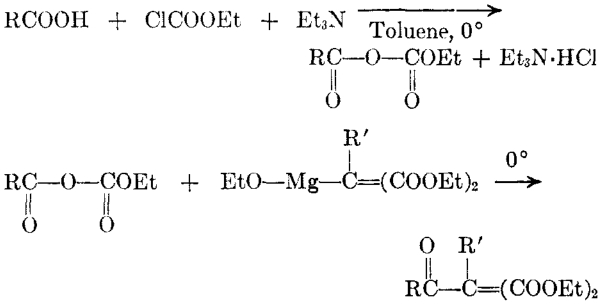
The Use of Mixed Carboxylic-Carbonic Anhydrides to Acylate Carbanions

Sir:

In connection with some projected synthetic sequences, we wished to know if the mixed carbonic anhydride procedure,[1] which has proved so useful for synthesis of peptide and amide linkages,[1,2] could be employed for the acylation of carbanions. We report in the present communication successful acylations, under very mild conditions, of the carbanions derived from diethyl malonate, diethyl ethylmalonate, and from diethyl cadmium.

Diethyl benzoylmalonate (V) was obtained in 70% yield by the action of the mixed anhydride I on the magnesium enolate[3] III in ether at 0° and room temperature; acetylmalonic ester VI was obtained similarly. The hitherto undescribed benzoylethylmalonate VII was prepared in 20% yield as a liquid, b.p. 126–127° (0.3 mm.); n_{D}^{20} 1.5021: Calc'd for $C_{16}H_{20}O_5$: C, 65.74; H, 6.90. Found: C, 65.40; H, 6.84.



$$\mathrm{RCOOH} + \mathrm{ClCOOEt} + \mathrm{Et_3N} \xrightarrow[\text{Toluene, }0^\circ]{} \underset{\mathrm{O}}{\underset{\|}{\mathrm{RC}}}\mathrm{{-}O{-}}\underset{\mathrm{O}}{\underset{\|}{\mathrm{C}}}\mathrm{OEt} + \mathrm{Et_3N{\cdot}HCl}$$

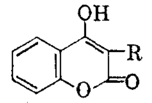
$$\underset{\mathrm{O}}{\underset{\|}{\mathrm{RC}}}\mathrm{{-}O{-}}\underset{\mathrm{O}}{\underset{\|}{\mathrm{C}}}\mathrm{OEt} + \mathrm{EtO{-}Mg{-}}\overset{\mathrm{R'}}{\overset{|}{\mathrm{C}}}\mathrm{{=}(COOEt)_2} \xrightarrow{0^\circ} \overset{\mathrm{O}}{\overset{\|}{\mathrm{RC}}}\mathrm{{-}}\overset{\mathrm{R'}}{\overset{|}{\mathrm{C}}}\mathrm{{=}(COOEt)_2}$$

I, R = C_6H_5 III, R' = H
II, R = CH_3 IV, R' = Et

V, R = C_6H_5, R' = H
VI, R = CH_3, R' = H
VII, R = C_6H_5, R' = Et

This compound deposited benzoic acid on standing for some months.[4]

Treatment of III with the mixed anhydride from acetylsalicylic acid yielded acetylsalicyloylmalonate, which was not isolated, but was converted by 10% alkali to 3-carbethoxy-4-hydroxycoumarin (VIII) in 45% over-all yield, and this in turn to IX; both VIII and IX were identified by comparison with authentic samples.[5]



VIII, R = COOEt
IX, R = H

Treatment of diethyl cadmium[6] in ether with the anhydride I gave propiophenone in 60% yield. In this reaction, but not in the malonic ester acylations, it was necessary to remove the triethylamine hydrochloride from the anhydride by filtration.

Acylation by mixed carbonic anhydrides thus appears to be a general reaction, and we are studying further applications. It appears to have advantages in cases where it is undesirable to prepare a carboxylic acid chloride, or where it is necessary to carry out acylations under very mild conditions.

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[2] *E.g.* J. R. Vaughan, Jr. and R. L. Osato, *J. Am. Chem. Soc.*, **73**, 5553 (1951); **74**, 676 (1952); V. du Vigneaud, *et al.*, *J. Am. Chem. Soc.* **75**, 4879 (1953); **76**, 3107 (1954); B. R. Baker, *et al.*, *J. Org. Chem.* **19**, 1786 (1954).

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[6] For use of cadmium compounds to prepare ketones from acid chlorides or anhydrides, see J. Cason, *Chem. Revs.*, **40**, 15 (1947).

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