4,4,4-trifluorobutanal (1) can be conveniently prepared by anodic trifluoromethylation of 2-propen-1-ol (allyl alcohol).

Solutions of trifluoroacetic acid, the alcohol, and a small amount of base were electrolyzed in a number of solvents. NMR spectra were used to obtain a preliminary indication of the nature of the product mixture and of the number of faradays required to maximize the product concentrations. Both the yield and product distribution were found to be markedly solvent dependent. In anhydrous methanol, the $^{19}F$ spectrum was dominated by a pair of overlapping triplets provisionally assigned to the dimethyl acetal of 1 and the corresponding hemiacetal, since the proton spectrum showed that little or no aldehyde was present. Apparently the radical, $CF_3CH_2\dot{C}HCH_2OH$, presumably formed at the anode, is very readily oxidized to $CF_3CH_2{}^+CHCH_2OH$. This ion can lose a proton to give the enol of 1 and then 1 itself, which is converted to the acetal with trifluoroacetic acid serving as the catalyst. Smaller peaks in the $^{19}F$ spectrum probably correspond to minor amounts of the expected byproducts, including $CF_3CH{=}CHCH_2OH$, $CF_3CH_2CH_2CH_2OH$, $CF_3CH_2CH(CF_3)CH_2OH$, and oligomeric products, but none of these was isolated.

Pouring the electrolyzed solution into water caused partial hydrolysis of the acetal. After isolation of the insoluble oil and extraction of the aqueous layer with dichloromethane, the $^1H$ and $^{19}F$ NMR spectra suggested that roughly equal amounts of aldehyde, acetal, and hemiacetal were present. These were separated from the less volatile byproducts by a preliminary distillation and further hydrolyzed by distilling with dilute aqueous sulfuric acid. Because the first distillate still contained considerable amounts of unhydrolyzed or partially hydrolyzed acetal, it was subjected to a second similar hydrolysis step and finally dried and distilled to give nearly pure 1. The method is much simpler than any of the several multistep procedures used to obtain this aldehyde previously.[7,8] If subjected to routine procedures for oxidation or reduction, the product provides good yields of 4,4,4-trifluorobutanoic acid or 4,4,4-trifluorobutanol.

## Experimental Section

Commercial trifluoroacetic acid, allyl alcohol, and sodium acetate were used as received. Methanol was refluxed over magnesium methoxide and distilled. Almost equally good results were obtained with untreated anhydrous methanol, but deliberate addition of increasing amounts of water as a cosolvent progressively lowered the yields. The electrolysis cell[5] was charged with 20.4 mL (300 mmol) of allyl alcohol, 30 mL (389 mmol) of the acid, and 1.6 g (20 mmol) of sodium acetate in 200 mL of methanol. The reaction was carried out by using a nearly constant current of 0.6 A until 0.48 faradays had been consumed. The mixture was then poured into 700 mL of water, the dense oil layer separated, and the aqueous layer extracted with several portions of dichloromethane. The combined nonaqueous solutions from four identical runs were distilled to recover the solvent and further distilled at 70 torr with the receiver cooled in dry ice until about 70–75 g of material, including some residual dichloromethane, had been collected and the temperature at the top of the short Vigreux column had reached 55 °C. The distillate was then subjected twice to the following three-step treatment: (1) Ten grams of 98% sulfuric acid in 350 mL of water were added and the resulting two-phase mixture was distilled until the temperature at the top of the column reached 100 °C and about 90 mL had been collected. Much of this material consisted of an azeotrope boiling at 79–81 °C. (2) The distillate was poured into 300 mL of water, the oil layer isolated, and the water layer extracted with several portions of dichloromethane. (3) The combined nonaqueous layers were distilled to remove the solvent. After the first treatment, the residue contained 1 and a significant amount of unhydrolyzed acetal or hemiacetal; after the second, hydrolysis was complete, and further distillation gave 37.8 g (300 mmol, 25% based on allyl alcohol) of colorless oil boiling between 91 and 96 °C (lit.[7] bp 94–96 °C). The $^1H$ and $^{19}F$ NMR spectra of a 12% solution in $CDCl_3$ (1% $Me_3Si$) showed only trace impurity peaks, indicating that the material was nearly pure 1: $^{19}F$ NMR (t, $J$ = 10.55 Hz), 11.75 ppm downfield from external trifluoroacetic acid; $^1H$ NMR $\delta$ 9.78 (br s, 1 H), 2.17–2.87 (complex m, 4 H).

