After the reaction was completed we used three procedures to isolate the product. One example of each method is described.

Method A. Isolation by Extraction. Methyl β-(β-Mercaptoethylamino)isobutyrate, S-Sulfonic Acid (16e).—To a solution of 70 g. (0.28 mole) of sodium thiosulfate pentahydrate in 280 ml. of water was added 20.0 g. (0.14 mole) of methyl 3-(1′-aziridinyl)-2-methylpropanoate. The pH rose to 9.8. Then 232 ml. of 1.0 *M* hydrochloric acid was added, which brought the pH to 7.2. The product was extracted thoroughly with ether. The aqueous phase was then further acidified to pH 3.4 and the solution was freeze dried. The solid residue was extracted twice with hot ethanol. The ethanol solution was evaporated to dryness *in vacuo*, and the resulting oil was crystallized slowly at room temperature from 500 ml. of a hot 1:4 (v./v.) methanol-ethanol mixture, yielding 7.82 g. (22%) of **16e**, m.p. 137–143°. Three further recrystallizations gave 2.84 g. of analytical material, m.p. 142–145.5°.

On paper in a BuOH-HOAc-water system (4:1:5) the product moved as a single spot with an R_f of 0.5. The isoelectric point was 5.2.

Method B. Isolation by Ion-Exchange Chromatography. Ethyl β-Mercaptoethylaminoacetate, S-Sulfonic Acid (16c).—The pure liquid adduct, ethyl N-ethyleniminoacetate (**2e**, 15.0 g., 0.117 mole) was added to 32.02 g. of sodium thiosulfate pentahydrate, in 129 ml. of water. The pH rose to 9.4. Then 113.6 ml. of 1.03 *M* hydrochloric acid (0.118 mole) was added, bringing the pH down to 7.1. The total crude reaction mixture was then charged directly onto a 75-mm. o.d. ion-exchange column packed with 1.75 l. of Rohm and Haas resin IRA-400 pretreated as follows. The column (originally in the chloride form) was washed with 4 l. of 4% sodium hydroxide solution, followed by 8 l. of a 29% aqueous solution of sodium acetate trihydrate. The column finally was washed with distilled water (*ca.* 1 l.) until the effluent pH was 9.5. The column was eluted with 25 l. of a continuous gradient of acetic acid. The first 5 l. was 0.001 *M* acetic acid which verged to 15 l. of 0.05 *M* and finally shifted to 5 l. of 0.1 *M* acetic acid. T.l.c. was used to monitor the 285 fractions of 100 ml. each. Fractions 132–278 contained chromatographically pure product with an approximate maximum concentration in tube 203.

The product was obtained virtually pure on the freeze drying of the fractions in the range indicated. A representative aliquot from the combined fractions showed the presence of 19.6 g. (69%) of ethyl β-mercaptoethylaminoacetate, S-sulfonic acid (**16c**). Fractions 218–250 were freeze dried *in toto* and yielded 6.35 g. of crystals, infrared spectrum identical with the once-recrystallized (from ethanol) analytical sample, m.p. 119.5–120.5° (5.67 g.).

Method C. Isolation by Countercurrent Distribution. N-Isopropyl-β-(β-mercaptoethylamino)propionamide, S-Sulfonic Acid (16f).—A solution of 5.0 g. (32.1 mmoles) of N-isopropyl-3-(1′-aziridinyl)propionamide (**21**) in water (10 ml.) was treated with 32.1 ml. of 1 *M* sodium thiosulfate solution. The product was then acidified to pH 5.2 with 6 *M* hydrochloric acid. From paper chromatography it was seen that the product had an R_f of somewhat less than 0.5 in a 1:1 butanol-water system, therefore this system was used for the countercurrent distribution. The total reaction product was diluted to 100 ml. with butanol-saturated water and placed in a 30-tube countercurrent apparatus which accommodated 100 ml. in each phase. The distribution was terminated after 55 transfers. The maximum concentration of amino acid was in tube 13 ($K = 0.32$). The product was isolated from tubes 8–18. The lower phases were freeze dried directly and the upper phases were combined with an equal volume of ether and extracted with water, and the aqueous fractions were freeze-dried. The total yield of crystalline product, m.p. 110–115°, was 4.5 g. (52%). Recrystallization was accomplished from acetonitrile-ether to yield 3.8 g. of analytically pure N-isopropyl-β-(β-mercaptoethylamino)propionamide, S-sulfonic acid (**16f**), m.p. 128–130°.

