Anal. Calcd. for $C_{22}H_{37}NO_3$: C, 72.68; H, 10.26. Found: C, 72.68; H, 10.26.

Formation of Glyoxal from Tetrahydroatidine. A solution of 83 mg. of the above "tetrahydroatidine" in 10 ml. of glacial acetic acid was treated with 217 mg. of lead tetraacetate and maintained at 62° for 22 hr. After dilution with 10 ml. of water, 200 mg. of *p*-nitrophenylhydrazine was added and then the mixture was heated at 100° for 21 hr. After cooling the bis-*p*-nitrophenylhydrazone of glyoxal was collected, m.p. 315–318°, 19.6 mg. (26%). Recrystallization from 125 ml. of boiling acetic acid gave 12.4 mg. of reddish purple crystals, m.p. 317–318°, with an infrared spectrum in Nujol identical with that of the authentic bis-*p*-nitrophenylhydrazone prepared from glyoxal.

Acetylation of Dihydroatidine to Give Dihydroajaconine Triacetate. A solution of 139 mg. of the mixture of epimeric dihydroatidines in 2.0 ml. of dry pyridine and 1.0 ml. acetic anhydride was allowed to stand overnight. Evaporation *in vacuo* gave a resin which was dissolved in chloroform and washed with dilute ammonium hydroxide. The chloroform phase yielded 180 mg. which on standing in methanol several days deposited heavy prisms, 52.8 mg., m.p. 122–127°. Recrystallization from methanol gave 44.5 mg., m.p.

131.5–133°. It was later observed that the crystalline isomer could be obtained easily by chromatography in benzene over Woelm neutral alumina. Recrystallization gave prisms of m.p. 133.5–135.5°, $[\alpha]_D$ −88.7° (c 1.9, EtOH), undepressed with an authentic sample of dihydroajaconine diacetate.[17] The infrared spectrum in KBr was identical with that of dihydroajaconine diacetate, ν_{max} 3448 (OH), 1745 and 1242 (OAc), 1718 (>C=O), and 1372 cm.$^{-1}$ (C—CH₃). Later experiments showed that acetylation of 257 mg. of dihydroatidine and work-up by chromatography gave 116 mg. of the dihydroajaconine triacetate, m.p. 131.5–134° cor.

Saponification of Dihydroajaconine Triacetate (from Dihydroatidine). A solution of 24.4 mg. of the triacetate in 1 ml. of methanol was treated with 69 mg. of potassium carbonate in 2 ml. of methanol and 1 ml. of water and allowed to stand for 17 hr. The reaction mixture was evaporated *in vacuo*, taken up in water, and extracted with chloroform. The product (19.3 mg.) was dissolved in a few drops of acetone, diluted until turbid, and seeded. Dihydroajaconine crystallized as fine needles, m.p. 90–91°. Recrystallization from aqueous acetone gave needles, m.p. 94.0–95.0°, undepressed by an authentic sample of m.p. 94.5–97.5°.[17]

A New Stable Radical, Bis(trifluoromethyl) Nitroxide[1]

W. D. Blackley and R. R. Reinhard

Contribution from Texaco, Inc., Beacon, New York. Received August 13, 1964

The stable free radical bis(trifluoromethyl) nitroxide has been synthesized, isolated, and characterized for the first time. This material is a stable purple gas at room temperature. It is unreactive with glass, stainless steel, copper, water, air, mercury, Freon 11, and 10% aqueous sodium hydroxide. Only reactions with other free radicals such as nitric oxide and nitrogen dioxide have been confirmed to date, the former yielding the known compound $(CF_3)_2NONO$.

Bis(trifluoromethyl) nitroxide ($(CF_3)_2NO$, I), a perfluorinated stable nitroxide radical, has been synthesized and isolated as a purple gas at room temperature. On cooling, the gas condenses to a brown liquid (b.p. −25°) and solidifies to a yellow solid (m.p. −70°). It is not affected chemically by water, 10% aqueous sodium hydroxide, air, stainless steel, copper, glass, fluorotrichloromethane, or benzene. However, it readily undergoes reactions with other free radical species. It combines readily with nitric oxide to form O-nitrosobis(trifluoromethyl)hydroxylamine ($(CF_3)_2$-NONO, II) and with nitrogen dioxide to form a compound believed to be the oxygen-substituted adduct O-nitrobis(trifluoromethyl)hydroxylamine ($(CF_3)_2$-NONO₂, III).

