Heterocycles from Fluoro Ketones and Alkyl Isocyanates, 1,3-Oxazetidinones, 1,3,5-Dioxazines, and 1,3,5-Oxadiazines

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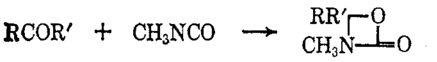
The reactions of fluoro ketones with alkyl isocyanates yield, depending on the reaction conditions, 1,3-oxazetidinones, 1,3,5-dioxazines, and 1,3,5-oxadiazines. In uncatalyzed and boron trifluoride catalyzed reactions, the oxazetidinones are the major products. In cesium fluoride catalyzed reactions at long reaction times, the six-membered ring products are formed predominantly. Preparative and mechanistic aspects of the reactions are discussed.

Few reports of 1,3-oxazetidinones appear in the literature.[1] Stallman[2] and Gaylord and Crowdle[3] proposed 1,3-oxazetidinone structures for certain aryl isocyanate dimers, but Brown[4] showed by X-ray analysis that solid phenyl isocyanate dimer is a 1,3-diazetidine. The transient existence of 1,3-oxazetidinones has been occasionally suggested in mechanistic accountings of product formation.[5] Reported in this paper are the preparation of stable 1,3-oxazetidones and the role of the compounds in the formation of related derivatives of 1,3,5-dioxazines and 1,3,5-oxadiazines.

The reactions of electronegatively substituted ketones with methyl isocyanate have been found to give 1,3-oxazetidinones in low to moderate conversions.

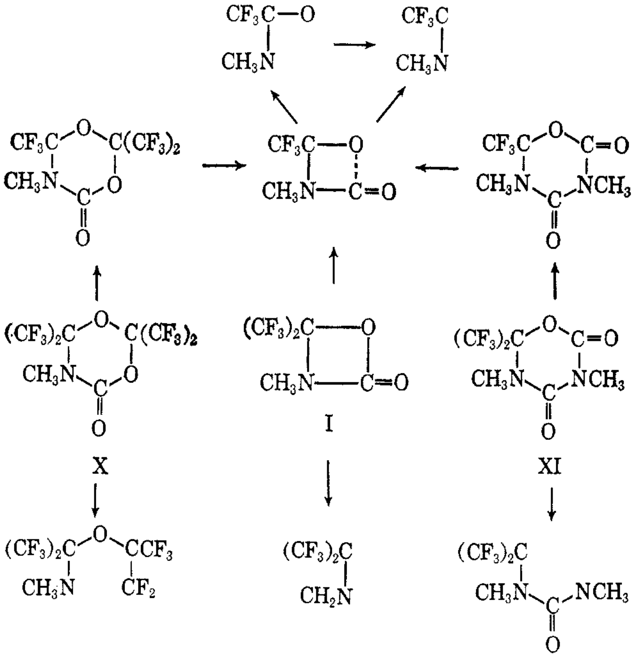


I-VI

I, $R = R' = CF_3$
II, $R = CF_3$; $R' = CF_2Cl$
III, $R = R' = CF_2Cl$
IV, $R = CF_2Cl$; $R' = CFCl_2$
V, $R = R' = CHF_2$
VI, R, $R' = CF_2CF_2CF_2$ (spiran)

In accordance with the strained four-membered ring structure, each product has an intense infrared carbonyl absorption in the 1950–1860-cm^{-1} region. The mass spectra provide strong evidence for the 1,3-oxazetidinone formulation (Scheme I).

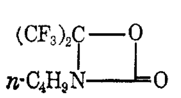
SCHEME I
PARTIAL MASS FRAGMENTATION SCHEMES FOR HEXAFLUOROACETONE–METHYL ISOCYANATE PRODUCTS



The appearance of proton–fluorine coupling in the nmr spectra of these compounds is significant. It is considered less likely that coupling would occur with alternative structures such as a 1,2-oxazetidinone (reverse addition) or a dioxetane (addition across the isocyanate carbonyl), since this would require the transmission of coupling effects through a larger number of bonds or through space. This view is supported by the nmr spectra of the dioxazines and oxadiazines which are described later. For example, splitting appears in the proton spectrum of the dioxazine X. Similar splitting is present in the proton spectrum of oxadiazine XI, but there also appears a singlet which can be attributed to the methyl group at the 3 position. The present evidence would therefore seem to favor the 1,3-oxazetidinone structure for compounds I-VI.

Cycloadduct formation is promoted when the ketone carbonyl group is flanked by two small electronegative groups. Acetone, 1,1,1-trifluoroacetone, and α,α,α-trifluoroacetophenone all failed to give detectable amounts of oxazetidinones in reactions with methyl isocyanate.

The reactions of hexafluoroacetone with a number of other isocyanates were also examined. The oxazetidinone VII was formed in low yield from *n*-butyl isocyanate.



VII

The single bands at 1885-1875 cm^{-1} in the infrared spectra of crude mixtures from cyclohexyl isocyanate, lauryl isocyanate, and ethyl isocyanato acetate indicated the presence of the corresponding oxazetidinones, but the pure products were not isolated from these mixtures.

