was then extracted with three 75-ml portions of chloroform. The chloroform extracts were dried with K_2CO_3 and evaporated to leave the 3,4-dihydroisoquinoline IV as an oily residue. To this residue was added 100 ml of diphenyl ether and 2 g of palladium black. The mixture was heated with gentle stirring under nitrogen at 200° for 2 hr and was then diluted with benzene. The catalyst was removed by filtration and the filtrate was extracted with five 25-ml portions of 10 *M* HCl. The aqueous layer was made basic with cold NaOH solution and extracted with three 30-ml portions of chloroform. The chloroform extracts were dried with K_2CO_3 and evaporated to dryness and the resulting white solid was recrystallized from ethanol to yield 1-(3,4-dimethoxyphenethyl)-6,7-dimethoxyisoquinoline (V), 19 g (80%), mp 147° (lit.[7] mp 147°).

(±)-Homoargemonine (6,11,12,13-Tetrahydro-2,3,8,9-tetramethoxy-14-methyl-5*H*-dibenzo[*a*,*e*]cyclononene-5,11-imine)(II).—V (14 g) was methylated with methyl iodide (60 ml) in 50 ml of methanol to yield 15 g of the *N*-methiodide VI. *N*-Methiodide VI was dried and was added to 2 g of $LiAlH_4$ in dry ether (250 ml). The mixture was stirred at room temperature for 3 hr and the excess $LiAlH_4$ was then decomposed by the addition of wet ether followed by a saturated solution of sodium potassium tartrate. The aqueous layer was further washed with ether (2 × 50 ml) and the ether portions were combined, dried with K_2CO_3, and evaporated to dryness to yield 1-(3,4-dimethoxyphenethyl)-6,7-dimethoxy-1,2-dihydro-2-methylisoquinoline, VII, as a yellow oil. This was then refluxed under N_2 with 100 ml of 7:5 $HCOOH-H_3PO_4$ for 8 hr. The reaction mixture was then diluted with water, washed with $CHCl_3$, made basic with NaOH solution, and extracted with three 50-ml portions of chloroform. The chloroform extract was dried with K_2CO_3 and evaporated to yield 9 g of brown oil. The oil was shown by tlc to be composed of two products. Column chromatography (Florisil 60–100 mesh) was used to separate the two products. The column yielded 2 g of a substance indicated by nmr and tlc to be 1-(3,4-dimethoxyphenethyl)-6,7-dimethoxy-1,2,3,4-tetrahydroisoquinoline and 6 g of (±)-homoargemonine (II): mp 196° (ethanol); uv (CH_3OH) λ_{max} 277 nm (log ϵ 3.53); nmr ($CDCl_3$) δ 6.67–6.5 (m, 4 H, aromatic protons), 3.90 (s, 6 H, OCH_3), 3.85 (s, 6 H, OCH_3), 2.53 (s, 3 H, NCH_3), 4.23–2.37 (m, 8 H, ring CH and CH_2); mass spectrum (70 eV) *m/e* (rel intensity) 369 (45), 204 (100), 218 (11), 368 (54).

Anal. Calcd for $C_{22}H_{27}NO_4$: C, 71.52; H, 7.37; N, 3.79. Found: C, 71.50; H, 7.65; N, 4.10.

Registry No.—II, 39013-26-8; III, 20944-13-2; IV, 20944-14-3; V, 39013-29-1; VI, 39013-30-4; VII, 39013-31-5; 3-(3,4-dimethoxyphenyl)propionic acid, 2107-70-2; 2-(3,4-dimethoxyphenyl)ethylamine, 120-20-7.

[7] G. Scheuing and B. Walach, German Patent 576,532 (1933); *Chem. Abstr.*, **27**, 5896 (1933).

