Preparation of (4*SR*,5*RS*)-4-Hydroxy-5-methyl-3,4-diphenyl-2-cyclopenten-1-one (7).—By a procedure analogous to that used to prepare 4, 6 was isomerized to give a 6:5 mixture of 7 and 6. Chromatography of 0.90 g of this mixture on 50 g of silica gel (elution with dilute ether in benzene mixtures) gave 0.24 g of 6, followed by 0.36 g of a mixture of 6 and 7, and finally 0.24 g of a 6:1 mixture of 7 and 6. Four recrystallizations of the last from carbon tetrachloride gave 0.10 g of 7: mp 159–160° (lit.[1a] mp 157°); nmr ($CDCl_3$) δ 7.2–7.7 (m, 10), 6.77 (s, 1), 2.92 (q, 1, J = 7 Hz), 2.88 (s, 1, OH), 0.72 (d, 3, J = 7 Hz); uv max (95% EtOH) 285 nm (log ϵ 4.29); ir ($CHCl_3$) 3600, 3400, 1705 cm^{-1}.

Equilibration of 3 and 4 in Basic Solution.—A solution of 0.23 g of 3 in 15 ml of ethanol was heated under reflux with 0.05 g of K_2CO_3. Aliquots were withdrawn at intervals and prepared for analysis by nmr by precipitation in water, extraction into ether, and evaporation of the ether. An equilibrium mixture containing 52% 4 and 48% 3 was formed after 90 min of heating. An identical mixture was formed by heating a 3:2 mixture of 4 and 3 in ethanol with K_2CO_3. A mixture containing a somewhat greater proportion of 4 was formed by allowing a solution of 3 in ethanol containing KOH to stand at room temperature. In another experiment, upon allowing a warm solution of 7.5 g of a mixture of 3 and 4 in 30 ml of ethanol containing 0.1 g of KOH to cool slowly, 5.5 g of a 16:1 crystalline mixture of 3 and 4 was slowly deposited. Analysis of the supernatant liquid at intervals showed it continuously to contain an equilibrium mixture of 3 and 4.

Action of Base upon 5, 6, and 7.—A solution of 0.96 g of a mixture of 6 and 7 in 5 ml of 1 *M* ethanolic KOH was heated under reflux for 1 hr. The solution became very dark. After neutralization with acetic acid, the solution was poured into water, and the precipitated material was extracted into ether. The ether was evaporated, and 0.8 g of the residue was chromatographed on 45 g of neutral alumina (activity grade III). Eluted by benzene were 0.2 g of material, the ir spectrum of which lacked hydroxyl absorption, and 0.1 g of highly colored material. Eluted by 1:10 ether–benzene was 0.39 g of a mixture of 5, 6, and 7 which contained, according to analysis by nmr, 0.08 g of 5. Other treatments of 5 and of mixtures of 6 and 7 did not effect interconversion of the structural isomers. Among the experiments in which no change was observed were treatment of 5 with boiling 1 *M* ethanolic KOH for 30 min, treatment of 5 with 0.1 *M* ethanolic KOH for 5 days, treatment of a mixture of 6 and 7 with 0.1 *M* ethanolic KOH for 5 days, and stirring, while heating under reflux, for 2 hr a heterogeneous mixture of 30% aqueous KOH and a solution of 6 and 7 in DME.

Registry No.—**1**, 5587-78-0; **2**, 38661-94-8; **3**, 38661-95-9; **4**, 38661-96-0; **5**, 38661-97-1; **6**, 38661-98-2; **7**, 38677-74-6; benzil, 134-81-6.

New Adducts of Hexafluoroacetone with Hydrogen Cyanide

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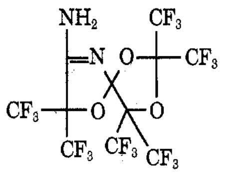
Two adducts of hexafluoroacetone with hydrogen cyanide are known. A 1:1 adduct, hexafluoroacetone cyanohydrin (6), was prepared by the piperidine-catalyzed addition of hydrogen cyanide to the ketone,[1] and a 2:1 adduct, 2,2,5,5-tetrakis(trifluoromethyl)-4-oxazolidinone (4), was prepared by reaction of hexafluoroacetone with sodium cyanide in acetonitrile.[2]

We noted that large, transparent crystals separated from a sample of hexafluoroacetone cyanohydrin that had been standing for more than a year in a clear glass bottle at room temperature. Elemental and mass spectral analysis showed that these crystals are a new, 3:2 adduct of hexafluoroacetone with hydrogen cyanide.