Electron-rich isocyanates of small steric size are more reactive in the cycloaddition reaction. Phenyl isocyanate, *p*-methoxyphenyl isocyanate, and chloro-

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(1) For 1,2-oxazetidinones, see H. Staudinger and S. Jelagin, *Ber.*, **44**, 365 (1911); S. P. Makarov, V. A. Shpanskii, V. A. Ginsberg, A. I. Shchekotikhin, A. S. Filatov, L. L. Martynova, I. V. Pavlovskaya, A. F. Golovaneva, and A. Ya. Yakubovich, *Chem. Abstr.*, **57**, 4527 (1962); *Dokl. Akad. Nauk SSSR*, **142**, 596 (1962); G. Kresze and A. Trede, *Tetrahedron*, **19**, 133 (1963).

(2) O. Stallman, U. S. Patent 2,723,265 (1955).

(3) N. G. Gaylord and J. H. Crowdle, *Chem. Ind.* (London), 145 (1955).

(4) C. J. Brown, *J. Chem. Soc.*, 2931 (1955).

(5) For example, P. A. Argabright and V. J. Sinkey, *Chem. Ind.* (London), 857 (1966); E. Niwa, H. Aoki, H. Tanaka, J. Munakata, and M. Namiki, *Ber.*, **99**, 3932 (1966); J. A. Moore in "The Chemistry of Heterocyclic Compounds," Vol. 19, Part 2, A. Weissberger, Ed., John Wiley and Sons, Inc., New York, N. Y., 1964, p 885; M. L. Weiner, *J. Org. Chem.*, **25**, 2245 (1960).

sulfonyl isocyanate[6] all failed to react with hexafluoroacetone under the conditions described here.[7]

The cycloaddition is promoted by either acidic or basic reagents. Catalytic amounts of boron trifluoride or cesium fluoride caused substantial increases in the conversions. A possible mechanism of cesium fluoride catalysis is presented later.[8] Boron trifluoride may catalyze the reaction by polarizing either reactant in the manner represented by intermediates VIII and IX.

$(CF_3)_2\overset{+}{C}O\overset{-}{B}F_3$
VIII

$CH_3N(\overset{-}{B}F_3)\overset{+}{C}O$
IX

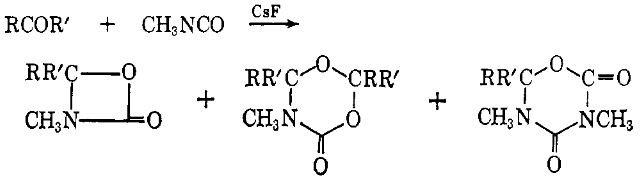
Evidence for the possible existence of these intermediates is given by reports that fluoro ketones[9] and isocyanates[10] yield Friedel–Crafts products when treated with aromatic compounds and acid catalysts.

The use of liquid sulfur dioxide as a medium for the cycloaddition reaction further increased the conversion to oxazetidinone I. On the other hand, the use of the moderately polar, but neutral, methylene chloride as a solvent gave conversions below those obtained when no solvent was used.

The oxazetidinone I is stable to both water and methanol at room temperature. It is thermally stable up to its boiling point, but further heating causes the regeneration of the starting materials. This is in marked contrast with the direction of bond cleavage of the transient oxazetidinones suggested by other workers.[5] In those compounds, the substituents at the 4 position are less electronegative, and bond scission leads to the formation of carbon dioxide and imino derivatives.

A parallel to this behavior has been noted with 4-imino-1,3-thiazetidinones.[11] Two cleavage paths are also observed with these compounds, and the extent to which either path operates is similarly determined by the electronegativities of the substituents at the 4 position.

The effect of cesium fluoride in the fluoro ketone–isocyanate systems was studied further. A striking change in the identity of the product occurs when the amount of cesium fluoride and the reaction time are increased. A nearly equimolar mixture of hexafluoroacetone and methyl isocyanate gave only oxazetidinone I when heated at 100° for 2 hr with a 2.5% charge of cesium fluoride. When the mixture was heated for 8 hr, only a small amount of oxazetidinone was present, and a good yield of a higher boiling liquid was formed. Distillation gave two compounds wihch were identified as the dioxazine derivative X[12] and the oxadiazine derivative XI.[13] A rationalization of the mass spectra of these compounds is shown in Scheme I.



X, XII, XIV XI, XIII, XV

X, XI, R = R′ = CF_3
XII, XIII, R = CF_3; R′ = CF_2Cl
XIV, R = R′ = CHF_2
XV, R, R′ = $CF_2CF_2CF_2$ (spiran)

Other fluoro ketones gave similar results with excess cesium fluoride.[14] Chloropentafluoroacetone was converted to compounds XII and XIII, while *sym*-tetrafluoroacetone afforded the dioxazine XIV and perfluorocyclobutanone gave the oxadiazine XV. Only the isocyanate trimer[15] was detected in the cesium fluoride catalyzed reaction of hexafluoroacetone and *p*-methoxyphenyl isocyanate.

As expected from the foregoing discussion, the oxazetidinones can serve as starting materials for the six-membered ring compounds, but it is more practical to begin with the ketone and isocyanate. Treatment of the pure oxazetidinone, I or II, with cesium fluoride produced a mixture of the dioxazine and oxadiazine, X and XI or XII and XIII.

