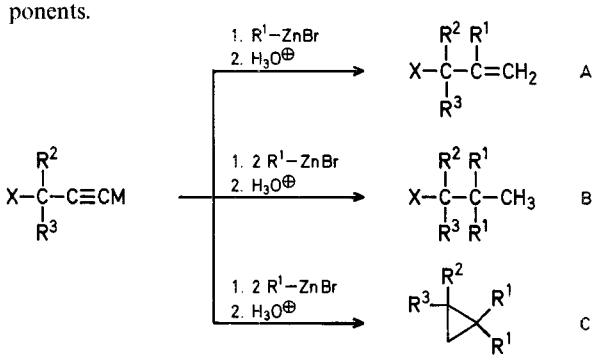
Synthesis of Substituted Cyclopropanes via Organozinc Reagents

M. Bellassoued, Y. Frangin

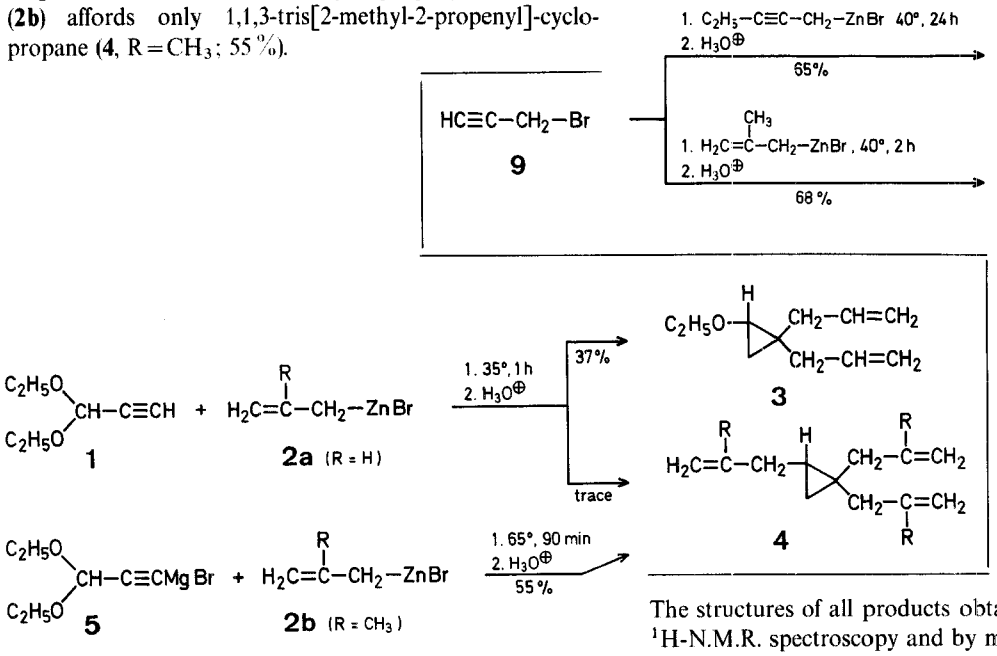
Laboratoire de Synthèse Organométallique, Université Pierre et Marie Curie, Bâtiment F, 4, Place Jussieu, F-75230 Paris CEDEX 05, France

In previous papers[1–5], we have reported that α,β-unsaturated organozinc reagents undergo single or twofold addition to acetylenic compounds to form open-chain or cyclopropane derivatives, the ratio of the three types of products (A, B, C) depending on nature and structure of the reaction components.

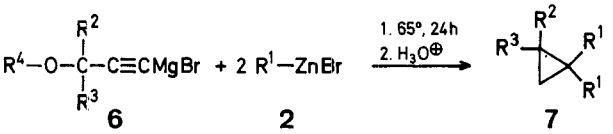


In the present paper, we show that the reaction of 1-alkynes and 1-alkynylmagnesium halides with organozinc halides can be conveniently applied to the synthesis of substituted cyclopropanes.

