Cross-Cyclizations of Alkylacetylenes to Cyclobutane Compounds via Vinyl Cations as Intermediates

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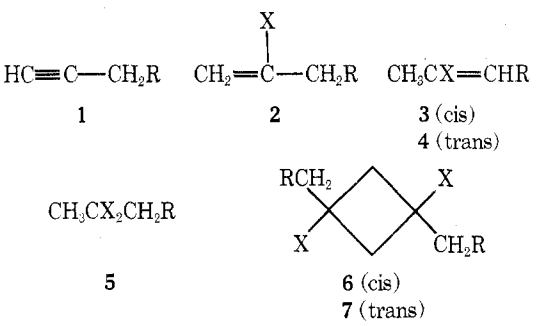
Reactions of anhydrous hydrogen chloride with mixtures of propyne and 1-butyne, of propyne and 1-pentyne, and of 1-butyne and 1-pentyne produced the corresponding 1,3-dialkyl-1,3-dichlorocyclobutane cross-cyclization products along with the addition and cyclodimerization products of the individual acetylenes.

In previous work we have shown that liquid-phase reactions of anhydrous hydrogen chloride[1] or hydrogen bromide[2,3] with the alkylacetylenes **1a–d** produce the corresponding cyclodimerization products **6** and **7**, along with the respective simple addition products **2–5**. The 1,3-dialkyl-1,3-dihalocyclobutanes **6** and **7**, which are thus easily



	a[1]	b[1]	c[1]	d[1]	e[2]	f[3]	g[3]	h[3]
R	H	CH_3	C_2H_5	C_3H_7	H	CH_3	C_2H_5	C_3H_7
X	Cl	Cl	Cl	Cl	Br	Br	Br	Br

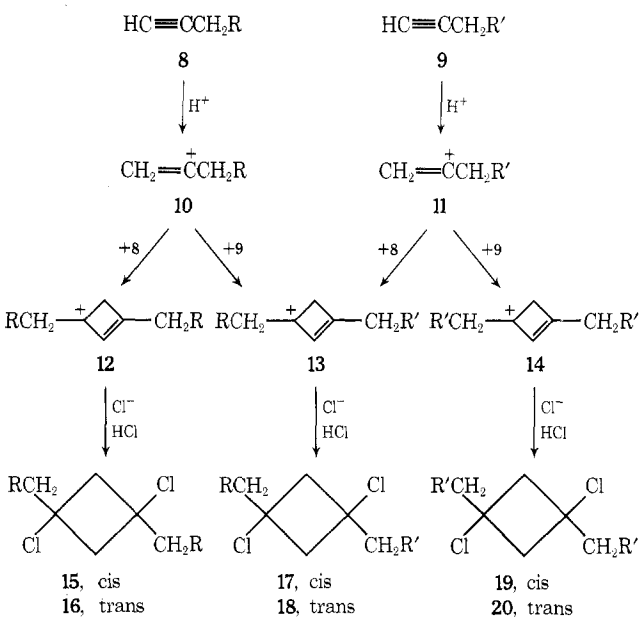
accessible in one-step reactions, are convenient starting materials for the short-path synthesis of other cyclobutane and cyclobutene compounds. Dehalogenation of **7e**[4,5] and of **7f**[3] produced the corresponding 1,3-dialkylbicyclo[1.1.0]butanes; reduction of **7e** yielded the stereoisomeric 1,3-dimethylcyclobutanes[6] and dehydrobromination of **7e** afforded 1,3-dimethylenecyclobutane and 1-methylene-3-methylcyclobutene.[7,8] The latter was used as a versatile starting material for the synthesis of a number of halogenated 1,3-dimethylcyclobutene and cyclobutane compounds.[8]

The scope of the synthetic utility of these 1,3-dialkyl-1,3-dihalocyclobutanes (**6, 7**) was thus far restricted, however, by the fact that cyclodimerizations of alkylacetylenes (**1**) can only afford cyclobutane derivatives which have two identical alkyl groups in 1,3 position. Since such cyclizations occur by cycloadditions of vinyl cations (e.g., **10** or **11**) to acetylenic substrates, it seemed possible that reactions of HCl with mixtures of two different acetylenes (**8** and **9**) could lead to cross-cyclizations by cycloaddition of the two vinyl cations **10** and **11** to the corresponding "foreign" acetylenes **9** and **8**, respectively. The products of such cross-cyclizations would be 1,3-dialkyl-1,3-dichlorocyclobutanes (**17** and **18**) bearing two different alkyl groups.