In these examples and when excess ketone was used, the dioxazine was the major product. However, when compound I was treated with cesium fluoride in an excess of methyl isocyanate, the oxadiazine XI became the dominant product. The dependency of the relative amounts of dioxazine and oxadiazine formed on the relative amount of ketone and isocyanate in the mixture suggests that there is a common intermediate for the two products.

The mechanism outlined in Scheme II is proposed to account for the observed results and represents a system of kinetic *vs.* thermodynamic control of the products.

The presence of intermediate, $RN\text{–}COF^-$, is supported by the observation that cesium fluoride initiated the polymerization of methyl isocyanate in a manner observed previously with other isocyanates and basic catalysts.[16]

With the acetone derivatives, the dioxazine is the normally preferred six-membered ring product. However, the oxadiazine is the preferred product when perfluorocyclobutanone is used.[17]

Additional evidence for the mechanism of Scheme II was provided by the isolation of a mixture of the dioxa-

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[6] R. Graf, *Ber.*, **89**, 1071 (1956); R. Appel and G. Eisenhauer, *ibid.*, **95**, 1753 (1962).

[7] F. W. Hoover, H. B. Stevenson, and H. S. Rothrock [*J. Org. Chem.*, **28**, 1825 (1963)] reported the addition of isocyanic acid to perhalo ketones to give bis(trihalomethyl)hydroxymethyl isocyanates.

[8] Because of the nature of the reaction systems, it is virtually impossible to rule out the presence of fluoride ions in "uncatalyzed" reactions. The word, "uncatalyzed," should be taken here to represent a description of intention.

[9] I. L. Knunyants, T. Y. Chen, N. P. Gambaryn, and E. M. Rokhlin, *Chem. Abstr.*, **54**, 20962 (1960); *Zh. Vses. Khim. Obshch. im. D.I. Mandeleeva*, **5**, 114 (1960).

[10] J. H. Saunders and R. J. Slocombe, *Chem. Rev.*, **43**, 203 (1948).

[11] W. Will, *Ber.*, **14**, 1486 (1881); H. Ulrich, B. Tucker, and A. A. R. Sayigh, *Tetrahedron*, **22**, 1565 (1966). 4-Imino-1,3-thiazetidinones bearing a less electronegative 4 substituent give, exclusively, carbonyl sulfide and a carbodiimide. Those with a more electronegative substituent also give an isocyanate and an isothiocyanate.

[12] For other 1,3,5-dioxazines, see B. Loev, K. M. Snader, and M. F. Kormendy, *J. Org. Chem.*, **29**, 245 (1964), and references cited therein.

[13] For other 1,3,5-oxadiazines, see G. Muller and R. Merten, U. S. Patent 3,294,792 (1966); M. C. Seidel, U. S. Patent 3,294,793 (1966); ref 8.

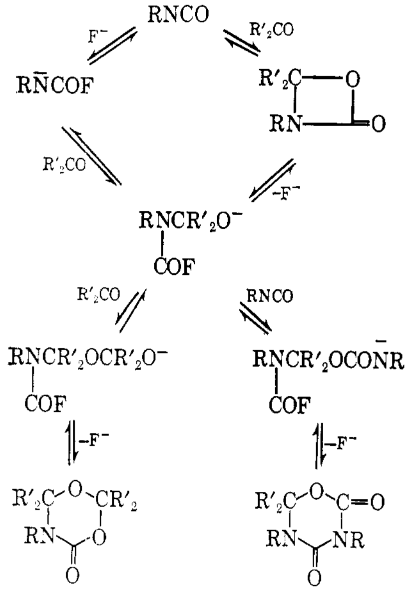
[14] A referee drew attention to the similarities in the reactions of isocyanates and ketenes and cited D. Borrmann and R. Wegler, *Ber.*, **99**, 1245 (1966). These authors reported the preparation of 1:1, 2:1, and 1:2 cycloadducts of halo ketones and ketenes.

[15] I. C. Kogon, *J. Am. Chem. Soc.*, **78**, 4911 (1956).

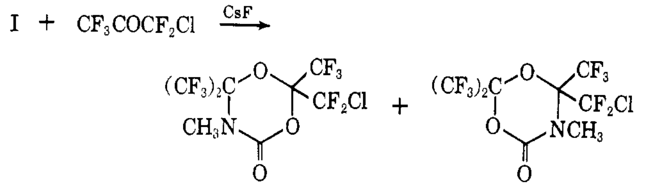
[16] V. E. Shashoua, *ibid.*, **81**, 3156 (1959); V. E. Shashoua, W. Sweeney, and R. F. Tietz, *ibid.*, **82**, 866 (1960).

[17] This result is not readily explained, but may indicate an unfavorable steric situation caused by the eclipsing of two cyclobutane rings in the dioxazine or its intermediate.

SCHEME II
CESIUM FLUORIDE CATALYZED REACTIONS OF FLUORO KETONES AND ALKYL ISOCYANATES



zine cross products XVI and XVII from the reaction of oxazetidinone I and chloropentafluoroacetone.


XVI XVII

This reaction also gave all of the other dioxazines and oxadiazines that can be formed in the system.