The reaction of 3,3-diethoxypropyne (**1**) with allylzinc bromide (**2a**) leads to the formation of 1,1-diallyl-2-ethoxycyclopropane (**3**; 37%) and a small amount of 1,1,2-triallylcyclopropane (**4**, R = H), as shown by ^{13}C-N.M.R. spectrometry. However, when the magnesium reagent **5** is used instead of **1** the reaction leads exclusively to the formation of **4** (R = H) in 37% yield. The reaction of 3,3-diethoxypropynylmagnesium bromide with 2-methyl-2-propenylzinc bromide (**2b**) affords only 1,1,3-tris[2-methyl-2-propenyl]-cyclopropane (**4**, R = CH_3; 55%).



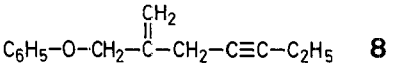
In a similar way, 3-methoxy-1-propynylmagnesium bromide (**6**, $R^2 = R^3 = H$, $R^4 = CH_3$) reacts with 2-butenylzinc bromide (**2d**, $R^1 = -CH_2-CH=CH-CH_3$) to give 1,1-bis[2-butenyl]cyclopropane (**7d**; 54%) whereas the analogous reaction with 3-methoxy-1-propyne instead of the Grignard reagent has been reported to lead to products of monoaddition and only traces of **7d**[6]. Further cyclopropanes obtained from the reaction of 1-alkynylmagnesium bromides of the type **6** with alkenyl- and alkynylzinc bromides (**2**) are listed below. It has to be noted that even in the case of a Grignard reagent **6** with a sterically hindered triple bond the reaction with allylzinc bromide affords a cyclopropane derivative (**7e**), albeit in low yield.



6 **2** **7**

	R^1	R^2	R^3	R^4	Yield [%] of **7**
a	$-CH_2-CH=CH_2$	H	CH_3	C_6H_5	62
b	$-CH_2-C(CH_3)=CH_2$	H	CH_3	C_6H_5	75
c	$-CH_2-C\equiv C-C_2H_5$	H	CH_3	C_6H_5	55
d	$-CH_2-CH=CH-CH_3$	H	H	CH_3	54
e	$-CH_2-CH=CH_2$	CH_3	CH_3		20
f	$-CH_2-C\equiv C-C_2H_5$	H	H	C_6H_5	46 [a]
g		H	CH_3	C_6H_5	42

[a] In this case, 2-phenoxymethyl-1-hepten-4-yne (**8**) is obtained as a side product in 10% yield.



8

1,1-Bis[2-pentynyl]-cyclopropane (**7f**) is more conveniently obtained in 65% yield by reaction of 3-bromo-1-propyne (**9**) with 2-pentynylzinc bromide. The analogous reaction of **9** with 2-methyl-2-propenylzinc bromide affords 1,1-bis[2-methyl-2-propenyl]-cyclopropane (**10**) in 68% yield.

7f **10**

The structures of all products obtained were confirmed by ^{1}H-N.M.R. spectroscopy and by microanalyses.

Preparation of Organozinc Reagents:

The preparations are carried out as described in Ref. [7].

Allylzinc Bromide (**2a**): Zinc (19.6 g, 0.30 g-atom) and allyl bromide (36.3 g, 0.30 mol) in dry tetrahydrofuran (150 ml) at 20° for 1 h.

