Vinyl-Copper Derivatives; X[1]. Alkylation of (*Z*)-Dialkenylcuprates

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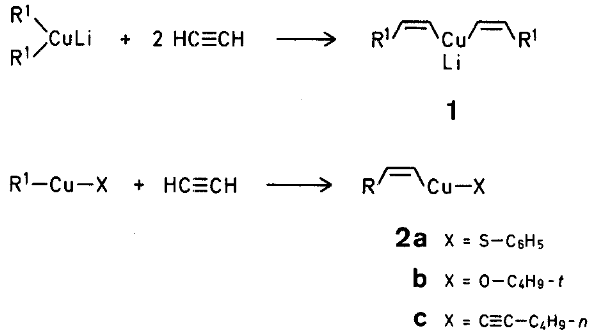
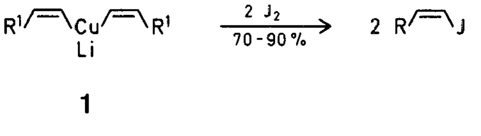
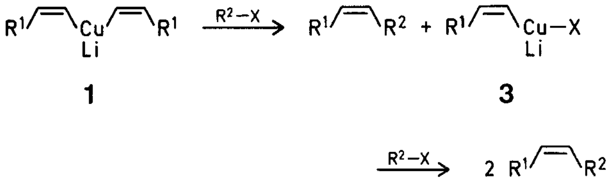
We have recently described[1,2] the *syn*-addition of various organocopper derivatives to acetylene, which affords (*Z*)-alkenyl-copper reagents in quantitative yield.



Iodination of the organometallic reagents **1** and **2**[1,2] gave the corresponding (*Z*)-iodoalkenes in high yield and with an excellent stereochemical purity ($\geq$99.95% as determined by G.L.C., 3 m LAC 860 column).



We report herein on the alkylation of cuprates **1** with various electrophiles under conditions where *both* alkenyl groups are used. Previously, the alkylation reaction has generally been performed with a large excess of the cuprate reagent[3,4], a significant drawback when the organometallic reagents are less available or more expensive than the electrophilic substrate. In order to circumvent this problem, the use of heterocuprates RCuX has been developed (X is a non-transferable hetero group such as S—C_6H_5[5], O—C_4H_9-*t*[5], C≡C—R[6,7]). Curiously, however, no efforts have been directed towards the use of *both* organic groups of the homocuprate reagent. Under our reaction conditions, cuprates **1** react with the first equivalent of electrophile to afford one equivalent of alkylated product and one equivalent of the less reactive vinyl-copper reagent **3**. The latter reacts, then, with the second equivalent of the electrophile, sometimes under more stringent conditions as shown below.



The complete reaction of the (*Z*)-dialkenyl cuprates **1** with the more reactive halides is simply achieved in the presence of 1 equivalent of hexamethylphosphoric triamide (with 2 equivalents the reaction is slightly faster). The results are summarised in Table 1.

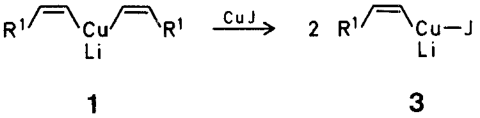
High yields of (*Z*)-alkenes are thus obtained with allylic and benzylic halides. Allylic phosphates, which constitute an interesting alternative to the corresponding halides, react as well. With substituted allylic substrates, both SN_2 and SN_2' attack occurs under our reaction conditions. However, a different ratio of cuprate and electrophile (5/1) permits a highly stereoselective SN_2 substitution[8].

α-Halo-ethers are also very reactive. Their reaction affords a general entry to allylic ethers with the (*Z*)-configuration.

The alkylation of (*Z*)-dialkenylcuprates **1** by less reactive alkyl halides can also be performed in high yield. The first equivalent of electrophile reacts readily in the presence of one or two equivalents of hexamethylphosphoric triamide (see Table 2). The reaction of the second equivalent of electrophile with the less reactive vinyl-copper reagent **3** is much slower and requires the addition of 3 equivalents of triethyl phosphite per copper atom which stabilises reagent **3** and prevents its decomposition at room temperature. Thus, a large variety of primary alkyl halides may be used (Table 2). It is also possible to perform the reaction with ω-functionalised halides, taking advantage of the non-reactivity of an ester group (entry 15 and 16) or the low reactivity of a chloride as compared to the iodide (entry 14). The reaction with a homoallylic halide (entry 12) is less satisfactory under the standard reaction conditions. However, a better yield (based on the electrophile used) is obtained when only one equivalent of halide is used in the absence of triethyl phosphite (entry 13). This result suggests a very low reactivity of the vinyl-copper reagent **3** towards such a halide.

