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ON THE REACTION OF MALEIC AND CITRACONIC ANHYDRIDES WITH ACETYLACETONE AND WITH ETHYL ACETOACETATE

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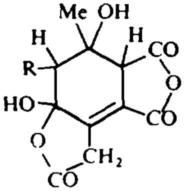
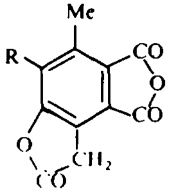
Abstract—The formation of 2:1-adducts between acetylacetone or ethyl acetoacetate and maleic anhydride may be visualized as a C-acylation of the β-dicarbonyl component followed by an intramolecular condensation in a Michael manner, forming a substituted furan which acts as diene in a Diels-Alder reaction with maleic anhydride. Hydrogenation and subsequent degradation of the adduct gives a furan derivative, 4-carboxy-5-methyl-2-furyl acetic acid ($C_8H_8O_5$), very similar to the proposed furan intermediate. PMR spectra supporting the proposed structures are given and discussed.

ADDUCTS of two molecules maleic anhydride with one molecule acetylacetone and one molecule ethyl acetoacetate, respectively, were first described in 1946.[1] The reaction was explained by suggesting that the two molecules of maleic anhydride linked together to form a double molecule, which after enolization could serve as a diene while the enolic forms of the β-dicarbonyl components could act as dienophiles. The structures Ia and b of the adducts were based upon the fact that on treatment with sulphuric acid, they lost two molecules of water, giving the aromatic compounds IIa and b, which on degradation gave *p*-xylenol.

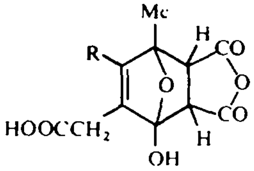


I



II

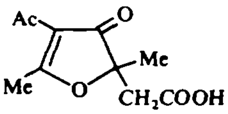
a: R = Ac
b: R = COOEt



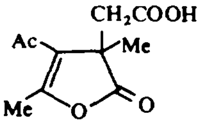
III

In a recent paper Bird and Molton[2] verified the formation of the 2:1-adducts and, based upon another scheme for the reaction, formulated the adducts as IIIa or b. In order to explain the formation of the aromatic compounds IIa and b, whose structures they confirmed, a complicated and unusual rearrangement was suggested to take place by the action of sulphuric acid. As we considered this rearrangement improbable, the question of the structure of the adducts was taken up anew.

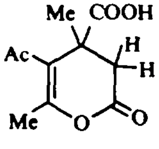
The reaction between acetylacetone and citraconic anhydride was reported in 1952.[3] A 1:1-adduct was formed, which was given the structure IV.



IV



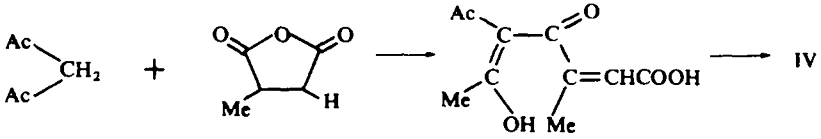
V



VI

Additional proof for this structure has now been obtained by use of IR and PMR spectroscopy. The mechanism for the formation of the adduct may be visualized as a C-acylation of acetylacetone followed by a cyclization which is similar to a Michael addition. The acylation with the unsymmetrical anhydride follows the established route[4] with nucleophilic attack on the carbonyl carbon next to the Me group of the anhydride.

