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Preparation of Fluorolactones from the Reaction of γ-Ketoacids with Diethylaminosulfur Trifluoride

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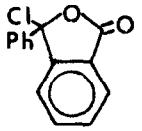
Summary. Levulinic acid and related γ-ketoacids react with diethylaminosulfur trifluoride to give γ-fluorobutyrolactones in good yield. The involvement of a bicyclic (3.2.1) mechanism is considered.

The reactions of o-benzoylbenzoic acid and levulinic acid with thionyl chloride are known to produce the γ-chlorolactones 1 and 2, respectively.[1]



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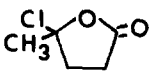


2

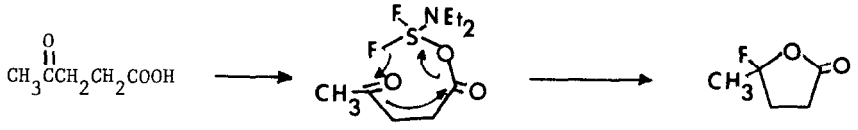
Newman, et al., proposed a novel bicyclic (3.2.1) mechanism from intermediate A to explain the formation of 1 and 2, and subsequently used the concept of bicyclic mechanisms to predict the products of many other reactions.[2,3]

A

The report by Middleton in 1975 that diethylaminosulfur trifluoride (DAST) converts hydroxyl groups into fluorides[4] led us to suspect that DAST would react with acids in a manner similar to that of thionyl chloride. Thus,

we investigated the reaction of several γ-ketoacids with DAST.

The reactions of ketoacids 3-6 with DAST in chloroform solution gave the corresponding fluorolactones, 7-10, respectively (Table I). The formation of the fluorolactones is postulated to occur through intermediate B, formed between the acid and DAST in a manner similar to that proposed by Middleton for reactions of alcohols with DAST. Intermediate B then transforms into product by a bicyclic (3.2.1) path similar to that proposed by Newman.



B 8

A mechanism in which the acid is first converted to an acid fluoride which adds to the γ-keto function cannot be ruled out entirely, but we assume that a one-step intramolecular cyclization would be preferred over a two-step mechanism in accord with previous work.[3]

We also studied the reaction between acetone, benzoic acid and DAST. The observed fluoroester product (11) can be postulated to occur by an intermolecular cyclic path (C). However, we observed that prior reaction of benzoic acid with DAST produces benzoyl fluoride which gives (11) on addition of acetone. Thus the mechanism depends on the timing of the competing processes.

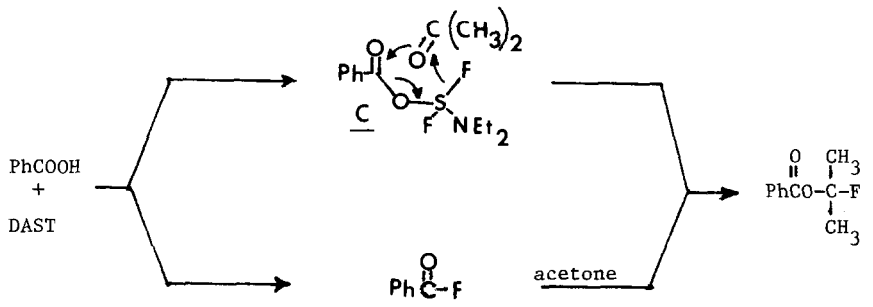
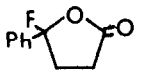
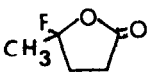
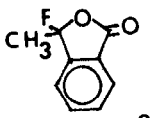
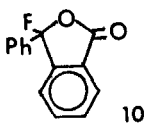
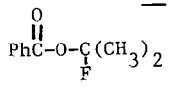


Table I
Properties of γ-Fluorolactones

Acid	Product	% Yield	^{13}C NMR[a]	^{1}H NMR[b]	^{19}F NMR[c]
benzoylpropionic **3**	 **7**	85	33.4(d,CH_2,J=15) 36.0(s,CH_2) 118.8(d,CF,J=228) 125.2-132.9(6, aromatic)	3.0(m,CH_2CH_2) 7.4,79(aromatic)	120.7(m)
levulinic **4**	 **8**	90	23.4(d,CH_3,J=29.3) 33.1(d,CH_2,J=28.3) 37.0(s,CH_2) 117.5(d,CF,J=225) 175(s,C=0)	1.31-2.9(m, aliphatic 1.75(d,CH_3,J=17.4)	93.4 (m,CF)
o-acetylbenzoic **5**	 **9**	95	22.7(d,CH_3,J=33) 114.6(d,CF,J=229) 122,126,130,132,135, (aromatic) 145.9(d, aromatic,J=21) 166.9(s, C=0)	1.95(d,CH , J=18) 7.7(m, aromatic)	95.6 (q,J=18)
o-benzoylbenzoic **6**	 **10**	93	114(d,CF,J=229) 123-135(seven, aromatic) 145.9(d, aromatic, J=225) 166.8(s, C=0)	7.46(m, aromatic)	101.6 (s)
acetone, benzoic acid	 **11**	95	24.5(d,CH_3,J=26) 115.2(d,CF,J=213) 128-235(six, aromatic) 163(s, C=0)	1.85(d,CH_3,J=19) 7.5,8.0(m,aromatic)	95.9 (seven,J=19)

a) $CDCl_3$ solution. Chemical shifts are in ppm relative to tetramethylsilane (TMS) (Ø.0). Coupling constants are in Hertz. The spectra are proton decoupled.
b) $CDCl_3$ solution. Chemical shifts are in ppm relative to TMS. Coupling constants are in Hertz.
c) $CDCl_3$ solution. Chemical shifts are in ppm relative to external Freon-11 ($CFCl_3$, Ø0.0). Coupling constants are in Hertz.

The fluoro products are easily characterized by a doublet for the CF carbon observed at 114-118 ppm (J_{CF} = 228 Hz) in the ^{13}C NMR spectrum, and by the high IR absorption band of 1790-1800 cm^{-1} for the carbonyl absorption frequency. The products are, however, relatively unstable, not amenable to C, H, F elemental analysis, and lose HF on standing several hours at room temperature, but they may be kept in a freezer for several days.

A typical reaction procedure consists of adding 0.01 mole of cold neat DAST to a solution consisting of 0.01 mole of ketoacid in 10 mL of dry reagent grade chloroform at 0° C. After 0.5 hours the yellow solution is extracted with dilute sodium bicarbonate solution and the organic solution is concentrated on a rotary evaporator to give the fluorinated product which is stored in a freezer.

Our work on the concept of using bicyclic and cyclic mechanisms to construct new fluorinated organic systems is continuing.[5]

References

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3) Newman, M.S.; Courduvelis, C., J. Am. Chem. Soc., (1966), 88, 781; Newman, M.S.; Gill, N.; Darre, B., J. Org. Chem., (1966), 31, 2713; Newman, M.S.; Mladenovic,S., J. Am. Chem. Soc., (1966), 88, 4523; Newman, M.S.; Lala, L., J. Org. Chem., (1967), 32, 3225; Newman, M.S.; Mladenovic, S.; Lala, L.; J. Am. Chem. Soc., (1968), 90, 747; Newman, M.S.; Gupte, S.,, J. Org. Chem., (1970), 35, 4176; Newman, M.S.; Gupte, S.; Sankarrappa, S.K.; J. Org. Chem., (1970), 35, 2757.

4) Middleton, W.J.; J. Org. Chem., (1975), 40, 574.

5) We thank Professor M.S. Newman for helpful comments about the mechanisms involved in our work.

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