Reactions of 1,4-enynes with the system CH_2I_2—Et_3Al

I. R. Ramazanov,[a] A. V. Yaroslavova,[a] U. M. Dzhemilev,[a] and O. M. Nefedov[b]*

[a] *Institute of Petrochemistry and Catalysis, Russian Academy of Sciences, 141 prosp. Oktyabrya, 450075 Ufa, Russian Federation. Fax: +7 (347 2) 84 2750. E-mail: iramazan@inbox.ru*
[b] *N. D. Zelinsky Institute of Organic Chemistry, Russian Academy of Sciences, 47 Leninsky prosp., 119991 Moscow, Russian Federation. Fax: +7 (499) 135 5328*

Reactions of alk-1-en-4-ynes with an excess of the system CH_2I_2—Et_3Al give 1-cyclopropylmethyl-1,2-diethylcyclopropanes. A decrease in the amount of either component of the system to two equivalents results in cyclopropanation of the double bond only. Under such conditions, conjugated enynes yield a complex mixture of products, while conjugated diynes are inert to the system CH_2I_2—Et_3Al.

Key words: cyclopropanation, 1,3-enynes, 1,3-diynes, 1,4-enynes, diiodomethane, triethylaluminum.

Reactions of unsaturated compounds with the system CH_2I_2—Zn/Cu have found wide use in the synthesis of cyclopropane derivatives.[1,2] Recently, we have proposed the novel system CH_2I_2—R_3Al that favors transformations of alkynes and allenes into substituted cyclopropanes[3,4] and spiropentanes,[5] respectively. In the present work, we further studied the behavior of enynes and diynes in reactions with CH_2I_2—R_3Al.

Preliminary experiments revealed that substituted vinylacetylenes (2-methyloct-1-en-3-yne and 1-ethynylcyclohexene) are completely consumed in reactions with CH_2I_2 and Et_3Al (the molar ratio [1,3-enyne] : [CH_2I_2] : [Et_3Al] is 1 : 4 : 6) at room temperature for 30 h to give a complex, difficult-to-identify mixture of oligomeric hydrocarbons containing no cyclopropane derivatives. At the same time, substituted 1,3-diynes (deca-4,6-diyne and hexadeca-7,9-diyne) proved to be inert to this system of reagents.

In contrast to 1,3-enynes and 1,3-diynes, reactions of allylacetylenes (non-1-en-4-yne and dec-1-en-4-yne) with the system CH_2I_2—Et_3Al under the above conditions followed by deuterolysis selectively yielded monodeuterated products of the conjectural formulas $C_{15}H_{27}D$ and $C_{16}H_{29}D$, respectively (GC-MS data, Scheme 1). Based on known experimental data,[3—5] we assumed that the reaction products are dicyclopropylmethanes **1a** and **1´a** or **1b** and **1´b** containing mono- and tetrasubstituted cyclopropane rings. The ^{13}C NMR spectra of the deuterated products show two high-field pairs of signals for the groups CH_2D and CH_3 of the deuteroethyl and ethyl fragments. This suggests the simultaneous formation of regioisomers **1a** and **1´a** or **1b** and **1´b** in equal proportions, which is evident from the integral intensities of the signals for the carbon atoms (C(9) and C(26) for **1a** and **1´a** and C(10) and C(28) for **1b** and **1´b**). At the same time, we ruled out the formation of *cis*- and *trans*-isomers since the ^{13}C NMR spectra contain no double signals for the asymmetric C atoms and their neighbors as observed in the spectrum of a product obtained from dec-5-yne.[4] The signals in the NMR spectra of compounds **1a**, **1b**, **1´a**, and **1´b** were assigned from COSY, HSQC, and HMBC data, as well as by comparison of their spectra with those of 1,2-dibutyl-1,2-diethylcyclopropane obtained earlier.[4] The presence of signals at δ 4.32 and 4.49 for the methylene group in the ^{13}C NMR spectrum of a mixture of regioisomers **1a** and **1´a** and a multiplet at δ 0.1—0.4 in their ^1H NMR spectrum suggests that these compounds contain a monosubstituted or 1,1-disubstituted cyclopropane ring. The APT and DEPT 135 spectrum exhibits signals for three CH_3, one CH, and eleven CH_2 groups and signals for two quaternary carbon atoms. The HMBC experiment revealed couplings of the methylene H atoms of the tetrasubstituted cyclopropane ring with the methylene C atoms of the cyclopropylmethyl fragment, the C atoms of the α-methylene group of the butyl substituent, and two quaternary C atoms. Apparently, the nonequivalence of the CH_2 groups in the monosubstituted cyclopropane ring results from their diasteretopic character. Available spectroscopic data are insufficient for making a conclusion about the stereoconfigurations of compounds **1a** and **1´a** or **1b** and **1´b**. In connection with this, it is interesting to note the difference of 1,4-enynes from symmetrical dialkylacetylenes (oct-4-yne and dec-5-yne), which react with the system Et_3Al—CH_2I_2 to give *cis*- and *trans*-isomers in a ratio of ~1 : 1.