The spiro structure 1 was assigned to this 3:2 adduct on the basis of infrared and nmr spectral analysis. The ^{19}F nmr showed six nonequivalent CF_3 groups. The ^1H nmr showed two different absorptions of equal intensity that coalesced on warming, similar to the ^1H nmr spectrum of the closely analogous 4-amino-2,2,5,5-tetrakis(trifluoromethyl)-3-oxazoline (2).[3] The ir spectra of both 1 and 2 were also similar, with a band at 5.88 μ for C=N.



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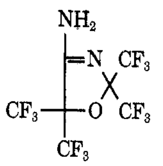
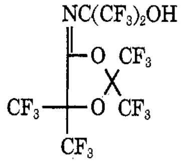


2

Chemically, the spiro compound 1 was also similar to 2. Both compounds are stable to concentrated sulfuric acid at 100°, and both compounds are nitrated by fuming nitric acid in fuming sulfuric acid to form nitramines.

Attempts to prepare 1 under controlled conditions resulted in additional new adducts of hexafluoroacetone with hydrogen cyanide. A 3:1 adduct resulted when excess hexafluoroacetone was added to either hydrogen cyanide or the preformed cyanohydrin in the presence of basic catalyst at or below room temperature. The structure of this new adduct is believed to be the dioxolane 3 instead of the isomeric oxazoline 3a, because attempts to distil the adduct at atmospheric pressure decomposed it to hexafluoroacetone and hexafluoroacetone cyanohydrin. Thermal decomposition of 3a should result in hexafluoroacetone and 2,2,5,5-tetrakis(trifluoromethyl)-4-oxazolidinone, a compound known to possess high thermal stability.[2] Although this new 3:1 adduct is somewhat thermally unstable, it can be distilled at reduced pressure. It can be dissolved in cold alkali and reprecipitated with acid, but warm alkali converts it to the cyanohydrin. Methylation of 3 with diazomethane gives a stable *O*-methyl ether. Reaction of 3 with sodium hydride followed by acidification gives the 2:1 adduct 4. Pyrolysis of 3 in the presence of a few drops of sulfuric acid gave a product that appeared to be a mixture of 3 and a new 2:1 adduct, 5. Evidence



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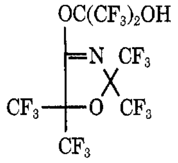

3a

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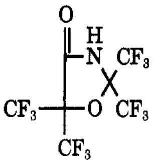

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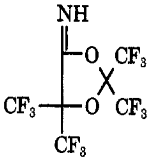


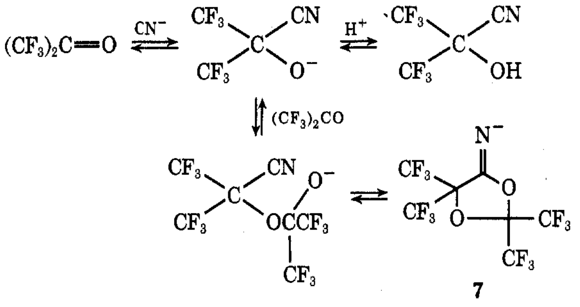
5

for formation of **5** consists of a new band in the ir spectrum at 5.73 μ, and two new absorptions in the ^{19}F nmr spectrum not due to the other known adducts.

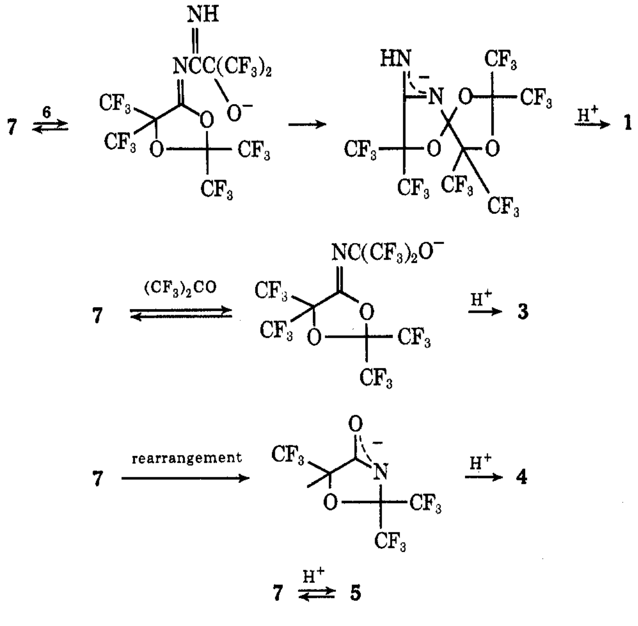
The 3:2 adduct **1** was eventually prepared in 40% yield by reaction of hexafluoroacetone cyanohydrin with excess hexafluoroacetone at 100° for 16 hr in the presence of an amine catalyst. Adduct **1** can also be prepared by adding trace amounts of amine to hexafluoroacetone cyanohydrin and allowing the equilibrating mixture to remain at room temperature for a prolonged period of time.

