2 h, and the mixture was recooled to −75 °C and quenched by general method E with acetic acid. The workup and Kugelrohr distillation [150 °C (10 mm)] gave **7a** (60.1 mg, 88.8%). The material was contaminated by 5.5% of the 1,2-addition product, 1-cycloheptylidene-2-propanol (**7b**), as judged by comparison (VPC, DEGS, 150 °C; ^1H NMR, 200 MHz) with an authentic sample.[69] **7a** had the following: NMR ($CDCl_3$, 200 MHz) δ 1.08 (s, 3 H), 1.2–1.8 (m, 12 H), 2.26 (d, J = 3.50 Hz, 2 H), 9.80 (d, J = 3.50 Hz, 1 H). For characterization the 2,4-dinitrophenylhydrazone was prepared;[63] mp 90–91 °C (from ethanol). Anal. Calcd for $C_{16}H_{22}N_4O_4$: C, 57.57; H, 6.63, N, 16.76. Found: C, 57.49; H, 6.69; N, 16.87.

Reaction of Cycloheptylideneacetaldehyde (7) with $Me_5Cu_3Li_2$ in Ether–Pentane. Enal **7** (131.3 mg, 0.950 mmol) in ether (2 mL plus 2 × 1 mL rinse) was added slowly (main portion over 5 min) to a cold (−75 °C) solution of $Me_5Cu_3Li_2$ in ether (5 mL) and pentane (15 mL) prepared according to procedure B. The reaction mixture was stirred for 2 h at −75 °C and then allowed to reach −10 °C over a 2-h period. Quenching with acetic acid by general method E and workup, gave, after Kugelrohr distillation [150 °C (10 mm)], a mixture of **7a** and **7b** (116.0 mg, 79.2%) in the ratio (VPC, DEGS, 150 °C) 95:5.

[[2-(1,2-Dimethylcyclohexyl)-1-propenyl]oxy]trimethylsilane (8a) and [[3-(2-Methylcyclohexylidene)-2-butyl]oxy]trimethylsilane (8b). Procedure B for reactions in ether–pentane was followed with 2-(2-methylcyclohexylidene)propionaldehyde (**8**; mixture of isomers, 114.3 mg, 0.751 mmol). The enal was added at −50 °C to the solution of $Me_5Cu_3Li_2$, and the reaction mixture was immediately allowed to warm to 0 °C over 1.5 h. The mixture was kept at this temperature for a further 30 min, cooled to −75 °C, and quenched by general method F with chlorotrimethylsilane. The workup and Kugelrohr distillation [145 °C (10 mm)] gave an oil (158.7 mg, 88.0%). The material consisted of **8a** and **8b** in the ratio 46:54 as judged by comparison (VPC, DEGS, 115 °C; ^1H NMR, 200 MHz) with an authentic sample of **8b**.[69] The 1,4-addition product **8a** was a 1:3 mixture (NMR) of diastereoisomers having the following: NMR ($CDCl_3$, 200 MHz) δ 0.158 and 0.162 (partially overlapping singlets, 9 H overall), 0.65 (d, J = 6.8 Hz, 2.25 H), 0.77 (d, J = 7.1 Hz, 0.75 H), 0.90 (s, 2.25 H), 1.17 (s, 0.75 Hz), 1.18–1.6 (m, 12 H, incorporating d, J = 1.5 Hz, at δ 1.55), 5.94 (q, J = 1.5 Hz, 0.25 H), 6.08 (q, J = 1.5 Hz, 0.75 H). For further characterization, **8a** was converted[63,71] to the derived 2,4-dinitrophenylhydrazone, mp 111–118 °C (from ethanol). Anal. Calcd for $C_{17}H_{24}N_4O_4$: C, 58.60; H, 6.94; N, 16.08. Found: C, 58.44; H, 6.90; N, 16.22.

(4aβ,8aβ)-2,4a-Dimethyldecahydronaphth-2-ylidene)acetaldehyde (9a). Procedure A was followed with (*cis*-4a-methyldecahydronaphth-2-ylidene)acetaldehyde (**9**; mixture of isomers, 157.5 mg, 0.819 mmol). The enal was added at −75 °C to the solution of $Me_5Cu_3Li_2$, and the reaction mixture was stirred at this temperature for 2 h. The temperature was then allowed to rise to −20 °C over 2 h, and the mixture was recooled to −75 °C and quenched by general procedure E with acetic acid. The workup, flash chromatography over silica gel (2 × 18 cm) with 3:97 ethyl acetate–hexane, and Kugelrohr distillation [140 °C (0.1 mm)] gave **9a** (144.2 mg, 84.5%) as an apparently homogeneous (TLC, silica, 1:20 ethyl acetate–hexane) oil. Examination by VPC (FFAP, 210 °C) showed two peaks (relative areas 1:19) corresponding to the two aldehydes epimeric at C-2. The crude reaction product (before chromatography) contained 2% of the 1,2-adduct, 1-(*cis*-4a-methyldecahydronaphth-2-ylidene)-2-propanol (**9b**) as judged by comparison (VPC) with an authentic sample.[69] **9a** had the following: IR (film) 2720, 1715 cm^{-1}; NMR ($CDCl_3$, 200 MHz) δ 0.75–1.95 (m, 21 H, including sharp singlets at δ 1.01 and 1.10, ca. 3 H each), 2.38 (d, J = 3.55 Hz, 2 H), 9.83 (t, J = 3.55 Hz, 1 H); exact mass 208.1825 (calcd for $C_{14}H_{24}O$ 208.1827). For further characterization, **9a** was converted[63] into its 2,4-dinitrophenylhydrazone, mp 180–183 °C (from ethanol). Anal. Calcd for $C_{20}H_{28}N_4O_4$: C, 61.83; H, 7.26; N, 14.42. Found: C, 61.75; H, 7.34; N, 14.37.