Organocopper Chemistry. Reactions of Lithium Dialkylcopper Reagents with Activated Vinylcyclopropanes. An Instance of 1,7 Addition

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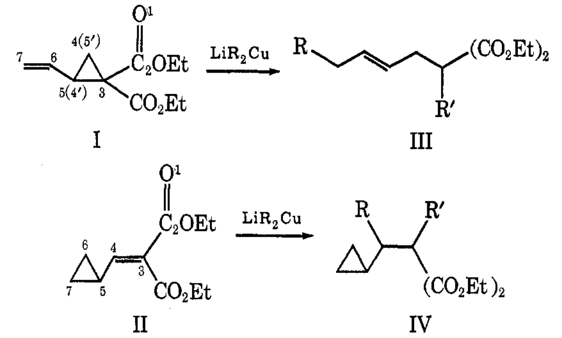
Received December 22, 1972

Alkylation of a wide variety of organic substrates using alkylcopper(I) "ate" complexes continues to be a subject of active interest.[1] The recently reported capabilities of organocopper species to perform 1,5 and 1,6 additions[2] (ω alkylation) prompts us to report our results concerning the reaction of I and II with lithium dimethylcopper ($LiMe_2Cu$) and lithium di-*n*-butylcopper ($LiBu_2Cu$). In addition we report further observations which allow for simultaneous ω (1,7 or 1,4)[3a] and α-alkylation *via* addition of an alkylcopper "ate" complex to either I or II followed by alkylation[3b] of the resultant malonate anion.



In principle, compounds I and II possess multiple electrophilic sites. In addition to the trivial possibility of 1,2 addition, compound II might be attacked by nucleophiles in a 1,4 or 1,7 sense. Likewise, compound I might suffer nucleophilic attack in a 1,5, 1,5′, or 1,7 sense.[4] Our studies demonstrate, in each case, remarkable specificity toward olefin attack.

Treatment of I[5] with $LiMe_2Cu$ (1.25 equiv) in ether at 0° for 1 hr afforded an 87% yield of IIIa ($R = CH_3$; $R' = H$). Its structure is assigned on the basis of the following data: ir max ($CHCl_3$) 5.80, 10.30 μ; nmr (CCl_4) δ 5.45 (m, 2 H, olefinic protons), 3.24 [t, 1 H, $CH(CO_2Et)_2$], 0.98 (t, 3 H, CH_2CH_3); *m/e* 228. This reaction constitutes a preferential and unambiguous 1,7 addition.[6–9] Similarly, $LiBu_2Cu$ underwent almost exclusive 1,7 addition in high yield (Table I).

In sharp contrast, treatment of II[10] with $LiMe_2Cu$ under similar conditions gave IVa ($R = CH_3$; $R' = H$) in 92% isolated yield. The structure is assigned on the basis of the following data: ir max ($CHCl_3$) 5.80 μ; nmr (CCl_4) δ 3.25 [d, 1 H, $CH(CO_2Et)_2$], 1.08 (d, 3 H, $CHCH_3$), 0.80–0.05 (m, 5 H, cyclopropyl moiety);

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[1] G. M. Whitesides, W. F. Fischer, Jr., J. SanFilippo, Jr., R. W. Bashe, and H. O. House, *J. Amer. Chem. Soc.*, **91**, 4871 (1968); E. J. Corey and G. H. Posner, *ibid.*, **89**, 3911 (1967), and **90**, 5615 (1968), and references cited therein.

[2] (a) E. J. Corey and P. L. Fuchs, *J. Amer. Chem. Soc.*, **94**, 4014 (1972); E. J. Corey, C. U. Kim, R. H. K. Chen, and M. Takeda, *ibid.*, **94**, 4395 (1972); G. Daviaud and P. Miginiac, *Tetrahedron Lett.*, 997 (1972). (b) For previous precedent in S_N2'-type displacements using $LiMe_2Cu$, see R. J. Anderson, C. A. Henrick, and J. B. Siddall, *J. Amer. Chem. Soc.*, **92**, 735 (1970); E. E. van Tamlen and J. P. McCormick, *ibid.*, **92**, 737 (1970); R. J. Anderson, *ibid.*, **92**, 4978 (1970); R. W. Herr and C. R. Johnson, *ibid.*, **92**, 4979 (1970).