Sterically Crowded Amines. VI. Quaternary Salts from the Alkylation of Trimethylamine with *t*-Propargylic Chlorides[1]

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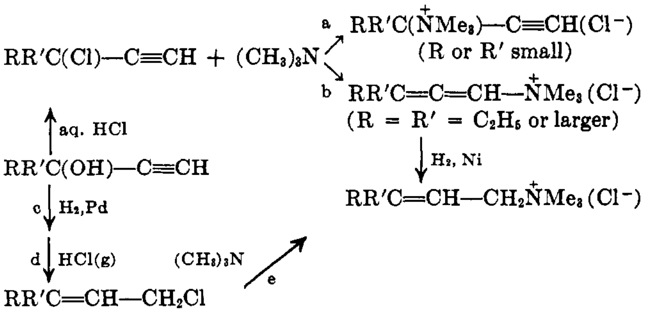
The reaction of trimethylamine with *t*-propargylic chlorides, RR′C(Cl)—C≡CH, produces quaternary ammonium chlorides; these have the propargylic structure when R *or* R′ is CH_3 and when RR′C comprise the cyclohexane ring. When R *and* R′ are larger than CH_3 (*e.g.*, R = R′ = C_2H_5), the products are allenic. The propargylic and the allenic products are believed to arise from intermediate zwitterion carbenes, ($RR'\overset{+}{C}—C≡C^- \longleftrightarrow RR'C=C=C:$).

The alkylation of ammonia[2] and primary and secondary amines[3,4] with *t*-propargylic chlorides leads to the corresponding propargylic amines, and such reactions may be used to prepare amines characterized by a remarkably high degree of steric crowding about the nitrogen atom.[5] The products are believed to arise from stable zwitterion carbenes ($RR'\overset{+}{C}—C≡C^- \longleftrightarrow RR'C=C=C:$), resistant to proton elimination from R or R′ and notably electrophilic at the tertiary carbon atom. Attempts to find halide–substrate combinations in which steric effects of necessity produce allenic amines have failed.[6] Several instances of steric control of this type have now been found, however, during a study of the reaction of *t*-propargylic chlorides with trimethylamine.



When R *or* R′ is small (one of them CH_3) or are parts of a cyclohexane ring, the products are quaternary *t*-propargylic ammonium salts (reaction a); when R *and* R′ are ethyl or larger, the isomeric allenic salts are formed (reaction b). In the original experiments the reactions were carried out with aqueous trimethyl-

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[1] Paper No. 81 on substituted acetylenes; previous paper, G. F. Hennion and A. C. Hazy, *J. Org. Chem.*, **30**, 2650 (1965).

[2] G. F. Hennion and E. G. Teach, *J. Am. Chem. Soc.*, **75**, 1653 (1953).

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TABLE I

QUATERNARY AMMONIUM SALTS

Compd.	R	R′	Yield, %[a]	Formula	M.p., °C.	% carbon Calcd.	% carbon Found	% hydrogen Calcd.	% hydrogen Found	% nitrogen Calcd.	% nitrogen Found
				A. Propargylic, $RR'C[\overset{+}{N}(CH_3)_3]C{\equiv}CH\ (Cl^-)$							
I	CH_3	CH_3	83	$C_8H_{16}ClN$	222–223	59.43	59.59	9.98	10.11	8.66	8.49
II	CH_3	C_2H_5	55	$C_9H_{18}ClN$	184–185	61.52	61.24	10.32	10.62	7.97	7.76
III	CH_3	*i*-C_4H_9	50	$C_{11}H_{22}ClN$	200[b]	64.84	64.70	10.89	10.95	6.87	6.92
IV[c]	C_2H_5	C_2H_5	52	$C_{10}H_{20}IN$	142–144	42.71	42.91	7.17	7.11	4.98	4.89
V	$-CH_2(CH_2)_3CH_2-$		100	$C_{11}H_{20}ClN$	211–213	65.49	65.33	9.99	10.24	6.94	6.65
				B. Allenic, $RR'C{=}C{=}CH{-}\overset{+}{N}(CH_3)_3\ (Cl^-)$							
VI	C_2H_5	C_2H_5	88	$C_{10}H_{20}ClN$	173–176	63.30	63.05	10.63	10.75	7.38	7.16
VII	C_2H_5	C_5H_{11}[d]	60	$C_{13}H_{26}ClN$	126–128	67.35	67.32	11.31	11.09	6.04	5.98

