An Efficient Synthesis of α-Diazo Carboxylic Esters from α-Amino Carboxylic Esters by Base-catalysed Cleavage of Triazenes

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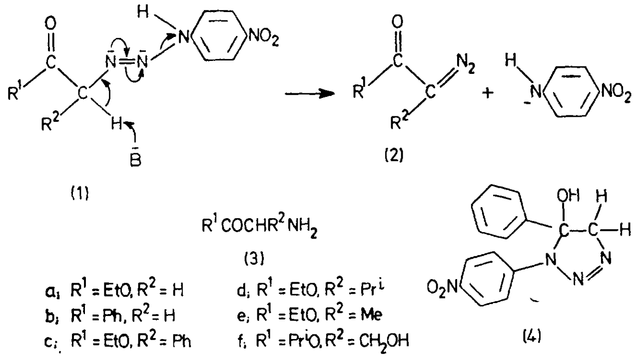
Summary Coupling of α-amino carboxylic esters with *p*-nitrobenzenediazonium tetrafluoroborate, or with 2,4-dinitrobenzenediazonium tetrafluoroborate in *NN*-dimethylformamide, in the presence of base, yields the corresponding α-diazo carboxylic esters and the corresponding aniline, by base-induced scission of the triazenes initially formed.

THE ethoxycarbonyl-triazene (**1a**) undergoes acid-catalysed scission[1] to form ethyl diazoacetate (**2a**), and *p*-nitroaniline in 66% yield.[2] We have observed that despite its reported[2] stability to base, (**1a**) is immediately and quantitatively transformed into the same products, by reaction with a catalytic quantity of potassium hydroxide in ethanol, or triethylamine in *NN*-dimethylformamide. Similarly, under the same reaction conditions, the analagous ketotriazene

(**1b**),†‡ yields quantitatively diazoacetophenone (**2b**). This base-catalysed scission (Scheme) is analogous to that observed in the diazo-group transfer reactions to carbonyl compounds, from tosyl azide,[3] and from aryl azides.[4] The synthetic utility of this reaction, applied to the formation of secondary diazo carboxylic esters, is unrestricted by the acid-sensitivity of the products, and the many possible side reactions of the diazonium ion intermediates in the acid-catalysed process.[1]


(1)

(2)

$R^1COCHR^2NH_2$

(3)

a; $R^1 = EtO, R^2 = H$
b; $R^1 = Ph, R^2 = H$
c; $R^1 = EtO, R^2 = Ph$
d; $R^1 = EtO, R^2 = Pr^i$
e; $R^1 = EtO, R^2 = Me$
f; $R^1 = Pr^iO, R^2 = CH_2OH$

(4)

SCHEME

(**2a**) can be formed quantitatively, without isolation of the intermediate triazene, by treating an equimolar solution of the *p*-nitrobenzenenediazonium salt and ethyl glycinate (**3a**), in dry *NN*-dimethylformamide with a slight molar excess of triethylamine. Subsequent partition of the reaction mixture between tetrachloromethane and water, allows complete extraction of spectroscopically pure (**2a**) into the organic layer.

The substituted amino esters (**3c**) and (**3d**) under the same reaction conditions, rapidly formed the corresponding triazenes (**1c**) and (**1d**), which required 12 h at 0° to yield only 40% of the desired diazo-compounds (**2c**) and (**2d**). The rate and efficiency of the latter step were improved by the use of 2,4-dinitrobenzenediazonium tetrafluoroborate[5] as the initial coupling reagent. The coupling reaction is carried out at —70° to avoid the spontaneous decomposition of the diazonium salt in *NN*-dimethylformamide, which occurs at —30°. Even at this low temperature, the addition of triethylamine gives immediate conversion to the diazo-compounds (**2c**) and (**2d**), preventing the observation of the intermediate triazenes. The only other reaction product formed was the triethylammonium salt of 1,3-di-2,4-dinitrophenyl-triazene, produced by the capture of the 2,4-dinitroanilide anion evolved in the reaction, by the aryl-diazonium reactant. The yields of (**2c**) and (**2d**) were raised to 80% by treatment of (**3c**) and (**3d**) with 2 equiv. of the diazonium salt and slightly more than 4 equiv. of triethylamine. Under these conditions, ethyl alanate (**3e**) and isopropyl serinate (**3f**) were diazotized in 75% and 40% (isolated) yields respectively.

This method of amine diazotization, involving very mild, essentially neutral conditions, is at present being extended to more elaborately substituted amino esters, nitriles, aldehydes and alkanes.

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† All new compounds have satisfactory elemental analyses and spectral properties.

‡ The keto-triazene (**1b**), precipitated by treatment of an ethanolic suspension of ω-amino-acetophenone hydrochloride and *p*-nitrobenzenediazonium tetrafluoroborate, with aqueous sodium carbonate at 0°, was found to exist, in the solid phase as in acetone solution, exclusively as its cyclic isomer, 1-*p*-nitrophenyl-5-hydroxy-5-phenyl-Δ^2-1,2,3,-triazoline (**4**). Compounds of this class have been prepared by the reaction of aryl azides with α-carbonyl carbanions,[6] and their further transformation into triazoles has been reported to be accompanied, in one case, by formation of the α-diazoketone.[4]

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