Ozonized oxygen was led into a solution of 0.4 g. (1.6 mmoles) of Ia in 300 ml. of methylene chloride, cooled in a Dry Ice–acetone bath for 24 hr. The solution was then flushed thoroughly with oxygen and concentrated to dryness under vacuum at room temperature. The infrared spectrum of the solid residue was identical with that of the starting material.

(b) A solution of 0.050 g. (0.2 mmole) of Ia in 30 ml. of methylene chloride was cooled in a Dry Ice–acetone bath and saturated with ozone (bright blue color). Zinc dust (0.85 g., 13 mmoles) and 1 ml. of 50% ethanol were then added, and the mixture was allowed to come to room temperature. After standing at room temperature for 1 hr., the mixture was dried over sodium sulfate, filtered, and concentrated to dryness under vacuum at room temperature. The residue was redissolved in methylene chloride, and the above procedure was repeated twice. Treatment of the resulting mixture with ether gave an insoluble fraction (mostly poly-β-anilino-β-phenylpropionate, as shown by the infrared). Evaporation of solvent left a residue which, by comparison of infrared spectra, was shown to be β-anilino-β-phenylpropionic acid *N*-carboxyanhydride (VI).

(c) In another run, 0.5 g. (2 mmoles) of Ia was oxidized as described under (b). The final reaction mixture was heated on the steam bath with 50 ml. of 1*N* hydrochloric acid for 0.5 hr. The aqueous solution was then decanted from insoluble material and rendered alkaline with aqueous sodium bicarbonate. The basic solution was washed three times with ether, treated with Norite on the steam bath, filtered, cooled, acidified to *p*H 4 with 1*N* hydrochloric acid, and then extracted three times with ether. The combined extracts were dried over sodium sulfate, filtered through a charcoal column, and concentrated to dryness under vacuum. The solid residue was submitted to sublimation at 110–114° (0.5 mm.). The infrared spectrum of the sublimate was superimposable on that of authentic β-anilino-β-phenylpropionic acid[11] (m.p. 133.5–134°). The admixture of the two samples melted at 133–134° (reported[11] m.p. 135–137°).

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NEW HAVEN, CONN.

[CONTRIBUTION NO. 689 FROM THE CENTRAL RESEARCH DEPARTMENT, EXPERIMENTAL STATION,
E. I. DU PONT DE NEMOURS & CO.]

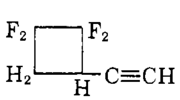
Cycloalkylation Reactions of Divinylacetylene

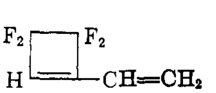
C. T. HANDY AND R. E. BENSON

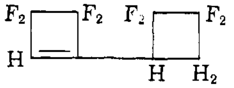
Received July 17, 1961

Bis(tetrahalocyclobutyl)acetylenes (Va and Vb) are formed in good yield by condensation of divinylacetylene with tetrafluoro- and chlorotrifluoroethylene. In contrast to the reaction of tetrafluoroethylene with monovinylacetylene, no product corresponding to the addition of tetrafluoroethylene to the acetylenic bond was found. The acetylenes Va and Vb are converted to bis(2-substituted 3,3-difluorocyclobutenyl)acetylenes by reaction with nucleophilic reagents.

Previous studies in this laboratory have established that acetylenes undergo cycloaddition reactions with tetrafluoroethylene to give cyclobutene structures. Thus, 3,3,4,4-tetrafluorocyclobutene is formed from acetylene and tetrafluoroethylene at 250°,[1] and monovinylacetylene with tetrafluoroethylene gives the products I–III derived from cycloalkylation reactions at both the acetylenic and olefinic bonds.[2] Furthermore, substituted tetrafluorocyclobutanes are also formed by condensation of activated olefins with tetrafluoroethylene.[2]

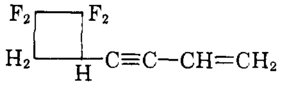

I

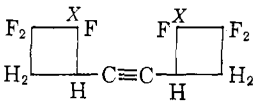

II


III

This paper reports the results of a study of the condensation of divinylacetylene with tetrafluoroethylene and chlorotrifluoroethylene together with an investigation of the resulting bis(tetrahalocyclobutyl)acetylenes.

