(2.01 min) from 1-amino-3,7,8-trichlorodibenzo-*p*-dioxin and 2,3,7,8-tetrachlorodibenzo-*p*-dioxin (3.65 min) from 1-amino-2,3,7,8-tetrachlorodibenzo-*p*-dioxin. The products had identical spectroscopic and chromatographic (NMR and GC–MS) properties with those of authentic standards.

In the synthesis of 1-nitro-2,3,7,8-tetrachlorodibenzo-*p*-dioxin, two other nitrotetrachlorodibenzo-*p*-dioxins were formed as by-products. These compounds, 1-nitro-3,4,7,8-tetrachlorodibenzo-*p*-dioxin and 2-nitro-1,4,7,8-tetrachlorodibenzo-*p*-dioxin, were isolated from the silica gel column as a mixture. The two compounds were separated on gas chromatography (relative retention times were 5.13 and 5.51) and identified by GC–MS ($M^+$ 365). However, no individual assignment was made to these two compounds. The mixture of nitro compounds was reduced to the corresponding amines and then deaminated via diazonium salts to form tetrachlorodibenzo-*p*-dioxin isomers. These two tetrachlorodibenzo-*p*-dioxins were identified by GC–MS ($M^+$ 320) and have GC retention times of 3.45 and 4.01 min which were not identical with that of the 2,3,7,8-tetrachlorodibenzo-*p*-dioxin isomer. No attempt was made to quantitate the deamination reactions but the expected products were the major GC peaks in all cases.

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# Formation of the *N*-Trifluoroacetate of Carbofuran

Carbofuran (2,3-dihydro-2,2-dimethylbenzofuranyl methylcarbamate) reacts rapidly and quantitatively with trifluoroacetic anhydride in deuteriochloroform in the presence of excess pyridine, which serves both as a catalyst and as a competitive base, preventing the formation of the unreactive trifluoroacetic acid conjugate of carbofuran.

Carbofuran (2,3-dihydro-2,2-dimethyl-7-benzofuranyl methylcarbamate) is a broad spectrum pesticide–nematocide with choline-esterase inhibiting properties. A number of analytical procedures, based on gas–liquid chromatography (GLC), have been developed for the detection of carbofuran and its metabolites. Seiber (1972) prepared the trifluoroacetate of carbofuran and a number of other *N*-methylcarbamates for GLC analysis and detection by both the alkaline-flame and electron-capture detectors. The derivatives were prepared in high yields by reaction of the *N*-methylcarbamates with a large excess of trifluoroacetic anhydride in benzene at elevated temperatures. Seiber concluded that two factors, solvent polarity and temperature, governed the rate of reaction and recommended either extended reaction times (16 h) for room temperature reactions or shorter periods (2 h) at elevated temperatures, e.g., 55 and 100 °C when ethyl acetate and benzene were used as solvents, respectively. Lau and Marxmiller (1970) previously *N*-trifluoroacetylated the commercial pesticide Landrin, a mixture of two isomeric *N*-methylcarbamates, for GLC electron-capture detection and employed ethyl acetate as solvent and overnight, room temperature reaction conditions. Wong and Fisher (1975) more recently reported on the determination of carbofuran and its toxic metabolites as their trifluoroacetates again prepared in ethyl acetate at elevated temperatures (45 °C) with a minimum reaction time of 16 h. In this work, it has been the practice (see Lau and Marxmiller, 1970, and Wong and Fisher, 1975)

Table I. Yield of *N*-Trifluoroacetylcarbofuran in the Presence of Deuteriotrifluoroacetic Acid

| Mol of $F_3CCOOD$/mol of carbofuran | Yield in 18 h, % |
|---|---|
| 0 | 35 |
| 0.1 | 29 |
| 0.2 | 18 |
| 0.4 | 9 |
| 0.8 | 6 |

to employ several thousand to more than 100 000 mol excess of trifluoroacetic anhydride in the derivatization of the *N*-methylcarbamates for GLC detection. These practices have the disadvantage of requiring the decomposition of large excesses of trifluoroacetic anhydride with the addition of water following dilution of the reaction mixture with a suitable solvent such as hexane. The excess trifluoroacetic acid is subsequently removed by washing the organic phase with water, and finally the organic phase is dried and concentrated to a convenient volume for GLC analysis.

In the course of attempting a room temperature preparative scale trifluoroacetylation of carbofuran in CDCl₃ and employing more nearly stoichiometric proportions of trifluoroacetic anhydride than is normally the practice, the reaction was observed by NMR to approach a limiting yield of 50% after about 18 h. The reaction was repeated several times with varying proportions of reactants without effectively improving the yield. From this observation it was surmised that for each mole of *N*-tri-

fluoroacetylcarbofuran (2) formed in the reaction mixture, 1 mol of carbofuran (1) was rendered virtually unreactive as the acid conjugate 3. The dissociation of 3 under stoichiometric conditions is assumed, therefore, to be rate limiting.
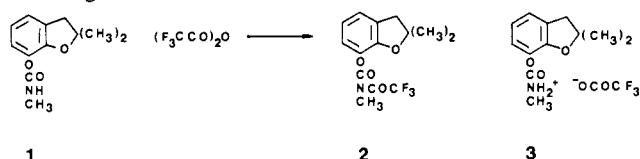


This communication describes the influence of trifluoroacetic acid on the extent of reaction of carbofuran with trifluoroacetic anhydride and the use of pyridine to accelerate the reaction and increase product yield.