**Registry No.** 1, 406-87-1; $CF_3CO_2H$, 76-05-1; $CH_2{=}CHCH_2OH$, 107-18-6; $CF_3(CH_2)_2CH(OMe)_2$, 92670-97-8; $CF_3(CH_2)_2CH(OH)OMe$, 92670-98-9.

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# Mechanism for the Reaction of *trans*-2-Phenylcyclopropylamine with Nitrous Acid

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*trans*-2-Phenylcyclopropylamine (2-PCPA) is an antidepressant drug which inactivates the enzyme monoamine oxidase (MAO); the mechanism of this enzyme inactivation and the structure of the enzyme adduct were reported recently.[2] Part of the structure proof for the enzyme adduct involved the conversion of 2-PCPA to cinnamaldehyde using sodium nitrite in HCl followed by chromic acid oxidation; the first of these reactions gives a mixture of cinnamyl chloride and cinnamyl alcohol.[2] Cyclopropylamine is known to give allyl alcohol upon treatment with aqueous sodium nitrite,[3] and Corey and Atkinson[4] showed that the $C_2$–$C_3$ bond is cleaved in the reaction. This is not a surprising result since the $C_1$–$C_2$ bond of cyclopropylamine is not polarized and the Woodward–Hoffmann rules[5] predict that for a concerted process, it is the $C_2$–$C_3$ bond of a substituted cyclopropane that should break. Kirmse and Schütte[6] investigated the diazotization and subsequent ring opening of *N*-nitroso-*N*-(2-phenylcyclopropyl)urea and suggested, however, that, in this case, the reaction is not concerted. Hausser and Uchic[7] found that the rate of solvolysis of *trans*-2-phenylcyclopropyl chloride was $4 \times 10^4$ times faster than that of cyclopropyl chloride and concluded that the increased rate was the result of phenyl stabilization of the positive charge in the transition state. Because of the increased polarization of the $C_1$–$C_2$ bond in 2-phenylcyclopropylamine relative to cyclopropylamine and the suggestion[6] that ring opening of (2-phenylcyclopropyl)diazonium ion is not concerted, we wanted to determine if there is a difference in 2-phenylcyclopropylamine from

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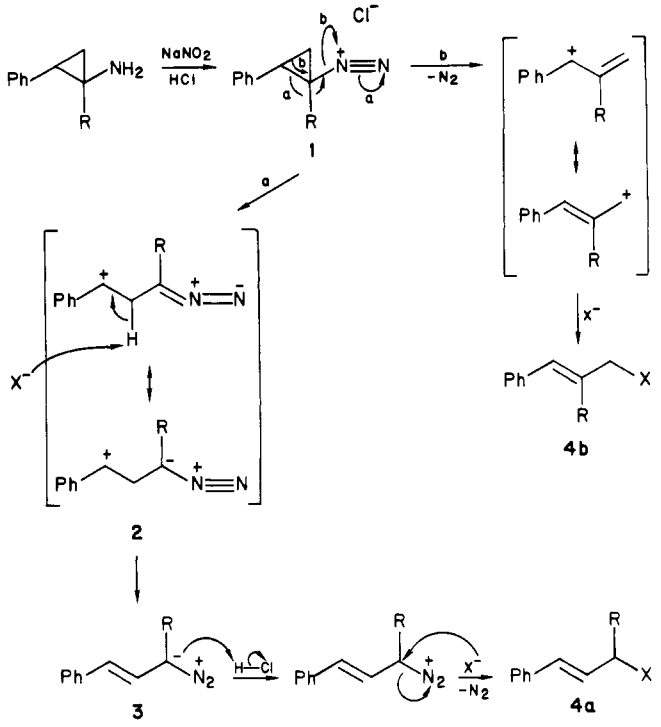
Scheme I. Two Possible Mechanisms for the Conversion of 2-PCPA to Cinnamyl Chloride and Cinnamyl Alcohol by Nitrous Acid ($X^-$ = $Cl^-$ or $H_2O$; R = H or D)



