Reactions of Hexafluoroacetone and Orthoformates

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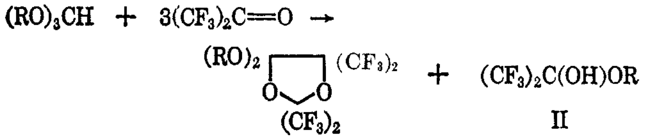
The reaction of orthoformates with hexafluoroacetone is quite general. Aliphatic and alicyclic orthoformates react with 3 molar equiv of a ketone to give cyclic ethers I and III and a mole of a hemiketal. This reaction may involve a dialkoxymethylene intermediate. The caged orthoformate VI and hexafluoroacetone give a formate ester as the only product. The product from the thermal rearrangement of Ia is the unusual methyl ester VIII.

The only reported reaction of an ortho ester with a halo ketone is that of dichloroacetone with triethyl orthoformate to give the diethyl acetal of dichloroacetone.[1] This paper describes several new reactions of hexafluoroacetone with orthoformates.

Aliphatic and alicyclic orthoformates react readily with hexafluoroacetone at 150° to give two products, a mole of 2,2,4,4-tetrakis(trifluoromethyl)-5,5-dialkoxy-1,3-dioxolane (I) and the hemiketal II.

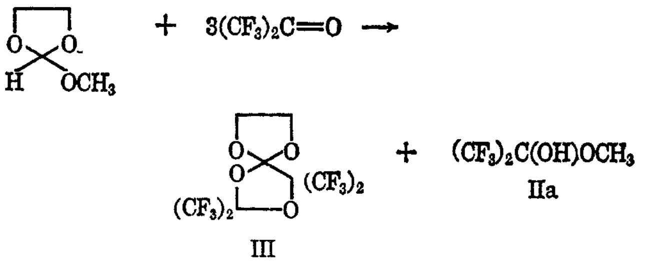


Ia, R = CH_3
b, R = C_2H_5
c, R = $n\text{-}C_5H_{11}$
d, R = $C_4H_9CH(C_2H_5)CH_2$
e, R = $CH_2{=}CHCH_2$
f, R = $ClCH_2CH_2$

The hemiketals of hexafluoroacetone are known substances and are easily removed from the reaction mixture by distillation at atmospheric pressure.[2]

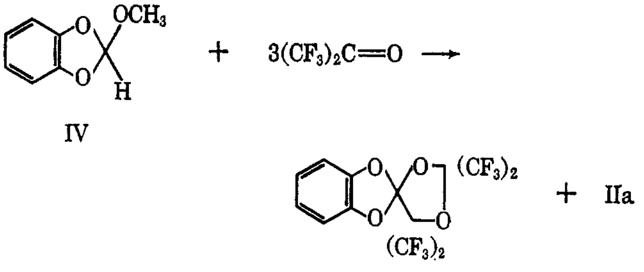
The new dioxolanes (I) are colorless liquids with unusual chemical stability. For example, Ia was unaffected by heating at 75° for 70 hr with thionyl chloride or by heating at 100° for 4 hr in a bomb with boron trifluoride gas. Compound Ib was inert to treatment with 50% sodium hydroxide solution at 25° and unaffected by heating with excess phosphorus pentachloride at 90° for 5 hr. The structure proof for Ia is based on elemental analysis and molecular weight. Its infrared spectrum shows the absence of OH, C=O, and C=C bonds. The proton nmr, fluorine nmr, and mass spectra were all in complete agreement with the proposed structure.

This reaction has been extended to cyclic orthoformates which on reaction with hexafluoroacetone yield spiroethers. For example, 2-methoxy-1,3-dioxolane and 3 moles of hexafluoroacetone give a mole of hemiketal IIa and 2,2,4,4-tetrakis(trifluoromethyl)-1,3,6,9-tetraoxa[4.4]nonane (III).