We believe that the very complex reactions of hexafluoroacetone with hydrogen cyanide to give the several different adducts (1:1, two 2:1, 3:1, and 3:2) can be represented by the following reaction schemes (Scheme I and II). Note that the intermediate anion **7** is common to all higher adducts. Which path the reaction takes depends on the temperature and the relative concentrations of catalyst, ketone, and hydrogen cyanide. All the adducts except the very unstable **5** can be prepared in pure form as the major product.

SCHEME I



SCHEME II



Experimental Section

8-Amino-2,2,4,4,7,7-hexakis(trifluoromethyl)-9-aza-1,3,6-trioxaspiro[4.4]non-8-ene (1).—A mixture of 19.3 g (0.10 mol) of hexafluoroacetone cyanohydrin,[1] 9.0 g (0.54 mol) of hexafluoroacetone, and 0.5 g of 1,4-diazabicyclo[2.2.2]octane (catalyst) was heated for 16 hr at 100° in a 125-ml Hastelloy-lined bomb. Excess hexafluoroacetone was allowed to evaporate and the residue was sublimed at 1 mm to give 10.9 g (40%) of **1** as a white, crystalline solid. Recrystallization from hexane gave the product as colorless prisms: mp 113–114°; ir (KBr) 5.86 μ; ^1H nmr (DMSO-d_6 at 30°) δ 8.60 (s) and 9.44 ppm (s); ^1H nmr (DMSO-d_6 at 50°) δ 9.12 ppm (broad s); ^{19}F nmr (acetone) δ −70.8 (A_3B_3, 6 F), −73.5 (A_3B_3, 6 F), and −78.3 ppm (A_3B_3, 6 F).

Anal. Calcd for $C_{11}H_2F_{18}N_2O_3$: C, 23.93; H, 0.36; F, 61.94; N, 5.07; mol wt, 552. Found: C, 23.71; H, 0.24; F, 61.93; N, 5.04; mol wt, 552 (mass spectrum).

Nitration of 1.—Red fuming nitric acid, 7 ml, was added to a solution of 2.76 g (0.005 mol) of **1** in 25 ml of fuming sulfuric acid (20% SO_3). The reaction mixture became warm. It was stirred for 5 min and then poured over ice. The white solid that formed was collected on a filter and recrystallized from benzene to give 1.70 g (58%) of 8-nitramino-2,2,4,4,7,7-hexakis(trifluoromethyl)-9-aza-1,3,6-trioxaspiro[4.4]non-8-ene (or tautomer) as colorless crystals: mp 43–44°; ir (KBr) 2.95 (NH) and 6.00 μ (C=N); uv (EtOH) λ_{max} 288 mμ (ϵ 12,200); ^{19}F nmr (CCl_3F) δ −71.3 (A_3B_3, 6 F), −74.0 (A_3B_3, 6 F), and −78.9 ppm (A_3B_3, 6 F).

Anal. Calcd for $C_{11}HF_{18}N_3O_5$: C, 22.12; H, 0.17; F, 57.27; N, 7.03; mol wt, 597. Found: C, 22.14; H, 0.43; F, 57.40; N, 6.87; mol wt, 597 (mass spectrum).

4-(1-Trifluoromethyl-1-hydroxy-2,2,2-trifluoroethylimino)-2,2,5,5-tetrakis(trifluoromethyl)-1,3-dioxolane (3). Method A.—Two drops of piperidine was added to a stirred mixture of 19.3 g (0.1 mol) of hexafluoroacetone cyanohydrin and 33.2 g (0.2 mol) of hexafluoroacetone cooled to −30°. The mixture solidified and the temperature rose to 15° in about 3 sec. There was obtained a quantitative crude yield of **3** as a colorless oil. A sample was purified by first dissolving it in cold 5% sodium hydroxide, and then precipitating it by adding 10% hydrochloric acid. The product was extracted with CCl_3F, and the extract was dried ($MgSO_4$) and then evaporated to dryness to give **3** as a colorless, crystalline solid, mp 29–30°.