that observed with cyclopropylamine[4] regarding which bond breaks subsequent to diazotization. (2-Phenylcyclopropyl)diazonium ion (1) could decompose by the two routes shown in Scheme I. Pathway a involves cleavage of the $C_1$–$C_2$ bond to give a diazo benzyl cation (2) followed by deprotonation (these steps could be concerted) to *trans*-2-diazomethylstyrene (3). In the presence of strong acid this would become protonated to the alkyl diazonium salt which would undergo rapid nucleophilic displacement of $N_2$ by $Cl^-$ or $H_2O$ giving either cinnamyl chloride or alcohol (**4a**). Pathway b involves concerted cleavage of the $C_2$–$C_3$ bond[5] with concomitant ejection of $N_2$ to give the cinnamyl cation which would be captured by $Cl^-$ or $H_2O$ to give the same two products (**4b**). Cleavage of $C_1$–$C_3$ is unlikely since a primary cation would be generated. The two pathways were differentiated by two experiments. The first experiment paralleled that of Corey and Atkinson[4] and used 1-deuterio-2-phenylcyclopropylamine as the starting material. In Scheme I when R = D, pathway a gives the cinnamyl derivatives with deuterium at $C_1$; pathway b gives $C_2$-deuterated products. Also, pathway a involves protonation at $C_1$ whereas pathway b does not. If DCl were used in the reaction with nonlabeled 2-PCPA, deuterium incorporation would occur only via pathway a, not b.

When 1-deuterio-2-PCPA was treated with sodium nitrite in HCl, both the cinnamyl chloride and cinnamyl alcohol isolated were completely (>95%) deuterated at $C_2$. Treatment of 2-PCPA with sodium nitrite in DCl gave only nondeuterated cinnamyl chloride and cinnamyl alcohol. Both of these results are consistent with pathway b and suggest that $C_2$–$C_3$ cyclopropane bond cleavage to give the cinnamyl cation is the lower energy pathway; phenyl stabilization is not sufficient to activate the $C_1$–$C_2$ bond for cleavage in favor of a concerted electrocyclic ring opening mechanism.[5] Capture by $Cl^-$ occurs 10–14 times faster than by $H_2O$ even though the concentration of $H_2O$ is 9 times greater than that of $Cl^-$. This is to be expected based on the greater nucleophilicity of $Cl^-$ than $H_2O$.[8]

## Experimental Section

**General Methods.** NMR spectra were recorded on a Varian EM 390 90-MHz spectrometer with internal $Me_4Si$ as standard. IR spectra were obtained with a Perkin-Elmer 283 spectrophotometer. Melting points were determined with a Fisher-Johns melting point apparatus and are uncorrected. Column chromatography was carried out on silica gel 60 by the method of Still et al.[9]

2-Phenylcyclopropanecarbonitrile, *trans*-2-phenylcyclopropylamine·HCl, methanol-*d* (99.5+ %), deuterium oxide (99.8%), and deuterium chloride (37 wt % in 99% $D_2O$) were purchased from Aldrich, sodium azide came from Fisher Scientific, and sodium nitrite was bought from Mallickrodt. Toluene was dried by distillation from sodium metal.

**1-Deuterio-2-phenylcyclopropanecarboxylic Acid.** The exchange of the $\alpha$-proton of 2-phenylcyclopropanecarbonitrile, catalyzed by sodium methoxide, is based on the work of Walborsky and Hornyak.[10] 2-Phenylcyclopropanecarbonitrile (1.0 g, 6.98 mmol) was added to 25 mL of a 1 M solution of sodium methoxide (prepared from 575 mg of sodium metal) in methanol-*d* and the solution was heated to reflux under argon for 16 h. The methanol-*d* was removed by distillation and replaced with 25 mL of fresh methanol-*d*. The solution was heated to reflux for an additional 26 h at which time complete exchange of the $\alpha$-proton was determined by the disappearance of the $\delta$ 1.25–1.7 signal in the NMR spectrum. The methanol-*d* was removed by distillation to give a yellow solution which was cooled and treated with 35 mL of a 4.7 N solution of sodium deuteroxide in $D_2O$ (prepared by the cautious addition of 5.4 g (0.235 mol) of sodium metal to 50 mL of $D_2O$ at 0 °C). The residual methanol was removed by heating until the vapor was >95 °C and then the basic solution was heated to reflux for 6 h. After being cooled to room temperature, 6 N HCl was added until the solution was very acidic, during which addition 1-deuterio-2-phenylcyclopropanecarboxylic acid precipitated. The product was extracted with 6 × 40 mL of ether and the combined extracts were washed with 4 mL of $H_2O$ and 2 × 4 mL of brine and dried ($MgSO_4$). After removal of the ether by rotary evaporation, the product was obtained as an off-white solid: 921 mg (81%); $^1H$ NMR ($CDCl_3$) $\delta$ 1.35 (t, 1 H), 1.60 (q, 1 H), 2.55 (t, 1 H), 7.0–7.4 (m, 5 H).