III

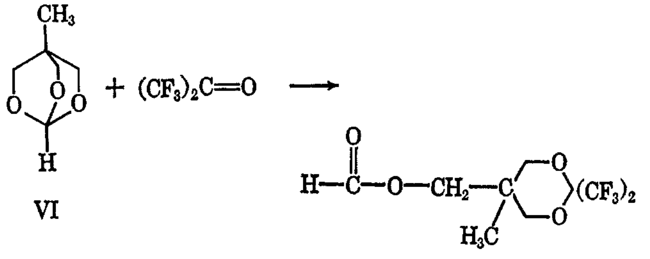
Similarly, 2-methoxy-1,3-benzodioxolane (IV) and 3 moles of hexafluoroacetone give V and IIa. The properties of these and related compounds are summarized in Table I.



V

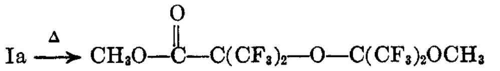
The reaction of triethyl orthoformate with chloropentafluoroacetone gives the analogous dioxolane. Using the more hindered and less electrophilic chlorofluoro ketones, such as 1,3-dichlorotetrafluoroacetone, other products are obtained which will be the subject of a later publication.

The cage orthoformate, 4-methyl-2,6,7-trioxabicyclo[2.2.2]octane, gives the formate ester VII with hexafluoroacetone.



VII

The new dioxolanes (Ia–f) are stable at 100 to 150° for several days but can decompose or rearrange at higher temperature. After heating Ia at 160° for 70 hr a new peak was observed in the infrared spectrum at 5.65 μ. Preparative-scale gas chromatography was used to isolate the pure liquid ester VIII.



$$\mathrm{Ia} \xrightarrow{\Delta} CH_3O{-}\overset{\overset{\displaystyle O}{\|}}{C}{-}C(CF_3)_2{-}O{-}C(CF_3)_2OCH_3$$

VIII

The spiro compounds, IXa and b, heated at 180 to 200°, degrade smoothly to allyl chloride, carbon dioxide, and hexafluoroacetone for IXa and phenyl allyl ether, carbon dioxide, and hexafluoroacetone for IXb.

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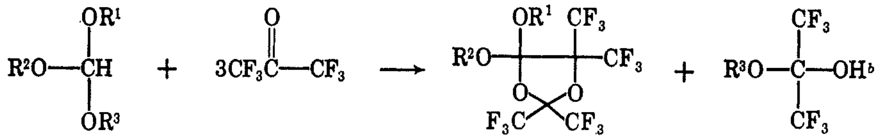
[1] A. Wohl, *Ber.*, **41**, 3599 (1908).

[2] C. Woolf, Abstracts, 32nd National Meeting of the American Chemical Society, New York, N. Y., Sept 1957, p 23M.

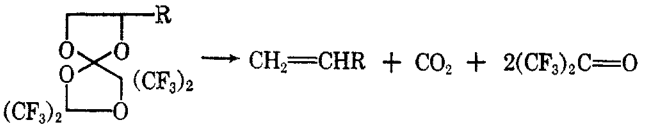
TABLE I

5,5-DIALKOXY-2,2,4,4-TETRAKIS(TRIFLUOROMETHYL)-1,3-DIOXOLANES[a]



