out by the absence of evidence for their formation[20] and the different positions of the minima for **1-OTs** and **4-Br**. The extent of ground-state solvation is not yet clear.

The decrease of α with X_{H_2O} has a precedent in the reaction of Ph_2CCl_2 in aqueous acetone.[25] A blend of effects (reduced recombination rate of R^+ with Br^-, enhanced cation solvation by water, reduced anion solvation by less TFE, change in the nucleophilicity of the medium, and possible intervention of ion pairs) account for this phenomenon.

A literature survey of solvolytic data in aqueous TFE reveals several peculiarities: (i) a minimum is also observable in Sunko's plot of log k_1 *vs.* Y for MNBOTs;[5] (ii) for cycloalkenyl triflates "m" (aqueous TFE) > "m" (aqueous EtOH), where "m" is based on two points[2j] (however, our data show that "high," "low," or "negative" m values may be obtained for different pairs of points, depending on the solvent mixtures chosen); (iii) "m" (aqueous TFE) for secondary brosylates are high,[2b] probably reflecting a high response to the solvent nucleophilicity; (iv) the solvent isotope effect for the solvolysis of t-BuCl[2a] and data on the addition of HCl to isobutene in TFE[26] suggest a rate determining dissociation of tight ion pairs in the trifluoroethanolysis.[2a,26] Since the extent of the ion pair return is unknown, Y values of aqueous TFE are inadequate as a measure of the "ionizing power" and they should be used with reservation in mechanistic studies.[27,28]

More work on solvolysis in aqueous TFE is now in progress.

Acknowledgments. We are indebted to the Volkswagen Foundation for support of this work and to Professors E. M. Kosower and P. v. R. Schleyer for helpful discussions and preprints.

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(27) For example, Y(97% TFE) = 2.27 when based on 1-adamantyl-Br,[2h] 1.15 when based on t-BuCl,[2a] and 0.79 when based on **4**-OTs.

(28) *E.g.*, the use of $(k_{\text{aq TFE}}/k_{\text{aq EtOH}})_Y$ for assessing the contribution of the k_s route (R. H. Summerville, C. A. Senkler, P. v. R. Schleyer, T. E. Dueber, and P. J. Stang, submitted for publication) may be highly misleading.

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Concerning Reported Nonnegligible Concentrations of Tetrahedral Intermediates in the Hydrolysis of Trifluoroacetanilides

Sir:

Tetrahedral species have long been postulated as intermediates in most reactions of carboxylic acid derivatives with nucleophiles.[1-3] More recently direct kinetic evidence for their intermediacy has been obtained in favorable cases,[1-9] and in a few cases such intermediates have been detected[10,11] or even (for cyclic or polycyclic systems) isolated.[12-14] Nevertheless it has been considered that such intermediates are ordinarily extremely unstable.[1,15] Consequently a recent report of kinetic studies of the alkaline hydrolysis of substituted trifluoroacetanilides, in which it was stated that the tetrahedral intermediate accumulated to the extent of 5–10%,[17] seemed quite startling. Furthermore the rate constants reported in this paper, from the kinetic analysis of the pH rate profile, correspond to an equilibrium constant of *ca.* 10^6 for the formation of I from A

$$\underset{\text{A}}{CF_3CONHC_6H_4Cl} + OH^- \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} \underset{\text{I}}{CF_3C(OH)(O^-)NHC_6H_4Cl} \xrightarrow[k_3(OH^-)]{k_2} \text{products}$$

Competitive ionization of the anilide (pK_a = 9.2[17]) prevents complete conversion of A into I.[18]

We have performed an independent test for the accumulation of the species I. This took the form of an ^{19}F nmr study of alkaline solutions of p-chlorotrifluoroacetanilide (A). In Table I are recorded ^{19}F chemical shifts for trifluoromethyl groups in chemical environments similar to that of I. From the table it appears that replacing O by N causes a downfield shift of δ 1–3, with a smaller shift if the N bears an electronegative substituent, and replacing OH by O^- causes a δ 1.5 downfield shift. Then from the shifts for orthoesters of trifluoroacetic acid one estimates that the