[3] (a) For a recent review of organocopper 1,4-addition reactions, see G. H. Posner, *Org. React.*, **19**, 1 (1972). (b) For alkylation of an enolate anion generated by addition of an organometallic reagent to an α,β-unsaturated ketone, see G. Stork, *Pure Appl. Chem.*, **17**, 383 (1968).

[4] We suggest the terms 1,5 and 1,5′ (which arises from alternative numbering) to signify alternate modes of homoconjugate addition and 1,7 to signify vinylogous homoconjugate addition. The terms 1,4 and 1,6 are thus reserved for classical Michael reactions.

[5] R. W. Kierstead, R. P. Linstead, and B. C. L. Weedon, *J. Chem. Soc.*, 3610 (1952).

[6] The normal mode of addition of nucleophiles to I is in the 1,5 sense.[7,8] The two serious exceptions to this rule are 1,7-mercaptan addition[7] and 1,7-enamine addition.[8] The former case is most probably the result of a free radical pathway.[9] The latter case may well be the result of 1,5-alkylation at nitrogen followed by Claisen rearrangement.

[7] J. M. Stewart and G. K. Pagenkopf, *J. Org. Chem.*, **34**, 7 (1969).

[8] S. Danishefsky, G. Rovnyak, and R. Cavanaugh, *Chem. Commun.*, 636 (1969).

[9] S. Danishefsky and R. Rovnyak, *J. Chem. Soc., Chem. Commun.*, 820 (1972).

[10] Prepared from the Knoevenagel condensation of diethyl malonate with cyclopropanecarboxaldehyde (see G. Rovnyak, Ph.D. Thesis, University of Pittsburgh, 1970).

Table I

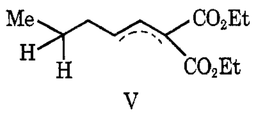
Reactions of I with LiR_2Cu Followed by R′X

$$\mathrm{I} \xrightarrow[2.\ \mathrm{R'X}]{1.\ \mathrm{LiR_2Cu}} \mathrm{III}$$

LiR_2Cu	R′X	Product[a]	Isolated yield, %
$LiMe_2Cu$		IIIa (R = CH_3; R′ = H)	87
$LiMe_2Cu$	CH_3I	IIIb (R = R′ = CH_3)	70
$LiMe_2Cu$	Allyl bromide	IIIc (R = CH_3; R′ = allyl)	75
$LiMe_2Cu$	$C_6H_5CH_2Cl$	IIId (R = CH_3; R′ = $CH_2C_6H_5$)	88
$LiBu_2Cu$		IIIe (R = C_4H_9; R′ = H)	90
$LiBu_2Cu$	CH_3I	IIIf (R = C_4H_9; R′ = CH_3)	75
$LiBu_2Cu$	Allyl bromide	IIIg (R = C_4H_9; R′ = allyl)	88

[a] All substances gave nmr, ir, and analytical data in agreement with the indicated structures.

m/e 228. It is important to note that, under these conditions, we were unable to detect the formation of compound V which would have resulted from 1,7



V

addition to II. This result is of particular interest in connection with two recent findings. Marshall reported[11] competitive 1,4 and 1,7 addition of $LiMe_2Cu$ to a vinylogous cyclopropyl ketone in a decalin system. Stewart,[12] on the other hand, reported exclusive (albeit in low yield) 1,7 addition of mercaptans to a substrate more closely related to II. The case at hand seems to indicate a very pronounced preference for 1,4 addition in the absence of compelling steric factors.

ω-Alkylation (1,7 or 1,4) employing $LiMe_2Cu$ or $LiBu_2Cu$ with either I or II results in the formation of a stabilized anion which should be capable of undergoing alkylation. We have examined this possibility and report that one can effectively alkylate such anions with several halides (see Tables I and II).