0039-7881/78/1132-0838 $ 03.00

Table. Preparation of Substituted Cyclopropanes

Organozinc reagent	Substrate	Product	Molar ratio[a]	Reaction conditions	Yield[b] [%]	b.p./torr	Molecular formula[c]	^{1}H-N.M.R. (60 MHz, CCl_4/TMS)[d] δ [ppm]
2a	**1**	**3**[e]	3.75	1 h, 35°	37	103–105°/60	$C_{11}H_{18}O$ (166.2)	4.75–5.2 (m, 4H, $2CH_2$=); 5.35–6.25 (m, 2H, 2-CH=); 1.75–2.3 (m, 4H, 2-CH_2—); 0.3–0.6 (m, 2H, —CH_2—, 3-membered ring); 2.85–3.1 (m, 1H, CH—O—, 3-membered ring); 3.42 (q, 2H, —CH_2—O—); 1.15 (t, 3H, CH_3)
2a	**5**	**4**[e] (R = H)	2.5	3 h, 65°	37	103–105°/60	$C_{12}H_{18}$ (162.3)	4.7–5.2 (m, 6H, $3CH_2$=); 5.35–6.2 (m, 3H, 3-CH=); 1.8–2.3 (m, 6H, 3-CH_2—); −0.1–1.25 (m, 3H, —CH_2—CH, 3-membered ring)
2b	**5**	**4** (R = CH_3)	4.8	90 min, 65°	55	105–107°/12	$C_{15}H_{24}$ (204.3)	4.75 (m, 6H, $3CH_2$=); 1.73 (m, 9H, $3CH_3$); 1.85–2.45 (m, 6H, 3-CH_2—); 0–1 (m, 3H, —CH_2—CH, 3-membered ring)
2d	**6d**	**7d**[f]	3.75	24 h, 65°	54	107–109°/71	$C_{11}H_{18}$ (150.2)	1.60 (m, 6H, $2CH_3$); 5.48 (m, 4H, 2-CH=CH—); 1.91 (m, 4H, 2-CH_2—); 0.22 (s, 4H, —CH_2—CH_2—, 3-membered ring)[g]
2a	**6c**	**7c**	3.75	24 h, 65°	62	77–79°/68	$C_{10}H_{16}$ (136.2)	4.7–5.2 (m, 4H, $2CH_2$=); 5.35–6.15 (m, 2H, 2-CH=); 1.8–2.2 (m, 4H, 2-CH_2—); −0.2–1.0 (m, 3H, —CH_2—CH, 3-membered ring); 1.09 (d, 3H, CH_3, J = 5 Hz)
2b	**6c**	**7b**	3.75	24 h, 65°	75	107–109°/68	$C_{12}H_{20}$ (164.3)	4.72 (s, 4H, $2CH_2$=); 1.69 (s, 6H, $2CH_3$); 1.8–2.3 (m, 4H, 2-CH_2—); −0.1–1.0 (m, 3H, —CH_2—CH, 3-membered ring); 1.07 (d, 3H, CH_3, J = 5 Hz)
2f	**6c**	**7f**	3.75	24 h, 65°	55	113–115°/12	$C_{14}H_{20}$ (188.3)	0.4–1.5 (m, 11H, $3CH_3$ + —CH_2, 3-membered ring); 1.9–2.6 (m, 8H, 4-CH_2—); −0.09 (m, 1H, CH—, 3-membered ring)
2g	**6c**	**7g**[h]	4.0	24 h, 65°	42	83–85°/0.05	$C_{16}H_{24}$ (216.3)	0.45–2.5 [m, 16H, —CH_2—, 3-membered ring + 2CH—$(CH_2)_3$—, 6-membered ring]; 5.67 (m, 2H, —CH=CH—); 0.13 (m, 1H, CH—, 3-membered ring); −1.13 (d, 3H, CH_3, J = 4 Hz)
2a	**6e**	**7e**	3.75	24 h, 65°	20	88–90°/70	$C_{11}H_{18}$ (150.2)	4.75–5.2 (m, 4H, $2CH_2$=); 5.4–6.2 (m, 2H, 2-CH=); 2.11 (d, 4H, 2-CH_2—); 1.15 (s, 6H, $2CH_3$); 0.18 (s, 2H, CH_2, 3-membered ring)
2f	**6f**	**7f**[i]	2.5	20 h, 65°	46	108–110°/12	$C_{13}H_{18}$ (174.3)	1.11 (t, 6H, $2CH_3$); 2.20 (m, 4H, 2-CH_2—); 2.26 (t, 4H, 2-CH_2—, J = 2 Hz); 0.42 (s, 4H, 2-CH_2—, 3-membered ring)
2f	**9**	**7f**	3.75	24 h, 40°	65			
2b	**9**	**10**	3.75	2 h, 40°	68	88–90°/57	$C_{11}H_{18}$ (150.2)	4.75 (s, 4H, $2CH_2$=); 1.71 (s, 6H, $2CH_3$); 1.93 (s, 4H, 2-CH_2—); 0.35 (m, 4H, 2-CH_2—, 3-membered ring)