Experimental Section

Optimum synthesis conditions were not determined in this study. The reactions were carried out in 3-oz glass aerosol compatibility tubes (Fischer-Porter Co.) fitted with a metal valve and a thermocouple which extended into the reaction mixture. Agitation was provided by a magnetic stirrer. Gaseous reactants were condensed in the tube by external cooling. The cold reactor was placed in a jacket supporting an electrical heating tape and a copper cooling coil and was pressured to 100 psig with dry nitrogen. Pressures up to 400 psig were developed in these reactions. After the heating period the reactor was cooled by passing liquid nitrogen through the coil and was then vented to 1 atm. Since volatile starting materials were lost on venting, the results are expressed in terms of conversions rather than yields, but the yields were probably high in all cases. The reaction mixture was distilled on a high vacuum line through a −45° trap (chlorobenzene slush) into a liquid nitrogen cooled trap. The products were recovered from either the first trap or the reactor. Further purification was done either by distillation or gas–liquid partition chromatography (glpc).

The glpc was done on a $^1/_4$ in. × 6 ft or on a $^3/_8$ in. × 12 ft column of 20% silicone oil 550 (Dow Corning Corp.) on 80–90 mesh Anakrom ABS (Analabs, Inc.) with a helium flow of 60 cc/min. Sample purity is expressed as the area percentage of component peaks or as the weight percentage determined by a comparison of peak sizes for known quantities of pure samples. The elution time (ET) is reported for each sample. Boiling points are uncorrected and were determined by differential thermal analysis. The thermograms showed no decomposition in any of the products. The infrared carbonyl stretching band position is noted for each compound. Proton nmr spectra were determined at 60 Mc. The chemical shifts are reported in cycles per second downfield from tetramethylsilane (internal standard). Fluorine nmr spectra were measured at 56.4 Mc and are referred to trichlorofluoromethane (internal standard). Significant peaks in the mass spectra are reported. Other peaks, including isotopic peaks, were observed and were consistent with the structures. In order to prevent the cracking of some of the products, it was necessary to keep the sample port near room temperature.

3-Methyl-4,4-bis(trifluoromethyl)-1,3-oxazetidinone (I).—Reaction of hexafluoroacetone (30 g, 0.18 mole) and methyl isocyanate (10 g, 0.175 mole) at 80° for 8 hr gave 11.1 g (28%) of I: bp 102°; infrared, 1935–1890 cm^{-1} (doublet); ET (6 ft, 60°), 2.2 min; density, 1.53 g/ml; mass spectrum, 223, 178, 154, 126, 110, 44: proton nmr, septet at 183 cps (J_{HF} = 0.6 cps); fluorine nmr, quartet at 4360 cps.

Anal. Calcd for $C_5H_3F_6NO_2$: C, 26.93; H, 1.36; F, 51.1; N, 6.28; mol wt, 223. Found: C, 27.06; H, 1.36; F, 48.6; N, 6.39; mol wt, 211 (cryoscopic in benzene).

When the reaction time was reduced to 1.5 hr, a 16% conversion into oxazetidinone was obtained. Scaling up by six times in a 300-ml stainless steel stirring autoclave gave a 25.6% conversion. Isolation and purification of the unreacted starting materials indicated a 59% yield.

Boron Trifluoride Catalysis.—Reaction of hexafluoroacetone (30 g), methyl isocyanate (10 g), and boron trifluoride etherate (75 μl.) at 80° for 8 hr gave 17.2 g (43.8%) I.

Cesium Fluoride Catalysis.—Reaction of hexafluoroacetone (30 g), methyl isocyanate (10 g), and cesium fluoride (1 g) at 100° for 1.5 hr gave 14.1 g (36.9%) of I. Also, see Table I.

TABLE I
VARIATION IN PRODUCT WITH CESIUM FLUORIDE CONCENTRATION[a,b]

CsF, g	I, g	X + XI, g
0	11.1	0
0.01	17.3	0
0.10	18.9	0
0.33	16.2	
0.50	14.1	1.9–2.8
1.0	2.8	33.8

[a] Reference 8. [b] Reaction time, 8 hr.

Sulfur Dioxide Solution.—Reaction of hexafluoroacetone (15 g, 0.09 mole), methyl isocyanate (5 g, 0.087 mole), and sulfur dioxide (25 g) at 100° for 8 hr gave 12 g (61%) I.

3-Methyl-4-chlorodifluoromethyl-4-trifluoromethyl-1,3-oxazetidinone (II).—Reaction of chloropentafluoroacetone (30 g, 0.164 mole) and methyl isocyanate (10 g, 0.175 mole) at 80° for 8 hr gave 6.5 g (16%) II: bp 135°; infrared, 1926–1890 cm^{-1} (doublet); ET (6 ft, 52°), 9.1 min; density, 1.50 g/ml; mass spectrum, 239, 126, 110, 44; proton nmr, multiplet centered at 183 cps; fluorine nmr, triplet at 4224 (CF_3) (J_{FF} = 9.6 cps) and two equal overlapping quartets centered at 3583 cps (CF_2Cl) (each quartet was offset by 3.3 cps).

Anal. Calcd for $C_5H_3ClF_5NO_2$: C, 25.07; H, 1.27; Cl, 14.81; F, 39.7; N, 5.85. Found: C, 24.84; H, 1.26; Cl, 14.58; F, 40.0; N, 5.95.