Compd	R¹	R²	R³	% yield	$n^{25}D$	Bp, °C (mm)	Mp, °C	Formula	Calcd, %			Found, %		
									C	H	F	C	H	F
Ia	CH_3	CH_3	CH_3	79.4	1.3225	161	−1 to 0	$C_9H_6F_{12}O_4$[c]	26.61	1.49	56.14	26.64	1.37	56.10
Ib	C_2H_5	C_2H_5	C_2H_5	84.7	1.3315	92 (45)	−12	$C_{11}H_{10}F_{12}O_4$	30.43	2.32	52.51	30.66	2.49	52.44
Ic	n-C_5H_{11}	n-C_5H_{11}	n-C_5H_{11}	57.0	1.3717	152 (45)		$C_{17}H_{22}F_{12}O_4$	39.39	4.28	43.98	39.57	4.14	43.65
Id	R¹ = R² = R³ = $C_4H_9CH(C_2H_5)CH_2$–			67.5	1.3870	130 (2.4)		$C_{23}H_{24}F_{12}O_4$	45.85	5.69	37.84	46.06	5.48	37.85
Ie	R¹ = R² = R³ = CH_2=$CHCH_2$–			64.2	1.3532	67 (4.3)		$C_{13}H_{10}F_{12}O_4$	34.07	2.20	49.76	34.00	2.51	49.63
III	–CH_2CH_2–		CH_3	74.7[c]		176	24	$C_9H_4F_{12}O_4$	26.75	1.00	56.42	26.98	0.89	56.23
IXb	–CH_2CH– $CH_2OC_6H_5$		C_2H_5	96.0	1.4044	120 (1.45)		$C_{16}H_{10}F_{12}O_4$	37.66	1.98	44.68	38.05	1.79	44.70
. . .	–CH_2–$C(CH_3)_2$–CH_2–		C_2H_5	81.8	1.3391	43 (0.18)		$C_{12}H_{10}F_{12}O_4$	32.30	2.26	51.10	32.39	2.67	51.35
. . .	–$CH_2C(CH_2)_2CH$– $CH(CH_3)_2$		CH_3	90.0			73–74[d]	$C_{15}H_{16}F_{12}O_4$	36.89	3.30	46.69	37.29	3.50	46.92
IXa	–$CH_2CH(CH_2Cl)$–		C_2H_5	89.9	1.3523	94 (12)		$C_{10}H_5ClF_{12}O_4$	26.54	1.11	7.83 (Cl)	26.77	1.01	7.95 (Cl)
V		CH_3	CH_3	75.2		207	71–72	$C_{13}H_4F_{12}O_4$	34.53	0.89	50.42	34.59	0.96	50.22
If	$(CH_2)_2Cl$	$(CH_2)_2Cl$	$(CH_2)_2Cl$	28.4	1.3684	86 (1.5)		$C_{11}H_9F_{12}ClO_4$	14.10 (Cl)		45.32	13.96 (Cl)		45.28

[a] All reactions were run in a stainless steel bomb. No solvent is required, but benzene has been used where the ortho ester is a crystalline solid at room temperature. Reaction conditions were 150° for 6 hr. Products were isolated by fractional distillation using a 3-ft spinning-band column. In all examples, the infrared and proton nmr spectra were in complete agreement with the proposed structures. [b] The hemiketals were isolated and characterized by comparison of their infrared and nmr spectra with authentic samples prepared from hexafluoroacetone or chloropentafluoroacetone and the appropriate alcohol. [c] The fluorine nmr spectra contained two equal peaks: +278 cycles [O–$C(CF_3)_2$–O fluorines] and +708 cycles [C–$C(CF_3)$–O fluorines]. (Freon 112 was used as external reference.) [d] Recrystallized from petroleum ether (bp 38–56°) to give white needles.



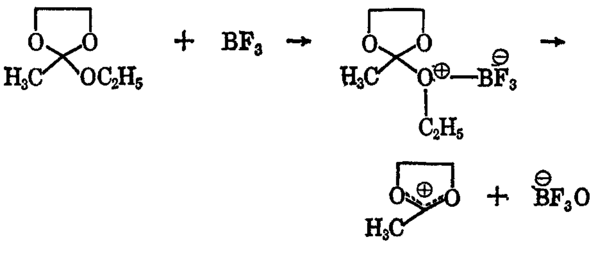
IXa, R = CH_2Cl
b, R = $OCH_2C_6H_5$

Discussion

A reaction mechanism is needed to explain the usual group of products from the reaction of orthoformates with perhalo ketones. The reactions are not solvent dependent, and, in fact, high yields of most of the products are obtained without solvent. Free-radical reactions are not involved, since addition of initiators such as di-*t*-butyl peroxide or inhibitors such as hydroquinone or 2,2-diphenyl-1-picrylhydrazyl did not alter the yield of Ia.