To our knowledge chlorotrimethylsilane had not been used in reactions with organocuprates. In the presence of hexamethylphosphoric triamide and triethylamine it reacts with only one (*Z*)-alkenyl group of **1** (entry 18). We were unable to transfer the second group under our standard reaction conditions. This behaviour reflects the inability of the organocopper reagent **3** to react with this compound.

Lastly, we have studied the alkylation of (*Z*)-dialkenylcuprates **1** by 1-haloalkynes, a reaction known to occur with vinyl-coppper reagents[9]. The reaction of **1** with 1-iodo-1-hexyne proceeds mainly by metal-halogen exchange, and poor yields of alkenynes are obtained. In order to circumvent these difficulties, we have transformed the cuprate **1** into the vinyl-copper reagent **3** by addition of 0.5 equivalents of copper iodide.



The vinyl copper **3**, thus obtained, can be now alkylated under the reaction conditions previously described (tetrahydrofuran/1-2 equivalents TMEDA) (see Table 3). It is worth note that the reaction proceeds at a sufficiently fast rate that a hydroxy function need not be protected (compare entry 20 and 21). The slight decrease in yield is largely

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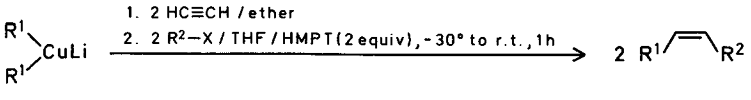
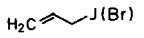
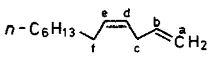
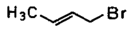
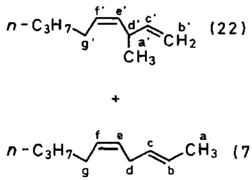
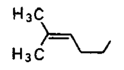
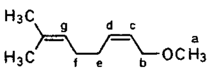
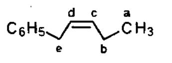
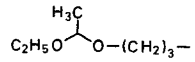
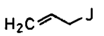
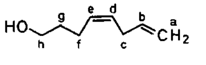
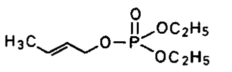
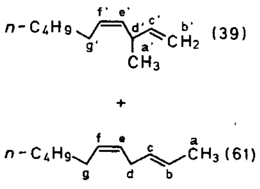
Table 1. Alkylation of (*Z*)-Dialkenylcuprates with Reactive Halides



Entry	R¹	Electrophile R²—X	Product(s)	Yield[a] [%]	b.p./torr	n_D^{20}	Molecular formula[b]	I.R. (neat) ν [cm⁻¹]	¹H-N.M.R. (CCl₄/TMS) δ [ppm]
1 (2)	n-C_7H_{15}			98 (71)	86–87°/15	1.4487	$C_{12}H_{22}$ (166.3)	3080; 3015; 1660; 1640; 990; 910; 725 (C=C)	5.64–5.28 (m, H-b); 5.10 (m, H-e, H-d); 4.83–4.62 (2d, 2H-a); 2.63 (t, 2H-c); 1.92 (q, 2H-f)
3	n-C_4H_9		 (22) (78)	67	55–61°/15	—	$C_{10}H_{18}$ (138.3)	3080; 3010; 1660; 1640; 990; 965; 910; 725 (C=C)	5.90–5.57 (m, H-c'); 5.44–5.14 (m, H-b, H-c, H-e, H-f, H-e', H-f'); 5.07–4.82 (2d, 2H-b'); 3.16 (m, H-d'); 2.71 (t, 2H-d); 2.06 (q, 2H-g, 2H-g'); 1.66 (d, 3H-a); 1.08 (d, 3H-a')
4		H_3CO-CH_2-Cl		79	76–77°/15	1.4533	$C_{10}H_{18}O$ (154.3)	3020; 1675; 1660; 1110 (C—O—C); 830; 710 (C=C)	5.50 (m, H-c, H-d); 5.12 (t, H-g); 3.90 (d, 2H-b); 3.24 (s, 3H-a); 2.08 (m, 2H-e, 2H-f)
5	C_2H_5	$C_6H_5-CH_2-Br$		84	82–83°/15 (82°/12)[11]	1.5246 (n_D^{23}: 1.5090)[11]	$C_{11}H_{14}$ (146.2)	3080; 1655 (C=C); 740; 695 (C_6H_5)	5.46 (m, H-c, H-d); 3.34 (d, 2H-e); 2.14 (m, 2H-b); 1.00 (t, 3H-a)
6				65[c]	90–91°/15	1.4640	$C_8H_{14}O$ (126.2)	3320 (OH); 3080; 3010; 1655; 1640; 990; 910; 720 (C=C)	6.00–5.62 (m, H-b); 5.56–5.32 (m, H-d, H-e); 5.12–4.84 (2d, 2H-a); 3.56 (t, 2H-h); 2.81 (t, 2H-c); 2.13 (q, 2H-f); 1.60 (m, 2H-g)
7	n-C_5H_{11}		 (39) (61)	72	67–73°/15	—	$C_{11}H_{20}$ (152.3)	3080; 3010; 1660; 1640; 990; 965; 910; 725 (C=C)	5.87–5.55 (m, H-c'); 5.40–5.12 (m, H-b, H-c, H-e, H-f, H-e', H-f'); 5.07–4.80 (2d, 2H-b'); 3.15 (m, H-d'); 2.69 (t, 2H-d); 2.08 (q, 2H-g, 2H-g'); 1.64 (d, 3H-a); 1.06 (d, 3H-a')