3-Methyl-4,4,-bis(chlorodifluoromethyl)-1,3-oxazetidinone (III).—Reaction of 1,3-dichlorotetrafluoroacetone (20 g, 0.1 mole) and methyl isocyanate (20 g, 0.35 mole) at 100° for 8 hr gave 2.6 g (10.5%) III: bp 154°; infrared, 1918–1885 cm^{-1} (doublet); ET (6 ft, 120°), 5.5 min; density, 1.55 g/ml; mass spectrum, 255, 170, 126, 44; proton nmr, multiplet at 183 cps; fluorine nmr, multiplet at 3426 cps.

Anal. Calcd for $C_5H_3Cl_2F_4NO_2$: C, 23.46; H, 1.18; Cl, 27.70; F, 29.7; N, 5.47. Found: C, 23.80; H, 1.21; Cl, 27.51; F, 28.4; N, 5.65.

3-Methyl-4-chlorodifluoromethyl-4-dichlorofluoromethyl-1,3-oxazetidinone (IV).—Reaction of 1,1,3-trichlorotrifluoroacetone (30 g, 0.14 mole) and methyl isocyanate (20 g, 0.35 mole) at 100° for 8 hr gave 1.1 g of a pasty solid. Filtration gave 0.6 g of a yellow liquid which was apparently too unstable to be purified further. Spectroscopic data indicated the presence of IV: infrared, 1870 cm^{-1}; proton nmr, broad peak at 185 cps; fluorine nmr, triplet at 3606 ($CFCl_2$) (J_{FF} = 14.2 cps) and two equally intense, overlapping doublets (CF_2Cl) with peaks at 3210.2, 3217.7, 3224.4, and 3231.9 cps.

3-Methyl-4,4-bis(difluoromethyl)-1,3-oxazetidinone (V).—Reaction of *sym*-tetrafluoroacetone (25 g, 0.192 mole) and methyl isocyanate at 100° for 8 hr gave 11 g of a light amber, high-boiling liquid. Distillation on a Hickman still under high vacuum up to a heater temperature of 60° separated V from a high-boiling liquid and a solid. Redistillation gave 1.7 g (5.2%) of V: bp 174°; infrared, 1860 cm^{-1}; ET (12 ft, 130°), 21.4 min; mass spectrum, 187, 136, 108, 92, 44; proton nmr, singlet at 181 (CH_3N) and a triplet centered at 375 cps (CHF_2) (J_{HF} = 54 cps); fluorine nmr, two equally intense, overlapping doublets with unresolved fine structure with peaks centered at 7732, 7562, 7582, and 7612 cps.

Anal. Calcd for $C_5H_5F_4NO_2$: C, 32.09; H, 2.70; F, 40.6; N, 7.49. Found: C, 31.94; H, 2.83; F, 40.1; N, 7.99.

3-Methyl-5,5,6,6,7,7-hexafluoro-1-oxa-3-azaspiro[3.3]heptan-2-one (VI).—Reaction of perfluorocyclobutanone (6.0 g, 0.034 mole) and methyl isocyanate (10 g, 0.175 mole) at 80° for 8 hr gave 5.5 g (69.6%) of pale yellow VI. Vacuum sublimation onto a Dry Ice cooled cold finger gave 3.6 g of white solid: mp 52–53°; infrared (chloroform solution), 1897–1873 cm^{-1} (doublet); proton nmr, single peak at 188 cps; fluorine nmr, three equally intense multiplets at 7271, 7295, and 7632 cps.

Anal. Calcd for $C_6H_3F_6NO_2$: C, 30.65; H, 1.29; F, 48.5; N, 5.96. Found: C, 30.45; H, 1.17; F, 48.9; N, 6.11.

3-*n*-Butyl-4,4-bis(trifluoromethyl-1,3-oxazetidinone (VII).—Reaction of hexafluoroacetone (40 g, 0.24 mole), *n*-butyl isocyanate (20 g, 0.35 mole), and boron trifluoride etherate (50 μl) at 75° for 8 hr gave 22.7 g of a residue of unreacted isocyanate and VII in the reactor. Vacuum distillation at room temperature in a Hickman still gave impure VII in the later fractions. A 600-mg sample was collected by glpc. Injection of small samples (10 μl) of the distillation heel into the gas chromatograph caused elution of VII before the isocyanate. Injection of larger samples (200 μl) caused the isocyanate to elute first, then VII: bp 161°; infrared, 1898 cm^{-1}; ET (6 ft, 65°), 6.7 min; proton nmr, similar to spectrum of *n*-butyl isocyanate; fluorine nmr, singlet at 4359 cps.

Anal. Calcd for $C_8H_9F_6NO_2$: F, 43.0; N, 5.29. Found: F, 42.4; N, 5.35.

5,6-Dihydro-5-methyl-2,2,6,6-tetrakis(trifluoromethyl)-4H-1,3,5-dioxazin-4-one (X) and Dihydro-3,5-dimethyl-6,6-bis(trifluoromethyl)-2H-1,3,5-oxadiazine-2,4(3H)-dione (XI). From Ketone and Isocyanate.—Reaction of hexafluoroacetone (30 g, 0.18 mole), methyl isocyanate (10 g, 0.175 mole), and cesium fluoride (1 g) at 100° for 8 hr gave 2.8 g of I, 30.8 g of X, and 3.0 g of XI. See Table I for variation in product with cesium fluoride concentration.