To the knowledge of the authors this is the first reported isolation of a stable nitroxide radical containing fluorinated substituents. The stable nature of this material cannot be ascribed to steric hindrance, but is believed to result from the strong electronegative character of the CF₃ groups and some delocalization of the unpaired electron by the six fluorine atoms as evidenced by its nine-line symmetrical electron spin resonance pattern.[2]

Nitroxide free radicals, R_2NO, have been known for many years. Prior to the present synthesis of I, a few such nitroxide radicals had been prepared and isolated, whereas several others had been observed as transient species in e.s.r. studies. Diphenyl nitroxide ($(C_6H_5)_2NO$) was first prepared by Wieland and Offenbacher.[3] It has a half-life of about 50 hr. in cumene at 100° according to Thomas and Tolmann.[4] Baird and Thomas[5] have recently made an e.s.r. study of seven disubstituted nitric oxide free radicals of unreported stability. The stable free radical di-*t*-butyl nitroxide has been synthesized by Hoffmann and

(1) This work was supported in part by the Rocket Propulsion Laboratory, Air Force Systems Command, United States Air Force, Edwards Air Force Base, Calif.

(2) We are indebted to a referee for pointing out that delocalization of the unpaired electron by the fluorine atoms is reasonable but is not proved by the observation of fluorine e.s.r. hyperfine splitting since β-substituent hyperfine splitting can occur *via* a spin-polarization mechanism without electron delocalization [A.D. McLachlan, *Mol. Phys.*, 1, 233 (1958)].
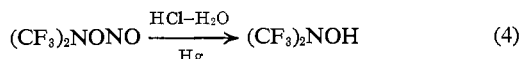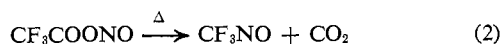
(3) H. Wieland and M. Offenbacher, *Ber.*, 47, 2111 (1914).

(4) J. R. Thomas and C. A. Tolmann, *J. Am. Chem. Soc.*, 84, 2930 (1962).

(5) J. C. Baird and J. R. Thomas, *J. Chem. Phys.*, 35, 1507 (1961).

Henderson[6] who have attributed its stability to the steric hindrance of the two *t*-butyl groups attached to nitrogen.

Other stable nitroxide radicals which have been reported are triacetoneamine N-oxide[7] and 1,1-dimethyl-3-(N-phenyloximino)butylphenyl nitroxide.[8] The oldest example of a nitroxide radical is the inorganic nitrosyl disulfonate ion also known as Fremy's salt.[9]

The present synthesis of the bis(trifluoromethyl) nitroxide was achieved by the following sequence of reactions.

$$CF_3COOAg + ClNO \longrightarrow CF_3COONO + AgCl \quad (1)$$

$$CF_3COONO \xrightarrow{\Delta} CF_3NO + CO_2 \quad (2)$$

$$2CF_3NO \xrightarrow{h\nu} (CF_3)_2NONO \quad (3)$$

$$(CF_3)_2NONO \xrightarrow[Hg]{HCl-H_2O} (CF_3)_2NOH \quad (4)$$

$$2(CF_3)_2NOH + F_2 \longrightarrow 2(CF_3)_2NO + 2HF \quad (5a)$$

$$2(CF_3)_2NOH + Ag_2O \xrightarrow{\Delta} 2(CF_3)_2NO + 2Ag + H_2O \quad (5b)$$

The yield of I by either reaction 5a or 5b was very good and no important side reactions were apparent. Fluorine degraded the material to smaller fragments when the reaction conditions were not sufficiently mild. The oxidation with fluorine proceeded readily at low temperature ($-70°$) whereas the silver oxide oxidation was carried out at 200° with no noticeable decomposition of I. Thus, I has considerable thermal stability, at least for short contact times.

The conversion of bis(trifluoromethyl)hydroxylamine (IV) to I could not be achieved with chlorine even in the presence of ultraviolet irradiation. This was in accord with the lack of reaction between IV and chlorine reported earlier by Haszeldine.[10]

The structure of bis(trifluoromethyl) nitroxide (I) was established unambiguously by physical techniques and chemical conversion to a known compound. The infrared spectrum of the radical material exhibited absorptions at 728, 995, and 1200–1300 cm.$^{-1}$ which are characteristic of compounds containing the $(CF_3)_2N-$ group.[11,12]

Nuclear magnetic resonance (n.m.r.) analysis gave a single F^{19} peak with a chemical shift of $+73.6$ ϕ.[13] A comparison of the n.m.r. spectrum of I with n.m.r. data for several related compounds in Table I indicates that all of its fluorine are equivalent and occur in trifluoromethyl groups probably attached to nitrogen.