[a] Yield of crude material. [b] Decomposes. [c] Methiodide. [d] $C_2H_5CH(CH_3)CH_2-$.

amine (25–40%), but the products were impure owing to contamination with trimethylamine hydrochloride, presumably due to a competitive hydrolysis reaction in the aqueous alkaline medium. This difficulty was overcome, however, by conducting the reactions in acetone. It is of interest to note that commercial acetone served much better for this purpose (solvent) than did pure acetone. The efficacy of pure acetone was much enhanced merely by adding small amounts of isopropyl alcohol and (or) water, indicating the importance of solvation effects during the reaction. Also significant is the fact that trace amounts of copper powder or cuprous chloride catalyze both reactions a and b as previously observed in amine alkylations.[4,5]

The propargylic structures assigned to compounds I–V, Table I, are supported by their infrared spectra (ethynyl bands near 3.0 and 4.75 μ, allene bands near 5.1 μ absent), p.m.r. data, and chemical behavior. Compound I was converted to the methiodide by reaction with sodium iodide in acetonitrile and found to be identical with a sample prepared unequivocally from 3-dimethylamino-3-methyl-1-butyne[3] by quaternization with methyl iodide. Furthermore, the hydrogenation of compounds I, II, III, and V using Raney nickel, platinum oxide, or palladium on charcoal, resulted only in hydrogenolysis to trimethylamine hydrochloride, a result typical of sterically crowded propargylic substrates.[4,5] Compounds VI and VII showed infrared bands at 5.1 (sharp) and 6.05–6.15 μ (weak, broad) but no ethynyl bands near 3 or 4.75 μ. Compound VI was converted to the methiodide (*via* sodium iodide in acetonitrile) and found to be very different from the isomeric methiodide IV, prepared from 3-dimethylamino-3-ethyl-1-pentyne by quaternization with methyl iodide. Furthermore, the p.m.r. spectrum of VI showed a triplet at τ 8.96 with $J = 6.6$ c.p.s. equivalent to 6.3 protons; two overlapping quartets at τ 7.8 equivalent to 4.1 protons assigned to the methylene protons split by the neighboring methyl protons, $J = 6.6$ c.p.s., and split by the allenic proton, $J = 3$ c.p.s.; a singlet at τ 6.43 equivalent to 9 protons; and a quintet at τ 2.65 with $J = 3$ c.p.s. equivalent to 1.2 protons. The long-range spin–spin coupling observed between the allenic and methylene protons with $J = 3$ c.p.s. is in agreement with data reported by Snyder and Roberts.[7] The p.m.r. spectrum of methiodide IV was notably different: a triplet at τ 8.98 equivalent to 5.9 protons; a split quartet at τ 7.9 equivalent to 4 protons; and two singlets, a small one at τ 6.6 and a larger at τ 6.58. The sum of the two singlets was equivalent to 10.8 protons. The smaller singlet is assigned to the acetylenic proton and the larger to the nine protons of the N-methyl groups. The error in integration is attributed to the overlap of the peaks.

Hydrogenation of VI using Raney nickel as the catalyst gave γ,γ-diethylallyltrimethylammonium chloride. The latter compound was prepared independently *via* the reactions c, d, and e; the two samples were identical in all regards. Hydrogenation of VII also led to an allylic quaternary salt, m.p. 157–164°, presumably a mixture of the two possible geometric isomers.