The proposed mechanism is shown in Scheme I.

The first step could be the attack of a mole of hexafluoroacetone on an ether oxygen of the orthoformate where the hexafluoroacetone acts as a Lewis acid and the orthoformate as a Lewis base. This step resembles the reaction of BF_3 with ortho esters.[3]



The electron-withdrawing CF_3 groups enhance the electrophilic character of the carbonyl carbon atom in hexafluoroacetone, making it a strong Lewis acid. The Lewis acid character of hexafluoroacetone makes possible the uncatalyzed reaction with aromatic amines,[4,5] phenols,[6,7] and amides[8] and the formation of stable hydrates[9] and hemiketals.[2,9]

The complex so formed decomposes to liberate the hemiketal and dialkoxymethylene (X). Hexafluoroacetone must be an effective trap for the carbene, and steric considerations are favorable for reaction with 2 moles of hexafluoroacetone and formation of the 1,3-dioxolane (I). There has been previous evidence for the formation of dialkoxymethylene from trialkyl orthoformates and weak acids[10] as well as indications of dialkoxymethylene intermediates in other reactions.[11,12]

In the case of the caged orthoformate VI, a mole of hemiketal cannot be eliminated, and the reaction takes

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(3) H. Meerwein, *Angew. Chem.*, **67**, 375 (1955).

(4) I. L. Knunyants, C. Ching-Yun, N. P. Gamaryan, and E. M. Rokhlin, *Zh. Vses. Khim. Obshchestva im. D. I. Mendeleeva*, **5**, 114 (1960); *Chem. Abstr.*, **54**, 20962 (1960).

(5) E. E. Gilbert, E. S. Jones, and J. P. Sibibia, *J. Org. Chem.*, **30**, 1001 (1965).

(6) B. S. Farah, E. E. Gilbert, M. Litt, J. A. Otto, and J. P. Sibilia, *ibid.*, **30**, 1003 (1965).

(7) D. C. England, French Patent 1,325,204 (1963); *Chem. Abstr.*, **59**, 11339 (1963).

(8) P. E. Newallis and E. J. Rumanowski, *J. Org. Chem.*, **29**, 3114 (1964).

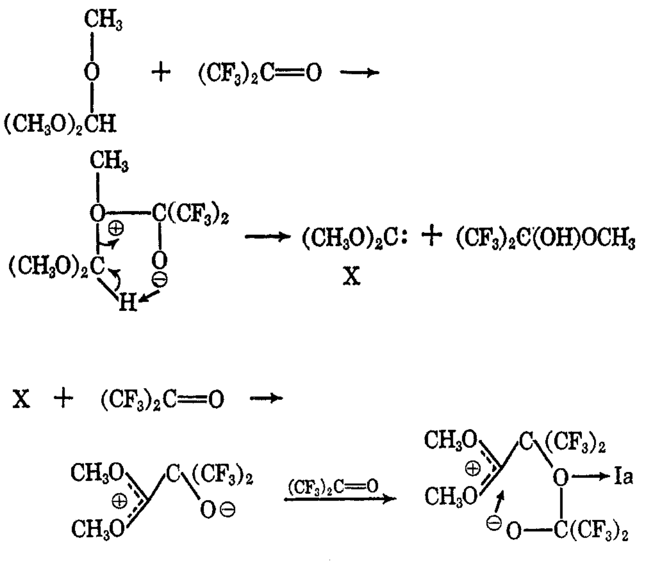
(9) A. L. Henne, J. W. Shepard, and E. J. Young, *J. Am. Chem. Soc.*, **72**, 3577 (1950).

(10) G. Crank and F. W. Eastwood, *Australian J. Chem.*, **17**, 1392 (1964).