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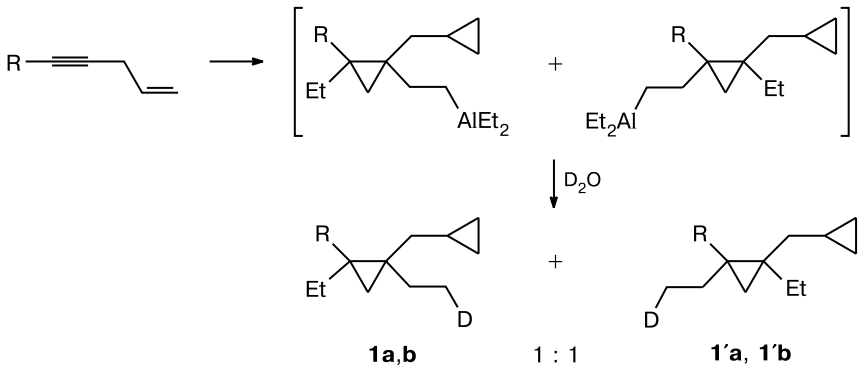
Scheme 1



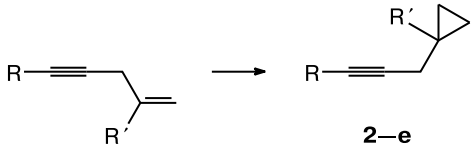
R = *n*-C_4H_9 (**a**), *n*-C_5H_{11} (**b**)

Reagents, conditions, and yields: CH_2I_2 (4 equiv.), Et_3Al (6 equiv.), CH_2Cl_2, ~20 °C, 30 h; 83% (**1a** + **1′a**), 77% (**1b** + **1′b**).

Earlier,[4] we have demonstrated that the stereoconfiguration of tetrasubstituted cyclopropane is formed in the transition state during the rearrangement of 1,1-disubstituted cyclopropane and depends on the size of substituents at the triple bond of acetylenes. When the substituents are close in size to each other and to the ethyl group, one can expect that the rearrangement will be nonstereoselective and yield both *cis*- and *trans*-isomers. Otherwise (as, *e.g.*, in the case of oct-2-yne), only one stereoisomer is produced.[3] Therefore, the formation of only one stereoisomer from the alkylallylacetylenes studied is indicative of a large difference in size between the substituents at the triple bond. Based on this, we assumed that alkylallylacetylenes are initially transformed into alkyl(cyclopropylmethyl)acetylenes.