While the mechanism of reaction a is not in doubt,[2–4,8] the outcome of reaction b may be explained in another way, namely *via* an SN2′ reaction across the propargylic halide system. This does not now appear to be an attractive explanation, particularly in view of studies by Hartzler,[8] who trapped zwitterion carbenes in the vinylidenecarbene structure with olefins (to form vinylidenecyclopropanes) and with certain acetylide ions (forming hexapentaenes). In order to obtain further information on this point, some preliminary reactions of the *t*-propargylic halides with triethylamine and with dimethylaniline have been attempted; no quaternary salts have been isolated from these experiments, however, and the matter is now being studied with assorted tertiary amines, varying in steric features and in basicity.

Experimental Section

The infrared spectra of the quaternary salts were obtained in chloroform solutions, the p.m.r. spectra as chloroform-*d* solutions with TMS as the internal standard. The *t*-propargylic chlorides were prepared as previously described.[9]

Preparation of Quaternary Chlorides. General Procedure.—One mole of *t*-propargylic chloride was added dropwise with stirring to 1.5 moles of trimethylamine in acetone solution (25–40%) containing a catalytic amount (*ca.* 0.1 g.) of copper powder or cuprous chloride. The temperature was maintained at 25–35° by periodic external cooling as necessary. When the precipitation was complete (1–12 hr.) the product was isolated by filtration and washed with cold acetone followed by anhydrous ether. Compounds I, II, III, and V were purified by crystallization from acetonitrile, VI by crystallization from acetone plus acetonitrile, and VII by crystallization from acetone.

Preparation of 3-Dimethylamino-3-ethyl-1-pentyne.—3-Chloro-3-ethyl-1-pentyne (32.6 g., 0.25 mole) was added dropwise with stirring at room temperature to 84.4 g. (0.75 mole) of 40% aque-

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(7) E. I. Snyder and J. D. Roberts, *J. Am. Chem. Soc.*, **84**, 1582 (1962).

(8) H. D. Hartzler, *ibid.*, **81**, 2024 (1959); **83**, 4990, 4997 (1961); *J. Org. Chem.*, **29**, 1311 (1964).

(9) G. F. Hennion and A. P. Boisselle, *ibid.*, **26**, 725 (1961).

ous dimethylamine containing *ca.* 0.1 g. of copper powder. After 5 hr. of stirring the layers were separated and the aqueous layer was extracted with two 50-ml. portions of ether which were added to the organic portion. The ethereal solution was dried over anhydrous potassium carbonate. Distillation gave 19.5 g. (56% yield), b.p. 80–84° (70 mm.), $n^{25}_{\rm D}$ 1.4440.

The methiodide (IV, Table I) was prepared from 12.9 g. (0.1 mole) of the amine and 21.3 g. (0.15 mole) of methyl iodide in 50 ml. of ethyl acetate. The product was collected by filtration and washed with acetone. The crude material (14.2 g., 52% yield) had m.p. 135–137°. Crystallization from methylene dichloride gave material with m.p. 142–144°.

Preparation of 1-Chloro-3-ethyl-2-pentene.—Dry hydrogen chloride was bubbled through 57 g. (0.5 mole) of 3-ethyl-1-penten-3-ol[10] with stirring while the temperature was maintained at 25–30° until 18 g. (0.5 mole) of hydrogen chloride had been taken up. The layers were separated and the organic portion was dried over anhydrous potassium carbonate. Distillation gave 39 g. (59% yield), b.p. 90–95° (112 mm.). Redistillation gave material with b.p. 78–79° (56 mm.), $n^{25}_{\rm D}$ 1.4513. The infrared spectrum showed no peaks at 7.1 μ characteristic of the $=CH_2$ in-plane deformation nor was there a peak at 10 μ characteristic of the $=CH$ out-of-plane deformation in vinyl groups. There was, however, a strong peak at 6.05 μ assigned to the $C=C$ stretch and a peak at 11.65 μ assigned to the $=CH$ out-of-plane deformation. The p.m.r. spectrum showed a triplet at τ 4.9 with J = 7.5 c.p.s. (0.82 proton), a doublet at τ 6.1 with J = 7.5 c.p.s. (2 protons), two overlapping quartets at about τ 7.9 with J = 7.5 c.p.s. (3.9 protons), and a triplet at τ 9.01 with J = 7.5 c.p.s. (6.2 protons). The quartets assigned to the methylene protons within the ethyl groups have slightly different chemical shifts due to the fact that one is *cis* to the chloromethylene group and is deshielded by the chlorine atom. The quartet at higher field is slightly less intense probably due to small long-range spin–spin splitting by the olefinic proton.

