Tetrahedron Letters, Vol.22, No.42, pp 4181 - 4184, 1981
Printed in Great Britain

0040-4039/81/424181-04$02.00/0

# A NEW CONVENIENT SYNTHESIS OF TRISUBSTITUTED 1,3-DIOXOLE-4-CARBOXYLATES FROM METHYL 2-DIAZO-3-OXOBUTYRATE AND ALDEHYDES

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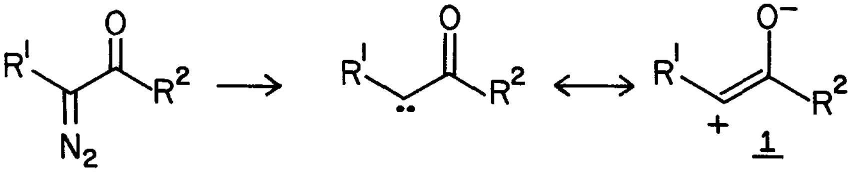
The interaction between methyl 2-diazo-3-oxobutyrate and the carbonyl group of aliphatic, aromatic, and α,β-unsaturated aldehydes under bis(hexafluoroacetoacetonato)copper(II) catalysis furnishes 1,3-dioxole-4-carboxylates in preparatively useful yields. The apparent 1,3-dipolar cycloaddition reaction of the metal carbene complex is remarkably free of competing processes.

The chemistry of α-diazocarbonyl compounds continues to attract the attention of organic chemists[1] over ninety years after the first explorations of their thermochemistry[2]. Besides the well known cyclopropanation, insertion and rearrangement processes of diazoesters and diazoketones that point towards the intervention of a free carbene or a metal carbene complex species in the photolytic or transition metal promoted reactions, α-diazocarbonyl compounds can also be envisioned as potentially effective precursors for dipolar synthons such as 1[3].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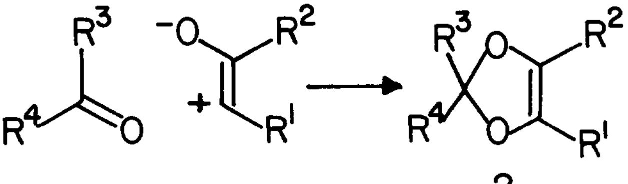
These intermediates have been detected as 1,3-cycloaddition products in reactions with some alkenes, alkynes[4], and nitriles[5]. The cycloaddition process appears conspicuously in the copper salt catalyzed thermolysis of α-diazocarbonyl compounds endowed with an additional carbonyl unit in the vicinity of the diazo functional group. Indeed methyl 2-diazo-3-oxobutyrate and 3-diazo-2,4-pentanedione have been reacted recently with alkyl vinyl ethers yielding solely dihydrofurans[6].

In principle, the carbonyl function of aldehydes and ketones should be a potentially adequate substrate for the construction of five membered rings containing two oxygen atoms in the cycle, i.e. dioxoles 2, owing to the dipolarophile nature of the C=O bond, if the carbene or metal carbene complex derived from the diazocarbonyl compound could be induced to operate as a 1,3-dipole such as 1.



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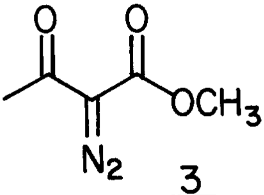

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Unfortunately,thorough investigations in recent decades of the interactions of diazomethane and diazoacetates with aldehydes and ketones[7] have shown the complexity of the process involved through the wide variety of products formed. Only the homologation of aldehydes and ketones[8], and the vinyl ether formation[9] from the Lewis acid promoted- and copper catalyzed reactions, respectively, of diazoacetic esters prevail in some instances.

