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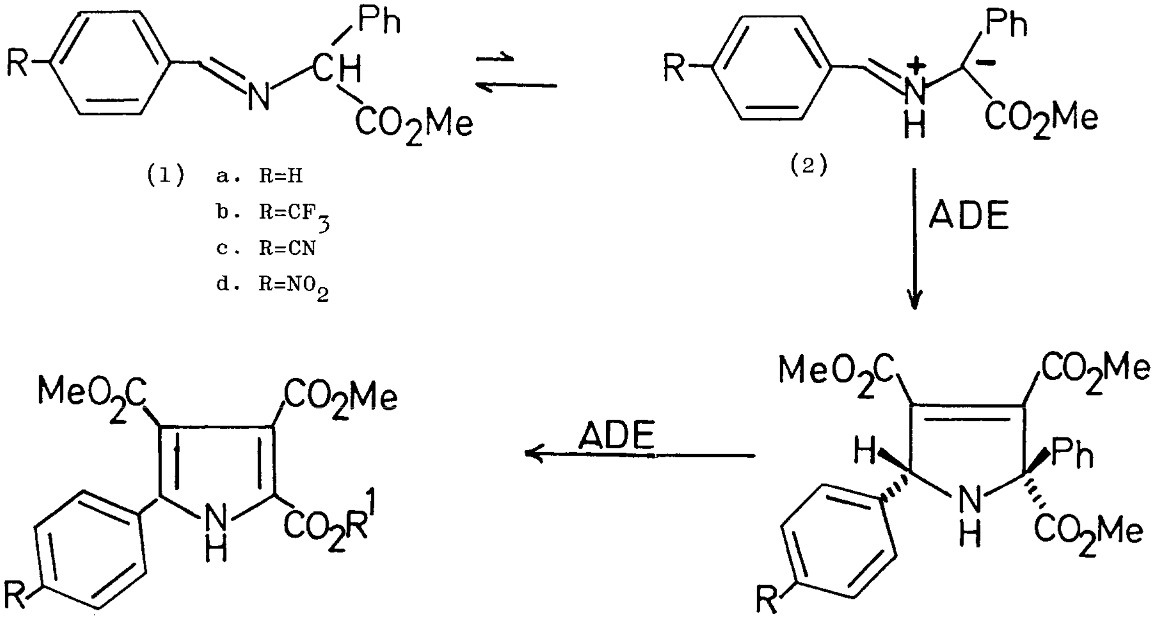
REACTION OF Δ^3-PYRROLINES WITH DIMETHYL ACETYLENEDICARBOXYLATE. A NOVEL PYRROLE FORMING REARRANGEMENT

by Ronald Grigg*, H.Q. Nimal Gunaratne and James Kemp
(Department of Chemistry, Queen's University,
Belfast BT9 5AG, Northern Ireland)

Summary. Reaction of arylidene imines of methyl phenylglycinate with 2 moles of dimethyl acetylenedicarboxylate (ADE) leads, via an intermediate Δ^3-pyrroline, to loss of the original methyl phenylglycinate moiety and formation of 2-aryl-3,4,5-tricarbo methoxypyrroles.

ADE is known to react with imines to give a variety of products depending on the nature of the imine and the reaction conditions.[1] Imines of α-amino acid esters (1) have been shown by us[2] to give rise to Δ^3-pyrrolines (3) via thermal generation of small amounts of the 1,3-dipolar species (2).[3]

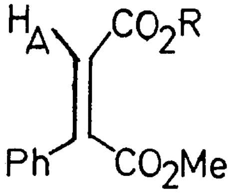


(1) a. R=H
b. R=CF_3
c. R=CN
d. R=NO_2

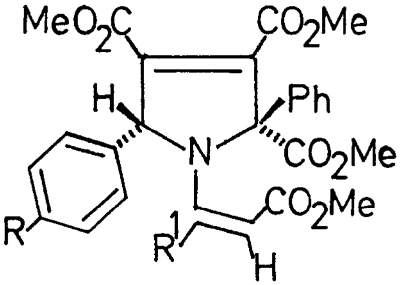
(2)

(4)

(3)