4,4-Diphenyl-3-buten-2-ol (10b). Procedure A was followed with 3,3-diphenylpropenal (**10**;[47b] 197.8 mg, 0.950 mmol). The enal was added at −75 °C to a solution of $Me_5Cu_3Li_2$, and the reaction mixture was stirred for 2 h while the temperature slowly reached 0 °C. The temperature was kept at 0 °C for 1 h. The mixture was then recooled to −75 °C and quenched by general procedure E with acetic acid. The workup and flash chromatography over silica gel (3 × 17 cm) with 2:1 hexane–ethyl acetate gave **10b** (156.1 g, 73.3%) as a homogeneous (TLC, silica, 7:4 hexane–ethyl acetate) oil: IR (film) 3330, 3080, 3059, 1600, 1055 cm^{-1}; NMR ($CDCl_3$, 80 MHz) δ 1.28 (d, J = 6.5 Hz, 3 H), 2.09 (br s, 1 H), 4.38 (m, 1 H), 6.09 (d, J = 9.3 Hz, 1 H), 7.0–7.55 (m, 10 H); exact mass 209.0968 (calcd for $C_{15}H_{13}O$ 209.0966).

Reactions with Me_2CuLi. These reactions were run under the same thermal conditions as their counterparts with $Me_5Cu_3Li_2$ but by using the general procedures given above for the Me_2CuLi experiments. After the workup and distillation the relative amounts of 1,2- and 1,4-addition products were determined by VPC and/or NMR (200 MHz). In the latter case the integration was performed on conveniently separated signals that were chosen from the NMR spectra of the pure 1,2- (obtained by use of MeLi) and 1,4-adducts (obtained usually by use of $Me_5Cu_3Li_2$). In most cases the olefinic signal of the trimethylsilyl enol ether or the aldehyde proton signal was used for estimation of the 1,4-adducts and the signal for the proton(s) on the carbon bearing the hydroxyl group (typically at δ 4.5–5.0) for the 1,2-adducts. The values obtained were checked by integration of any other suitable sets of signals, including the singlets due to the trimethylsilyl groups, in which case a relaxation delay of 30 s between scans was used to allow complete relaxation.

Reaction of Cyclohexylideneacetaldehyde (1) with Me_2CuLi in Ether. Procedure C was followed with cyclohexylideneacetaldehyde (**1**; 180 mg, 1.449 mmol). The enal was added at −75 °C to the solution of Me_2CuLi, and the reaction mixture was stirred at this temperature for 2 h. The temperature was then allowed to rise to −40 °C over 1.5 h, the cooling bath was then removed, and the reaction was quenched by rapid injection of saturated aqueous ammonium chloride (10 mL) with stirring.[72] When the mixture had reached room temperature, it was extracted with ether (2 × 30 mL), and the combined organic phase was washed with saturated aqueous sodium hydrogen carbonate (2 × 30 mL) and with brine (2 × 30 mL). The solution was dried (Na_2SO_4) and evaporated, and the product (148.4 mg) was obtained by Kugelrohr distillation. The material consisted (NMR, 200 MHz) of starting enal and reaction product in the ratio of 1:10. The reaction product itself was comprised of **1a** and **1b**[69] in the ratio 87:13 (71% combined yield after correction for recovered starting material).

Reaction of 3-Methyl-2-octenal (2) with Me_2CuLi in Ether. Procedure C was followed with 3-methyl-2-octenal (**2**; 140.0 mg, 0.998 mmol) in ether. The enal was added at −75 °C to the solution of Me_2CuLi, and the reaction mixture was stirred at this temperature for 2 h. The temperature was then allowed to rise to −40 °C over 1.5 h, and the mixture was recooled to −75 °C and quenched by general procedure E with acetic acid. The workup and Kugelrohr distillation gave a mixture of **2a** and **2b**[69] (140.9 mg total, 90.3%) in the ratio (NMR, 200 MHz) of 91.5:8.5.

Reaction of 3,3,7-Trimethyl-6-octenal (3) with Me_2CuLi in Ether. Procedure C was followed with 3,3,7-trimethyl-6-octenal (**3**; mixture of isomers, 519.9 mg, 3.380 mmol). The enal was added at −75 °C to the solution of Me_2CuLi, and the mixture was immediately allowed to warm so that it reached 0 °C over 4 h. The mixture was then cooled to −75 °C and quenched by general procedure E with acetic acid. The workup and Kugelrohr distillation gave a mixture of **3a** and **3b**[69] (445.9 mg, total 78.5%) in the ratio (NMR, 200 MHz) of 9:1. Flash chromatography over silica gel (3 × 17 cm) with heptane containing increasing amounts (5–10% v/v) of ethyl acetate gave after Kugelrohr distillation (140 °C, 12 mm) **3a** (391.1 mg, 68.9%) of better than 98% purity (VPC)

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(71) Hydrolysis occurred in situ on treatment of **8a** (in the presence of **8b**) with the (2,4-dinitrophenyl)hydrazine reagent.