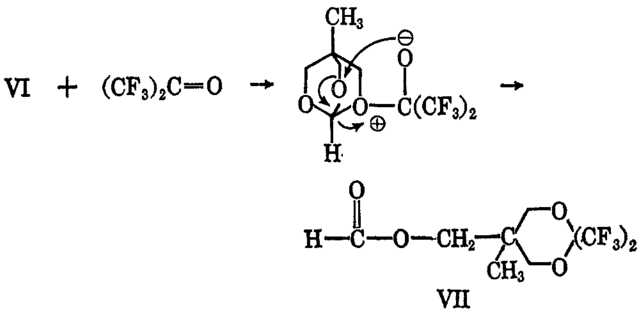
(11) E. J. Corez and R. A. E. Winter, *J. Am. Chem. Soc.*, **85**, 2677 (1963).

(12) R. W. Hoffmann and H. Hauser, *Tetrahedron*, **21**, 891 (1965).

Scheme I

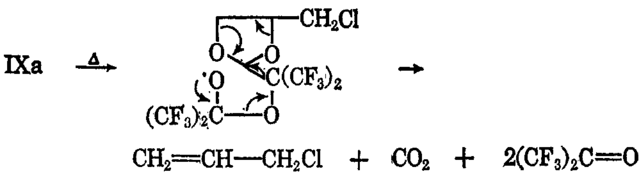


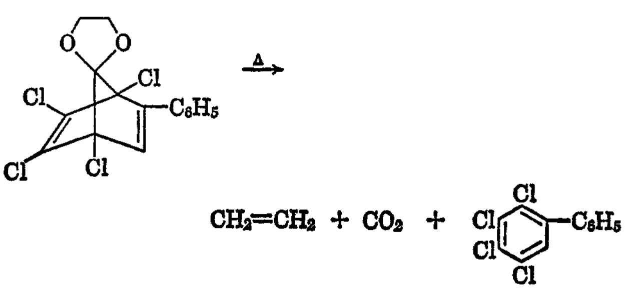
a different path after the initial attack of the ketone on the ether oxygen.



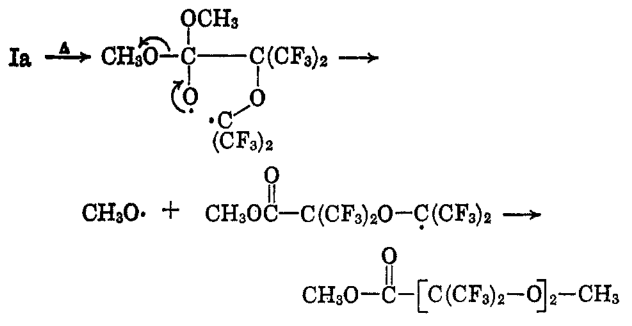
VII

The decomposition of IXa probably occurs synchronously after an initial cleavage of a carbon–oxygen bond. A fragmentation similar to that of IXa was reported recently.[13]





From products isolated from the thermal rearrangement or decomposition of Ia and IXa, it appears likely that the ring carbon–oxygen bond of the ortho ester is initially broken with the formation of a diradical or perhaps an ionic species which rearranges to the methyl ester VIII.



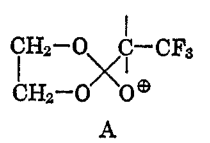
VIII

Subsequent papers will deal with the reaction of hexafluoroacetone with ortho esters other than orthoformates, acetals, and ketals.

Experimental Section[14]