Table II

Reactions of II with LiR_2Cu, Followed by R′X

$$\mathrm{II} \xrightarrow[2.\ \mathrm{R'X}]{1.\ \mathrm{LiR_2Cu}} \mathrm{IV}$$

LiR_2Cu	R′X	Product[a]	Isolated yield, %
$LiMe_2Cu$		IVa (R = CH_3; R′ = H)	92
$LiMe_2Cu$	CH_3I	IVb (R = R′ = CH_3)	93
$LiMe_2Cu$	Allyl bromide	IVc (R = CH_3; R′ = allyl)	95
$LiBu_2Cu$	CH_3I	IVd (R = C_4H_9; R′ = CH_3)	99
$LiBu_2Cu$	Allyl bromide	IVe (R = C_4H_9; R′ = allyl)	98

[a] All substances gave nmr, ir, and analytical data in agreement with the indicated structures.

The conjugate 1,4- and vinylogous homoconjugate 1,7-addition processes involving organocopper species accompanied by α-alkylation illustrates a number of effective, specific operations which can be employed in organic synthesis.

Experimental Section[13]

Procedure for the Reaction of I or II with Lithium Dimethylcopper.—To a cooled (0°) stirred suspension of CuI (289 mg, 1.5 mmol) in 12 ml of anhydrous ether under an atmosphere of nitrogen was added 1.8 ml of 1.66 *M* ethereal methyllithium (3.0 mmol). To this colorless solution was added 212 mg of vinylcyclopropane I. After 1 hr at 0°, the reaction mixture was quenched by pouring it into a solution of ammonium chloride. Isolation with ether followed by short-path distillation [bp 80° (bath temperature) at 0.1 mm] afforded 198 mg (87%) of 1,7-addition product IIIa: ir max ($CHCl_3$) 5.80, 10.30 μ; nmr (CCl_4) δ 5.45 (m, 2 H, olefinic protons), 4.15 (q, *J* = 7 Hz, 4 H), 3.24 [t, 1 H, $CH(CO_2Et)_2$], 2.53 (m, 2 H), 1.28 (t, *J* = 7 Hz, 6 H), 0.98 (t, 3 H, CH_2CH_3); *m/e* 228.1362.

Anal. Calcd for $C_{12}H_{20}O_4$: C, 63.13; H, 8.83. Found: C, 62.97; H, 8.77.

Procedure for the Reaction of I or II with Lithium Di-*n*-butylcopper.—To a cooled (−20°) stirred suspension of CuI (240 mg, 1.25 mmol) in 12.5 ml of anhydrous ether under an atmosphere of nitrogen was added 1.0 ml (2.5 mmol) of 2.5 *M* *n*-BuLi in hexane. After 30 min at −20°, vinylcyclopropane I (214 mg, 1.0 mmol) in 2.0 ml of ether was added dropwise and stirring at −20° was continued for 3 hr. The reaction mixture was quenched by pouring it into a solution of ammonium chloride. Isolation with ether and short-path distillation [bp 90° (bath temperature) at 0.1 mm] afforded 243 mg (90%) of 1,7-addition product IIIe: ir max (film) 5.80, 10.32 μ; nmr (CCl_4) δ 5.38 (m, 2 H, CH═CH), 4.14 (q, *J* = 7 Hz, 4 H), 3.24 [t, 1 H, $CH(CO_2Et)_2$], 2.50 (m, 2 H), 1.95 (m, 2 H), 1.25 (t, *J* = 7 Hz, 6 H), 0.88 (t, 3 H); *m/e* 270.

Anal. Calcd for $C_{15}H_{26}O_4$: C, 66.63; H, 9.69. Found: C, 66.40; H, 9.62.