(72) This is the only case where the workup of an experiment with Me_2CuLi is different from that used with $Me_5Cu_3Li_2$.

which was identical (IR; NMR, 200 MHz) with a sample made by using $Me_5Cu_3Li_2$. The flash chromatography also gave **3b**[69] [39.0 mg, 6.8%; after Kugelrohr distillation, 150 °C (10 mm)] which was a mixture of *E* and *Z* isomers (NMR, 200 MHz) and was better than 95% pure (VPC). **3a**[9] had the following: NMR ($CDCl_3$, 200 MHz) δ 1.0–2.2 (m, 15 H, incorporating doublets at δ 1.22 and 1,23, J = 7 Hz, 3 H overall), 4.4–4.7 (m, 1 H), 6.0–6.3 (m, 2 H); exact mass 168.1502 (calcd for $C_{11}H_{20}O$ 168.1514).

Reaction of 2-Methyl-2-nonenal (4) with Me_2CuLi in Ether. Procedure C was followed with 2-methyl-2-nonenal (**4**; mixture of isomers, 120.0 mg, 0.865 mmol). The enal was added at −75 °C to the solution of Me_2CuLi, and the mixture was stirred at this temperature for 2 h. The temperature was then allowed to rise to −20 °C over 2 h, and the mixture was recooled to −75 °C and quenched by general procedure F with chlorotrimethylsilane. The workup and Kugelrohr distillation gave a mixture (209.4 mg, 92.2%) consisting (VPC; NMR, 200 MHz) of **4a**[73] and **4b**[69] in the ratio of 94.5:5.5.

Reaction of 2-Cyclohexylidenepropionaldehyde (5) with Me_2CuLi in Ether–Pentane. Procedure D for reactions in ether–pentane was followed with 2-cyclohexylidenepropionaldehyde (**5**; 120.0 mg, 0.865 mmol). The enal was added at −50 °C to the solution of Me_2CuLi, and the reaction mixture was immediately allowed to warm to 0 °C over 2 h. The mixture was kept at this temperature for a further 30 min, cooled to −75 °C, and quenched by general procedure F with chlorotrimethylsilane. The workup and Kugelrohr distillation gave an oil (180.3 mg, 91.7%) of better than 99% purity (VPC, DEGS, 115 °C). The material consisted (NMR, 200 MHz) of **5a**[73] and **5b**[69] in the ratio of 80:20.

Reaction of Cycloheptylideneacetaldehyde (7) with Me_2CuLi in Ether. Procedure C was followed with cycloheptylideneacetaldehyde (**7**; 104.2 mg, 0.754 mmol) in ether. The enal was added at −75 °C to the solution of Me_2CuLi, and the mixture was stirred at this temperature for 2 h. The temperature was then allowed to rise to −20 °C over 2 h, and the mixture was recooled to −75 °C and quenched by general procedure E with acetic acid. The workup and Kugelrohr distillation gave an oil (102.5 mg, 88.1%) of better than 97% purity (VPC, DEGS, 150 °C). The material consisted (NMR, 200 MHz) of **7a** and **7b**[69] in the ratio of 83:17.

Reaction of 2-(2-Methylcyclohexylidene)propionaldehyde (8) with Me_2CuLi in Ether–Pentane. Procedure D was followed with 2-(2-methylcyclohexylidene)propionaldehyde (118.5 mg, 0.778 mmol). The enal was added at −50 °C to the solution of Me_2CuLi, and the reaction mixture was immediately allowed to warm to 0 °C over 1.5 h. The mixture was kept at this temperature for a further 30 min, cooled to −75 °C, and quenched by general method F with chlorotrimethylsilane. The workup and Kugelrohr distillation gave a mixture (162.8 mg, 87.0%) of better than 99% purity (VPC, DEGS, 115 °C). The material consisted (NMR, 200 MHz) of **8a**[74] and **8b**[69] in the ratio of 48.5:51.5.

Reaction of (*cis*-4a-Methyldecahydronaphth-2-ylidene)acetaldehyde (9) with Me_2CuLi in Ether. Procedure C was followed with (*cis*-4a-methyldecahydronaphth-2-ylidene)acetaldehyde (**9**; 146.5 mg, 0.762 mmol). The enal was added at −75 °C to the solution of Me_2CuLi, and the reaction mixture was stirred at this temperature for 2 h. The temperature was then allowed to rise to −20 °C over 2 h, and the mixture was recooled to −75 °C and quenched by general procedure E with acetic acid. The workup and Kugelrohr distillation gave a mixture (144.1 mg, 90.8%) consisting (VPC) of **9a** and **9b**[69] in the ratio of 97.5:2.5 and small amounts of other materials. Flash chromatography over silica gel (2 × 18 cm) with 3:97 ethyl acetate–hexane and Kugelrohr distillation gave pure (VPC) **9a** (129.9 mg, 81.9%) consisting (VPC) of two diastereoisomers in the ratio[75] of 94:6.

Reaction of 3,3-Diphenylpropenal (10) with Me_2CuLi in Ether. Procedure C was followed with **10** (187.4 mg, 0.90 mmol). The enal was added at −75 °C to the solution of Me_2CuLi, and the reaction mixture was stirred at this temperature for 2 h. The temperature was then allowed to rise to 0 °C over 2 h, and the mixture was stirred 2 h at 0 °C. It was then recooled to −75 °C and quenched by general procedure E with acetic acid. The workup and flash chromatography over silica gel (3 × 17 cm) with 2:1 hexane–ethyl acetate gave 4,4-diphenyl-3-buten-2-ol (**10b**;[76] 85.0 mg, 42%) identical (IR, NMR) with the sample obtained in the $Me_5Cu_3Li_2$ reaction.

Reactions of 2-(Cyclopentylidene)propionaldehyde (6) with Various Copper Reagents. (i) Reaction with Me_2CuLi in Ether. This reaction is described in the literature and gives[3] (86% yield) a mixture of **6a**[3,70] and **6b**[3] in the ratio of 36:64.