In the present paper we report about the reaction of anhydrous hydrogen chloride with mixtures of propyne and 1-butyne, of propyne and 1-pentyne, as well as of 1-butyne and 1-pentyne. The reactions were carried out in the liquid phase at ambient temperatures and afforded in each case liquid product mixtures. GLC analysis showed that these product mixtures contained the respective addition (**2–5**) and cyclodimerization products (**6, 7**) of the individual acetylenes **8** and **9**[9] as well as two additional components. The latter were in each case isolated as colorless liquids by preparative GLC and identified as the respective cross-cyclization products **17** and **18** on the basis of the following spectral data.

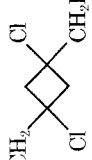
The mass spectra (Table I) exhibited the expected molecular ion triplets and a number of fragment ions which are typical for 1,3-dialkyl-1,3-dihalocyclobutanes.[1,10,11] These are the ions $(M - Cl)^+$, $(M - HCl)^+$, $(M - Cl_2)^+$, $(M - HCl_2)^+$ and the fragments $(C_3H_4ClR)^+$ and $(C_3H_4ClR')^+$ which result from bisection of the cyclobutane ring. The ^1H NMR spectra of the cis isomers **17** showed AA'BB' quartets for the signals of the methylene groups in the cyclobutane ring; the corresponding CH_2 groups in the trans isomers **18** appeared as singlet signals (Table II). This is in agreement with the ^1H NMR spectra of other stereoisomeric 1,3-dialkyl-1,3-dihalocyclobutanes.[1,10,11]

The quantitative results are summarized in Table III. The amounts of the total (i.e., homo- and cross-) cyclization products ranged from 9 to 35%. The highest selectivities of cyclization products (30 and 35%, respectively) were obtained from the reactions of equimolar mixtures of propyne–butyne and butyne–pentyne with equivalent amounts of hydrogen chloride. The use of excess hydrogen chloride led to a noticeable decrease of the cyclization reactions: reaction of HCl, butyne, and pentyne produced 35% of the combined 1,3-dialkyl-1,3-dichlorocyclobutanes when the reactants were applied in a molar ratio of 2:1:1, while a reactant ratio of 20:1:1 yielded only 10% of cyclic products.



	a	b	c
R	H	H	CH_3
R'	CH_3	C_2H_5	C_2H_5

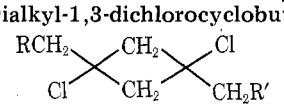
Table I. Mass Spectroscopic Data of *trans*-1,3-Dialkyl-1,3-dichlorocyclobutanes[a]



R	R'	Molecular ions	Rel abundances of corresponding ions[b]					
			M^+	$(M - Cl)^+$	$(M - HCl)^+$	$(M - CH_2Cl)^+$	$(M - Cl_2)^+$ $(M - HCl_2)^+$	$(C_3H_4ClR')^+$
H	CH_3	170, 168, 166	12, 65, 100	1037, 3289	2365, 6687	5665, 17 510	7013 9623	11 091, 29 870
H	C_2H_5	184, 182, 180	12, 67, 100	4168, 12 867	2136, 3148	11 444, 35 477	4666 30 328	90 367, 284 655
CH_3	C_2H_5	198, 196, 194	21, 63, 100	1012, 3284	886, 1771	5301, 16 718	1898 17 533	16 738, 46 350
								26 323, 123 351
								34 641, 114 464
								12 875, 42 488

[a] The mass spectra of the corresponding cis isomers showed the same ions, albeit with different intensities. [b] Based on the lowest molecular weight molecular ion as 100.