Dioxazine X had bp 140°, 72° (65 mm); infrared, 1803 cm^{-1}; ET (12 ft, 200°), 3.9 min; density, 1.82 g/ml; mass spectrum, 326, 320, 154, 126, 110, 44; proton nmr, multiplet at 198.1 cps; fluorine nmr, two equally intense multiplets centered at 4274 (C-6 CF_3's) and 4514 cps (C-2 CF_3's).

Anal. Calcd for $C_8H_3F_{12}NO_3$: C, 24.69; H, 0.78; F, 58.6; N, 3.60; mol wt, 389. Found: C, 24.63; H, 0.75; F, 58.2; N, 3.84; mol wt, 397 (cryoscopic in benzene).

A stirred mixture of 3.64 g of X and 0.5 g of cesium fluoride was heated 6 hr at 100° under vacuum in a sealed glass reactor. Infrared analysis showed the gases above the liquid contained hexafluoroacetone and methyl isocyanate; 92% of X was recovered.

Oxadiazine XI had bp 187°; infrared, 1749 (2-C=O) and 1720 cm^{-1} (4-C=O); ET (12 ft, 200°), 7.8 min; density, 1.70 g/ml; mass spectrum, 280, 236, 211, 154, 126, 110, 44; proton nmr, peak at 195 cps (3-NCH_3) overlapped by an incompletely resolved multiplet spanning 192.4 to 197.2 cps (5-NCH_3) (J_{HF} = *ca.* 1.2 cps); fluorine nmr, narrow multiplet at 4314 cps.

Anal. Calcd for $C_7H_6F_6N_2O_3$: C, 30.02; H, 2.16; F, 40.7; N, 10.01. Found: C, 30.01; H, 2.43; F, 40.3; N, 10.01.

A stirred mixture of 1 g of XI and 0.5 g of cesium fluoride was heated 6 hr at 100° under vacuum in a sealed glass reactor. Infrared and mass spectra showed the presence of trifluoromethane and carbon dioxide in the gas above the liquid. A trace of water apparently caused some decomposition. A 72% recovery of XI was achieved.

From Oxazetidinone I.—Reaction of oxazetidinone (7.65 g) and cesium fluoride (0.1 g) in a sealed glass reactor under vacuum at room temperature for 1 day gave methyl isocyanate and 3.3 g of a mixture of X and XI. Reaction of oxazetidinone (11 g), hexafluoroacetone (10 g), and cesium fluoride (1 g) at 100° for 8 hr gave 0.5 g of I and 6.5 g of a mixture of X and XI in which X was the predominant product. Reaction of oxazetidinone (5 g), methyl isocyanate (15 g), and cesium fluoride (0.5 g) overnight at room temperature gave 1.6 g of a mixture of X and XI in a ratio of 1:2.

5,6-Dihydro-5-methyl-2,6-bis(chlorodifluoromethyl)-2,6-bis(trifluoromethyl)-4H-1,3,5-dioxazin-4-one (XII) and Dihydro-3,5-dimethyl-6-chlorodifluoromethyl-6-trifluoromethyl-2H-1,3,5-oxadiazin-2,4(3H)-dione (XIII). From Ketone and Isocyanate.—Reaction of chloropentafluoroacetone (30 g, 0.16 mole), methyl isocyanate (30 g, 0.53 mole), and cesium fluoride (1 g) at 100° for 8 hr gave, from two combined runs, 29.3 g (38.4%) of II and 13.4 g of a mixture of XII and XIII. The mixture was distilled under high vacuum in a Hickman still and the fraction collected at a heater temperature of 60–70° was gas chromatographed to collect the pure components.

Dioxazine XII (5.9 g) had bp 193°; infrared, 1810 cm^{-1}; ET (12 ft, 200°), 8.4 min; mass spectrum, 352, 336, 154, 126, 110, 44; proton nmr, sextet centered at 195.8 cps (J_{HF} = 1.2–1.4 cps); fluorine nmr, multiplets centered at 3471 (C-6 CF_2Cl), 3752 (C-2 CF_2Cl), 4101 (C-6 CF_3), and 4356 cps (C-2 CF_3).

Anal. Calcd for $C_8H_3Cl_2F_{10}NO_3$: C, 22.77; H, 0.72; Cl, 16.80; F, 45.0; N, 3.32. Found: C, 23.09; H, 0.84; Cl, 16.56; F, 44.8; N, 3.21.

Oxadiazine XIII (6.2 g) had bp 213°; infrared, 1790 (2-C=O) and 1710 (4-C=O) cm^{-1}; ET (12 ft, 200°), 20 min; mass spectrum, 296, 252, 227, 211, 170, 154, 126, 110, 44; proton nmr, singlet at 195.3 (3-NCH_3) bracketed by a multiplet ranging from 190 to 197 cps (5-NCH_3) (J_{HF} = *ca.* 1.2 cps); fluorine nmr, pentuplet centered at 3480 (CF_2Cl) arising from overlapping quartets for each fluorine (frequencies between adjacent peaks varied from 8 to 14 cps), triplet centered at 4180 cps (CF_3) (J_{FF} = 11 cps) (incompletely resolved fine structure was evident in each peak of the triplet).