To identify possible intermediates, we studied the time dependence of the composition of the reaction products and found that, indeed, the first step involves selective cyclopropanation of the double bond in the starting 1,4-enyne and the formation of (cyclopropylmethyl)-acetylenes **2a**—**c** (Scheme 2). Therefore, the double bond is more nucleophilic than the triple bond in a reaction with a methylenating Al intermediate. Methallylacetylenes were even more reactive in this reaction than allylacetylenes (the half-conversion time of 2-methylnon-1-en-4-yne is about half that of non-1-en-4-yne), which is consistent with the concept of the electrophilic nature of the methylenating Al intermediate. The reactivities were compared using the competitive reaction method. For the ratio [1,4-enyne] : [CH_2I_2] : [Et_3Al]=1 : 2 : 2, (cyclopropylmethyl)acetylenes **2a**—**e** were selectively obtained in 43—58% yields. When the reaction time is extended to 6 h, the final reaction mixture contains, along with the nonconsumed alkylallylacetylene, tetrasubstituted cyclopropanes **1a** and **1a′** or **1b** and **1′b** in 7—9% yields (GLC data).

Scheme 2



Compound	R	R′	Yield (%)
a	*n*-C_4H_9	H	45
b	*n*-C_5H_{11}	H	43
c	*n*-C_4H_9	Me	49
d	Ph	H	51
e	Ph	Me	58

Reagents and conditions: CH_2I_2 (2 equiv.), Et_3Al (2 equiv.), CH_2Cl_2, ~20 °C, 6 h (R = allyl) and 3 h (R = methallyl).

Apparently, the next steps of the reactions of (cyclopropylmethyl)acetylenes with the system CH_2I_2—Et_3Al follow the pattern proposed earlier for similar reactions with monoacetylenes.[4]

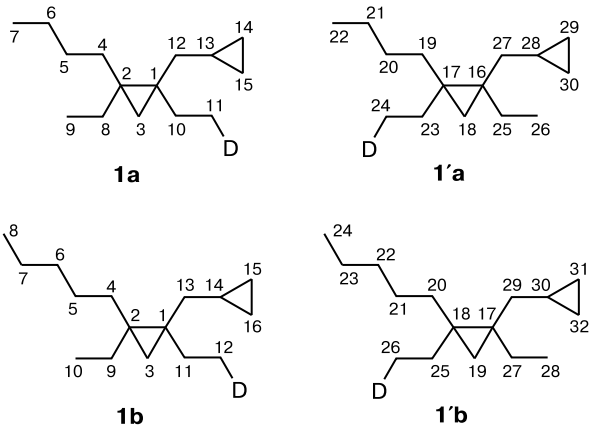
To sum up, we discovered that the system CH_2I_2—Et_3Al affords cyclopropane derivatives in reactions with 1,4-enynes only, not with 1,3-enynes or 1,3-diynes.

Experimental

1,3-Enynes (1-ethynylcyclohexene and 2-methyloct-1-en-3-yne) were prepared by dehydration of appropriate propargylic alcohols with $POCl_3$ (see Ref. 6). 1,3-Diynes (deca-4,6-diyne and hexadeca-7,9-diyne) were prepared by the CuCl-catalyzed oxidative Glaser coupling of terminal acetylenes under the action of atmospheric oxygen. 1,4-Enynes (non-1-en-4-yne, dec-1-en-4-yne, 2-methylnon-1-en-4-yne, 5-phenylpent-1-en-4-yne, and 2-methyl-5-phenylpent-1-en-4-yne) were prepared by cross-coupling of magnesium acetylenides with allyl bromide or methallyl bromide in THF in the presence of catalytic amounts of CuCl.[7] Reactions with organoaluminum compounds were car-

ried out under argon. Dichloromethane was distilled over P_2O_5 before use. Reaction products were analyzed on a Carlo Erba chromatograph (Ultra-1 glass capillary column (Hewlett Packard), 25 000×0.2 mm, flame ionization detector, programmed thermostat temperature 50—170 °C, helium as a carrier gas). Mass spectra were measured on a Finnigan 4021 instrument (ionization potential 70 eV, ionization chamber temperature 200 °C). Elemental analysis was carried out on a Carlo Erba 1106 analyzer. ^1H and ^{13}C NMR spectra were recorded on a Bruker Avance 400 spectrometer (400 (^1H) and 100 MHz (^{13}C)) with $SiMe_4$ and $CDCl_3$, respectively, as the internal standards. The yields of the products were determined by gas chromatography with *n*-undecane and *n*-hexadecane as the internal standards.