**1-Deuterio-2-phenylcyclopropylamine Hydrochloride.** This procedure is a modification of the procedure of Burger and Yost.[11] Thionyl chloride (0.334 mL, 4.63 mmol) was added via syringe to a stirred solution of 1-deuterio-2-phenylcyclopropanecarboxylic acid (771 mg, 4.72 mmol) in 25 mL of dry toluene under argon. The mixture was stirred and heated at 60 °C for 6 h.[12] The reaction flask was flushed with a stream of argon, and the solution was syringed into a mixture of sodium azide (610 mg, 9.37 mmol) in 4 mL of dry, refluxing toluene. After 9 h, fresh sodium azide (1.156 g, 17.78 mmol) was added and the mixture was heated to reflux for an additional 4 h.[13] An off-white precipitate of inorganic salts was removed by filtration and washed well with dry toluene. The combined washes and filtrate were concentrated to ~5 mL by rotary evaporation, cooled in an ice bath, and treated cautiously with 18.4 mL of 4 N HCl. After most of the gas evolution had ceased, the mixture was heated to reflux with vigorous stirring for 10 h. After being cooled, the organic layer was separated and extracted with 3 × 5 mL of $H_2O$. The combined acid layer and aqueous extracts were washed with 3 × 4 mL of ether, and the water was removed in vacuo to give the product as an off-white solid, 517 mg (64%). After recrystallization from MeOH-EtOAc, the product was obtained as white crystals: mp 151–155 °C dec; $^1H$ NMR ($D_2O$) $\delta$ 1.25–1.60 (m, 2 H), 2.48 (t, 1 H), 7.10–7.55 (m, 5 H).

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(12) The reaction was monitored by the disappearance of the carboxyl carbonyl IR absorption at 1690 $cm^{-1}$ and the appearance of the acid chloride carbonyl IR absorption at 1780 $cm^{-1}$.
(13) The conversion of the acid chloride to the isocyanate was monitored by the disappearance of the 1780-$cm^{-1}$ IR absorption and appearance of the 2265-$cm^{-1}$ peak.

**Reaction of 1-Deuterio-2-phenylcyclopropylamine Hydrochloride with Sodium Nitrite in HCl.** 1-Deuterio-2-phenylcyclopropylamine hydrochloride (485 mg, 2.84 mmol) was suspended in 6 N HCl (1.46 mL) and stirred in an ice bath while a solution of sodium nitrite (201 mg, 2.91 mmol) in 1.2 mL of $H_2O$ was added dropwise. After 5 min, a few granules of urea were added, and the mixture was heated on a steam bath for 5 min, cooled, and extracted with 3 × 10 mL of ether. The combined ether extracts were washed with saturated $NaHCO_3$, $H_2O$, and brine, dried ($MgSO_4$), and rotary evaporated to an orange-yellow liquid (119 mg). TLC (ether) revealed five spots ($R_f$ 0.65, 0.56, 0.40, 0.29, 0.0); the spots at $R_f$ 0.65 and 0.40 comigrated with cinnamyl chloride and cinnamyl alcohol, respectively.[14] Silica gel column chromatography (2.8 × 28 cm; ether) was used to isolate the compounds having $R_f$ values of 0.65 (61.7 mg) and 0.40 (4.4 mg). NMR ($CDCl_3$) of the cinnamyl chloride: δ 4.20 (s with deuterium coupling, 2 H), 6.60 (s with deuterium coupling, 1 H), 7.2–7.5 (m, 5 H). NMR ($CDCl_3$) of the cinnamyl alcohol: δ 4.30 (s, 2 H), 6.60 (s with deuterium coupling, 1 H), 7.2–7.5 (m, 5 H).

(14) In a reaction starting with nonlabeled 2-phenylcyclopropylamine, these compounds were identified by comparison of their NMR and IR spectra with those of authentic samples of cinnamyl chloride and cinnamyl alcohol.