Divinylacetylene reacts readily with tetrafluoroethylene at 125–140° and autogenous pressure to give 1,1,2,2-tetrafluoro-3-vinylethynylcyclobutane (IV) and bis(2,2,3,3-tetrafluorocyclobutyl)acetylene (Va). Either compound can be prepared as the major product by controlling the concentration of tetrafluoroethylene. In contrast to the reactions with either acetylene or monovinylacetylene, no product corresponding to the addition of tetrafluoroethylene to the acetylenic bond of divinylacetylene was isolated from these reactions. The structure assignments are based on elemental analyses and interpretation of the infrared, Raman, and NMR spectral data.


IV


Va. $X = F$
b. $X = Cl$

Similarly, reaction of divinylacetylene with chlorotrifluoroethylene at 150° and autogenous pressure produced bis(2-chloro-2,3,3-trifluorocyclobutyl)-acetylene (Vb), apparently as a mixture of stereoisomers. The structure assignment of Vb was made

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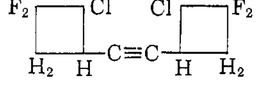
(1) J. L. Anderson, R. E. Putnam, and W. H. Sharkey, *J. Am. Chem. Soc.*, **83**, 382 (1961).

(2) D. D. Coffman, P. L. Barrick, R. D. Cramer, and M. S. Raasch, *J. Am. Chem. Soc.*, **71**, 490 (1949).

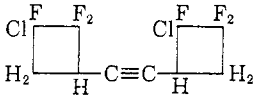
on the basis of elemental analysis, chemical studies, and NMR analyses.

The fluorine NMR spectrum of Vb clearly shows two overlapping spectra of equal intensity, each consisting of a weak, strong, strong, and weak pattern together with another peak. This weak, strong, strong, and weak pattern accompanied by another peak is the characteristic spectrum of chlorotrifluorocyclobutanes.[3] This evidence indicates that at least two isomers are produced in the reaction, but efforts to separate them by vapor phase chromatography were unsuccessful.

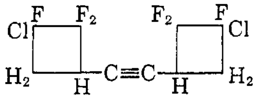
A priori, the addition of chlorotrifluoroethylene to the vinyl groups of divinylacetylene would be expected to give a mixture of Vb, VI, and VII. The possibility existed that products containing a 3-chloro substituent would give one set of spectral data, while products containing a 2-chloro substituent would give another set of spectral data. The combination of the two, although derived from a mixture consisting of more than two products, would appear as a 1:1 mixture. If this were the case, the reaction product should contain only 25% of Vb on a statistical basis. However, reaction of the product with methanolic potassium hydroxide gave bis(2-methoxy-3,3-difluorocyclobutenyl)acetylene, which was also the product of the methanolysis of Va, in 83% yield, thus establishing the product Vb to be a mixture of stereoisomers.



Vb

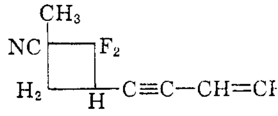


VI

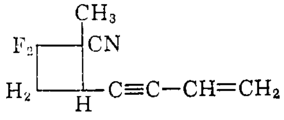


VII

The high reactivity of divinylacetylene for cycloaddition was shown by reaction with β,β-difluoromethacrylonitrile to give what appears to be the first example of a cycloalkylation reaction of the nitrile with a nonfluorinated olefin. The product was a mixture of mono- and diadducts derived from addition at the olefinic bonds of divinylacetylene. Studies of the monoadduct indicated that it was a mixture of isomers VIII and IX. Thus, whereas the condensation with chlorotrifluoroethylene appears to give a single position isomer, the condensation of divinylacetylene with β,β-difluoromethacrylonitrile gives a mixture of position isomers.

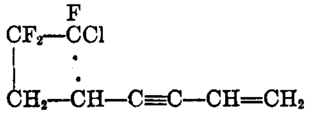


VIII

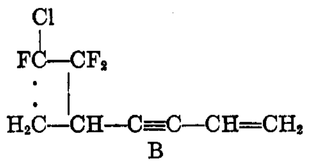


IX

These results are believed to be consistent with the concept[4,5] that the structure of the product obtained in a cycloalkylation reaction can be predicted on the basis of the degree of radical stabilization in the transition state. Haszeldine[6] has shown that the radical $RCF_2CFCl\cdot$ is more stable than $RCFClCF_2\cdot$. Presumably, $RCH_2\dot{C}HC{=}CCH{=}CH_2$ would be more stable than $\cdot CH_2\underset{R}{\underset{|}{C}}HC{=}CCH{=}CH_2$ because of resonance contribution from the adjacent acetylenic bond. Thus, in the transition state the diradical A is stabilized to a greater extent than the diradical B, and the formation of Vb would be predicted.