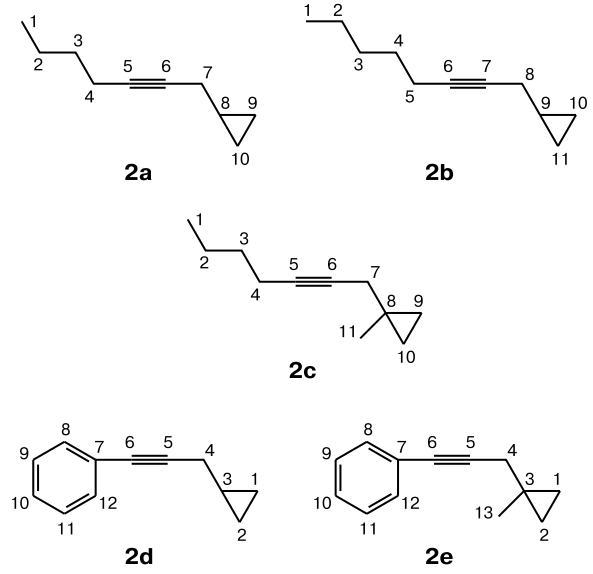
Reactions of 1,4-enynes with the system Et_3Al—CH_2I_2 (general procedure). A 50-mL glass reaction vessel immersed in an ice bath and equipped with a magnetic stirring bar was charged in an inert atmosphere at 0 °C with CH_2Cl_2 (15 mL), an enyne (2 mmol), CH_2I_2 (0.64 mL, 8 mmol), and Et_3Al (12 mmol). The mixture was stirred at ~20 °C for 30 h, cooled on the ice bath, and subjected to deuterolysis with D_2O (3 mL). The precipitate of $Al(OD)_3$ that formed was filtered off. The product from the aqueous layer was extracted with diethyl ether (3×10 mL). The organic layers were combined, washed with a saturated solution of $NaHCO_3$, and dried over $CaCl_2$. The solvent was removed *in vacuo* and the residue was distilled to give compounds **1a**, **1a´**, **1b**, and **1b´**.



A mixture of 2-butyl-1-cyclopropylmethyl-1-deuteroethyl-2-ethylcyclopropane (1a) and 2-butyl-1-cyclopropylmethyl-2-deuteroethyl-1-ethylcyclopropane (1´a). Yield 83%, b.p. 68—72 °C (1 Torr). Found (%): C, 86.21. $C_{15}H_{27}D$. Calculated (%): C, 86.04. ^{13}C NMR, δ: 4.32 (2 C, C(15) and C(30)); 4.49 (2 C, C(14) and C(29)); 9.11 (2 C, C(13) and C(28)); 10.81 (t, C(24), J = 19 Hz); 10.95 (t, C(11), J = 19 Hz); 11.13 (C(9)); 11.22 (C(26)); 14.19 (2 C, C(7) and C(22)); 23.28 (2 C, C(6) and C(21)); 24.48 (2 C, C(3) and C(18)); 24.61 (2 C, C(10) and C(25)); 24.84 (2 C, C(8) and C(23)); 29.30 (2 C, C(5) and C(20)); 29.91 (2 C, C(2) and C(17)); 30.83 (2 C, C(1) and C(16)); 35.81 (2 C, C(12) and C(27)). MS, m/z (I_{rel} (%)): 209 $[M]^+$ (1), 180 $[M - C_2H_5]^+$ (10), 154 (18), 152 (11).