(ii) Reaction with $Me_5Cu_3Li_2$ in Ether. Procedure A was followed with 2-(cyclopentylidene)propionaldehyde (**6**; 132.8 mg, 1.069 mmol). The enal was added at −50 °C to the solution of $Me_5Cu_3Li_2$, and the mixture was stirred at this temperature for 30 min. The temperature was then allowed to rise to 0 °C over 2 h and was maintained at 0 °C for a further 30 min. The mixture was recooled to −75 °C and quenched by general procedure F with chlorotrimethylsilane. The workup and Kugelrohr distillation [120 °C (10 mm)] gave an oil (194.2 mg, 85.5%) of better than 99% purity (VPC, DEGS, 100 °C) consisting (NMR,[77] 200 MHz) of **6a**[3] and **6b**[3] in the ratio of 77.5:22.5.

(iii) Reaction with $Me_5Cu_3Li_2$ in Ether–Pentane. Procedure B was followed with 2-(cyclopentylidene)propionaldehyde (**6**; 132.8 mg, 1.069 mmol). The enal was added at −50 °C to the solution of $Me_5Cu_3Li_2$, and the mixture was stirred at this temperature for 30 min. The temperature was then allowed to rise to 0 °C over 2 h and was maintained at 0 °C for a further 30 min. The mixture was recooled to −75 °C and quenched by general procedure F with chlorotrimethylsilane. The workup and Kugelrohr distillation [120 °C (10 mm)] gave an oil (210.6 mg, 88%) of better than 99% purity (VPC, DEGS, 100 °C) consisting (NMR, 200 MHz) of **6a**[3] and **6b**[3] in the ratio of 85:15.

(iv) Reaction with Me_3CuLi_2[21] in Ether. Ethereal MeLi (2.1 M, 2.0 mL, 4.2 mmol) was injected slowly into a stirred and cooled (0 °C) slurry of purified cuprous iodide (265.4 mg, 1.394 mmol) in ether (14 mL). The cuprate solution was cooled to −50 °C, and the enal **6** (173.4 mg, 1.396 mmol) in ether (1 mL plus 3 × 1 mL rinse) was added (main portion over 5 min). After the addition, the mixture was kept for 30 min at −50 °C. The temperature was then allowed to rise to 0 °C over 2 h. The mixture was kept at this temperature for 30 min, recooled to −75 °C, and quenched by general method F with chlorotrimethylsilane (0.6 mL), triethylamine (0.75 mL), and HMPA (0.4 mL). The cold bath was removed, and the mixture was worked up in the usual way. Kugelrohr distillation (120 °C, 10 mm) gave an oil (251.5 mg, 84.8%) of better than 99% purity (VPC, DEGS, 100 °C) consisting (NMR, 200 MHz) of **6a**[3] and **6b**[3] in the ratio of 4:96.

Reaction with $Me_5Cu_3(MgBr)_2$[23] in Ether. Ethereal MeLi (1.91 M, 0.58 mL, 1.1 mmol) was injected dropwise into a stirred and cooled (0 °C) slurry of purified cuprous iodide (635 mg, 3.330 mmol) in ether (12 mL). Five minutes after the end of the addition the yellow suspension was cooled to −40 °C, and an ether solution of methylmagnesium bromide (2.74 M, 1.6 mL, 4.40 mmol) was added. The temperature was allowed to reach −10 °C over 30 min and then lowered to −40 °C again. The enal (136.5 mg, 1.10 mmol) in ether (1 mL plus 2 × 1 mL rinse) was injected (main portion over 4 min). The temperature was then allowed to rise to 0 °C over 1 h and kept at 0 °C for 30 min. The mixture was recooled to −75 °C and quenched by general procedure F with chlorotrimethylsilane (0.7 mL), triethylamine (0.9 mL), and HMPA (0.45 mL). The cold bath was removed, and the mixture was worked up in the usual way. Kugelrohr distillation [120 °C (10 mm)] gave an oil (145.4 mg, 92%) consisting (NMR, 200 MHz) of **6a**,[3] **6b**,[3] and **6c**[69] in the ratio of 4:1:95. Consequently, the amounts of 1,2- and 1,4-adducts are in the ratio of 96:4.

Reaction with Me_3Cu_2Li[20] in THF. Ethereal MeLi (1.91 M, 1.90 mL, 3.63 mmol) was injected dropwise into a stirred and cooled (0 °C) slurry of purified cuprous iodide (461.0 mg, 2.420 mmol) in THF (15 mL). Ten minutes after the end of the addition the pale pink solution was cooled to −50 °C. The enal (147.4 mg, 1.19 mmol) in THF (1 mL plus 2 × 1 mL rinse) was added (main portion added over 5 min). The temperature was then allowed

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[73] Isomerically pure (NMR, 200 MHz).

[74] Mixture of two diastereoisomers.

[75] Relative peak areas.

[76] Cheminat, B.; Rambaud, R. *C. R. Hebd. Seances Acad. Sci., Ser. C* **1967**, *264*, 897.

[77] The following signals were compared: olefinic signal of **6a** (δ 6.09, q, J = 2 Hz) and methine signal of **6b** (δ 4.57, q, J = 6.4 Hz).

to rise to 0 °C over 1 h and kept at 0 °C for 1 h. The mixture was recooled to −75 °C and quenched by general procedure F with chlorotrimethylsilane (0.6 mL), triethylamine (0.75 mL), and HMPA (0.4 mL). The cold bath was removed, and the mixture was worked up in the usual way. Kugelrohr distillation [120 °C (10 mm)] afforded an oil (204.4 mg) consisting (DEGS, 100 °C) of **6a**[3] and **6b**[3] in the ratio of 20:80 as well as two other unidentified substances. The latter accounted for ca. 50% of the total product (VPC, relative peak areas).