Anal. Calcd for $C_7H_6ClF_5N_2O_3$: C, 28.35; H, 2.04; Cl, 11.94; F, 32.0; N, 9.45. Found: C, 28.37; H, 2.35; Cl, 11.96; F, 31.9; N, 9.38.

From Oxazetidinone II.—Reaction of oxazetidinone (4.8 g) and cesium fluoride (0.3 g) in a sealed glass reactor under vacuum at 85° overnight gave chloropentafluoroacetone, methyl isocyanate, and a mixture of 0.97 g of II, 0.58 g of XII, and 0.22 g of XIII.

5,6-Dihydro-5-methyl-2,2,6,6-tetrakis(difluoromethyl)-4H-1,3,5-dioxazin-4-one (XIV).—*sym*-tetrafluoroacetone (20 g, 0.152 mole), methyl isocyanate (20 g, 0.35 mole), and cesium fluoride (1 g) gave a vigorous exothermic reaction which was checked at 134° by cooling. The temperature was held at 90° for 8 hr. After distillation of the volatile materials, including some V, the reactor residue (27.9 g), a viscous liquid, was distilled under high vacuum on a Hickman still. The liquid (2.0 g) boiling up to a heater temperature of 75° was collected and found to be nearly pure XIV. Further purification by glpc gave an analytical sample: bp 238°; infrared, 1773 cm^{-1}; ET (12 ft, 200°), 16.4 min; mass spectrum, 266, 222, 136, 108, 92, 44; proton nmr, singlet at 194 (CH_3) and a triplet centered at 362 cps (CHF_2) (J_{HF} = 54 cps); fluorine nmr, multiplet at 7484–7667 (6-CHF_2) and a doublet at 7701–7751 cps (2-CHF_2).

1,1,2,2,3,3-Hexafluoro-7,9-dimethyl-5-oxa-7,9-diazaspiro[3.5]-nonan-6,8-dione (XV).—Reaction of perfluorocyclobutanone (15 g, 0.084 mole), methyl isocyanate (20 g, 0.35 mole), and cesium fluoride (0.5 g) at 90° for 8 hr gave 13.0 g of high-boiling liquid. Preparative glpc gave 6.3 g of XV: bp 217°; infrared, 1805 (5-C=O) and 1730 (7-C=O) cm^{-1}; ET (12 ft, 200°), 16 min; mass spectrum, 292, 206, 191, 44; proton nmr, singlet at 191 (7-NCH_3) and a septet centered at 195.6 cps (9-NCH_3) (J_{HF} = 1.1–1.2 cps); fluorine nmr, three equally intense multiplets at 7125, 7144 (1,3-CF_2's), and 7474 cps (2-CF_2).

Anal. Calcd for $C_8H_6F_6N_2O_3$: C, 32.87; H, 2.07; F, 39.0; N, 9.59; mol wt, 292. Found: C, 33.15; H, 2.32; F, 38.7; N, 9.65; mol wt, 280 (cryoscopic in benzene).

Mixture of 5,6-Dihydro-5-methyl-2-chlorodifluoromethyl-2,6,6-tris(trifluoromethyl)-4H-1,3,5-dioxazin-4-one (XVI) and 5,6-Dihydro-5-methyl-6-chlorodifluoromethyl-2,2,6-tris(trifluoromethyl)-4H-1,3,5-dioxazin-4-one (XVII). From I.—Reaction of oxazetidinone (15 g, 0.067 mole), chloropentafluoroacetone (30 g, 0.14 mole), and cesium fluoride (2 g) at 100° for 8 hr gave 9.1 g of I and 1.1 g of a high-boiling liquid. Glpc and infrared analysis of the collected peaks showed the following composition of the higher boiling product: 8.4% dioxazine X, 8.9% oxadiazine XI, 9.4% dioxazine XII, and 25.0% oxadiazine XIII; 35.6% was a mixture of cross products XVI and XVII. A sample of the cross products was collected for analysis. bp 167°; infrared, 1810 cm^{-1}; ET (12 ft, 125°), 12.7 min; mass spectrum, 342, 336, 326, 320, 292, 276, 170, 154, 126, 110, 44; proton nmr, multiplet at 198 cps; fluorine nmr, multiplets assigned to dioxazine XVI at 3495 (2-CF_2Cl), 4129 (2-CF_3), and 4517 cps (6-CF_3's), multiplets assigned to dioxazine XVII at 3774 (6-CF_2Cl), 4274 (2-CF_3's), and 4398 cps (6-CF_3). (The relative areas of each set of multiplets indicated the composition of 1:2 dioxazine XVI to dioxazine XVII.)

Anal. Calcd for $C_8H_3ClF_{11}NO_3$: Cl, 8.74; N, 3.45. Found: Cl, 8.64; N, 3.64.

From Ketone Mixture.—Reaction of hexafluoroacetone (15 g, 0.09 mole), chloropentafluoroacetone (17 g, 0.09 mole), methyl isocyanate (10 g, 0.175 mole), and cesium fluoride (1 g) at 100° for 8 hr gave 28 g of product. Analysis by glpc indicated the following composition: I, 18.2%; II, 17.2%; X, 39.8%; XI, 2.9%; XII, trace; XIII, trace; XVI and XVII, 21.4%.