Table II. Parameters of ^1H NMR Spectra of 1,3-Dialkyl-1,3-dichlorocyclobutanes



R	R'	Isomer	Chemical shifts[a] of CH_2 groups in the ring, ppm
H	CH_3	Cis	2.95 (m)[b]
H	CH_3	Trans	2.87 (s)
H	C_2H_5	Cis	2.94 (m)[c]
H	C_2H_5	Trans	2.87 (s)
CH_3	C_2H_5	Cis	2.86 (m)[d]
CH_3	C_2H_5	Trans	2.82 (s)

[a] In CCl_4 as solvent, using Me_4Si as internal standard. [b] AA'BB' spin system (J_{AB} = 15 Hz, δ_A 2.71, δ_B 3.18) which is further split due to diagonal spin coupling of ca. 2 Hz. [c] Same as *b* with J_{AB} = 15 Hz, δ_A 2.70, δ_B 3.18, and diagonal coupling ca. 2 Hz. [d] Same as *b* with J_{AB} = 15 Hz, δ_A 2.65, δ_B 3.07, and diagonal coupling ca. 2 Hz.

Of the possible stereoisomers, the *trans*-1,3-dialkyl-1,3-dichlorocyclobutanes were always formed predominantly with selectivities ranging between 79 and 88%. The amounts of the cross-cyclization products (**17, 18**) were always approximately equal to the sum of the homocyclization products (**15, 16, 19, 20**) of the individual alkylacetylenes.

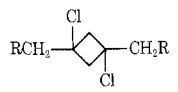
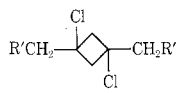
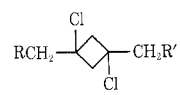
The quantitative results in Table III allow some conclusions concerning the relative reactivities of the alkylacetylenes applied: 1-butyne and 1-pentyne showed almost equal reactivities (column E, Table III), while propyne was considerably less reactive than either 1-butyne (column A, Table III) or 1-pentyne (column C, Table III) both in the HCl addition and in the cyclodimerization reactions. This is probably indicative of different rates of protonation of propyne on one hand and of butyne or of pentyne on the other hand. By contrast, it appears that in the cycloalkylation reactions, the vinyl cations which were formed in these experiments do not discriminate between the alkylacetylene from which they were derived and the corresponding "foreign" alkylacetylene, since, as mentioned above, the sum of homocyclization products was approximately equal to the sum of the cross-cyclization products, no matter whether pairs of substrates exhibiting similar or dissimilar reactivities were applied.

Experimental Section

Analytical Methods. The ^1H NMR spectra were recorded on a Varian-A-60, the ir spectra on a Beckman IR-8, and mass spectra on a Varian MAT CH-5 instrument. GLC analyses were carried out on a Varian Aerograph 1400-1 instrument, using the following conditions: column 5 m, 5 mm i.d., 5% nitrile silicone oil XE-60 on Chromosorb G; 24 ml N_2/min; 60–160 °C at 2 °C/min; injection port 180 °C. Preparative GLC was carried out on a Perkin-Elmer F-21, column 15 ft, 0.375 in. i.d., 5% Carbowax 20M on Chromosorb G. Conditions varied with the nature of the feed material.