Reaction with $Me_2CuMgCl$ in THF.[8] Methylmagnesium chloride in THF (2.8 M, 1.33 mL, 3.72 mmol) was added at 0 °C to a suspension of commercial cuprous bromide (268 mg, 1.86 mmol) in dry THF (3 mL), and the suspension was stirred for 15 min at room temperature. 2-(Cyclopentylidene)propionaldehyde (**6**; 196.4 mg, 1.582 mmol) was added in THF (1 mL plus 2 × 1 mL rinse) at −5 °C. The mixture was kept 1 h in an ice–water bath and then for 15 min at room temperature. The mixture was cooled to −75 °C and quenched by rapid successive addition of chlorotrimethylsilane (0.6 mL), triethylamine (0.75 mL), and HMPA (0.4 mL). Stirring was continued overnight during which period the bath attained room temperature. The stirred mixture was diluted with pentane (20 mL), ether (15 mL), and saturated aqueous ammonium chloride (20 mL). The resulting suspension was filtered, and the organic phase was washed with water (3 × 30 mL) and dried ($MgSO_4$). Evaporation and Kugelrohr distillation [120 °C (10 mm)] gave an oil (301.1 mg, 89.6%) consisting (VPC, NMR) of the 1,2-adduct **6b** (75%) and the 1,4-adduct **6a** (25%).

A similar experiment, but with cuprous iodide, gave an 80:20 mixture of the 1,2- and 1,4-adducts in an overall yield of 84%.

Preparation of 1,2-Adducts. 1-(Cyclohexylidene)-2-propanol (1b). Ether (10 mL) was added to ethereal MeLi (1.52 M, 1.6 mL, 2.43 mmol). The solution was cooled to 0 °C, and cyclohexylideneacetaldehyde (**1**; 200 mg, 1.61 mmol) in ether (1 mL plus 2 × 1 mL rinse) was injected (main portion added over ca. 2 min). The mixture was stirred for 2 h at 0 °C, and the reaction was then quenched by addition of saturated aqueous ammonium chloride (20 mL). The product was extracted with ether, and the solution was dried and evaporated. Kugelrohr distillation [140 °C (10 mm)] of the residue gave **1b** (205.2 mg, 90.8%) as an oil of better than 98% purity (VPC, DEGS., 120 °C): IR (film) 3300, 1668, 1050 cm^{-1}; NMR ($CDCl_3$, 200 MHz) δ 1.22 (d, J = 6.8 Hz, 3 H), 1.3–2.3 (m, 11 H), 4.60 (m, 1 H), 5.15 (m, 1 H); exact mass 140.1199 (calcd for $C_9H_{16}O$ 140.1201). Anal. Calcd for $C_9H_{16}O$: C, 77.09; H, 11.50. Found: C, 77.34; H, 11.40.

4-Methyl-3-nonen-2-ol (2b). The procedure for **1b** was followed with 3-methyl-2-octenal (109 mg, 0.777 mmol) in ether (1 mL plus 2 × 1 mL rinse) and ethereal MeLi (1.52 M, 0.8 mL, 1.216 mmol) in ether (7 mL). Kugelrohr distillation [140 °C (10 mm)] gave **2b** (108.7 mg, 87.5%) as a mixture (VPC, DEGS, 130 °C) of *E* and *Z* isomers of better than 99% purity: IR (film) 3320, 1665, 1060 cm^{-1}; NMR ($CDCl_3$, 200 MHz) δ 0.88 (t, J = 7.5 Hz, 3 H), 1.15–1.65 (m, 10 H, incorporating d, J = 6.25 Hz, at δ 1.22), 1.66 (d, J = 1.0 Hz, 2.25 H), 1.68 (d, J = 1.0 Hz, 0.75 H), 1.9–2.2 (m, 2 H), 4.53 (m, 1 H), 5.16 (m, 1 H); exact mass 156.1512 (calcd for $C_{10}H_{20}O$ 156.1514). Anal. Calcd for $C_{10}H_{20}O$: C, 76.86; H, 12.90. Found: C, 76.63; H, 12.86.

[(3-Methyl-3-decan-2-yl)oxy]trimethylsilane (4b). The procedure for **1b** was followed with 2-methyl-2-nonenal (mixture of isomers, 553.6 mg, 3.589 mmol) in ether (3 mL plus 2 × 1 mL rinse) and ethereal MeLi (1.52 M, 3.55 mL, 5.396 mmol) in ether (10 mL). Kugelrohr distillation [150 °C (10 mm)] gave 3-methyl-3-decen-2-ol (550 mg, 90%) as a homogeneous (TLC, silica, 1:5 ethyl acetate–hexane) oil. A portion (278.8 mg, 1.637 mmol) was dissolved in ether (10 mL), and chlorotrimethylsilane (0.25 mL) and triethylamine (0.28 mL) were added. The mixture was refluxed for 2 h, cooled, filtered through a pad (5 × 2 cm) of Celite, and evaporated. Flash chromatography over silica gel (2 × 8 cm) with hexane containing increasing amounts (1–20% v/v) of ethyl acetate gave, after Kugelrohr distillation [140 °C (10 mm)], **4b** (101 mg, 25.4%) of better than 99% purity (VPC, DEGS, 95 °C). The material was a mixture (NMR) of *E* and *Z* isomers in the ratio of 85:15: IR (film) 1080, 840 cm^{-1}; NMR ($CDCl_3$, 200 MHz) δ 0.08 (s, 7.65 H), 0.09 (s, 1.35 H), 0.88 (br t, J = 6.7 Hz, 3 H), 1.18 (d, J = 6.4 Hz, 0.45 H), 1.20 (d, J = 6.4 Hz, 2.55 H), 1.25–1.60 (m, 7 H), 1.57 (d, J = 1.0 Hz, 2.55 H), 1.67 (q, J = 1.2 Hz, 0.45 H), 1.98 (m, 2 H), 4.16 (q, J = 6.4 Hz, 0.85 H), 4.72 (q, J = 6.4 Hz, 0.15 H), 5.06 (br t, J = 7.0 Hz, 0.15 H), 5.32 (br t, J = 7.3 Hz, 0.85 H); exact mass 242.2064 (calcd for $C_{14}H_{30}OSi$ 242.2066). Anal. Calcd for $C_{14}H_{30}OSi$: C, 69.35; H, 12.47. Found: C, 69.07; H, 12.45.