A mixture of 1-cyclopropylmethyl-1-deuteroethyl-2-ethyl-2-pentylcyclopropane (1b) and 1-cyclopropylmethyl-2-deuteroethyl-1-ethyl-2-pentylcyclopropane (1´b). Yield 77%, b.p. 80—84 °C (1 Torr). Found (%): C, 86.31. $C_{16}H_{29}D$. Calculated (%): C, 86.02. ^{13}C NMR, δ: 4.30 (2 C, C(16) and C(31)); 4.45 (2 C, C(15) and C(32)); 9.09 (2 C, C(14) and C(30)); 10.81 (t, C(26), J = 19 Hz); 10.97 (t, C(12), J = 19 Hz); 11.20 (C(10)); 11.25 (C(28)); 14.14 (2 C, C(8) and C(24)); 22.79 (2 C, C(7) and C(23)); 24.43 (2 C, C(3) and C(19)); 24.55 (2 C, C(9) and C(25)); 24.72 (2 C, C(11) and C(27)); 26.65 (2 C, C(5) and C(21)); 29.86 (2 C, C(2) and C(18)); 30.89 (2 C, C(1) and C(17)); 32.48 (2 C, C(6) and C(22)); 35.68 (2 C, C(13) and C(29)). MS, m/z (I_{rel} (%)): 223 $[M]^+$ (1), 194 $[M - C_2H_5]^+$ (10), 168 (14), 152 (12).

Synthesis of (cyclopropylmethyl)acetylenes 2a—e (general procedure). A 50-mL glass reaction vessel immersed in an ice bath and equipped with a magnetic stirring bar was charged in an inert atmosphere at 0 °C with CH_2Cl_2 (15 mL), an enyne (2 mmol), CH_2I_2 (0.32 mL, 4 mmol), and Et_3Al (4 mmol). The mixture was stirred for 3 h for methallylacetylenes and for 6 h for allylacetylenes. Then the reaction mixture was cooled on the ice bath, diluted with hexane (50 mL), and treated with aqueous 15% HCl. The product from the aqueous layer was extracted with diethyl ether (3×10 mL). The organic layers were combined, washed with a saturated solution of $NaHCO_3$ and dried over $CaCl_2$. The solvent was removed *in vacuo* and the residue was distilled to give compounds **2a**—**e** as oily products.



1-Cyclopropylhept-2-yne (2a). Yield 45%, b.p. 65—69 °C (15 Torr). Found (%): C, 88.01; H, 11.75. $C_{10}H_{16}$. Calculated (%): C, 88.16; H, 11.84. ^1H NMR, δ: 0.1—0.7 (m, 5 H, C(9)H_2, C(10)H_2, C(8)H); 0.89 (t, 3 H, C(1)H_3, J = 6.7 Hz); 1.1—1.9 (m, 4 H, C(3)H_2, C(4)H_2); 2.0—2.7 (m, 4 H, C(4, 7)H_2). ^{13}C NMR, δ: 3.64 (2 C, C(9), C(10)); 9.63 (C(8)); 13.60 (C(1)); 18.46 (C(4)); 21.97 (C(7)); 22.88 (C(2)); 31.29 (C(3)). MS, m/z (I_{rel} (%)): 136 $[M]^+$ (9), 121 $[M - CH_3]^+$ (5), 107 $[M - C_2H_5]^+$ (16), 94 (22), 93 $[M - C_3H_7]^+$ (43), 91 (33), 79 (100).

1-Cyclopropyloct-2-yne (2b). Yield 43%, b.p. 72—74 °C (10 Torr). Found (%): C, 87.80; H, 12.14. $C_{11}H_{18}$. Calculated (%): C, 87.93; H, 12.07. ^1H NMR, δ: 0.1—0.7 (m, 5 H, C(10)H_2, C(11)H_2, C(9)H); 0.88 (t, 3 H, C(1)H_3, J = 6.8 Hz); 1.1—1.8 (m, 6 H, C(2)H_2, C(3)H_2, C(4)H_2); 2.0—2.4 (m, 4 H, C(5)H_2, C(8)H_2). ^{13}C NMR, δ: 3.67 (2 C, C(10), C(11)); 9.60 (C(8)); 13.96 (C(1)); 18.45 (C(5)); 22.14 (C(2)); 28.84 (s, C(4)); 31.09 (C(3)). MS, m/z (I_{rel} (%)): 150 $[M]^+$ (1), 135 $[M - CH_3]^+$ (2), 121 $[M - C_2H_5]^+$ (6), 107 $[M - C_3H_7]^+$ (19), 94 (20), 93 $[M - C_4H_9]^+$ (40), 91 (34).