General Procedure for the Reaction of Anhydrous Hydrogen Chloride with Alkylacetylenes. The reactions were carried out in thick-walled (3.5 mm) sealed glass tubes at ambient temperatures. Liquid reactants were directly introduced into the glass tube, while gaseous reactants, including anhydrous HCl, were condensed into the cooled (liquid air cooling) tube via a vacuum line system. The frozen reaction mixture was then evacuated, and the tube was sealed and transferred into a water bath which was kept at ambient temperatures. After the reaction was over, the tube was again cooled with liquid air and then opened. The unreacted gases were allowed to distill off via a drying tower while the tube was gradually warmed up from −70 to −10 °C in a cold bath. The crude reaction products were immediately analyzed by GLC and subsequently distilled in order to gain fractions in which the cross-cyclization products (**17, 18**) were enriched. These distillations

Table III. Typical Product Distributions from the Reactions xHCl + yHC≡C–CH_2R + zHC≡C–CH_2R'

Column		A	B	C	D	E	F
R; R′		H; CH_3	H; CH_3	H; C_2H_5	H; C_2H_5	CH_3; C_2H_5	CH_3; C_2H_5
x:y:z		2:1:1	4:3:1	2:1:1	4:3:1	2:1:1	20:1:1
Products, mol %[a]							
CH_2=C(Cl)CH_2R		11.2	17.3	7.6	17.2	7.8	
CH_3CCl=CHR						11.7	
$CH_3CCl_2CH_2R$		9.8	24.0	10.0	33.7	14.2	47.1
CH_2=C(Cl)CH_2R'		8.8	4.6	23.6	16.4	18.6	
CH_3CCl=CHR′		20.6	15.4				0.5
$CH_3CCl_2CH_2R'$		23.1	18.8	28.4	21.9	13.2	42.9
	cis	0.4	1.2	0.4	0.6	1.9	0.5
	trans	1.7	4.4	2.6	2.9	9.1	2.3
	cis	1.5	0.6	1.5	0.3	1.0	0.3
	trans	9.3	2.8	10.2	1.3	7.2	1.7
	cis	2.0	2.0	2.0	1.1	2.6	0.7
	trans	11.6	8.9	13.7	4.6	12.7	4.0
Molar ratios of							
R:R′ linear adducts		1:2.5	1:0.9	1:3.0	1:0.8	1:1.1	1:1.2
R:R′ cycloadducts		1:5.0	1:0.6	1:3.9	1:0.5	1:0.8	1:0.8
Homo-:cross-cyclizations		1:1.05	1:1.2	1:1.07	1:1.1	1:0.8	1:1

[a] Determined by GLC analysis, using the specific response factors of the individual compounds.

were carried out under mild conditions, i.e., low temperatures and reduced pressure. Partial fractionation was achieved by applying a series of receivers at different temperatures (0, −40, −78 °C).

Reaction of Anhydrous Hydrogen Chloride and an Equimolar Mixture of Propyne and 1-Butyne. A mixture of 12.8 g (0.35 mol) of hydrogen chloride, 7.1 g (0.18 mol) of propyne, and 9.5 g (0.18 mol) of 1-butyne was allowed to react at ambient temperatures for 20 days in a 350-ml glass tube. After removal of unreacted gases, 22.5 g of a reddish-brown, mobile liquid was obtained. The combined crude products (62.8 g) of three reactions were distilled and the fraction (15.1 g) obtained by distillation at ambient temperatures at 0.1 Torr in a receiver at −40 °C was submitted to preparative GLC (column temperature 90 °C, injection port 150 °C, 110 ml N_2/min).

***trans*-1,3-Dichloro-1-ethyl-3-methylcyclobutane (18a):** bp 164 °C; n^{20}D 1.4576; ^{1}H NMR (CCl_4, Me_4Si) 1.02 (t), 2.05 (q), J = 7 Hz, 1.91 (s), 2.87 ppm (s); ir (neat) 2970, 2940, 2880, 1460, 1420, 1380, 1290, 1270, 1165, 1120, 1090, 1020, 1000, 960, 930, 865, 800, 725 cm^{-1}.

Anal. Calcd for $C_7H_{12}Cl_2$: C, 50.32; H, 7.24; Cl, 42.44. Found C, 51.00; H, 7.38; Cl, 41.73.

***cis*-1,3-Dichloro-1-ethyl-3-methylcyclobutane (17a):**[12] ^{1}H NMR (CCl_4, Me_4Si) 1.01 (t), 1.85 (q), J = 7 Hz, 1.70 (s), 2.95 ppm (AA′BB′ system; see Table II).