The flash chromatography also afforded, after Kugelrohr distillation [150 °C (10 mm)], 3-methyl-3-decen-2-ol[78] (258.4 mg, 65.1%) as an apparently homogeneous (TLC, silica, 1:5 ethyl acetate–hexane) oil: NMR ($CDCl_3$, 200 MHz) δ 0.88 (br t, J = 6.7 Hz, 3 H), 1.2–1.5 (m, 11 H, incorporating doublets at δ 1.23, J = 6.4 Hz, ca. 2.5 H, and at δ 1.22, J = 6.4 Hz, ca. 0.5 H), 1.62 (s, 2.55 H), 1.70 (m, 0.45 H), 2.00 (m, 3 H), 4.18 (q, J = 6.4 Hz, 0.85 H), 4.77 (q, J = 6.4 Hz, 0.15 H), 5.17 (br t, J = 7.1 Hz, 0.15 H), 5.39 (br t, J = 7.0 Hz, 0.85 H).

[(3-Cyclohexylidene-2-butyl)oxy]trimethylsilane (5b). The procedure for **1b** was followed with 2-cyclohexylidenepropionaldehyde (**5**; 634.6 mg, 4.591 mmol) in ether (5 mL plus 2 × 1 mL rinse) and ethereal MeLi (1.52 M, 4.5 mL, 6.84 mmol) in ether (25 mL). The workup, flash chromatography over silica gel (3 × 18 cm) using 1:10 ethyl acetate–hexane, and Kugelrohr distillation [120 °C (0.3 mm)] gave 3-cyclohexylidene-2-butanol (590 mg, 83.3%) as a homogeneous (TLC, silica, 1:10 ethyl acetate–hexane) oil. A portion (220 mg, 1.426 mmol) of this material was dissolved in ether (10 mL), and chlorotrimethylsilane (0.22 mL) and triethylamine (0.24 mL) were added. The mixture was refluxed for 2 h, cooled, filtered through a pad (5 × 2 cm) of Celite, and evaporated. Flash chromatography over silica gel (2 × 17 cm) with hexane containing increasing amounts (1–10% v/v) of ethyl acetate gave, after Kugelrohr distillation [110 °C (0.3 mm)], **5b** (91 mg, 28.1%) of better than 99% purity (VPC, DEGS, 115 °C): IR (film) 1078 cm^{-1}; NMR ($CDCl_3$, 200 MHz) δ 0.07 (s, 9 H), 1.14 (d, J = 6.3 Hz, 3 H), 1.4–1.6 (m, 6 H), 1.60 (s, 3 H), 2.14 (m, 4 H), 4.85 (q, J = 6.3 Hz, 1 H); exact mass 211.1516 [calcd for $C_{12}H_{23}OSi$ (M − CH_3) 211.1518]. Anal. Calcd for $C_{13}H_{26}OSi$: C, 68.96; H, 11.58. Found: C, 69.02; H, 11.41.

The flash chromatography also afforded, after Kugelrohr distillation [115 °C (0.3 mm)], 3-cyclohexylidene-2-butanol (145 mg, 65.9%) as a homogeneous (TLC, silica, 1:10 ethyl acetate–hexane) oil: NMR ($CDCl_3$, 200 MHz) δ 1.21 (d, J = 6.4 Hz, 3 H), 1.3–1.6 (m, 10 H), 1.65 (s, 3 H), 2.2–2.4 (m, 4 H), 4.92 (q, J = 6.4 Hz, 1 H).

3-Cyclopentylidene-2-butanol (6c). The procedure for **1b** was followed with 2-cyclopentylidenepropionaldehyde (**6**; 132.1 mg, 1.063 mmol) in ether (1 mL plus 2 × 1 mL rinse) and ethereal MeLi (1.80 M, 0.7 mL, 1.26 mmol) in ether (10 mL). Kugelrohr distillation [85 °C (0.5 mm)] gave **6c** (131.7 mg, 88.3%) as a homogeneous (TLC, silica, 1:10 ethyl acetate–hexane) oil: IR (film) 3330, 1072 cm^{-1}; NMR ($CDCl_3$, 200 MHz), δ 1.20 (d, J = 6.8 Hz, 3 H), 1.3–2.6 (m, 12 H), 4.63 (q, J = 6.8 Hz, 1 H); exact mass 140.1202 (calcd for $C_9H_{16}O$ 140.1201). Anal. Calcd for $C_9H_{16}O$: C, 77.09; H, 11.50. Found: C, 77.25; H, 11.58.