**Reaction of 2-Phenylcyclopropylamine Hydrochloride with Sodium Nitrite in DCl.** The same procedure as above was followed starting with 500 mg of 2-phenylcyclopropylamine hydrochloride in 1.5 mL of 6 N DCl. The sodium nitrite was dissolved in 1.2 mL of $D_2O$ before addition. The crude reaction product (182 mg) was chromatographed as above, and the cinnamyl chloride (112.7 mg) and cinnamyl alcohol (11.1 mg) were isolated. The NMR spectra were identical with those of cinnamyl chloride and cinnamyl alcohol, respectively; no deuteration was evident.

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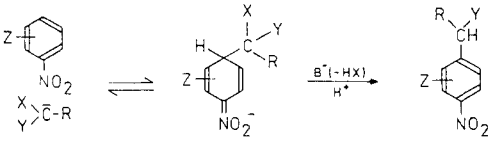
**Registry No.** 2-PCPA, 95-62-5; 1-deuterio-2-phenylcyclopropanecarboxylic acid, 92456-24-1; 1-deuterio-2-phenylcyclopropylamine hydrochloride, 92456-25-2.

# Communications

## Vicarious Nucleophilic Substitution of Hydrogen in Nitrophenols and Polynitroarenes. Examples of Nucleophilic Addition to Nitrocyclohexadienonenitronate Anions[1]

*Summary:* The vicarious nucleophilic substitution of hydrogen in dinitrophenols with chloromethyl phenyl sulfone carbanion 1 follows an orientation pattern due to quinoid resonance structures of the dinitrophenolate anions which behave as dinitrocyclohexadiene derivatives; di- and even trisubstitution is observed in the reaction with polynitroarenes leading to a sixfold-substituted benzene ring.

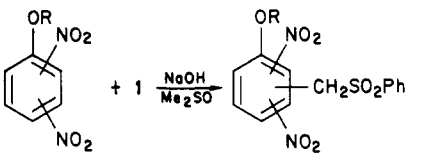
*Sir:* Vicarious nucleophilic substitution of hydrogen in nitroaromatic compounds proceeds via the addition of carbanions RCYX (X = leaving group, Y = carbanion stabilizing group) to the ortho and para positions of the nitroarene ring, with the formation of anionic σ complexes which undergo β-elimination of HX, giving rise to the anions of the substituted products.[2,3]



The reaction of nitroarenes with the carbanion of chloromethyl phenyl sulfone, 1, practically has no limitations as far as the substituents in the nitroarene ring are concerned. Electron donating ($NMe_2$, OR, $CH_3$) as well as electron accepting substituents (CN, $SO_2Ph$, $CF_3$) and even negatively charged ($COO^-$) groups located in the ortho, meta, and para positions to the nitro group usually do not impede this reaction.[4] However ortho, meta, and para nitrophenols do not enter this reaction. This is obviously due to the fact that the negative charge of the nitrophenolate anion is mostly located on the nitro group, or on the ring as in *m*-nitrophenol, hence the nucleophilic addition of the carbanion is hindered. Here we would like to report that this effect can be circumvented by the introduction of a second nitro group into the nitroarene ring. One can roughly consider that in a dinitrophenolate anion one of the nitro groups is engaged in the delocalization of the negative charge, whereas the second can sufficiently activate the ring toward nucleophilic attack.

Indeed dinitrophenols, which in the presence of strong alkali exist in the form of corresponding phenolate anions, react with 1 according to the vicarious nucleophilic sub-

**Table I.[a] Reactions of Dinitrophenols and Dinitroanisoles with 1**



| substrate | product | yield, % | mp, °C |
|---|---|---|---|
| **24** | **243**[b] | 89 | 226–228 |
| **24a** | **245a** | 61 | 180–183 |
| **25** | **256**[c] | 64 | 197–199 |
| **25a** | **256a** | 42 | 177–180 |
| **26** | **263** | 69 | 214–217 |
| **34** | **342**[c] | 23 | 216–218 |
| **34a** | **342a** | 26 | 170–172.5 |
| **35** | **352**[c] | 20 | 255 dec |
| **35a** | **352a** | 78 | 173–175 |

[a] Notations: see ref 5. [b] **243a** obtained via methylation of **243**; mp 200–203 °C. [c] Methylation of these phenols gives anisoles identical with **256a**, **342a**, and **352a**, respectively.

(1) Part 120 in the series Reactions of Organic Anions. Part 119: Mąkosza, M.; Wojciechowski, K. *Bull. Acad. Polon. Sci., Ser. Sci. Chim.*, in press.

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