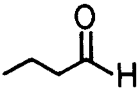
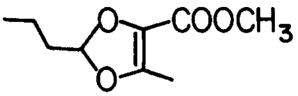
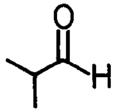
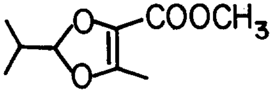
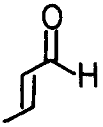
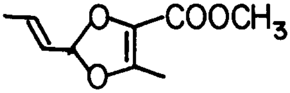
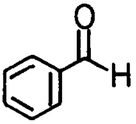
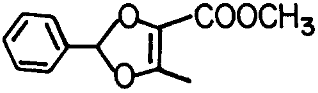
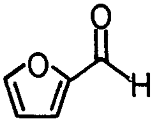
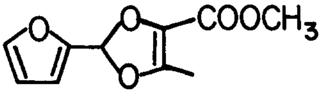
We now report the successful construction of little known 1,3-dioxole-4-carboxylates 2 ($R_1$= $COOCH_3$; $R_2$= $CH_3$; $R_3$= H; $R_4$= alkyl, alkenyl, aryl) in preparatively useful yields from the copper chelate catalyzed thermolysis of methyl 2-diazo-3--oxobutyrate 3 in the presence of aldehydes (Table I). In a typical experiment, the copper catalyst {bis(hexafluoroacetoacetonato)copper(II), 151 mg, 0.32 mmol} was suspended in degassed fluorobenzene (2 mL) under an inert atmosphere (nitrogen) and heated to reflux temperature. To this stirred mixture, a fluorobenzene solution (15 mL) of the diazoester 3 (1.5 g; 11 mmol) and the aldehyde (25 mmol) was added dropwise during a two hour period. Heating was continued until complete disappearance of the diazo group - typically five hours - by monitoring the mixture with infrared spectrometry ( 2150 $cm^{-1}$ ). The cold reaction mixture was filtered through a short column of neutral alumina act III and eluted with benzene. Evaporation of solvents and distillation of the remaining crude material under vacuum furnished the pure dioxole derivative. The non-volatile material consisted of intractable tar.

The formation of dioxoles is remarkably free of the several competing transformations expected[7]. Products of epoxidation, C-H insertion, O-insertion, homologation, aldol condensation, carbene dimerization, and Wolff rearrangement anticipated for this type of addition were not detected in any of the experiments performed. Although several copper salts display catalytic activity towards diazoesters, bis(hexafluoroacetoacetonato)copper(II) was found more effective. Also, an increase in the catalyst to diazoester molar ratio from the amount indicated above only decreased the yield of dioxole product.

Notably, compound 3 interacted with $\alpha,\beta$-unsaturated aldehydes such as crotonaldehyde only at the carbonyl synthon leaving unaffected the alkene moiety. Similarly cyclopropanation-rearrangement at the furan nucleus[10] in the reaction with furfural was not witnessed. These facts are in striking contrast to the recently reported

TABLE I

Isolated yields and boiling points of dioxoles obtained from the copper (II) catalyzed thermolysis of compound 3 with aldehydes.(a)

| $R_4$-CHO | DIOXOLE 2 | bp (mmHg) | yield (%)(b) |
|---|---|---|---|
|  |  | 56-58°(1.1) | 79 |
|  |  | 49-50°(0.15) | 80 |
|  |  | 99-101°(2.5) | 83 |
|  |  | 104-5°(0.025) | 81 |
|  |  | 99-101°(0.2) | 76 |

(a) Spectroscopical and chemical analyses were obtained for all compounds.

(b) The purity of distilled products was confirmed by GLC using a 12 ft, 5% SE-30 column.

cyclopropanation of α,β-unsaturated carbonyl compounds by diazocarbonyl systems[11] under $SbF_5$ catalysis.If activation of the electrophilic character of the α,β-unsaturated substrate by antimony and subsequent nucleophilic attack of the diazocarbon is alleged there to account for the 1+2 cycloaddition to the C=C bond, the divergent behavior of compound 3 towards crotonaldehyde under copper chelate catalysis suggests the operation of a different mechanistic pathway, namely interaction of 3 with the copper atom to yield an electrophilic metal carbene complex, followed by attack onto the carbonyl moiety of the aldehyde, and not onto the electron deficient carbon carbon double bond[1c], whereby the metal complex acts as a 1,3-dipole. The degree of concert of this dipolar cycloaddition cannot be properly evaluated with the preliminary experiments at hand, but the lack of rearrangement or double bond migration products in the addition of 3 to crotonaldehyde indicates that there is probably no significant charge development at any intermediary stage. Further experiments in this area continue in our laboratory.[12]

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12. The financial support of the Consejo Nacional de Investigaciones Científicas y Tecnológicas, CONICIT, of Venezuela, is acknowledged.

(Received in USA 20 May 1981)

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