Reaction of Anhydrous Hydrogen Chloride with an Equimolar Mixture of Propyne and 1-Pentyne. A mixture of 12.8 g (0.35 mol) of hydrogen chloride, 7.1 g (0.18 mol) of propyne, and 12.0 g (0.18 mol) of 1-pentyne was allowed to react for 23 days in a 350-ml glass tube. The crude product (24.7 g) was a reddish-brown, mobile liquid. The combined products (64 g) of three reactions were distilled and the fraction (10.3 g) boiling at 30–32 °C (0.07 Torr), collected at 0 °C, was submitted to preparative GLC (column temperature 100 °C, injection port 160 °C, 120 ml N_2/min).

***trans*-1,3-Dichloro-1-methyl-3-propylcyclobutane (18b):** bp 183 °C; n^{20}D 1.4579; ^{1}H NMR (CCl_4, Me_4Si) 0.97 (t, J = 6 Hz), 1.20–2.18 (m), 1.87 (s), 2.87 ppm (s); ir (neat) 2970, 2940, 2880, 2840, 1470, 1420, 1380, 1310, 1275, 1250, 1170, 1130, 1105, 1030, 950, 905, 810, 735 cm^{-1}.

Anal. Calcd for $C_8H_{14}Cl_2$: C, 53.06; H, 7.79; Cl, 39.15. Found: C, 53.75; H, 8.00; Cl, 38.46.

***cis*-1,3-Dichloro-1-methyl-3-propylcyclobutane (17b):**[12] ^{1}H NMR (CCl_4, Me_4Si) 0.95 (t, J = 6 Hz), 1.17–2.15 (m), 1.67 (s), 2.94 ppm (AA′BB′ system; see Table II).

Reaction of Anhydrous Hydrogen Chloride with an Equimolar Mixture of 1-Butyne and 1-Pentyne. A mixture of 18.2 g (0.5 mol) of hydrogen chloride, 13.5 g (0.25 mol) of 1-butyne, and 16.9 g (0.25 mol) of 1-pentyne was allowed to react for 26 days in a 350-ml glass tube to yield 46 g of a reddish-brown, mobile liquid. The combined products (82 g) of two reactions were distilled and the fraction (18.3 g) boiling at 34–37 °C (0.09 Torr), collected at 0 °C, was submitted to preparative GLC (column temperature 105 °C, injection port 160 °C, 140 ml N_2/min).

***trans*-1,3-Dichloro-1-ethyl-3-propylcyclobutane (18c):** bp 206–207 °C; n^{20}D 1.4584; ^{1}H NMR (CCl_4, Me_4Si) the signals of the ethyl and of the propyl group are mutually overlapped, the CH_2 group in the ring appears as singlet signal at 2.82 ppm; ir (neat) 2970, 2940, 2880, 1460, 1415, 1380, 1285, 1270, 1240, 1170, 1145, 1135, 1100, 990, 975, 945, 905, 860, 810, 730 cm^{-1}.

Anal. Calcd for $C_9H_{16}Cl_2$: C, 55.40; H, 8.27; Cl, 36.34. Found: C, 56.06; H, 8.32; Cl, 35.87.

***cis*-1,3-Dichloro-1-ethyl-3-propylcyclobutane (17c):**[12] ^{1}H NMR (CCl_4, Me_4Si) the signals of the ethyl and of the propyl group are mutually overlapped, the CH_2 group in the ring appears as a AA′BB′ quartet at 2.86 ppm (see Table II).

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Registry No.—**17a,** 57637-65-7; **17b,** 57637-66-8; **17c,** 57637-67-9; **18a,** 57637-68-0; **18b,** 57637-69-1; **18c,** 57637-70-4; propyne, 74-99-7; 1-butyne, 107-00-6; 1-pentyne, 627-19-0.

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(12) This compound was isolated in amounts insufficient for elemental analysis.