A. **Preparation of Orthoformates.**—The orthoformates which were not available from commercial sources were prepared by the transorthoesterification reaction between glycols and trimethyl or triethyl orthoformate catalyzed by *p*-toluenesulfonic acid:[15] 2-methoxy-4-isopropyl-5,5-dimethyl-1,3-dioxane, bp 100° (17 mm) (*Anal.* Calcd for $C_{10}H_{20}O_3$: C, 63.79; H, 10.71. Found: C, 64.17; H, 10.68.); 2-ethoxy-4-chloromethyl-1,3-dioxane, bp 100° (22 mm) (*Anal.* Calcd for $C_6H_{11}ClO_3$: Cl, 21.28. Found: Cl, 21.11.); 2-ethoxy-4-phenoxymethyl-1,3-dioxolane (from 3-phenoxy-1,2-propanediol[16]), bp 173–174° (12 mm) (*Anal.* Calcd for $C_{12}H_{16}O_4$: C, 64.27; H, 7.19. Found: C, 63.95; H, 7.16.); 2-ethoxy-5,5-dimethyl-1,3-dioxane, bp 91° (41 mm) (*Anal.* Calcd for $C_8H_{16}O_3$: C, 59.97; H, 10.07. Found: C, 59.65; H, 9.84.); and 2-methoxy-1,3-benzodioxolane, bp 110–111° (46 mm) (*Anal.* Calcd for $C_{15}H_{14}O_2$: C, 63.15; H, 5.30. Found: C, 63.06; H, 5.25.).

B. **2,2,4,4-Tetrakis(trifluoromethyl)-1,3,6,9-tetraoxaspiro[4.4]nonane (III).**—Hexafluoroacetone (66.5 g, 0.4 mole) and 2-methoxy-1,3-dioxolane (13.9 g, 0.133 mole) were heated in a stainless steel bomb at 150° for 6 hr at autogenous pressure. The bomb was vented, and the liquid product was fractionated on a spinning-band column to give the hemiketal IIa, bp 40° (62 mm), 26.8 g (68.0% based on 2-methyl-1,3-dioxolane). The infrared and proton nmr spectra of IIa were identical with those of an authentic sample prepared from hexafluoroacetone and methanol. The residue was fractionated to give III, bp 108° (62 mm), 40.2 g (74.7%). The infrared spectrum showed no absorption due to OH, C═O, or C═C. A sample of III gave a single gc peak on three different columns, which confirmed its homogeneity. The proton nmr spectrum contained a single peak at 4.20 ppm ($-O-CH_2-CH_2-O-$ protons). The mass spectrum contained the parent ion *m/e* 403 (calcd mol wt 403) and fragments which further support the proposed structure: *m/e* 385 (parent − F), 335 (parent − CF_3), 204 [parent − $-O-\overset{|}{C}(CF_3)_2-$], 178 [$(CF_3)_2C—\overset{|}{\underset{|}{C}}—O^{\oplus}$], 169 (A). See Table I for analytical data.



A

Similar experimental procedures were used for the preparation of all the compounds of Table I.

C. **2,4-Bis(trifluoromethyl)-2,4-bis(chlorodifluoromethyl)-5,5-diethoxy-1,3-dioxolane.**—Using the same experimental pro-

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[13] D. M. Lemal, E. P. Bosselink, and A. Ault, *Tetrahedron Letters*, No. 11, 579 (1964).

[14] Fluorine nmr spectra were obtained with Varian Associates high-resolution nmr spectrometer operating at 56.4 Mc/sec. Spectra were calibrated in parts per million from the F^{19} resonance of 1,2-difluoro-1,1,2,2-tetrachloroethane used as an external reference. Proton spectra were obtained with a Varian Associates A-60 spectrometer. Spectra were calibrated (in parts per million) from the proton resonance of tetramethylsilane used as an external reference. Melting points and boiling points are uncorrected.

[15] H. Baganz and L. Damaschke, *Ber.*, **91**, 650 (1958).

[16] J. O. Hoppe, *J. Med. Chem.*, **6**, 246 (1963).

cedure as shown above, triethyl orthoformate (29.6 g, 0.20 mole) and chloropentafluoroacetone (110.0 g, 0.60 mole) gave 2,4-bis(trifluoromethyl)-2,4-bis(chlorodifluoromethyl)-5,5-diethoxy-1,3-dioxolane, 60.5 g (64.7%), bp 110° (23 mm), n^{25}_{D} 1.3728. The infrared spectrum contained no OH, C═O, or C═C bonds.