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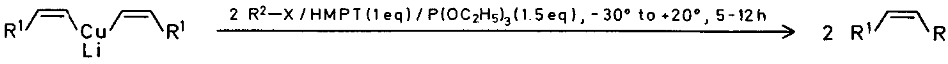
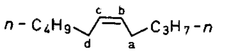
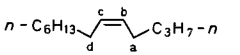
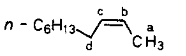
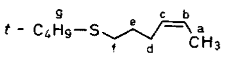
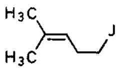
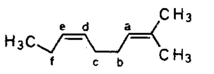
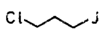
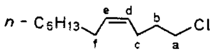
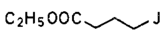
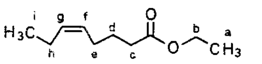
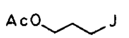
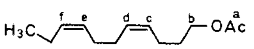
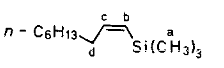
[a] Yield of isolated product based on electrophile used.

[b] The microanalyses were in satisfactory agreement with the calculated values (C ±0.18, H ±0.19).

[c] Yield based on the (*Z*)-dialkenylcuprate which is formed in ~80% yield.

Table 2. Alkylation of (*Z*)-Dialkenylcuprates with Less Reactive Halides



Entry	R¹	Electrophile R²—X	Product(s)	Yield [%]ᵃ	b.p./torr	n_D^{20}	Molecular formulaᵇ	I.R. (neat) ν [cm⁻¹]	¹H-N.M.R. (CCl_4/TMS) δ [ppm]
8	*n*-C_5H_{11}	*n*-C_4H_9—Br		81	71–72°/15 (191°/760)[13]	1.4292 (1.4295)[13]	$C_{12}H_{22}$ (154.3)	3010; 1655; 720 (C=C)	.29 (m, H-b, H-c); 2.00 (q, 2H-a, 2H-d)
9	*n*-C_7H_{15}	*n*-C_4H_9—Br		81ᶜ	109–110°/15 (104°/12)[12]	1.4357 (1.4362)[12]	$C_{13}H_{26}$ (182.4)	3010; 1655; 720 (C=C)	5.32 (m, H-b, H-c); 2.02 (q, 2H-a, 2H-d)
10	*n*-C_7H_{15}	H_3C—J		82	60–61°/15 (60–61°/13)[10]	1.4264	$C_{10}H_{20}$ (140.3)	3010; 1655; 720 (C=C)	5.32 (m, H-b, H-c); 2.00 (q, 2H-d); 1.58 (d, 3H-a)
11	*t*-C_4H_9—S—$(CH_2)_3$—	H_3C—J		81	85–87°/15	1.4689	$C_{10}H_{20}S$ (172.3)	3020; 1655; 700 (C=C)	5.40 (m, H-b, H-c); 2.29 (t, 2H-f); 2.16 (q, 2H-d); 1.64 (d, 3H-a); 1.60 (m, 2H-e); 1.27 (s, 9H-g)
12 (13)ᵈ	C_2H_5			63 (84)ᵈ,ᵉ	59°/15	1.4545	$C_{10}H_{18}$ (138.3)	3010; 1665; 825; 725 (C=C)	5.32 (m, H-d, H-e); 5.13 (t, H-a); 2.04 (m, 2H-b, 2H-c, 2H-f)
14	*n*-C_7H_{15}			77ᶜ	75–76°/0.2	1.4550	$C_{12}H_{23}Cl$ (202.8)	3010; 1665; 730 (C=C)	5.08 (m, H-d, H-e); 3.20 (t, 2H-a); 2.06 (m, 2H-c); 1.96 (m, 2H-f); 1.76 (m, 2H-b)