1-Cycloheptylidene-2-propanol (7b). The procedure for **1b** was followed with cycloheptylideneacetaldehyde (**7**; 246.5 mg, 1.784 mmol) in ether (1 mL plus 2 × 1 mL rinse) and ethereal MeLi (1.52 M, 1.80 mL, 2.736 mmol) in ether (15 mL). The workup and flash chromatography over silica gel (2 × 20 cm) with 1:5 ethyl acetate–hexane followed by Kugelrohr distillation [110 °C (0.3 mm)] gave **7b** (207 mg, 75.2%) as a homogeneous (TLC, silica, 1:5 ethyl acetate–hexane) oil of better than 99% purity (VPC, FFAP, 150 °C): IR (film) 3330, 1652, 1053 cm^{-1}; NMR ($CDCl_3$, 200 MHz) δ 1.23 (d, J = 6.0 Hz, 3 H), 1.3–1.9 (m, 9 H), 2.15–2.45 (m, 4 H), 4.57 (m, 1 H), 5.21 (m, 1 H); exact mass 154.1358 (calcd for $C_{10}H_{18}O$ 154.1358). Anal. Calcd for $C_{10}H_{18}O$: C, 77.86; H, 11.76. Found: C, 77.84; H, 11.67.

[[3-(2-Methylcyclohexylidene)-2-butyl]oxy]trimethylsilane (8b). The procedure for **1b** was followed with 2-(2-methylcyclohexylidene)propionaldehyde (**8**; 787.0 mg, 5.177 mmol) in ether (5 mL plus 2 × 1 mL rinse) and ethereal MeLi (1.50 M, 6.9 mL, 10.35 mmol) in ether (25 mL). Kugelrohr distillation [110 °C (0.3 mm)] gave 3-(2-methylcyclohexylidene)-2-butanol (761 mg, 87.5%) as a homogeneous (TLC, silica, 1:5 ethyl acetate–hexane) oil: NMR ($CDCl_3$, 200 MHz) δ 1.0–1.3 (series of 8 overlapping d, 6 H overall), 1.3–3.2 (m, 12 H), 4.80–5.05 (m, 1 H).

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[78] This was a mixture of geometric isomers.

A portion (421.2 mg, 2.50 mmol) was dissolved in ether (10 mL), and chlorotrimethylsilane (0.38 mL) and triethylamine (0.42 mL) were added. The mixture was refluxed for 2 h and worked up as described for **4b**. The crude product was purified by flash chromatography over silica gel (2 × 18 cm) with hexane containing increasing amounts of ethyl acetate (1–20% v/v). Kugelrohr distillation [160 °C (10 mm)] gave **8b** as a mixture of isomers (200.5 mg, 33.2%) of better than 98% purity (VPC, DEGS, 115 °C): IR (film) 1252, 1085 cm^{-1}; NMR ($CDCl_3$, 200 MHz) δ 0.088, 0.079, 0.044, 0.041 (4 s, 9 H overall), 0.95–1.2 (series of 8 overlapping d, 6 H overall), 1.2–3.0 (m, 12 H), 4.75–5.00 (m, 1 H); exact mass 240.1907 (calcd for $C_{14}H_{28}OSi$ 240.1909). Anal. Calcd for $C_{14}H_{28}OSi$: C, 69.93; H, 11.74. Found: C, 70.18; H, 11.84.

The flash chromatography also afforded, after Kugelrohr distillation, the starting alcohol (240.9 mg, 57.2%) as an apparently homogeneous (TLC, silica, 1:4 ethyl acetate–hexane) oil.

(4aβ,8aβ)-(4a-Methyldecahydronaphth-2-ylidene)-2-propanol (9b). The procedure for **1b** was followed with **9** (148.2 mg, 0.771 mmol) in ether (1 mL plus 2 × 1 mL rinse) and ethereal MeLi (1.52 M, 0.75 mL, 1.156 mmol) in ether (10 mL). The workup, flash chromatography over silica gel (2 × 18 cm) with 1:8 ethyl acetate–hexane, and Kugelrohr distillation [160 °C (0.15 mm)] gave **9b** (124 mg, 77.2%) as an apparently homogeneous (TLC, silica, 1:8 ethyl acetate–hexane) oil of better than 98% purity (VPC, FFAP, 210 °C). The material was a mixture (NMR) of four diastereoisomers: IR (film) 3330, 1660, 1055 cm^{-1}; NMR ($CDCl_3$, 200 MHz) δ 0.9–2.5 (m, 22 H, incorporating 4 sharp d with J = 8 Hz at δ 1.240, 1.230, 1.222, and 1.220 and 2 s at δ 1.032 and 1.026, all of comparable intensity), 4.58 (m, 1 H), 5.11 (br d, J = 8 Hz, 0.5 H), 5.22 (br d, J = 8 Hz, 0.5 H); exact mass 208.1829 (calcd for $C_{14}H_{24}O$ 208.1827). Anal. Calcd for $C_{14}H_{24}O$: C, 80.70; H, 11.61. Found: C, 80.74; H, 11.54.

2,3,4-Trimethyl-3-penten-2-ol. Ethereal methyllithium (1.53 M, 3 mL, 4.59 mmol) was diluted with ether (10 mL) and treated at 0 °C with 3,4-dimethyl-3-penten-2-one (**12**;[79] 275.8 mg, 2.458 mmol) in ether (1 mL plus 2 × 1 mL rinse). After 1 h at 0 °C the mixture was poured onto a saturated aqueous solution of ammonium chloride and extracted with ether (2 × 30 mL). The organic extract was dried, and evaporation gave an oil that was purified by flash chromatography over silica gel (2 × 18 cm with 1:8 ethyl acetate–hexane. Kugelrohr distillation [110 °C (10 mm)] gave 2,3,4-trimethyl-3-penten-2-ol as a white solid: 236.9 mg (75%); mp 37–39 °C; better than 99% pure (VPC, DEGS, 95 °C); IR (film) 3345, 1650, 1143 cm^{-1}; NMR ($CDCl_3$, 200 MHz) δ 1.37 (s, 6 H), 1.66 (m, 6 H), 1.80 (br s, 1 H), 1.94 (m, 3 H); exact mass 128.1197 (calcd for $C_8H_{16}O$ 128.1201), 110.1096 [calcd for C_8H_{14} ($M^{+\cdot} - H_2O$) 110.1096].