Electron spin resonance indicated the presence of free radicals giving the pattern shown in Figure 1. The intensity ratio of the nine lines was found experimentally to be $1:6:20.5:40:50:40:20.5:6:1$, which is in close agreement with the theoretical assignments

(6) A. K. Hoffmann and A. T. Henderson, *J. Am. Chem. Soc.*, **83**, 4672 (1961).

(7) M. B. Neiman, E. G. Rozanstev, and Yu. G. Mamedova, *Nature*, **196**, 472 (1962); *Chem. Abstr.*, **58**, 5625 (1963).

(8) D. M. McQueen, U. S. Patent 2,619,479 (Nov. 25, 1952); *Chem. Abstr.*, **47**, 4652 (1953).

(9) E. Fremy, *Ann. Chim. Phys.*, [3] **15**, 408 (1845); J. H. Murib and D. M. Ritter, *J. Am. Chem. Soc.*, **74**, 3394 (1952).

(10) R. N. Haszeldine and B. J. H. Mattinson, *J. Chem. Soc.*, 1741 (1957).

(11) J. A. Young, S. N. Tsoukalas, and R. D. Dresdner, *J. Am. Chem. Soc.*, **82**, 396 (1960).

(12) J. Mason, *J. Chem. Soc.*, 4531 (1963).

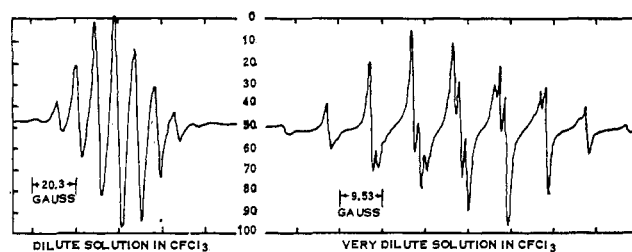(13) All n.m.r. chemical shift data measured relative to fluorotrichloromethane.

Figure 1. Electron spin resonance spectra of $(CF_3)_2NO$.

$(1:7:22:41:50:41:22:7:1)$ for six equivalent fluorine atoms of two trifluoromethyl groups attached to nitrogen with the splitting due to fluorine and nitrogen being equal. At very low concentrations, the central peaks were observed to split into triplets with the splitting for nitrogen and fluorine being 9.3 and 8.2 gauss, respectively. A *g* value of 2.0046 was obtained.

A concentrated solution (*ca.* 30%) of $(CF_3)_2NO$ in $CFCl_3$ was cooled to $-60°$ giving a color change from purple to brown, and on further cooling to $-160°$ the solution became a yellow solid. These color changes suggested a change in radical concentration which was borne out by e.s.r. measurements. The e.s.r. results indicated a gradual decrease in radical concentration on cooling the sample from 25° to about $-160°$, at which temperature an abrupt decrease in radical concentration was noted which closely corresponded to the solidification of the solution to a yellow solid.

Table I.

Compound	F^{19} n.m.r. shift,^{a} ϕ	Peak shape
$(CF_3)_2NO$	$+73.6$	Singlet
$(CF_3)_2NONO$	$+67.5$	Singlet
$(CF_3)_2NOH$	$+70$	Singlet
$(CF_3)_2NOCF_3$	$+65.7$	Septet^b
	$+67.6$	Quartet
$(CF_3)_2NF$	$+71.1$	Doublet
	$+87.5$	Broad singlet

^{a} All data obtained in $CFCl_3$ at 25°. ^{b} $J = 5$ c.p.s.