Anal. Calcd for $C_{11}H_{10}Cl_2F_{10}O_4$: C, 28.22; H, 2.37; Cl, 15.15. Found: C, 28.50; H, 2.09; Cl, 14.79.

D. **2,2-Bis(trifluoromethyl)-5-methyl-5-formyloxymethyl-1,3-dioxane (VII).**—A mixture of 2-ethyl-2,6,7-trioxabicyclo-[2.2.2]octane (Kay-Fries Chemicals, Inc., 13.0 g, 0.1 mole), benzene (50.0 g), and hexafluoroacetone (50.0 g, 0.3 mole) was heated in a bomb at 150° for 6 hr. The bomb was cooled and vented to remove unreacted hexafluoroacetone. The liquid residue was fractionated on a spinning-band column to give 16.4 g (55.4%) of VIII, bp 60–62° (0.25 mm), n^{25}_{D} 1.3772. The infrared absorption spectrum contained no hydroxyl or C═C bands but did show an ester carbonyl band at 5.74 μ. The doublet at 8.77 and 8.95 μ is due to the C–O–C of the dioxane ring. The proton nmr spectrum showed singlets at 8.0 (area 1, –COOH proton), 4.20 [area 2, –C(═O)–O–CH_2–C protons), 3.94 (area 4, ring C–CH_2–O protons), and 0.98 ppm (area 3, C–CH_3 protons).

Anal. Calcd for $C_9H_{10}F_6O_4$: C, 36.50; H, 3.40; F, 38.49; mol wt, 296. Found: C, 36.41; H, 3.45; F, 38.00; sapon equiv, 285.

E. **Methyl 1,1,3,3-Tetrakis(trifluoromethyl)-3,5-oxacaproate (VIII).**—5,5-Dimethoxy-2,2,4,4-tetrakis(trifluoromethyl)-1,3-dioxolane (Ia, 20.0 g, 0.049 mole) was heated at reflux (160 ± 5°) for 75 hr. The residue in the flask was 90% Ia and 10% VIII, and the separation was made by preparative-scale gc on a 3 ft × 0.75 in. column packed with 25% tetra[fluoroalkyl (C_5 and C_7)]pyromellitate on Chromosorb P at 150° (flow, 860 cc of He/min). The first peak was Ia (6.6 min), and the only other peak was VIII (25.6 min), bp 156°, fp −6°, n^{25}_{D} 1.3678. The infrared spectrum of VIII contained no OH or C═C peaks but did show a C═O peak at 5.65 μ. The C═O band is not due to an aldehyde or ketone, since the compound did not react with 2,4-dinitrophenylhydrazine reagent. The proton nmr spectrum contains two singlets of equal area at 2.68 and 2.79 ppm. The mass spectrum of VIII contained m/e 375 (parent − OCH_3), 171 [$C(OCH_3)(CF_3)COOCH_3$)], and 59 (–$COOCH_3$).

Anal. Calcd for $C_9H_6F_{12}O_4$: C, 26.61; H, 1.49; F, 56.14. Found: C, 27.24; H, 1.85; F, 56.19.

F. **Decomposition of 2,2,4,4-Tetrakis(trifluoromethyl)-7-chloromethyl-1,3,6,9-tetraoxaspiro[4.4]nonane (IXa).**—Thirty grams (0.066 mole) of IXa was heated at 190–200° in a flask fitted with a water-cooled condenser leading to an ice trap followed by a Dry Ice trap. After 3 hr 2.5 g of IXa remained in the flask. The ice trap contained 0.7 g and the Dry Ice trap contained 29.2 g which was separated by trap-to-trap transfer into a fraction with boiling point less than −30° (13.4 g). Gc analysis showed this to be a mixture of CO_2 (28%) and hexafluoroacetone (69%). A fraction with boiling point greater than −30° was also obtained. Gc analysis showed this to be a mixture of hexafluoroacetone (10%) and allyl chloride (83%). The allyl chloride was further identified by fractional distillation of the high-boiling fraction, bp 45–46° (lit.[17] bp for allyl chloride 45–45.5°). The infrared and proton nmr spectra were identical with those of an authentic sample of allyl chloride.