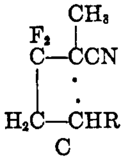


A

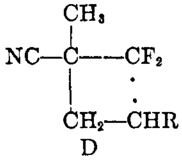


B

The formation of isomers in the β,β-difluoromethacrylonitrile–divinylacetylene condensation can be attributed to the similar stability of the diradicals C and D in the transition state.



C



D

The bis(tetrahalocyclobutyl)acetylenes underwent reactions with nucleophilic reagents to give bis(substituted cyclobutenyl)acetylene derivatives. Thus, heating the bis(tetrafluoro) compound Va with aqueous alkali or with trimethylamine in benzene brought about dehydrofluorination to produce bis(2,3,3-trifluorocyclobutenyl)acetylene (X). Compound X could also be obtained from the bis(chlorotrifluoro) derivative Vb under similar conditions. The preferential loss of chlorine under similar conditions has been observed previously.[1] Reaction of the bis(chlorotrifluoro) compound Vb with diethylamine yielded the vinylamine derivative, bis(2-diethylamino-3,3-difluorocyclobutenyl)-acetylene (XIa).

Reaction of either the bis(tetrafluoro) compound

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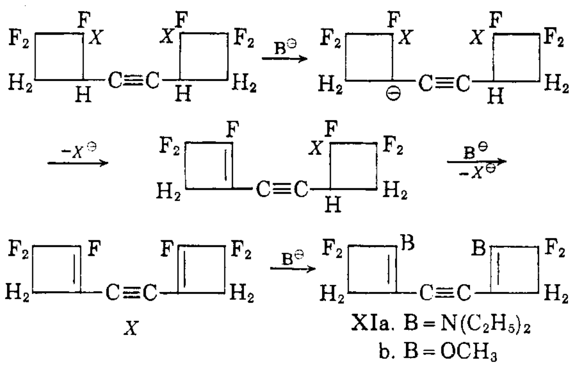
[3] We are indebted to Dr. W. D. Phillips of this laboratory for determination and interpretation of the NMR data.

[4] E. E. Lewis and M. A. Naylor, *J. Am. Chem. Soc.*, 69, 1968 (1947).

[5] E. C. Coyner and W. S. Hillman, *J. Am. Chem. Soc.*, 71, 324 (1949).

[6] R. N. Haszeldine and B. R. Steele, *J. Chem. Soc.*, 1592 (1953).



(Va) or the bis(chlorotrifluoro) compound (Vb) with alkoxides yielded the corresponding 2-alkoxydifluorocyclobutenylacetylene derivatives. In this manner substituted ethers derived from methanol, ethanol, allyl alcohol, and phenol were prepared.

These reactions are believed to proceed through initial formation of the anion obtained by removal of the hydrogen atom adjacent to the activating acetylene group. The resulting anion eliminates fluoride or chloride ion to give the bis(trifluorocyclobutenyl) structure. A displacement-type reaction of the latter with alcohols or with diethylamine yields the observed products.

Verification for this mechanism was found in the reaction of the bis(trifluoro) compound X with methanolic sodium hydroxide to produce the ether XIb, although in low yield. Considerable unidentified ketonic product was formed in this reaction, presumably by reaction of the excess base with the ether.

EXPERIMENTAL

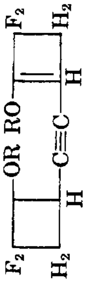
1,1,2,2-Tetrafluoro-3-vinylethynylcyclobutane (IV). A mixture of 25 ml. (0.25 mole) of divinylacetylene,[7,8] 25 g. (0.25 mole) of tetrafluoroethylene, and 0.1 g. of *N*-phenyl-β-naphthylamine was heated in a stainless steel pressure vessel at 135° for 4 hr. Four grams of unchanged tetrafluoroethylene was recovered and distillation of the liquid products gave 13.2 g. (40% conversion) of IV, b.p. 56–61° (50 mm.), n_D^{25} 1.4081. Analytical data were obtained on a sample of b.p. 59–60.5° (50 mm.), n_D^{25} 1.4086.

Anal. Calcd. for $C_8H_6F_4$: C, 53.94; H, 3.40. Found: C, 54.07; H, 3.62.

The infrared absorption spectrum indicates the presence of a vinyl group (10.3 and 11.2 μ). The proton magnetic resonance spectrum is consistent with the proposed structure.