If we assume that dimerization of $(CF_3)_2NO$ follows the equation $2A \rightleftharpoons A_2$ where $(B - 2X)$ describes the concentration of radical as measured by e.s.r. with B the initial concentration of radical and X the concentration of dimer, the equilibrium constant for dimerization becomes $Ke = X/[(B - 2X)^2]$. A plot of log Ke vs. $1/T$ for temperatures 232–126°K. (Figure 2) gave a straight line from which a slope was obtained corresponding to a heat of dimerization of -2.5 kcal./mole.[14]

Combining the radical I with nitric oxide produced II. This product was identical with the material prepared as an intermediate by ultraviolet irradiation of CF_3NO according to reaction 3. The structure of II has been established by Haszeldine and Mattinson.[10] Reaction 6 is consistent with the observed results and

(14) The radical concentrations were corrected for changes in spectrometer sensitivity with temperature. The values of B and ΔH were selected to provide a least-squares fit of log Ke = constant $- \Delta H/R \cdot (1/T)$ to the data.
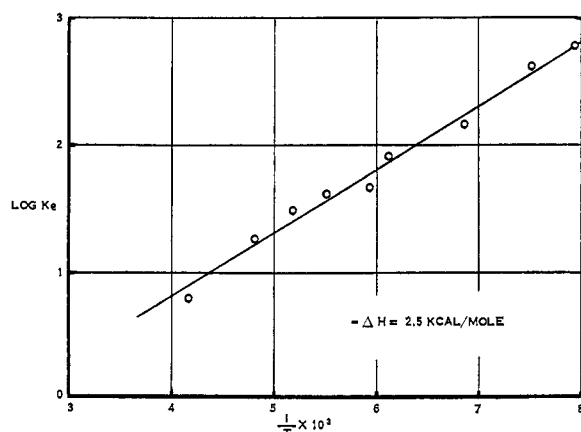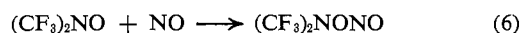
Figure 2. Dimerization of $(CF_3)_2NO$.

chemically establishes the structure of I as being that proposed.

$$(CF_3)_2NO + NO \longrightarrow (CF_3)_2NONO \qquad (6)$$

Experimental

Trifluoroacetyl Nitrite. Trifluoroacetyl nitrite, CF_3-COONO, was prepared by the method of Taylor, Brice, and Wear[15] and was used without further purification.

Trifluoronitrosomethane. Trifluoroacetyl nitrite was thermally decomposed at 200–230° and the product purified according to the procedure of Taylor, Brice, and Wear.[15] The material obtained was 80–90% CF_3NO, with CF_3NO_2 as the major impurity, and was used without further purification.

O-Nitrosobis(trifluoromethyl)hydroxylamine. The procedure of Haszeldine and Mattinson[10] involving irradiation of CF_3NO was employed. A second preparation eliminating the isolation of CF_3NO by extending the procedure of Rosser[16] gave results equivalent to those obtained in the above two-step process. Trifluoroacetyl nitrite (20–25 g.) was charged to a 5-l. bulb and irradiated with sunlight until all the liquid and the blue color of the trifluoronitrosomethane disappeared. The gaseous products were then purified by trap-to-trap fractionation giving the brown O-nitroso-bis(trifluoromethyl)hydroxylamine, which was used without further purification.

A high purity sample was obtained by gas chromatography on a 32 ft. $\times$ $^3/_8$ in. copper column packed with 33% FC-43 on chromosorb P and was used to obtain the n.m.r. results in Table I.

Bis(trifluoromethyl)hydroxylamine. The method of Haszeldine and Mattinson[10] was used with the exception that 5-l. bulbs at subatmospheric pressure were employed in place of Carius tubes. Vapor phase chromatography indicated the product was better than 90% pure. Trapping fractions from a vapor phase chromatographic separation gave pure material which gave the n.m.r. results recorded in Table I.

Bis(trifluoromethyl) Nitroxide. Bis(trifluoromethyl) nitroxide was prepared from $(CF_3)_2NOH$ by two separate routes.

(15) C. W. Taylor, T. J. Brice, and R. L. Wear, *J. Org. Chem.*, 27, 1064 (1962).
(16) R. W. Rosser, Ph.D. Thesis, University of Colorado, 1961, p. 23.

1. Via Fluorine Oxidation. Bis(trifluoromethyl)-hydroxylamine (1.5 g., 8.9 mmoles) was condensed into a U-shaped pyrex reactor and maintained as a solid by cooling the reactor with powdered Dry Ice. A fluorine–nitrogen mixture (1:3) was passed over the solid and the effluent gases passed through a liquid nitrogen cooled product trap. After excess fluorine had been introduced the noncondensable gases were pumped off and the reaction products partially purified by trap-to-trap fractionation. SiF_4 and a small amount of CF_4 were identified by infrared analysis. The major product, $(CF_3)_2NO$, was a yellow solid at Dry Ice temperatures which melted to a brown liquid and vaporized to a purple gas. The yield of radical was over 90%, containing as the major impurity the known compound $(CF_3)_2NOCF_3$.