15	C_2H_5			85ᶜ	86–88°/15	1.4352	$C_{10}H_{18}O_2$ (170.3)	3010; 1740 (COO); 1655; 710 (C=C)	5.34 (m, H-f, H-g); 4.10 (q, 2H-b); 2.26 (t, 2H-c); 2.06 (m, 2H-e, 2H-h); 1.70 (m, 2H-d); 1.25 (t, 3H-a); 0.98 (t, 3H-i)
16				67	86–88°/0.01	1.4567	$C_{14}H_{24}O_2$ (224.3)	1740; 1240 (COO); 3010; 1655; 730 (C=C)	5.37 (m, H-c, H-d, H-e, H-f); 4.02 (t, 2H-b); 1.96 (s, 3H-a)
17 (18)ᵈ	*n*-C_7H_{15}	$(H_3C)_3Si$—Cl		43 (80)ᵈ,ᵉ,ᶠ	98–100°/15	1.4383	$C_{12}H_{26}Si$ (198.4)	1250; 840; 765 [Si(CH_3)$_3$]; 1610; 740 (C=C)	6.20 (dt, H-c); 5.38 (d, H-b); 2.11 (q, 2H-d); 0.10 (s, 9H-a); $J_{H\text{-}b,H\text{-}c}$ = 14 Hz

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[a] Yield of isolated product based on electrophile used.

[b] The microanalyses were in satisfactory agreement with the calculated values (C ±0.31, H ±0.21).

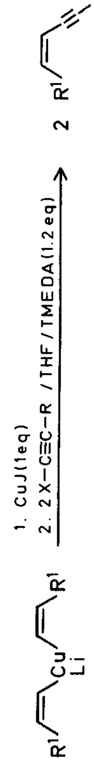
[c] 2 equivalents of hexamethylphosphoric triamide used instead of 1.

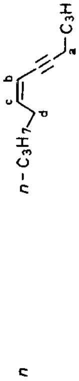
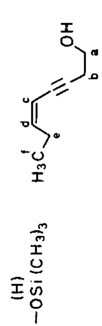
[d] Reaction with 1 equivalent of electrophile instead of 2.

[e] Reaction performed without addition of triethyl phosphite.

[f] 1 equivalent of triethylamine is admixed with chlorotrimethylsilane prior to addition.

Table 3. Alkylation of (Z)-Dialkenylcuprates with 1-Halo-1-alkynes

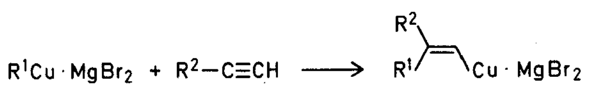


Entry	R'	Haloalkyne	Product	Yield[a] [%]	b.p./torr	n_D^{20}	Molecular formula[b]	I.R. (neat) ν [cm^{-1}]	^{1}H-N.M.R. (CCl$_4$/TMS) δ [ppm]
19	n-C_4H_9	J–C≡C–C_4H_9-n		82	95–96°/15 (70°/3.5)[14]	1.4649 (n_D^{22}: 1.4626)[14]	$C_{12}H_{20}$ (164.3)	2210 (C≡C); 1620; 735 (C=C)	5.73 (d of t, H-c); 5.35 (dd, H-b); 2.22–2.14 (m, 2H-a, 2H-d); $J_{H-b,H-c}$ = 11 Hz
20 (21)	C_2H_5	Br–C≡C–CH_2–CH_2–OSi(CH_3)$_3$ (H)		83 (75)	61–62°/0.1 (61°/0.3)[9b]	1.4952 (1.4942)[9b]	$C_8H_{12}O$ (124.2)	3350; 2220 (C≡C); 1045 (OH); 1620; 735 (C=C)	5.73 (d of t, H-d); 5.31 (d, H-c); 3.63 (t, 2H-a); 2.53 (t, 2H-b); 2.26 (m, 2H-c); 1.00 (t, 3H-f); $J_{H-c,H-d}$ = 11 Hz

[a] Yield of isolated product based on electrophile used.