Method B.—A mixture of 42 g (0.27 mol) of hexafluoroacetone, 4 ml (0.1 mol) of hydrogen cyanide, and a few crystals of potassium cyanide was sealed in a Carius tube at liquid nitrogen temperature. When the tube was warmed to room temperature and shaken, an exothermic reaction took place. Distillation gave 44 g (93%) of **3** as a colorless liquid, bp 58° (20 mm), $n^{25}D$ 1.3022. A 6-g sample was dissolved with cooling in 5 ml of 10% sodium hydroxide and 10 ml of water. Concentrated hydrochloric acid (2 ml) was added with cooling and the crystals that formed were collected on a filter and recrystallized from petroleum ether (bp 30–60°) to give 5.1 g of **3** as a colorless crystal: mp 29–30°; ir (neat) 5.61 μ (C=N); ^1H nmr (CCl_3F) δ 3.8 ppm (s); ^{19}F nmr (CCl_3F) δ −73.1 (septet, J = 5.5 Hz, 6 F), −78.8 (septet, J = 5.5 Hz, 6 F), and 80.0 ppm (s, 6 F).

Anal. Calcd for $C_{10}HF_{18}NO_3$: C, 22.88; H, 0.19; F, 65.14; N, 2.67. Found: C, 23.46; H, 0.54; F, 65.05; N, 2.80.

4-(1-Trifluoromethyl-1-methoxy-2,2,2-trifluoroethylimino)-2,2,5,5-tetrakis(trifluoromethyl)-1,3-dioxolane.—To 100 ml of dry ether and 19.3 g (0.1 mol) of hexafluoroacetone cyanohydrin at −30° was added 0.2 mol of hexafluoroacetone followed by 0.1 g of 1,4-diazabicyclo[2.2.2]octane. The mixture was brought to room temperature and filtered to remove a small amount of solid. A 3% solution of diazomethane in ether was added to the filtrate until no further evolution of nitrogen was observed, and the reaction mixture was distilled to give 17.5 g of the methyl ether as a colorless liquid: bp 135–148°; ir (neat) 5.63 μ (C=N); ^{19}F nmr (CCl_3F) δ −73.0 (septet, J = 6 Hz, 6 F), −75.7 (q, J = 1 Hz, 6 F), and −79.0 ppm (septet, J = 6 Hz, 6 F); ^1H nmr δ 3.63 ppm (septet, J = 1.0 Hz).

Anal. Calcd for $C_{11}H_3O_3NF_{18}$: C, 24.50; H, 0.56; F, 63.44; N, 2.60. Found: C, 24.38; H, 0.79; F, 63.30; N, 2.56.

Distillation of 3 from Acid.—A few drops of sulfuric acid was added to a crude sample of **3**, and the mixture was distilled to give a liquid, bp 43° (10 mm). Analysis by glc, ir, and ^{19}F nmr indicated that two compounds were present in about equal amounts. One product was **3**. The other product (probably **5**) showed an ir band at 5.73 μ for C=N and two septets of equal intensity in the ^{19}F nmr spectrum. Attempts to isolate this second product were unsuccessful, for it apparently decomposes easily to hexafluoroacetone and hexafluoroacetone cyanohydrin.

Conversion of 3 to 2,2,5,5-Tetrakis(trifluoromethyl)-4-oxazolidinone (4) by Sodium Hydride.—A solution of 8.5 g of **3** in 10 ml of ethylene glycol dimethyl ether was added to a slurry of 1 g of sodium hydride in mineral oil (50%) in 15 ml of ethylene glycol dimethyl ether. The mixture was then warmed to 50° and the resulting solution was poured into ice and acidified with hydrochloric acid. The oil that formed was extracted with methylene chloride, dried, and distilled to give 3.2 g (38%) of **4**, bp 89° (20 mm), mp 104–106° (after recrystallization from benzene), identified by comparison with an authentic sample.[2]

Registry No.—**1**, 38868-31-4; **1** nitro derivative, 38868-32-5; **2**, 22038-16-0; **3**, 38868-34-7; **3** methyl ether derivative, 38868-35-8; **4**, 7730-28-1; **6**, 677-77-0; hexafluoroacetone, 684-16-2; hydrogen cyanide, 74-90-8.