Registry No.—I, 13619-24-4; II, 13619-25-5; III, 13619-26-6; IV, 13639-87-7; V, 13619-27-7; VI, 13639-88-8; VII, 13618-60-5; X, 13618-61-6; XI, 13618-62-7; XII, 13618-63-8; XIII, 13618-64-9; XIV, 13618-65-0; XV, 13639-89-9; XVI, 13618-66-1; XVII, 13618-67-2.

4-Aroylbenzils and Related Compounds

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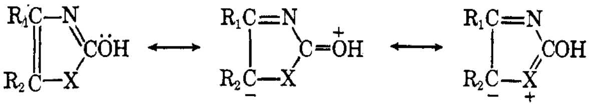
A number of *ortho*-mono- and -diacylated benzils have been reported in the literature,[1-5] but *para*-mono- and -diacylated benzils are unknown. We have previously shown that 4,5-diphenyl-2-imidazolone[6] and 4,5-diphenyloxazoles[7] undergo electrophilic substitution in the *para* position of the phenyl group(s), and are smoothly oxidized by bromine in acetic acid to benzils. The acylation of these heterocycles has now been investigated in order to provide a convenient pathway to the *para*-acylated benzils.

Attempted acylation of either 2-methyl-4,5-diphenyl-, 2,4,5-triphenyl, 4,5-diphenyl-, or 2,5-diphenyloxazole and 2-methyl-4,5-diphenyl- or 4,5-diphenylimidazole under different conditions (eq 1, X = O or


(1)

NH) furnished only starting materials. The presence of an oxygen atom at C_2 would increase the electron density of C_4 (C_5) and should facilitate acylation. When 4,5-diphenyl-2-imidazolone was treated with benzoyl chloride in nitrobenzene in the presence of anhydrous aluminium chloride or in nitromethane with silver perchlorate,[8] only starting material was recovered. However, the imidazolone was monoacylated by heating it with various aromatic acids in polyphosphoric acid at 140–150°. The products were frequently difficult to purify and were then oxidized directly to the benzils in poor yield (see Tables I and II).

High yields of monoacylated oxazolones were obtained when 4,5-diphenyl-2-oxazolone (I) was heated with an aromatic acid in the presence of polyphosphoric acid. The monoacylated oxazolones were oxidized to their corresponding benzils in excellent yield (see Tables I and II).

The oxidation of the oxazolone (I) by bromine in acetic acid in the presence and absence of anhydrous sodium acetate buffer was investigated to establish optimum conditions for benzil formation. The maximum yield of benzil was obtained when the oxidation was carried out under reflux in the presence of aqueous acetic acid. These conditions were then used for the oxidation of the acylated oxazolones.

The structure of the acylated benzils was determined by cleavage of the benzil with cyanide ion[7] to give the corresponding *p*-benzoylbenzoic acids and benzaldehyde. The unknown *p*-(4 chlorobenzoyl)benzoic acid was reduced with Raney alloy in alkaline solution to give *p*-diphenylmethanecarboxylic acid. Hence the acylated oxazolone was designated 5(4)-*p*-aroylphenyl-

TABLE I

ACYLATION OF 4,5-DIPHENYL-2-IMIDAZOLONE (A) AND 4,5-DIPHENYL-2-OXAZOLONE (B) TO THE CORRESPONDING 4(5)-BENZOYLATED PRODUCTS

Starting material	Acylating acid	Yield, %	Mp, °C	Recrystn solvent	Formula	Registry no.	Calcd, % C	Calcd, % H	Calcd, % N	Found, % C	Found, % H	Found, % N
A	Benzoic	68	145–147	Dil EtOH	$C_{22}H_{16}N_2O_2$	13342-52-4	77.7	4.7	8.2	77.5	4.5	8.1
B	Benzoic	97	239–240	EtOH	$C_{22}H_{15}NO_3$	13342-53-5	77.5	4.4	4.1	77.5	4.4	4.1
A	*p*-Bromobenzoic[a]		240–260			13342-54-6						
B	*p*-Bromobenzoic[a]	90	260–263	Dil AcOH	$C_{22}H_{14}BrNO_3$	13342-55-7	62.9	3.3	3.3	62.7	3.2	3.3
B	*p*-Chlorobenzoic	95	252–255	AcOH	$C_{22}H_{14}ClNO_3$	13342-56-8	70.3	3.7	3.7	69.9	3.6	3.8
A	*p*-Nitrobenzoic[b]	61	291–294	Dil EtOH		13342-57-9						
B	*p*-Nitrobenzoic[a]		215–230			13342-58-0						
A	3,4-Dichlorobenzoic											
B	3,4-Dichlorobenzoic	81	266–268	Dil DMFA	$C_{22}H_{13}Cl_2NO_3$	13342-60-4	64.4	3.2	3.4	64.1	3.1	3.3

[a] Product could not be purified and was oxidized directly to the benzil. [b] The crude product was refluxed with EtOH–concentrated HCl (1:1) for 1 hr, the solution evaporated, and the solid washed with sodium bicarbonate solution. The product was oxidized directly to the benzil.

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