Bis(2,2,3,3-tetrafluorocyclobutyl)acetylene (Va). A metal pressure vessel of 80 ml. capacity was charged with 7.8 g. (0.1 mole) of divinylacetylene, 40 g. (0.4 mole) of tetra-

TABLE I



R	Reactants	Solvent Temperature	Time, Hr.	Conversion, %	M.P. (b.p.)	n_D^{25}	Formula	Calcd., % C	Calcd., % H	Found, % C	Found, % H
C_2H_5	Vb, C_2H_5OH KOH	C_2H_5OH Reflux	1.5	51	(109/2 mm.)	1.4939	$C_{14}H_{14}O_2F_4$	57.93 (F, 26.18)	4.86	58.41 (F, 26.10)	5.02
C_6H_5	Vb, C_6H_5OH KOH	Dioxane Reflux	2	46	105		$C_{22}H_{14}O_2F_4$	68.39	3.64	68.56	3.81
$CH_2{=}CHCH_2$	Vb, $CH_2{=}CHCH_2OH$ KOH	$CH_2{=}CHCH_2OH$ Reflux	1	22	(88/0.3)	1.4469	$C_{16}H_{14}O_2F_4$	61.14	4.49	61.06	4.73

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(7) Divinylacetylene is an extremely hazardous chemical. It reacts readily with oxygen to form an unstable, explosive, peroxidic polymer. All experiments involving divinylacetylene should be conducted in an oxygen-free atmosphere. After completion of the experiments, the equipment should be rinsed immediately with solvents containing a polymerization inhibitor to avoid formation of unstable films. All experiments should be conducted with adequate shielding.

(8) J. A. Nieuwland, W. S. Calcott, F. B. Downing, and A. S. Carter, *J. Am. Chem. Soc.*, **53**, 4197 (1931).

fluoroethylene, and 0.1 g. of *N*-phenyl-β-naphthylamine. The vessel was sealed and heated at 125° for 11 hr. The pressure fell from 65 to 43 atm. during this time. Distillation of the reaction product yielded 18.6 g. of colorless liquid, b.p. 75–77° (14 mm.), n_D^{25} 1.3742, d_{20}^{4} 1.4433, m.p. 19.8° (73% conversion based on divinylacetylene charged).

Anal. Calcd. for $C_{10}H_6F_8$: C, 43.18; H, 2.17; F, 54.65; mol. wt., 278. Found: C, 43.35; H, 2.44; F, 54.63; mol. wt., 274.

The infrared spectrum of Va shows weak absorption at 4.4 μ, indicative of an internal acetylene bond, and considerable absorption in the 7–10-μ region, indicative of C—F bonds (6.96, 7.35, 7.48, 7.86, 8.62, 8.88, 9.73, and 10.07 μ). The Raman spectrum shows strong absorption at 2260 cm.$^{-1}$, confirming the presence of an internal acetylene group. The fluorine NMR spectrum shows two overlapping sets of bands of the weak, strong, strong, weak pattern characteristic of tetrafluorocyclobutanes[3] (−1126, −1340, −1490, and −1708; and −1168, −1368, −1756, and −1970 c.p.s. from trifluoroacetic acid[9] at 40 mc.). The product reacted readily with potassium permanganate but did not decolorize bromine in carbon tetrachloride solution.

Bis(2-chloro-3,3,3-trifluorocyclobutyl)acetylene (Vb). A metal pressure vessel was charged with 25 ml. (0.25 mole) of divinylacetylene, 85 g. (0.75 mole) of chlorotrifluoroethylene and 0.1 g. of *N*-phenyl-β-naphthylamine. The vessel was sealed and heated at 150° for 6.5 hr., during which time the pressure fell from 32 to 19 atm. Distillation gave 52.0 g. (67% conversion) of a colorless liquid, b.p. 66–68° (0.7 mm.), n_D^{25} 1.4251.

Anal. Calcd. for $C_{10}H_6Cl_2F_6$: C, 38.61; H, 1.94; Cl, 22.80. Found: C, 39.19; H, 2.50; Cl, 22.23.

The infrared spectrum shows weak absorption at 4.42 μ, which may be attributed to an internal acetylene bond, and strong absorption in the 7–11-μ region attributable to C—F bonds (6.96, 7.65, 8.14, 9.00, 10.01, and 10.69 μ).