Preparation of 1-Dimethylamino-3-ethyl-2-pentene Methochloride.—To 11.1 g. (0.075 mole) of 40% trimethylamine in acetone solution was added dropwise with stirring 6.6 g. (0.05 mole) of 1-chloro-3-ethyl-2-pentene. After 1 hr. the mixture was cooled to 10° and the product was collected by filtration. The crude product (4.4 g., 46% yield) had m.p. 204–205°. Crystallization from acetone plus acetonitrile gave material with m.p. 206–207°.

The compound was also prepared by hydrogenating 19.0 g. (0.1 mole) of 1-dimethylamino-3-ethyl-1,2-pentadiene methochloride (VI) in 55 ml. of ethanol containing 2 g. of Raney nickel (wet with ethanol) at an initial pressure of 50 p.s.i.g. The catalyst was removed by filtration and the solvent was removed by vacuum distillation. The crude solid weighed 17 g. Recrystallization from acetone plus acetonitrile gave material with m.p. 205–207°. A mixture melting point with the material described above showed no depression and the infrared spectra were superimposable.

Preparation of Methiodides from Methochlorides.—A boiling solution of 7.5 g. (0.05 mole) of sodium iodide in 20 ml. of acetonitrile was added to a boiling solution of 8.1 g. (0.05 mole) of 3-dimethylamino-3-methyl-1-butyne methochloride (I) in 80 ml. of acetonitrile. The resulting mixture was filtered hot and the solvent was removed on a rotary evaporator. The residue, crystallized from ethanol, had m.p. 205–207° dec.; lit.[11] m.p. 210° dec.

1-Dimethylamino-3-ethyl-1,2-pentadiene methiodide was prepared in a similar manner from 8 g. (0.05 mole) of sodium iodide and 9.5 g. (0.05 mole) 1-dimethylamino-3-ethyl-1,2-pentadiene methochloride (VI). The product (10.3 g., 54% yield) crystallized from ethyl acetate plus acetone had m.p. 137–139°.

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Reaction of Amines with Cyclic Fluorinated Olefins[1,2]

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A series of perfluoro- and per(chlorofluoro)cycloalkenes was treated with methylamine and ethylamine to give 1-alkylamino-2-chloro- (or fluoro-) 3-alkyliminopolyfluorocycloalkenes which were hydrolyzed to the corresponding amino ketones. The same series of olefins also reacted with hydroxylamine to give 1,2,3-trioximinopolyfluorocycloalkanes. A monooxime was isolated and shown to be an intermediate in the trioxime formation. The 1-methylamino-2-chloro- (or fluoro-) 3-alkyliminopolyfluorocycloalkenes reacted with ethylamine and hydroxylamine and a methylamino group was replaced by an ethylamino and hydroxylamino group, respectively. Mechanisms for these reactions are presented.

Several examples of the reaction[3] of polyfluorinated cyclic olefins with primary amines,[3–6] secondary[4,7–9] amines, and ammonia have been reported.[4–6] With secondary amines, monosubstitution in a vinylic position was obtained, but with primary amines and ammonia only iminoamines were isolated. Addition–elimination and S_N2' mechanisms have been proposed to account for the products.

We now report a comprehensive study of the reaction of five cyclic olefins (I–V) with primary alkylamines and the more nucleophilic but sterically similar hydroxylamine.

Reactions with Methylamine and Ethylamine.—The cyclic olefins I–V reacted with gaseous methylamine and III and IV with gaseous ethylamine to give the iminoamines VI–XI, which were hydrolyzed on a chromatography column packed with acid-washed alumina to give the 1,3-amino ketones XII–XVII. The 1,3-iminoamines and the 1,3-amino ketones were

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(1) This paper is based on a thesis submitted by J. J. Turner to the Graduate School of Purdue University in partial fulfillment of the requirements for the degree of Doctor of Philosophy.

(2) Presented at the Third International Symposium of Fluorine Chemistry, Munich, Sept. 1965.

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