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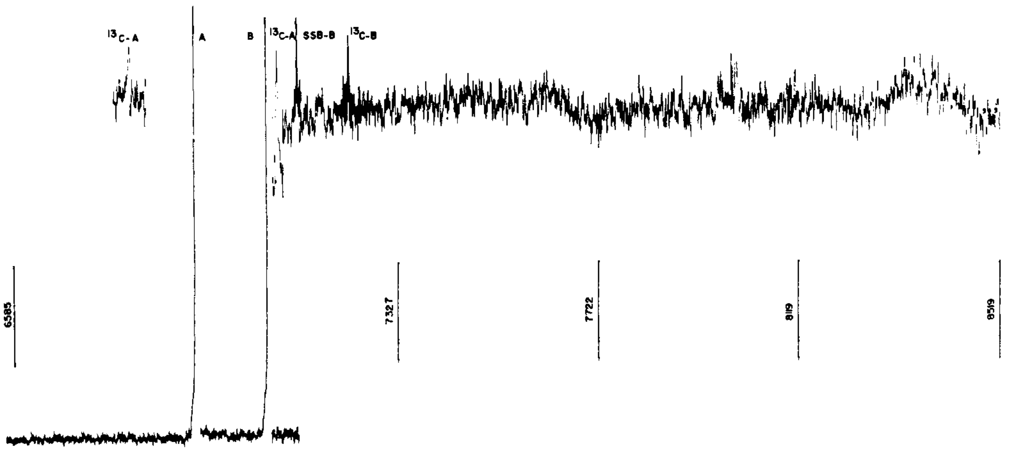

Figure 1. ^{19}F nmr spectrum of a solution initially 0.5 *M* in A, in aqueous solution containing 20% methanol, at pH 11.8, and at 32.5°. Scale markings are Hz from $CFCl_3$ (coaxial capillary). The spectrum was recorded after 45 min of reaction. Peak A is the starting material (present as its conjugate base) peak B is trifluoroacetate ion. At high amplitude the ^{13}C satellites can be seen, but no other peaks are visible up to δ 85.19.

Table I. ^{19}F Chemical Shifts of CF_3–$CX_1X_2X_3$ Compounds

X_1	X_2	X_3	δ[a]
CH_2–	ON=	OH	83.7[b,c]
CH_2–	$NHOCH_3$	OH	83.0[c,d]
CF_3	NH_2	OCH_3	79.6[c,e]
CF_3	OH	OH	82.7[c,e]
			82.3[f,g]
CF_3	$NHNH_2$	NH_2	79.1[h,i]
COOH	OH	OH	83.1[f,j]
CF_3	OCs	OH	81.5[f,g]
OCH_2–	OCH_2–	OCH_2–	84.9[k,l]
OCF_2–	OCF_2–	OCF_2–	84.8[l,m]

[a] Ppm relative to $CFCl_3$. [b] $CH_2C(CH_3)=NOC(OH)\mathit{CF}_3$ in $CDCl_3$. [c] W. H. Dawson, personal communication. [d] $\mathit{CF}_3C(OH)(NHOCH_3)CH_2C(OH)(NHOCH_3)\mathit{CF}_3$ in CCl_4. [e] In $CHCl_3$. [f] In acetone. [g] J. H. Prager and P. H. Ogden, *J. Org. Chem.*, **33,** 2100 (1968). [h] Neat. [i] W. J. Middleton and C. G. Krespan, *J. Org. Chem.*, **30,** 1398 (1965). [j] R. E. Bak, D. Berry, and G. J. Moore, *J. Chem. Soc. C*, 2598 (1969). [k] $CF_3C(OCH_2)_3CCH_3$ in benzene. [l] R. L. Talbot, *J. Org. Chem.*, **32,** 834 (1967). [m] $\mathit{CF}_3C(OCF_2)_3CCF_3$ in $CFCl_3$.

shift for I should be *ca.* δ 81.5 and certainly should lie between δ 75 and 85.

Because of the low solubility of neutral A in water, it was necessary to add a concentrated solution of A in methanol to an aqueous sodium hydroxide–triethylamine solution of suitable concentration to give a final solution of the anion of A in a triethylamine–triethylammonium ion buffer. Results of such an experiment are shown in Figure 1; the low amplitude scans show signals from A at δ 69.45 and product trifluoroacetate at δ 70.87. At high amplitude, where the ^{13}C satellites are clearly visible, *no* additional high field peaks can be seen. Therefore I can only be present to a maximum extent of less than 0.5% of the total anilide concentration.[27]

The source of the discrepancy between this experiment and the conclusion that I accumulates,[17] lies in the kinetic analysis used to reach this conclusion. Extrapolation[17] of a graph of $1/k_{obsd}$ *vs.* (H^+) to (H^+) = 0 gave a nonzero intercept from which k_2 was calculated; however, the data are such that a line with zero intercept, corresponding to $k_2 = \infty$ passes within *ca.* 10% of all experimental points (Figure 1B of ref 17).[28] Furthermore the kinetic analysis[17] leads to the conclusion that I is present as a nonnegligible fraction of total anilide, which invalidates the assumption that I is a steady-state intermediate (ref 22 of ref 17). If the intermediate accumulates, and the mechanism proposed[17] is correct, then rigorously correct integrated rate equations can be derived[29] describing the concentration of A, I, and products as a function of time. In particular

$$\mathrm{I} = \frac{A_0k_1(\mathrm{OH}^-)}{(1 + K_a/(\mathrm{H}^+))(\lambda_2 - \lambda_3)}[-e^{-\lambda_2 t} + e^{-\lambda_3 t}]$$

where λ_2 and λ_3 are functions of the rate constants.[30] From this expression one can deduce expressions for the maximum concentration of I which will accumulate. Using these correct expressions and reported[17] rate constants one finds that for the conditions used for the experiment described above, 35% of the initial anilide should have been present as I after 45 min of reaction. This is *not* what was observed, and therefore the kinetic analysis[17] must be incorrect.[31]