2. Via Silver Oxide Oxidation. Bis(trifluoromethyl-hydroxylamine (4.4 g., 26 mmoles) was passed through a 19.3 $\times$ 12 mm. o.d. Pyrex tube containing silver oxide (5.5 g.) heated to 180–200°. The effluent gases were passed through a trap at $-22°$ (CCl_4 slush) and condensed into a storage cylinder at $-196°$. Essentially no noncondensable gases were formed and infrared analysis of the stored product indicated that the material was $(CF_3)_2NO$. The yield calculated by pressure–volume measurements was quantitative.

Pure bis(trifluoromethyl) nitroxide was obtained by trapping fractions from a vapor phase chromatographic separation. A 32 ft. $\times$ $^3/_8$ in. copper column packed with 33% FC-43[17] (perfluorinated tri-n-butylamine) on chromosorb P was used at 0°. The infrared spectrum was obtained on 11 mm. of radical material in a 5-cm. minimum volume cell: 1395 (m), 1290 (vs), 1230 (vs), 995 (s), and 728 (m) (pqr) cm.$^{-1}$. The n.m.r. results (Table I) were obtained on the purified material. The molecular weight was determined by the Regnault method giving values of 167.5 and 168.0 vs. a theoretical value of 168.0.

Electron spin resonance data were obtained on a Varian e.s.r. spectrometer at a field of 3300 gauss and a frequency of 9.2 kMc./sec. with 100-kc. field modulation and a Harvey-Wells 12-in. electromagnet. The radical material was diluted with $CFCl_3$ or benzene and gave the nine-line pattern recorded in Figure 1. The log K_e obtained for nine temperatures by e.s.r. measurements were plotted vs. the reciprocal of the temperature, $1/T$, to give the straight line shown in Figure 2.

The mass cracking pattern exhibited the following fragments in the order of their decreasing relative intensity: CF_3 (>100), NO (100), CF (43.8), CF_2 (32.4), CF_3NOCF_2 (25.1), N_2 (23.7), CO (23), $(CF_3)_2NO$ (13.5), C (12), CF_3NO (5.8), O (5.1), F_2CN (4.9), FCN (4.8), O_2 (4.6), N (4.0), F (3.7).

Reactions of Bis(trifluoromethyl) Nitroxide. Bis-(trifluoromethyl) nitroxide was changed to an infrared cell and a spectrum taken. Nitric oxide was added to the cell and on reanalysis the infrared spectrum was identical with that of $(CF_3)_2NONO$.

Nitrogen dioxide combined very quickly with the radical I in the gas phase at 25° to give a new compound with infrared absorptions at 720 (s), 783 (s), 985 (s), 1220–1320 (vs), 1385 (w), 1770 (s), and 1820 (w) cm.$^{-1}$.

(17) Product of Minnesota Mining and Manufacturing Co.

This product reacted quickly with mercury to form O-nitrosobis(trifluoromethyl)hydroxylamine ((CF$_3$)$_2$-NONO), indicating the new compound to be O-nitro-bis(trifluoromethyl)hydroxylamine ((CF$_3$)$_2$NONO$_2$).

The radical material I was allowed to contact air, water, and 10% sodium hydroxide with no reaction based on visual observation and infrared analysis. It has been found to be compatible with stainless steel, copper, and glass over long periods of time.
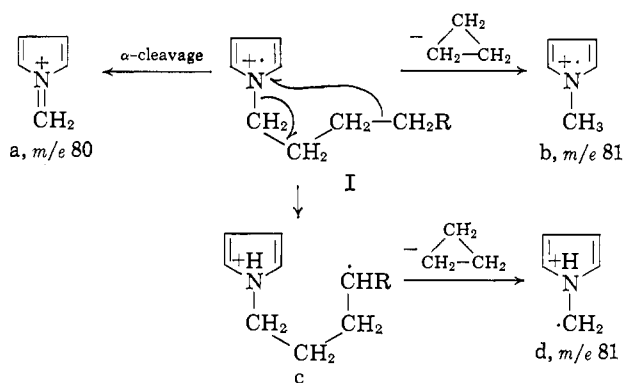
Mass Spectrometry in Structural and Stereochemical Problems. LXIII.[1] Hydrogen Rearrangements Induced by Electron Impact on N-*n*-Butyl- and N-*n*-Pentylpyrroles[2]