The fluorine NMR spectrum (determined in an equal volume of carbon tetrachloride) shows two overlapping sets of bands of the weak, strong, strong, weak pattern together with another band (1645, 1845, 2735, 2935, and 3465 c.p.s.; and 1960, 2160, 2265, 2465, and 2735 c.p.s. at 56.4 mc. with 1,2-difluorotetrachloroethane as reference.[3,9]

Condensation of divinylacetylene with β,β-difluoromethacrylonitrile. A mixture of 5 ml. (0.05 mole) of divinylacetylene, 15 g. (0.145 mole) of β,β-difluoromethacrylonitrile and 0.1 g. of *N*-phenyl-β-naphthylamine was heated in a pressure vessel at 150° for 7 hr. Distillation of the product gave 1.84 g. (20% conversion, based on divinylacetylene) of the 1:1 adduct (VIII and IX), b.p. 69° (5 mm.), n_D^{25} 1.4608. Analysis by fluorine NMR spectroscopy indicated that this fraction was a mixture of VIII and IX.

Anal. Calcd. for $C_{10}H_9NF_2$: C, 66.29; H, 5.00; N, 7.73. Found: C, 66.14; H, 5.07; N, 7.80.

Bis(2,3,3-trifluorocyclobutenyl)acetylene (X). A solution of 15.6 g. (0.05 mole) of the acetylene Vb and 25 g. (0.25 mole) of triethylamine in 100 ml. of benzene was refluxed for 1.5 hr. The resulting mixture was cooled and filtered to remove the amine salt. The filtrate was diluted with ether and washed with water to remove the excess amine. Distillation gave 5.5 g. (46% conversion) of colorless liquid, b.p. 49–60° (6 mm.). An analytical sample had b.p. 45–51° (6 mm.), n_D^{25} 1.4537.

Anal. Calcd. for $C_{10}H_4F_6$: C, 50.43; H, 1.69. Found: C, 50.52; H, 1.61.

The cyclobutenyl derivative X was also formed in 50% conversion when the bis(tetrafluoro) derivative Va was refluxed in water with two equivalents of potassium hydroxide and three drops of "Duponol," a commercial wetting agent.

Bis(2-diethylamino-3,3-difluorocyclobutenyl)acetylene (XIa). A solution of 6.2 g. (0.02 mole) of the acetylene Vb and 20.5 ml. (0.2 mole) of diethylamine in 50 ml. of benzene was refluxed for 4 hr. The precipitated amine salt was removed by filtration and the filtrate was washed with water to remove the excess amine. The resulting benzene solution was distilled to give 4.0 g. of amber oil, b.p. 132–138° (0.2 mm.) with evidence of decomposition. The oil was chromatographed on an alumina column with petroleum ether to give 2.88 g. of XIa as a lemon yellow, nonviscous liquid, n_D^{25} 1.5568. The proton magnetic resonance spectrum is consistent with the proposed structure.

Anal. Calcd. for $C_{18}H_{24}N_2F_4$: N, 8.13; F, 22.07. Found: N, 8.41; F, 21.53.

Bis(3,3-difluoro-2-methoxycyclobutenyl)acetylene (XIb). To a stirred solution of 7.4 g. (0.15 mole) of potassium hydroxide in 50 ml. of methanol was added slowly 9.3 g. (0.03 mole) of the acetylene Vb. After the exothermic reaction had subsided, the solution was refluxed for 2 hr. After cooling, the precipitated yellow crystals were recovered by filtration and washed with water. Recrystallization from 50 ml. of 90% methanol gave 6.5 g. (83% conversion) of pale yellow prisms melting at 67°. Further recrystallization from methanol yielded colorless prisms of XIb, m.p. 69°.

Anal. Calcd. for $C_{12}H_{10}O_2F_4$: C, 54.96; H, 3.84; F, 28.99. Found: C, 55.04; H, 3.78; F, 28.32.

The structure was confirmed by ultraviolet and fluorine NMR spectral analyses. The ultraviolet absorption spectrum, determined in chloroform, showed λ_{max} 280 mμ (ϵ = 14,400), λ_{max} 294 mμ (ϵ = 19,400), and λ_{max} 312 mμ (ϵ = 16,700).

The reaction of the chlorotrifluoro compound Vb with several alcohols in the presence of base gave the bis(2-alkoxy-3,3-difluorocyclobutenyl)acetylenes listed in Table I.

Acknowledgment. We wish to acknowledge the helpful suggestions of Dr. R. M. Joyce and Dr. O. W. Webster.

WILMINGTON 98, DEL.

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[9] The NMR spectra were determined with a Varian Associates High Resolution NMR spectrometer.