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(27) (a) To observe the trifluoromethyl group in a transient reaction intermediate by nmr spectroscopy, the decomposition of the intermediate must be slow with respect to the difference in chemical shift between that of the intermediate and the starting material or product.[27b] In the present case the difference in chemical shift must be at least 500 Hz and probably 1000 Hz. If the intermediate is to accumulate to $\geq 0.5\%$ of total anilide, then $(k_1(\mathrm{OH}^-)/(1 + K_a/(\mathrm{H}^+))/(k_{-1} + k_2 + k_3(\mathrm{OH}^-)) \geq 0.005$. Substituting measured values for K_a and k_1 (based on steady-state analysis of the kinetics), this implies that $(k_{-1} + k_2 + k_3(\mathrm{OH}^-)) \leq 5\ \mathrm{sec}^{-1}$. Thus the condition is satisfied *if* I accumulates, and *if* I were present it would be observable. (b) E. D. Becker, "High Resolution NMR," Academic Press, New York, N. Y., 1969, p 214.

(28) (a) The error limits for slope and intercept evaluated by a least-squares procedure are themselves subject to error and are not reliable unless 15–20 independent points are used to define the line.[28b] With a limited number of data points it is preferable to estimate error limits for the intercept by drawing the extreme lines which can fit the points within their error limits.[28c] (b) W. E. Deming, "Statistical Adjustment of Data," Dover, New York, N. Y., 1964, p 30; (c) D. P. Shoemaker and C. W. Garland, "Experiments in Physical Chemistry," 2nd ed, McGraw Hill, New York, N. Y., 1967.

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(30) $\lambda_2 = {}^1/_2(p + q)$; $\lambda_3 = {}^1/_2(p - q)$; where $p = k_1(\mathrm{OH}^-)/(1 + K_a/\mathrm{H}^+) + k_{-1} + k_2 + k_3(\mathrm{OH}^-)$ and $q = (p^2 - 4k_1(\mathrm{OH}^-)(k_2 + k_3(\mathrm{OH}^-))^{1/2}$ using the kinetics scheme of ref 17. When the steady-state approximation is valid, λ_2 is the rate of approach to steady state and λ_3 is the observable steady-state rate constant, $\lambda_3 \simeq k_{obsd} = (k_2 + k_3(\mathrm{OH}^-))k_1(\mathrm{OH}^-)/(1 + K_a/(\mathrm{H}^+))(k_{-1} + k_2 + k_3(\mathrm{OH}^-))$.

(31) In addition, the rigorous equation for the concentration of A as a function of time predicts (using the rate constants reported[17]) biphasic kinetics for the disappearance of A; this is contrary to observation[17,18] and constitutes further evidence that the analysis leading to these rate constants[17] is incorrect.

In conclusion, although there is strong evidence for the existence of a tetrahedral intermediate as an obligatory species along the reaction path for hydrolysis of trifluoroacetanilide,[19–26] there is no evidence concerning the concentration of this species except that it is less than 0.5% of the total at all times.

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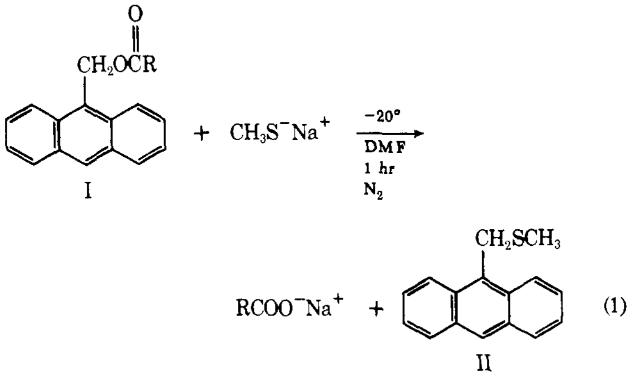
A New Method for Protecting Carboxylic Acids, Phenols, Thiophenols, and Mercaptans

Sir:

We describe a new blocking group for carboxylic acids, phenols, thiophenols, and mercaptans which is readily attached to these functions, which remains in place under a variety of circumstances, and which is rapidly detached under mild, highly specific conditions. This protective device derives from the unusual chemical properties of the 9-anthrylmethyl system, a system which has recently been found to undergo a new type of substitution at the saturated carbon atom.[1]

Carboxylic acids are protected as esters (I).[2,3] The general procedure for deblocking these esters involves treatment for 1 hr at −20° with the sodium salt of methyl mercaptan in DMF (eq 1); the yields given in Table I refer to pure, isolated acids.[4] In hexamethylphosphoramide (HMPA) the reaction of eq 1 is extraordinarily fast; at 25° 9-anthrylmethyl mesitoate is completely deblocked in less than 30 sec and a 93% yield of pure mesitoic acid is obtained.



