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# NEW SYNTHESIS OF PROTECTED α-DEHYDRO α-AMINOACIDS FROM SUBSTITUTED OXAMIC ACID

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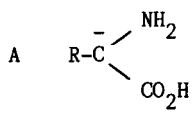
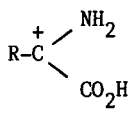
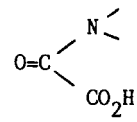
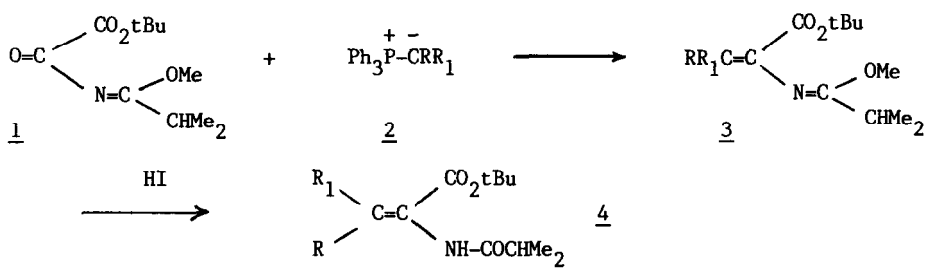
Abstract : the condensation of a phosphorus ylid with t-butoxalyl iminoether gives 3-carbobutoxy 2-aza 1,3-dienes ; subsequent reaction with hydriodic acid provides protected α-dehydro α-amino acids (1).

Syntheses of α-amino acids from nucleophilic amino acid synthons A are well established. In comparison, there are considerably fewer general routes which involve the reaction of nucleophiles with cationic amino acid synthons B (2) or C.

A  B  C 

In this preliminary account we report the first method of preparation of protected α-dehydroα-amino acids via C-C bond formation with substituted oxamic acids C. Previous work has demonstrated that oxamic esters react with ylids but acylation occurs and the product is a ketophosphorane (3). We envisioned that, by changing hybridisation of the nitrogen atom and lowering the reactivity of ester group by steric hindrance, it should be possible to reverse the reactivity of the two carbonyl groups. Results presented here confirm our prediction.

The t-butoxalyl imidate 1 is a very reactive electrophilic compound, which reacts with non-stabilized, semi-stabilized and stabilized ylids to give azadienes 3 in 80-90 % yields. Subsequent reaction of imidates 3 with aqueous hydriodic acid gives α - dehydro α-acylamino ester 4.



A typical procedure is as follows : 1 equ. of acyliminoether 1 was added to a stirred solution of 1 equ. of ylid in dry toluene. After completion of the reaction (Table), the solvent was evaporated and the azadiene separated from triphenylphosphine oxide with hexane. Yields of 3 or 4 are for pure products obtained by distillation or recrystallisation.

Transformation of 3 to 4 was obtained by stirring (20-50 mn) 1 equ. of 3 in chloroform with 1,3 equ. of aqueous hydriodic acid (57 %).

The requisite acyliminoether 1 is readily available (70 % yield) from crude t-butoxalyl chloride (4) and methyl isopropylimidate prepared by Pinner's method (5).

Table - Derivatives 3 and 4 prepared

| | | | | 3 | | 4 | |
|---|---|---|---|---|---|---|---|
| R | $R_1$ | Reaction | | yield | bp | yield | m.p. or b.p. |
| | | Temp. | Time (h) | (%) | (°C/mm) | (%) | (°C) or (°C/mm) |
| a $CH_3$ | H | 0°C | 0.5 | 80 | 95-97/2 | 86 | 84-86 |
| b $n\text{-}C_3H_7$ | H | 0°C | 0.5 | 87 | 138-140/1.5 | 86 | 108-110 |
| c $C_6H_5$ | H | reflux | 5 | 96 | 88-90/1.2 | 87 | 112-114 |
| d $CO_2Me$ | H | reflux | 48 | 94 | 108-110/1 | 72 | 115-118/0.8 |
| e $-(CH_2)_3-$ | | 0°C | 0.5 | 63 | 114-116 | 79 | 123-125 |

This synthesis is stereoselective. The magnitude of $^3J_{C-H}$ coupling constant between the ethylenic proton and the carbon atom of the ester group (4.8-6.7 Hz) shows that the double bond of 4 is Z. The dehydroamino compounds can be enantioselectively hydrogenated using a chiral rhodium-phosphine catalyst (6). Of particular interest is the possibility of using such a condensation for direct access to β-deutero α-amino acids from readily available deutero-ylids.

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