1-(Hept-2-yn-1-yl)-1-methylcyclopropane (2c). Yield 49%, b.p. 81—84 °C (15 Torr). Found (%): C, 87.68; H, 11.88. $C_{11}H_{18}$. Calculated (%): C, 87.93; H, 12.07. ^{1}H NMR, δ: 0.1—0.6 (m, 4 H, C(9)H_2, C(10)H_2); 0.91 (s, 3 H, C(1)H_3, J = 7.2 Hz); 1.12 (s, 3 H, C(11)H_3); 1.3—1.7 (m, 4 H, C(2)H_2, C(3)H_2); 2.1—2.3 (m, 4 H, C(4)H_2, C(7)H_2). ^{13}C NMR, δ: 11.91 (2 C, C(9), C(10)); 13.60 (C(1)); 18.36 (C(4)); 22.94 (C(2)); 23.21 (C(11)); 28.49 (C(7)); 31.29 (C(3)).

3-Cyclopropyl-1-phenylprop-1-yne (2d). Yield 51%, b.p. 61—65 °C (1 Torr). Found (%): C, 92.05; H, 7.83. $C_{12}H_{12}$. Calculated (%): C, 92.26; H, 7.74. ^{1}H NMR, δ: 0.2—0.9 (m, 4 H, C(1)H_2, C(2)H_2); 2.55 (s, 2 H, C(4)H_2); 7.1—8.0 (m, Ph). ^{13}C NMR, δ: 3.87 (2 C, C(1), C(2)); 9.47 (C(3)); 23.57 (C(4)); 127.67 (C(10)); 128.32 (2 C, C(9), C(11)); 131.77 (2 C, C(8), C(12)). MS, m/z (I_{rel} (%)): 156 $[M]^+$ (50), 155 $[M - 1]^+$ (30), 141 $[M - CH_3]^+$ (28), 128 (66), 115 (100).

3-(1-Methylcyclopropyl)-1-phenylprop-1-yne (2e). Yield 58%, b.p. 77—80 °C (1 Torr). Found (%): C, 91.56; H, 8.13. $C_{13}H_{14}$. Calculated (%): C, 91.71; H, 8.29. ^{1}H NMR, δ: 0.3—0.8 (m, 4 H, C(1)H_2, C(2)H_2); 1.23 (s, 3 H, C(13)H_3); 2.46 (s, 2 H, C(4)H_2); 7.1—7.9 (m, Ph). ^{13}C NMR, δ: 12.14 (2 C, C(1), C(2)); 14.74 (C(3)); 23.28 (C(13)); 29.14 (C(4)); 127.64 (C(10)); 128.29 (2 C, C(9), C(11)); 131.77 (2 C, C(8), C(12)). MS, m/z (I_{rel} (%)): 170 $[M]^+$ (23), 155 $[M - CH_3]^+$ (41), 141 $[M - C_2H_5]^+$ (39), 128 (66), 115 (100).

Reactions of 1,3-enynes (1-ethynylcyclohexene and 2-methyloct-1-en-3-yne) and 1,3-diynes (deca-4,6-diyne and hexadeca-7,9-diyne) with the system $Et_3Al—CH_2I_2$ were carried out as described above for 1,4-enynes.

Comparison of the relative reactivities of 2-methylnon-1-en-4-yne and non-1-en-4-yne by the competitive reaction method. A 50-mL glass reaction vessel immersed in an ice bath and equipped with a magnetic stirring bar was charged in an inert atmosphere at 0 °C with CH_2Cl_2 (15 mL), *n*-hexadecane (1 mmol), 2-methylnon-1-en-4-yne (1 mmol), non-1-en-4-yne (1 mmol), CH_2I_2 (0.32 mL, 4 mmol), and Et_3Al (4 mmol). The hydrolysis products were analyzed by gas chromatography 10, 15, 30, 60, 90, 120, 180, 240, and 480 min after the addition of the reagents. The bath temperature was maintained at 0 °C throughout the experiment.

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