(1)

The study of 9-anthrylmethyl mesitoate provides an insight into the intrinsic properties of 9-anthrylmethyl esters for, here, the usual acid and base catalyzed acyl–oxygen cleavage processes do not occur easily. Thus, the mesitoate ester is recovered quantitatively after a 24-hr treatment with 24 mol of anhydrous ethylamine in DMF at 25°. In aqueous dioxane the mesitoate is completely unaffected by 2 mol of lithium hydroxide (0.07 M) after 8 hr at 25°.

Table I. 9-Anthrylmethyl Esters Deblocked at −20° [a]

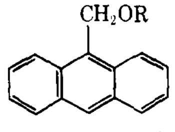
Ester (I)	Acid	% yield
p-Toluate	*p*-Toluic	95
Mesitoate	Mesitoic	99
p-Methoxyphenylacetate	*p*-Methoxyphenylacetic	93
n-Heptanoate	*n*-Heptanoic	89
m-Nitrobenzoate	*m*-Nitrobenzoic	86
trans-Cinnamate	*trans*-Cinnamic[b]	94

[a] In DMF; 0.1 M in ester, 0.2 M in CH_3SNa; 1 hr, under N_2.
[b] 0.1 M in ester and in CH_3SNa, 6 hr reaction time.

The behavior of 9-anthrylmethyl mesitoate toward acids is noteworthy. An aqueous dioxane solution containing 4 equiv of 0.14 N sulfuric acid is without effect after 3 hr at 25°; nor is there any reaction on exposure to 10 equiv of trifluoroacetic acid in dioxane for 1 hr at 25°. However, when the mesitoate ester is treated with a methylene chloride solution containing 10 equiv of trifluoroacetic acid, it is completely deblocked after 10 min at 0° and a 97% yield of pure mesitoic acid is isolated. Thus the ester is stable to acids in oxygenated solvents such as dioxane or aqueous dioxane but is rapidly and cleanly cleaved by trifluoroacetic acid in an oxygen free solvent—presumably as an alkyl–oxygen cleavage process involving the 9-anthrylmethyl carbonium ion. This selective sensitivity to acid provides a valuable alternative deblocking procedure.

Some of the other esters of Table I are also of interest. The fact that the *m*-nitrobenzoate gives an excellent yield of *m*-nitrobenzoic acid shows that reduction of a nitro group does not compete with the reaction of eq 1. The cinnamate is an example of an ester capable of undergoing the Michael condensation; it turns out that this complication can be avoided merely by using 1 equiv of the mercaptide salt (Table I).[5]

Phenols, thiophenols, and mercaptans are protected as the 9-anthrylmethyl ethers or thioethers—readily prepared by the reaction of their sodium salts with 9-chloromethylanthracene at room temperature in DMF. Two phenolic ethers were studied: III and IV. At 25° they are completely deblocked by treatment with a DMF solution of the sodium salt of methyl mercaptan for 20 min; ether III gives an 86% yield of pure *p-tert*-butylphenol while from ether IV a 99% yield of pure *p*-benzylphenol is isolated.



III, R = *p-tert*-butylphenyl
IV, R = *p*-benzylphenyl

The cleavage of thioethers V and VI by the sodium salt of methyl mercaptan is also a rapid process; in DMF deblocking is complete after 2 hr at 0°. From thioether V a 92% yield of *p*-bromothiophenol is obtained while thioether VI gives *p*-thiocresol in 85% yield. Thioethers derived from mercaptans are, not

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(1) C. W. Jaeger and N. Kornblum, *J. Amer. Chem. Soc.*, **94**, 2545 (1972).

(2) Readily obtained from the acid, 9-chloromethylanthracene and triethylamine in acetonitrile solution; *cf.* F. H. C. Stewart, *Aust. J. Chem.*, 18, 1701(1965). Esterification with 9-hydroxymethylanthracene should be equally effective.

(3) Satisfactory elemental analyses and nmr and ir spectra were obtained for all new compounds.

(4) Thioether II is not completely stable to CH_3SNa; this matter will be discussed in the full paper.

(5) The *trans*-crotonate is also completely deblocked under these conditions but quantitative isolation of crotonic acid is relatively difficult, and the matter was not pursued.