Synthetic Reactions by Complex Catalsts. XXIX. Esterification of Carboxylic Acid with Alkyl Halide by Means of Copper(I)-Isonitrile Complex

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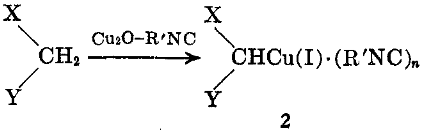
In a preliminary paper,[1] we have reported that carboxylic acid is readily esterified with alkyl halide in the presence of Cu_2O–isonitrile complex. A reaction scheme was presented in which Cu(I) carboxylate–isonitrile complex (**1**) was first generated from Cu_2O–isonitrile complex and carboxylic acid, and then **1** reacted with alkyl halide to produce the corresponding carboxylic ester (Scheme I).

SCHEME I

$$RCO_2H \xrightarrow{Cu_2O\text{–}R'NC} \underset{\mathbf{1}}{RCO_2Cu(I)\cdot(R'NC)_n} \xrightarrow{R''X} RCO_2R'' + Cu(I)X\cdot(R'NC)_n \quad (1)$$

In the present paper, we wish to report the isolation of Cu(I) carboxylate–isonitrile complex (**1**) as a key intermediate in the above reaction and the stereochemistry of the reaction. It is of interest to note that **1** in Scheme I constitutes a counterpart of organocopper(I)–isonitrile complex (**2**) derived from the reaction of acidic carbon acid such as acetylacetone and malonate with the Cu_2O–isonitrile complex.[2,3]



(2)

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Isolation of Cu(I) Carboxylate–Isonitrile Complex.—On heating, Cu_2O was dissolved in acetic acid in the presence of *tert*-butyl isocyanide under nitrogen. From the reaction mixture, Cu(I) acetate–*t*-BuNC complex (**3**) was isolated. **3** is a white, crystalline

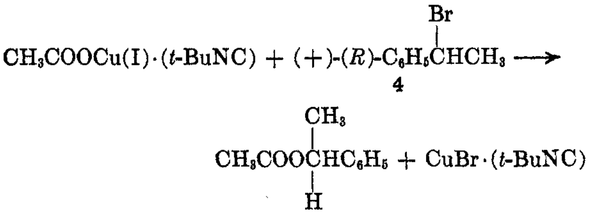
$$CH_3COOCu(I)\cdot(t\text{-}BuNC)$$

3

solid, which is soluble in acetonitrile and hot benzene, and air sensitive. **3** could be purified by recrystallization from hot benzene under nitrogen. In the presence of an additional amount of *t*-BuNC, **3** is readily soluble in benzene even at room temperature. The elemental analysis, nmr, and ir were in accord with the structure of **3** (see Experimental Section). By a similar way, Cu(I) benzoate–*t*-BuNC complex was prepared.

3 reacted with alkyl halide even at room temperature to give the corresponding acetate. In the reaction of **3** with phenethyl bromide and chloride, phenethyl acetate was obtained in the yields of 88 and 12%, respectively. For the purpose of comparison, Cu(I) acetate prepared by Calvin's procedure[4,5] was also treated with alkyl halide. The results are summarized in Table I. Here it is seen that the isonitrile ligand enhances the reactivity of Cu(I) carboxylate toward alkyl halide.

Reaction of Cu(I) Acetate–*t*-BuNC Complex with (+)-(*R*)-Phenethyl Bromide.—The stereochemical course of the reaction of Cu(I) carboxylate–*t*-BuNC with alkyl halide was examined using an optically active halide, (+)-(*R*)-phenethyl bromide (**4**), having $[\alpha]^{25}D$ +58.6°. The optical purity of **4** employed in the present study was 45%.[6]



$$CH_3COOCu(I)\cdot(t\text{-}BuNC) + \underset{\mathbf{4}}{(+)\text{-}(R)\text{-}C_6H_5\overset{\displaystyle Br}{\overset{|}{C}}HCH_3} \longrightarrow CH_3COO\overset{\displaystyle CH_3}{\overset{|}{\underset{\displaystyle H}{\underset{|}{C}}}}HC_6H_5 + CuBr\cdot(t\text{-}BuNC) \quad (3)$$

$[\alpha]^{25}D$ −41.6° (*c* 6.27, cyclohexane)

The reaction proceeded quantitatively (Table I). The product was purified by preparative glpc, which showed an optical rotation of $[\alpha]^{25}D$ −41.6° (Table I). The optical purity was calculated at 33% on the basis of the known rotation of optically pure phenethyl acetate.[7] As the authentic ester, (−)-(*S*)-phenethyl acetate was prepared by the reaction of (−)-(*S*)-phenethyl alcohol with acetic anhydride in pyridine, which was known to proceed with the retention of configuration.[7] It has been established that the bromination of alcohol using PBr_3 proceeds with the inversion of

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