A. M. Duffield,[3a] R. Beugelmans,[3b] H. Budzikiewicz, D. A. Lightner,[3c] D. H. Williams, and Carl Djerassi

Contribution from the Department of Chemistry, Stanford University, Stanford, California. Received October 19, 1964

A study of the mass spectra of deuterated analogs of N-n-butyl- and N-n-pentylpyrroles has uncovered and clarified the rather complex origin of the peaks at m/e 80 and 81 in the spectra of the parent compounds. High-resolution mass spectrometry established the composition of these species as C$_5$H$_6$N$^+$ and C$_5$H$_7$N$^+$. The former results from α-cleavage of the respective molecular ions and also from loss of a hydrogen radical from m/e 81 and is assigned structure a. The fragment of mass 81 is formed predominantly by transfer of hydrogen from C-3 of the alkyl chains through any one of three mechanisms. Anomalous quantitative shifts in m/e 81 observed in some of the deuterated analogs of N-n-butyl and N-n-pentylpyrroles can be explained by a process involving exchange of deuterium and hydrogen between C-3 of the alkyl chain and an α-carbon atom of the heterocyclic ring. The formation of the less abundant ions at m/e 67 and 53 is also rationalized.

Introduction

Systematic work on the mass spectrometric fragmentation of pyrroles has been performed only recently.[4,5] In that connection relatively few N-alkylpyrroles have been studied and an analysis of the recorded[6a] mass spectrum of N-*n*-butylpyrrole (I, R = H) has been attempted,[5] especially as far as the major peaks at *m/e* 80 and 81 (see Figure 1) are concerned. The *m/e* 80 species was suggested[5] to have its genesis from α-cleavage of the molecular ion (I, R = H) of N-*n*-

butylpyrrole, and to be represented by a. This cleavage corresponds to that observed with alkyl amines (α-cleavage) as well as to the fission of benzylic bonds in alkyl-substituted aromatic systems.

Two possibilities were suggested for the ion of mass 81 in the spectrum of N-*n*-butylpyrrole[5]: (1) transfer of the terminal methyl group of the side chain to nitrogen with concomitant homolysis of the nitrogen–carbon bond (I (R = H) → b) and elimination of cyclopropane, or (2) hydrogen transfer from the terminal methyl group *via* a six-membered intermediate to nitrogen (I (R = H) → c (R = H)) followed by α-cleavage and formation of d.

In view of our great interest[6b] in demonstrating possible methyl migrations in mass spectrometric fragmentation processes, N-*n*-(butyl-4,4,4-*d*$_3$)pyrrole was prepared but no migration of the labeled methyl group was found to occur (Table I). The mass spectrum of this labeled analog showed the second possibility, I → c → d, to operate only to the extent of 8% as deduced from the shift of the *m/e* 81 peak to *m/e* 82. Consequently, we decided to prepare N-*n*-butylpyrroles labeled with deuterium in all positions of the alkyl chain in order to determine precisely the source of the hydrogen transferred in the formation of the ion of mass 81. It was observed that the spectra (Figures 1 and 2) of N-*n*-pentyl- and N-*n*-butylpyrroles were identical with

(1) Paper LXII: J. Karliner, H. Budzikiewicz, and C. Djerassi, *J. Am. Chem. Soc.*, 87, 580 (1965).

(2) We are indebted to the National Institutes of Health of the U. S. Public Health Service for financial assistance (Grants No. GM-11309 and AM-04257).

(3) (a) Postdoctoral Research Fellow 1963–1965; (b) recipient of a N.A.T.O. (Paris) travel grant; (c) N.S.F. Postdoctorate Fellow 1963–1964.

(4) H. Budzikiewicz, C. Djerassi, A. H. Jackson, G. W. Kenner, D. J. Newman, and J. M. Wilson, *J. Chem. Soc.*, 1949 (1964).

(5) H. Budzikiewicz, C. Djerassi, and D. H. Williams, "Interpretation of Mass Spectra of Organic Compounds," Holden-Day, Inc., San Francisco, Calif., 1964, p. 237.

(6) (a) "Catalog of Mass Spectral Data," American Petroleum Institute Project 44, Carnegie Institute of Technology, Pittsburgh, Pa., spectrum no. 624; (b) F. Komitsky, J. E. Gurst, and C. Djerassi, in press.