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Registry No. 1, 1713-63-9; **1a**, 79405-31-5; **1b**, 79405-36-0; (*E*)-**2**, 60934-89-6; (*Z*)-**2**, 60934-90-9; **2a**, 79405-32-6; **2a** 2,4-dinitrophenylhydrazone, 81535-49-1; (*E*)-**2b**, 81535-50-4; (*Z*)-**2b**, 81535-51-5; (*E*)-**3**, 74063-65-3; (*Z*)-**3**, 81535-52-6; **3a**, 17920-90-0; (*E*)-**3b**, 34562-09-9; (*Z*)-**3b**, 81535-53-7; (*E*)-**4**, 69625-48-5; (*Z*)-**4**, 81535-54-8; **4a**, 79405-33-7; (*E*)-**4b**, 81535-55-9; (*Z*)-**4b**, 81535-56-0; **5**, 7062-12-6; **5a**, 79405-34-8; **5b**, 79405-39-3; **6**, 76966-13-7; **6a**, 76966-34-2; **6b**, 76966-35-3; **6c**, 81535-57-1; **7**, 79405-30-4; **7** 2,4-dinitrophenylhydrazone, 81535-58-2; **7a**, 79405-35-9; **7a** 2,4-dinitrophenylhydrazone, 81535-59-3; **7b**, 79405-40-6; (*E*)-**8**, 81535-60-6; (*Z*)-**8**, 81535-61-7; (*E*)-**8** 2,4-dinitrophenylhydrazone, 81535-62-8; (*Z*)-**8** 2,4-dinitrophenylhydrazone, 81535-63-9; **8a** (isomer 1), 81535-64-0; **8a** (isomer 2), 81535-65-1; **8a** 2,4-dinitrophenylhydrazone, 81535-66-2; **8b**, 81535-67-3; (*E*)-**9**, 81535-68-4; (*Z*)-**9**, 81535-69-5; (*E*)-**9** 2,4-dinitrophenylhydrazone, 81535-70-8; (*Z*)-**9** 2,4-dinitrophenylhydrazone, 81600-21-7; **9a** (epimer 1), 81535-71-9; **9a** (epimer 2), 81535-72-0; **9a** (epimer 1) 2,4-dinitrophenylhydrazone, 81535-73-1; **9a** (epimer 2) 2,4-dinitrophenylhydrazone, 81535-74-2; **9b** (epimer 1), 81600-70-6; **9b** (epimer 2), 81535-75-3; **9b** (epimer 3), 81600-22-8; **9b** (epimer 4), 81600-23-9; **10**, 1210-39-5; **10b**, 15295-29-1; **12**, 684-94-6; (trimethylsilyl)acetaldehyde *tert*-butylimine, 73198-78-4; cycloheptanone, 502-42-1; 2-(trimethylsilyl)propionaldehyde *tert*-butylimine, 58707-01-0; 2-methylcyclohexanone, 583-60-8; (*Z*)-1-bromo-2-ethoxyethylene, 23521-49-5; *cis*-4a-methyloctahydro-2-naphthalenone, 938-06-7; (*E*)-3-methyl-3-decen-2-ol, 26560-10-1; (*Z*)-3-methyl-3-decen-2-ol, 81535-76-4; 3-cyclohexylidene-2-butanol, 69986-44-3; 3-(2-methylcyclohexylidene)-2-butanol, 81535-77-5; 2,3,4-trimethyl-3-penten-2-ol, 72486-21-6; $Me_5Cu_3Li_2$, 61701-36-8.

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Dimerization of 3-Benzoyl-4-phenylisocrotonic Acid†

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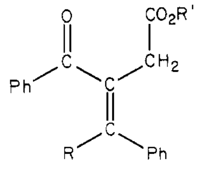
The acid-catalyzed self-condensation of acid **1a** formed the tricyclic pseudoacid dichloride **3a**, which on pyrolysis underwent a ring-expansion rearrangement to produce the dilactone **5a**. The structures and stereochemistries of these dimeric compounds are deduced by a study of their chemical transformations involving extensive use of deuterium incorporation.

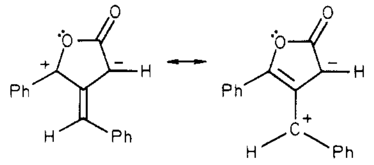
In the course of the attempted synthesis of the zwitterionic species **2** from 3-benzoyl-4-phenylisocrotonic acid[2] (**1a**) for a study of its participation in 1,3 dipolar cycloaddition reactions, an interesting dimerization took place. The details of this investigation are described in this paper.[3]

Results and Discussion

The acid-catalyzed dehydration of the acid **1a** was carried out under a variety of conditions. Reaction with acetyl chloride produced the tricyclic pseudoacid chlorides **3a** (40% yield) and **4a** (5% yield).[4] The use of oxalyl



1a, R' = H; R = H
b, R' = H; R = D
c, R' = CH_3; R = H



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† Dedicated to Professor Gilbert Stork on his 60th birthday.