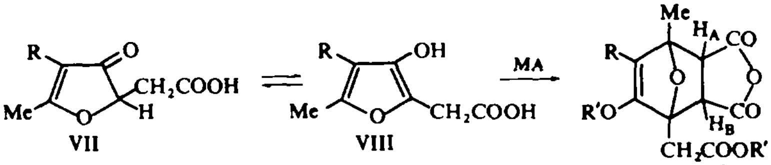
(i)



A mechanism similar to the one proposed by Bird and Molton[2] could theoretically lead to four structures for the adduct with citraconic anhydride. Two of these are highly improbable on mechanistic grounds, since they would imply a Michael addition starting at the least electrophilic carbon atom of the anhydride. They should also give complex coupling patterns in the PMR spectra, which showed only singlet signals (τ in ppm) at $\tau = 8{\cdot}52$ (3 protons), $\tau = 7{\cdot}54$ (3 protons), $\tau = 7{\cdot}39$ (3 protons), $\tau = 7{\cdot}07$ (2 protons), and $\tau = -0{\cdot}46$ (1 proton). Of the other two, structure VI ought to give an AB quartet due to magnetic non-equivalence of the two methylene protons as in the case of α-methylsuccinic anhydride. Absence of IR absorption at around 1800 cm^{-1} expected for V[5] should rule out this structure.

A mechanism similar to (i) for the reaction between maleic anhydride and ethyl acetoacetate or acetylacetone seems reasonable. In this case enolization of the primary adduct VII is possible and the tautomer 3-hydroxyfuran VIII could then react with a second molecule of maleic anhydride (MA) to form the final adduct IX (a or b).

(ii)



VII VIII IX

a: R = Ac, R' = H

b: R = COOEt, R' = H

c: R = COOEt, R' = Me

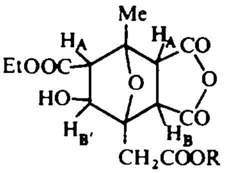
Compound IXb (or its ketonic tautomer) absorbs one molecule of hydrogen upon hydrogenation to give $C_{14}H_{16}O_9$ (Xa), m.p. 202°. It reacted with diazomethane to give $C_{15}H_{18}O_9$ (Xb), m.p. 134°.

TABLE I[a]

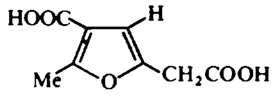
		$\underline{CH_3}CH_2O$	$\underline{CH_3}C$	$\underline{CH_2}COOR$	$-\overset{H_A}{\underset{\vert}{\overset{\vert}{C}}}-\overset{H_B}{\underset{\vert}{\overset{\vert}{C}}}-$	$CH_3\underline{CH_2}O$	OH	$>CH$	OCH_3	$-\overset{H_{A'}}{\underset{\vert}{\overset{\vert}{C}}}-\overset{H_{B'}}{\underset{\vert}{\overset{\vert}{C}}}-$
IXb	τ	8·65 Tripl.	8·25 Singl.	7·02; 6·70 2 Doubl. AB	6·23; 5·88 2 Doubl. AB	5·68 Quart.	3·5 Broad signal	6·43 Singl.		
	J	7·2		18·2	7·6	7·0	(1H)			
IXc	τ	8·65 Tripl.	8·22 Singl.	6·97; 6·82 2 Doubl. AB	6·37; 6·26 2 Doubl. AB	5·70 Quart.			6·28; 5·95 2 Singl.	
	J	7·1		17·2	7·0	7·1				
Xa	τ	8·71 Tripl.	8·45 Singl.	6·92 2 Deg. Doubl. AB → A_2	5·84; 5·57 2 Doubl. AB	5·74 Quart.	4–5 Broad signal			6·92; 5·32 2 Doubl. AX
	J	7·2		17·0	7·7	7·0	(2H)			10·2
Xb	τ	8·70 Tripl.	8·40 Singl.	7·00; 6·81 2 Doubl. AB	5·89; 5·53 2 Doubl. AB	5·64 Quart.	~5·9 Broad signal[b]		6·19 Singl.	7·02; 5·32 2 Doubl. AX
	J	7·0		17·7	8·0	7·0	(1H)			10·0

[a] Chemical shifts (τ) are given in ppm, coupling constants (J) in c/s.

[b] Signal found by integration. Disappears when adding trifluoroacetic acid.