General Procedure for the Reaction of I or II with Lithium Di-*n*-butylcopper Followed by Treatment with R′X.—To a suspension of CuI (241 mg, 1.25 mmol) in 12.5 ml of anhydrous ether cooled to −20° under an atmosphere of nitrogen was added 1.0 ml (2.5 mmol) of *n*-BuLi (2.55 *M* in hexane) followed by the dropwise addition of 212 mg (1.0 mmol) of vinylcyclopropane II in 2.0 ml of ether. After 2 hr at −20°, the reaction mixture was warmed to room temperature and excess methyl iodide was added. The reaction mixture was stirred overnight at room temperature (18 hr) and was quenched by pouring it into an ammonium chloride solution. Isolation with ether followed by short-path distillation [bp 94° (bath temperature) at 0.15 mm] afforded 280 mg (99%) of ω (1,4), α dialkylated product IVd: ir max ($CHCl_3$) 5.81 μ; nmr (CCl_4) δ 4.11 (q, *J* = 7 Hz, 4 H), 1.35 (s, 3 H), 1.23 (t, *J* = 7 Hz, 6 H), 0.88 (t, 3 H), 0.70–0.05 (cyclopropyl moiety, 5 H); *m/e* 284.

Anal. Calcd for $C_{16}H_{28}O_4$: C, 67.57; H, 9.92. Found: C, 67.80; H, 9.77.

General Procedure for the Reaction of I and II with Lithium Dimethylcopper Followed by Treatment with R′X.—To a suspension of CuI (240 mg, 1.25 mmol) in 12.5 ml of anhydrous ether at 0° under an atmosphere of nitrogen was added 1.5 ml (2.5 mmol) of 1.66 *M* ethereal methyllithium followed by 214 mg (1.0 mmol) of vinylcyclopropane I in 2.0 ml of ether. After 1 hr at 0°, the reaction mixture was treated with excess benzyl chloride, warmed to room temperature, and allowed to stir overnight (18 hr). Usual work-up afforded after short-path distillation [bp 127° (bath temperature) at 0.13 mm] 278 mg (88%) of ω (1,7), α dialkylated product IIId: ir max (film) 5.79, 10.38 μ; nmr (CCl_4) δ 7.12 (s, 5 H), 5.42 (m, 2 H), 4.09 (q, *J* = 7 Hz, 4 H), 3.16 (s, 2 H), 2.43 (d, 2 H), 2.02 (m, 2 H), 1.19 (t, *J* = 7 Hz, 6 H), 0.98 (t, 3 H); *m/e* 318.

Calcd for $C_{19}H_{26}O_4$: C, 71.67; H, 8.23. Found: C, 71.45; H, 8.29.

Registry No.—I, 7686-78-4; II, 39000-53-8; IIIa, 36276-65-0; IIId, 39000-72-1; IIIe, 36276-67-2; IVa, 39013-57-5; IVd, 39013-58-6; $LiMe_2Cu$, 15681-48-8; $LiBu_2Cu$, 24406-16-4; CH_3I, 74-88-4; allyl bromide, 106-95-6; $C_6H_5CH_2Cl$, 100-44-7.

Acknowledgments.—We thank Professor S. Danishefsky for many stimulating discussions and Mr. P. Cain for the preparation of compound I. Acknowledgment is to the Science Development Program of the National Science Foundation (GU 3184) for support of this research.

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[11] J. A. Marshall and R. A. Ruden, *J. Org. Chem.*, **37**, 659 (1972).

[12] J. M. Stewart and B. R. Olsen, *J. Org. Chem.*, **33**, 4534 (1968).

[13] Nmr measurements were carried out on a Varian A-60D spectrometer using TMS as an internal reference. A Perkin-Elmer Model 247 was used for ir studies. Mass spectral data were obtained on an LKB-9 spectrometer. Elemental analyses were determined by Galbraith Laboratories, Knoxville, Tenn. Anhydrous cuprous iodide was purchased from Alpha Inorganics, Inc., and was sufficiently dry and pure for direct use.