Anal. Calcd for C_3H_5Cl: C, 47.09; H, 6.59. Found: C, 46.98; H, 6.44.

G. **Decomposition of 2,2,4,4-Tetrakis(trifluoromethyl)-7-phenoxymethyl-1,3,6,9-tetraoxaspiro[4.4]nonane (IXb).**—Using the same procedure as in the previous experiment, IXb (39.0 g, 0.076 mole) was decomposed by heating at 180° for 6 hr. Hexafluoroacetone and carbon dioxide were identified as the primary volatile products by mass spectral analysis. The residue was fractionated to give 6.2 g (77.5%) of allyl phenyl ether, bp 95° (31 mm), n^{25}_{D} 1.5191. The infrared and proton nmr spectra are in complete agreement with that expected for allyl phenyl ether.

Anal. Calcd for $C_9H_{10}O$: C, 80.56; H, 7.51. Found: C, 80.66; H, 7.68.

The residue from the distillation was undecomposed IXb (8.3 g).

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(17) R. L. Shriner, R. C. Fuson, and D. Y. Curtin, "The Systematic Identification of Organic Compounds," John Wiley and Sons, Inc., New York, N. Y., 1956, p 308.

Nuclear Magnetic Resonance Study of Some N,N-Dimethylcarbamates

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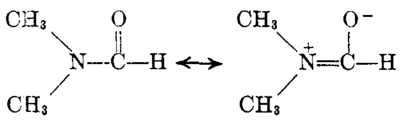
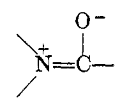
The nmr spectra of 26 N,N-dimethylcarbamates were obtained. The effect on the splitting and chemical shifts of the N,N-dimethylamino protons induced by varying the substituents on the carbonyl carbon atom is reported.

N,N-Dimethylformamide is the classic example of nuclear magnetic nonequivalence of two methyl groups attached to nitrogen.[1-3] At room temperature, rotation about the nitrogen–carbonyl carbon bond in this compound is so reduced, because of resonance interaction, that the methyl groups are magnetically nonequivalent. This gives rise to a distinct peak for each methyl group in the nmr spectrum. By measuring C^{13}–H coupling constants of N,N-dimethylacetamide, Haake, *et al.*,[4] have verified Pauling's conclusion that the dipolar form of such amides contributes about 40% to the total structure.





There have been several recent studies of the magnetic nonequivalence of protons of alkyl groups attached to nitrogen, *e.g.*, in N,N-disubstituted amides by LaPlanche and Rogers,[5] 3-(dimethylamino)acrolein by Martin and Martin,[6] N-methylcyclohexylacetamide,[7] N,N-dimethyl-*t*-hexylsulfinamide,[7] and N,N-diethylmethanesulfinamide[8] by Moriarty.

The present paper reports the effect on the splitting and chemical shifts of the methyl protons of some N,N-dimethylcarbamates when the substituent on the car-

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(1) J. D. Roberts, "Nuclear Magnetic Resonance," McGraw-Hill Book Co., Inc., New York, N. Y., 1959, pp 69–71.

(2) M. T. Rogers and J. C. Woodbrey, *J. Phys. Chem.*, **66**, 540 (1962).

(3) A. G. Whittaker and S. Siegel, *J. Chem. Phys.*, **42**, 3320 (1965).

(4) P. Haake, W. B. Miller, and D. A. Tyssee, *J. Am. Chem. Soc.*, **86**, 3577 (1964).

(5) L. A. LaPlanche and M. T. Rogers, *ibid.*, **85**, 3728 (1963).

(6) M. Martin and G. Martin, *Compt. Rend.*, **256**, 403 (1963).

(7) R. M. Moriarty, *J. Org. Chem.*, **28**, 1296 (1963).

(8) R. M. Moriarty, *ibid.*, **30**, 600 (1965).