X



XI

a : R = H
b : R = Me

A survey of the PMR spectra of IXb, its reaction product with diazomethane (IXc), Xa and Xb is given in Table 1. The results agree very well with the above structures. Compound IIIb should give a more complex coupling pattern for the methylene protons and even more so for one of the protons introduced during the hydrogenation. An interesting feature of the spectra is the large coupling constant (17–18 c/s) between the two magnetic non-equivalent methylene protons. It appears from the PMR spectrum that the adduct IXb exists mainly in the keto form. The singlet at τ = 6·43 could then be assigned to the methine proton, an expected resonance position based on current correlation tables.[6] One would also have expected exchange between the enol proton and the carboxyl proton, which is not observed in the spectrum of IXb.

When Xa was treated with sulphuric acid and subsequently with alkali, a compound, $C_8H_8O_5$, m.p. 208°, was obtained. It was shown, by comparison with an authentic sample, to be 4-carboxy-5-methyl-2-furylacetic acid. The course of this degradation could possibly be interpreted as a sulphuric ester formation, giving a water-soluble product which by the alkaline treatment eliminated sulphuric acid, giving as intermediate the Diels–Alder adduct from XI and maleic anhydride. However, a retro-Diels–Alder reaction is obviously thermodynamically favoured, thus yielding XI as the ultimate degradation product. Indeed, so far it has been proved impossible to get a reaction between XI and maleic anhydride. The aspect of a retro-Diels–Alder reaction in this connection will be studied further.

During our reinvestigation of these reactions a paper by Bailey and Strunz[7] appeared, in which the acetylacetone–maleic anhydride adduct was studied. They arrived at a conclusion similar to ours and proposed the same reaction mechanism.

EXPERIMENTAL

General. M.ps are not corrected. IR spectra were recorded on a Beckman IR 5A spectrophotometer (KBr-pellets). PMR spectra were recorded on a Varian A-60A spectrophotometer with TMS as internal reference. The solvent used was trideuteroacetonitrile except for Xb where $CDCl_3$ was used.

Ethyl acetoacetate adduct and diazomethane. On adding pulverized adduct to an ethereal soln of diazomethane the adduct dissolved but shortly afterwards the reaction product IXc separated. After recrystallization from diethyl ether it melted at 133°.

Hydrogenation of ethyl acetoacetate adduct. A soln of the adduct (4 g) in anhyd methylal (60 ml) to which PtO_2 (0·3 g) had been added, absorbed one mole H_2 on shaking in H_2 atmosphere for 2 days at room temp and atm press. The filtrate on evaporation left a crystalline reaction product (Xa) which after washing with AcOEt weighed 2·4 g. After recrystallization twice from AcOEt, m.p. 202°. (Found: C, 51·21; H, 5·07. $C_{14}H_{16}O_9$ requires: C, 51·22; H, 4·91%.)

The hydrogenated adduct reacted with diazomethane to give *a methoxy derivative* (Xb), m.p. 134°. (Found: C, 52·99; H, 5·23. $C_{15}H_{18}O_9$ requires: C, 52·63; H, 5·30%.)

Degradation of hydrogenated adduct. The hydrogenated adduct (1·5 g) was dissolved in H_2SO_4 (5 ml) whereby the temp rose to about 30°. After heating to 45° for 1 hr the soln was poured on ice-water. An insignificant amount of ppt was removed by filtration and the soln shaken with ether, but no substance could be extracted. To the soln NaOH (8 g) dissolved in a little water was added. The soln became very warm and was kept warm on the waterbath for a short time. After cooling and adding 5N H_2SO_4 (15 ml) the soln was extracted twice with ether (300 ml). The crude product (0·6 g) thus obtained partly crystallized. After washing with AcOEt the crystalline fraction had m.p. 202° which on recrystallization from AcOEt had m.p. 207°. (Found: C, 52·30; H, 4·59; calc. for $C_8H_8O_5$: C, 52·18; H, 4·38%.) It was identified by IR and PMR spectra as 4-carboxy-5-methyl-2-furylacetic acid; an authentic sample of the acid was made according to the method of Fittig.[8]

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