(5) a. R=Me
b. R=Et



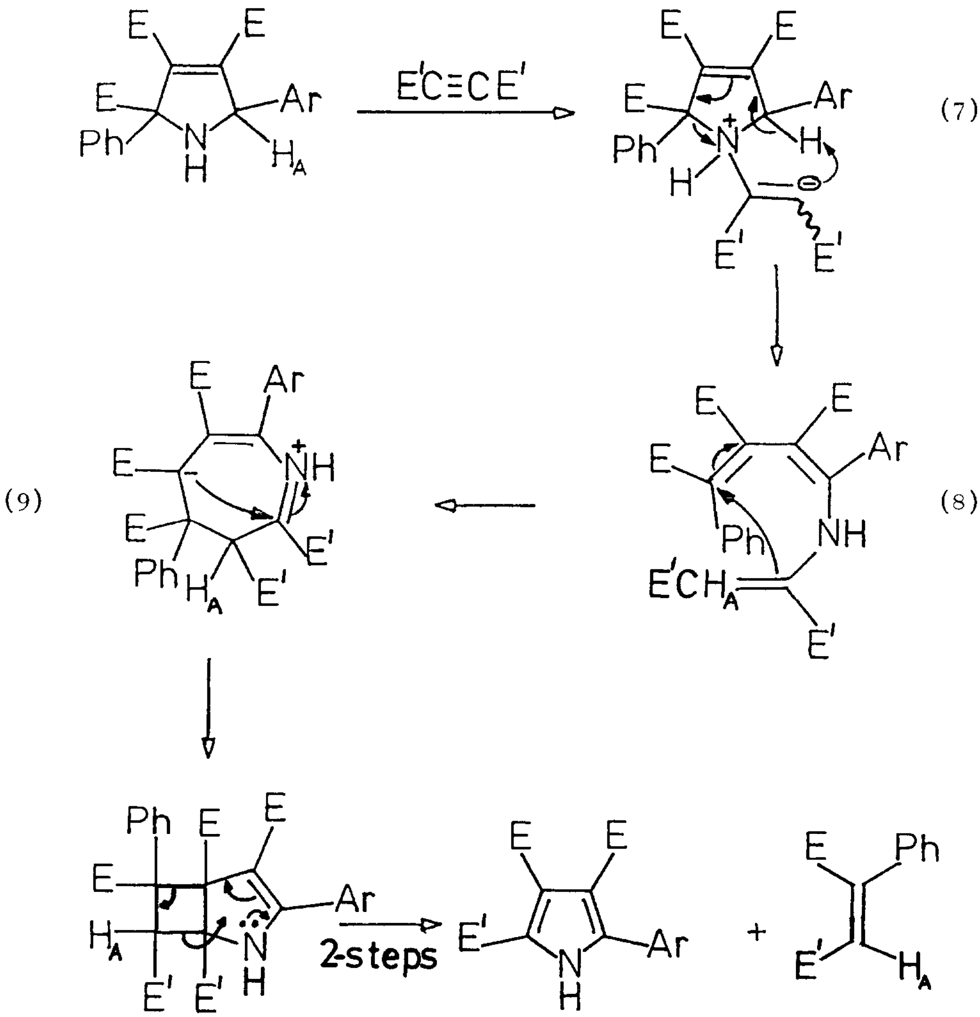
(6)

When the arylidene phenylglycine esters (1b-d) are heated with 2.2 moles of ADE in toluene at 110°C the products are the pyrroles (4b-d, R^1= Me) and the olefin (5a). Monitoring the reaction by nmr provided clear evidence for the intermediacy of (3). Indeed, on heating (3b-d)[2] with one mole of ADE (toluene, 110°C) the same two products (4b-d, R^1= Me) and (5a) were obtained. The pyrroline (3a) reacted with one mole of ADE under similar conditions to give a ca 1.4:1 mixture of (4a, R^1= Me)[4] and (6a, R^1= CO_2Me)[4] which could be separated by fractional crystallisation. The configuration of the olefin (5a) was established by NOE difference spectroscopy. Thus irradiation of H_A results in a ca. 22% enhancement of the ortho-protons of the adjacent phenyl ring.

The mechanistic possibilities for the process (3)→(4) + (5) are limited by the following observations: (i) Michael adducts (6; R^1= CO_2Me) are not intermediates in the process since (6a, R^1= CO_2Me) is thermally stable even at 140°C, (ii) reaction of (3a and c) with methyl propiolate (110°C, toluene) gives the Michael adducts (6a, R^1= H) and (6c, R^1= H) but no pyrrole, (iii) both (1c) and the p-cyanobenzylidene phenylglycine ethyl ester give the same pyrrole (4c, R^1= Me), with 2.2 moles of ADE, showing that it is the original phenylglycine ester group that is lost, (iv) heating (3c) with one mole of diethyl acetylene dicarboxylate gives a tricarbalkoxypyrrole containing only one ethyl ester moiety together with (5b). The precise location of the ethyl ester moiety has not been established but is tentatively placed at C(5), (v) pyrrole formation is favoured by electron withdrawing p-substituents in (1) or (3).

A mechanism which does not conflict with (i-v) is presented in the Scheme.

It is **suggested** that the function of the electron withdrawing p-substituent in (3) is to promote deprotonation at C(5) [Scheme, (7), arrows] at the expense of proton transfer from nitrogen. The latter process leads to the Michael adducts (6; $R^1 = CO_2Me$). Literature precedents exist for the 8π-electrocyclisation (8, arrows)[5] and the 1,5-dipolar cyclisation (9, arrows).[6]



$E = CO_2Me$ $E' = CO_2Et$

SCHEME

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References

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4. (4a, R^1= Me), colourless prisms m.p. 165°C from methanol/ether. The phenyl group was assigned to C(2) by NOE difference spectroscopy ($CDCl_3$). Thus irradiation of the NH proton resulted in a 14% enhancement of the ortho-protons of the phenyl group. (6a, R^1= CO_2Me), colourless prisms m.p. 166°C from methanol/ether.
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