[b] The microanalyses were in satisfactory agreement with the calculated values (C ±0.07, H ±0.17).

compensated by the fact that the protection of the alcohol function of 1-bromo-4-hydroxy-1-butyne is effected in only 70–80% yield[9b]. The reactivity of vinyl-copper compounds **3** towards other 1-haloalkynes has not been studied. However, it may be expected that it does not differ from that of vinyl-copper reagents **4**.



4

In all the alkylation reactions presented here, we have used the cuprates **1** instead of **2**. Hetero-cuprates **2a** and **2b** are less suited since the hetero group X competes with the alkenyl group for transfer, thus lowering the yield based on the electrophile. Cuprates **2c** react as well as cuprates **1** when only one equivalent of electrophile is used, but they are more expensive and consume one copper atom per mol electrophile.

It must be emphasised that all the products described here are obtained in a purity up to 99.9% (Z)-configuration. For example, in the case of (Z)-2-decene (entry 10), gas chromatographic analysis (SE 30 capillary column, 50 m) shows the presence of only 0.03% of the E isomer by comparison with authentic samples of both isomers[10]. These compounds are simply isolated by distillation through a Vigreux column, without any chromatographic separation, thus allowing a large scale preparation.

In conclusion, our synthesis of (Z)-alkenes seems very suited when alkenes of very high (Z)-purity are needed (for example, synthesis of natural products). We are currently applying this method to the synthesis of some insect sex pheromones where the (E)-isomer has often an inhibiting effect on their biological activity.

Alkylation with Reactive Halides (Table 1); General Procedure:
To a stirred solution of the (Z)-dialkenyl-cuprate **1** (25 mmol), in ether under a nitrogen atmosphere are added at −30° hexamethylphosphoric triamide (10 ml, 50 mmol) mixed with tetrahydrofuran (30 ml) and then a solution of the halide (50 mmol) in tetrahydrofuran (10 ml). The mixture is allowed to reach room temperature, stirred for 1 h at +20°, then hydrolysed at −20° with 5 normal hydrochloric acid (80 ml). The precipitate is filtered, the aqueous layer is extracted once with ether (100 ml) or hexane (100 ml), and the combined organic layers are successively washed once with 17% ammonium hydroxide solution (50 ml), then with a saturated ammonium chloride solution (50 ml), and finally dried with magnesium sulfate. After removal of the solvents on a rotatory evaporator, the crude product is distilled on a 10 cm Vigreux column.

Alkylation with Less Reactive Halides (Table 2); General Procedure:
To a stirred solution of the (Z)-dialkenylcuprate **1** (25 mmol) in ether under a nitrogen atmosphere are successively added at −30° hexamethylphosphoric triamide (10 ml, 50 mmol) mixed with tetrahydrofuran (30 ml), then a solution of the halide (50 mmol) in tetrahydrofuran (10 ml), and finally triethyl phosphite (15 ml, 75 mmol). The mixture is slowly allowed to reach (1–2 h) room temperature, stirred for 5–12 h at +20°, then hydrolysed at −20°, with 5 normal hydrochloric acid (80 ml), and worked up as described above.

Alkylation with 1-Halo-1-alkynes (Table 3); General Procedure:
To a stirred solution of (Z)-dialkenyl-cuprate **1** (25 mmol), in ether under a nitrogen atmosphere are added at −50° copper(I) iodide (4.75 g, 25 mmol), tetrahydrofuran (60 ml), and tetramethylethylenediamine (7.0 g, 60 mmol). The mixture is stirred for 90 min at

−25° until all copper(I) iodide has dissolved. To this dark-green solution is slowly added a solution of the halide (50 mmol) in tetrahydrofuran (10 ml), the mixture is stirred for 60 min at −15°, then hydrolysed with 5 normal hydrochloric acid (80 ml), and worked up as described above.

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