[a] Molar ratio RBr/acetylenic derivative.
[b] Yield of isolated product calculated from acetylenic derivative.
[c] All products gave satisfactory microanalyses: C, ±0.2; H, ±0.3.
[d] Recorded with a Perkin Elmer R-12 spectrometer (TMS as external reference for 3-membered ring).
[e] ^{13}C-N.M.R. (25.2 MHz/$CDCl_3$/TMS) (Varian XL-100 spectrometer):
3: δ = 116.4, 115.85 ($2CH_2$=); 136.75, 135.3 (2-CH=); 39.3, 33.8 (2-CH_2—); 24.7 (C cycle); 17.2 (—CH_2— cycle); 62.2 (O—CH cycle); 66.15 (—CH_2—O—); 15.2 ppm (CH_3).
4: δ = 116.0, 115.9, 114.2 ($3CH_2$=); 138.1, 136.65, 135.95 (3-CH=); 41.8, 35.6, 33.55 (3-CH_2—); 22.85 (C cycle); 17.0 (—CH_2— cycle); 22.45 ppm (CH— cycle).
[f] *Z*/*E* isomer mixture.
[g] Ref. [6].
[h] Mixture of diastereoisomers.
[i] We also isolated compound **10** (yield: 10%; b.p. 88–90°/0.05 torr).
^{1}H-N.M.R.: δ = 1.11 (t, 3H, CH_3); 2.65 (m, 2H, —CH_2—); 2.96 (m, 2H, ≡C—CH_2—C); 5.20 (m, 2H, CH_2=); 4.45 (s, 2H, —CH_2—O—); 6.7–7.4 ppm (m, 5H_{arom}).

2-Methyl-2-propenylzinc Bromide (**2b**): Zinc (19.6 g, 0.30 g-atom) and 3-bromo-2-methylpropene (40.5 g, 0.30 mol) in dry tetrahydrofuran (250 ml) at 0° for 3 h.

2-Butenylzinc Bromide (**2d**): Zinc (19.6 g, 0.30 g-atom) and 1-bromo-2-butene (40.5 g, 0.30 mol) in dry tetrahydrofuran (300 ml) at 0° for 4 h.

2-Pentynylzinc Bromide (**2f**): Zinc (19.6 g, 0.30 g-atom) and 1-bromo-2-pentyne (44 g, 0.30 mol) in dry tetrahydrofuran (280 ml) at −15° for 4 h.

2-Cyclohexenylzinc Bromide (**2g**): This reagent is prepared from zinc (14.4 g, 0.22 g-atom) and 3-bromocyclohexene (32.2 g, 0.2 mol) in dry tetrahydrofuran (200 ml) at −15° during 8 h, as indicated in Ref. [4].

Reaction of Organozinc Reagents with 1-Alkynes; General Procedure:

To the organozinc reagent, prepared as described above, the 1-alkyne (**1**, **9**) is added rapidly under the reaction conditions given in the Table. Then, the mixture is poured into dilute hydrochloric acid/crushed ice. After extraction with ether (3 × 100 ml), the

organic layer is neutralised with potassium carbonate, washed with water, dried with magnesium sulfate, and distilled.

Reaction of Organozinc Reagents with 1-Alkynylmagnesium Halides; General Procedure:

The Grignard reagents are prepared in tetrahydrofuran following a classical procedure: the 1-alkyne is added to ethylmagnesium bromide at 20° and then the reaction mixture is heated at 60° for 3 h. The product thus prepared is added rapidly to the organozinc reagent, prepared as described above, under the reaction conditions given in the Table. Hydrolysis and extraction are carried out as described above.

Received: January 23, 1978

[1] Y. Frangin, M. Gaudemar, *C. R. Acad. Sci. Ser. C* **278**, 885 (1974).
[2] Y. Frangin, M. Gaudemar, *C. R. Acad. Sci. Ser. C* **280**, 1389 (1975).
[3] Y. Frangin, E. Favre, M. Gaudemar, *C. R. Acad. Sci. Ser. C* **282**, 277 (1976).
[4] M. Bellassoued, Y. Frangin, M. Gaudemar, *Synthesis* **1977**, 205.
[5] Y. Frangin, M. Gaudemar, *J. Organometal. Chem.* **142**, 9 (1977).
[6] F. Bernadou, L. Miginiac, *J. Organometal. Chem.* **125/1**, 23 (1977).
[7] M. Gaudemar, *Bull. Soc. Chim. Fr.* **1962**, 974.

0039–7881/78/1132–0840 $ 03.00