## EXPERIMENTAL SECTION

All reactions were conducted at room temperature. Trifluoroacetic anhydride and pyridine were used without purification. Carbofuran was a product of the Niagara Chemical Co. and was stated to be 98.8% pure. Deuteriochloroform and deuteriotrifluoroacetic acid were commerical NMR solvent grade. The NMR spectra were recorded at 100 MHz in the field lock mode on a Varian HA 100 NMR spectrometer, and the usual conditions for quantitative NMR were observed (Kasler, 1973). The yield of $N$-trifluoroacetylcarbofuran was determined directly from the integrals for the sharp singlet at $\delta$ 3.44 ppm from tetramethylsilane for the $N$-methyl protons in the derivative and the doublet at $\delta$ 2.84 ppm for the $N$-methyl protons in carbofuran which collapses to a broad singlet, without change in chemical shift, in the salt. The low-resolution mass spectrum was obtained at 70-eV ionization potential on a Nuclide 12-90-G mass spectrometer employing a direct solids inlet probe.

## RESULTS AND DISCUSSION

For convenience the reactions were conducted in deuteriochloroform rather than perdeuterioethyl acetate or other appropriate solvent system for trifluoroacetylation. That the apparent limiting yield of approximately 50% arose from the formation of the trifluoroacetate salt of carbofuran was supported by the observation that when 0.73 mmol of deuteriotrifluoroacetic acid was added to 0.50 mmol of trifluoroacetic anhydride and reacted with 0.13 mmol of carbofuran, the yield of $N$-trifluoroacetylcarbofuran was not measurable after 18 h and was less than 4% even after 7 days. As the presence of relatively small quantities of trifluoroacetic acid in the reagent directly, or generated indirectly by the presence of water in the pesticide sample, could adversely affect the product yield for GLC analysis, varying levels of deuteriotrifluoroacetic acid were added to a series of 0.25-mL aliquots of a 1.5-mL deuteriochloroform solution of 0.19 g (0.86 mmol) of carbofuran and 0.75 g (3.6 mmol) of trifluoroacetic anhydride. The yields of $N$-trifluoroacetylcarbofuran after 18 h are given in Table I.

That the apparent interference in the yield, caused by the free acid, could be overcome by the addition of base was considered in the preparation of the derivative in quantity for GLC reference usage. When trifluoroacetic anhydride and pyridine were mixed in equal quantity and added to a deuteriochloroform solution of carbofuran, the reaction was quantitative and complete before the NMR spectrum could be recorded, and the reaction product, when isolated in the usual way, gave a mass spectrum (not previously recorded) in accordance with the assigned structure $m/e$ 65 (13), 69 (85), 77 (18), 91 (23), 107 (15), 110 (11), 126 (42), 131 (27), 135 (14), 145 (12), 147 (22), 154 (16), 163 (24), 164 (16), 190 (21), 191 (8), 218 (5), 220 (5),

Table II. Influence of Pyridine on the Extent of Reaction Between Trifluoroacetic Anhydride and Carbofuran in CDCl$_3$

| Mol of pyridine/mol of carbofuran | Time, min | Yield, % |
|---|---|---|
| 0 | 33 | 5 |
| 0.18 | 37 | 14 |
| 0.36 | 21 | 20 |
| 0.71 | 17 | 34 |
| 1.43 | 13 | 58 |
| 2.86 | 7 | 96 |

245 (45), 246 (6), 260 (100), 261 (16), M$^+$ 317 (70), 318 (12).

A second experiment was conducted to determine if lesser quantities of pyridine would substantially affect the course of the reaction. Varying quantities of pyridine were added to 0.25-mL aliquots of a deuteriochloroform solution (1.5 mL) of carbofuran (0.18 g, 3.6 mmol) and trifluoroacetic anhydride (0.75 g, 3.6 mmol). The extent of reaction was measured immediately after addition in the mixture containing the greatest proportion of pyridine, and as quickly as possible thereafter in the remaining solutions in order of decreasing proportions of pyridine. Because of the time taken to record each NMR spectrum, the solution containing the least pyridine could not be analyzed earlier than 30 min from initiation. The addition of near stoichiometric quantities of pyridine substantially affected both the rate and extent of the reaction (Table II).

While the use of pyridine, as a catalyst, in the acylation of carbamates has not been previously reported, pyridine has been employed as a catalyst in the reaction of heptafluorobutyric anhydride and $N$-nitrosamines in chloroform (Brooks et al., 1972, and Gough et al., 1975). Brooks and Moore (1969) have observed that pyridine had not only a catalytic affect on the rate of reaction of trifluoroacetic anhydride with biologic amines but also affected product yields. The mechanism by which pyridine acts in the course of these reactions has not been previously described. However, from this study, it would appear probable that pyridine acts both as a catalyst and as a competitive base with respect to the formation of the trifluoroacetic acid conjugate of carbofuran.

The results of this investigation provide a simple rapid method for preparing $N$-trifluoroacetylcarbofuran, and by inference possibly the $N$-trifluoroacetates of other carbamates, in high yields for GLC analysis under mild conditions and without resorting to the use of excessive quantities of the anhydride and elevated temperature, which serves only to further complicate the isolation of the derivatives in a pure state. Further, this work suggests modifications to existing procedures for the GLC analysis of carbamate pesticides which may obviate the necessity for decomposing the excess anhydride and removal of the rather excessive quantity of trifluoroacetic acid in a subsequent step prior to GLC analysis.

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