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REACTIONS OF CYCLIC ANHYDRIDES XI. A FACILE APPROACH TO PYRROLO-3, 1-BENZOXAZINONES VIA ANILIC ACIDS.

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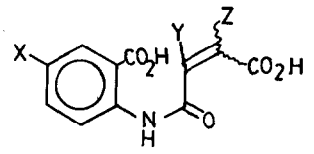
Summary :*ortho*-Carboxymaleanilic acids (I) undergo intramolecular double cyclisation to give pyrrolobenzoxazinones (II) in excellent yields when treated with sodium acetate-acetic anhydride whereas the corresponding fumaranilic acids (III) under these conditions furnish 3, 1-benzoxazinones (IV.)

Recent publications from our laboratories have highlighted the applications of cyclic anhydrides for novel synthetic approaches[1] to organic heterocycles. The overall strategy involves Michael-type addition in maleanilic acids (I) derived from suitably ortho substituted anilines and maleic anhydride (MA) (quinolines[2], 4,1-benzoxazines[3], quinoxalines[4], benzothiazines[4-6] and benzothiazoles[7]). We have now examined the behaviour of IA-F derived from reaction of anthranilic acids with MA. Their reactions have revealed interesting chemistry. The system I offers multiple pathways for intramolecular dehydration to give imide, isoimide or benzoxazinone.

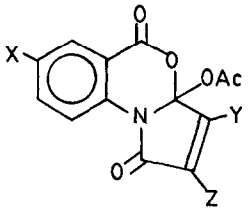
When dicarboxylic acids IA-F were treated with sodium acetate-acetic anhydride, none of the expected dehydration products was obtained. Instead, it was transformed to the angular tricyclic system pyrrolobenzoxazinone II in excellent yields. In a typical experiment, to o-carboxymaleanilic acid (IA) (2.35g, 0.01 mole) were added anhydrous sodium acetate (0.5g) and acetic anhydride (15 ml); the resulting slurry was kept at room temperature for 8 hrs. Aqueous work up followed by crystallisation from benzene afforded IIA (m.p. 160°c; 77%). Predictably, o-carboxyfumaranilic acid (IIIA, m.p. 235°c, obtained from IA; aqueous methanol, thiourea, reflux 3.5 hrs.) under identical conditions gave only the bicyclic 3, 1-benzoxazinone (IVA) which revealed that cis geometry in anilic acid is essential for generation of IIA requiring double cyclisation. The structural assignments made for IIA-F are consistent with elemental analysis and spectral data[9].

Structures related to II with angular oxygen functions are of current interest in synthesising mitomycin congeners[10,11].

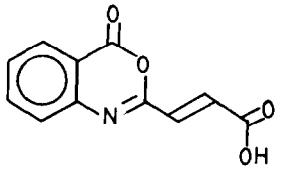
Part X. Ref. 6. Part IX. V. Balasubramaniyan, V.G.Bhatia and S.B.Wagh, Tetrahedron, 39, 1475 (1983).



I OR III



II



IV

Table 1. Reactions of o-carboxymaleanilic and o-carboxyfumaranilic acids with sodium acetate-acetic anhydride.

	X	Y	Z	m.p.°c.	% yield
IIA	H	H	H	160	77
B	Cl	H	H	170	75
C	Br	H	H	182	75
D	H	Me	H	142	72[8]
E	H	H	Me		
F	H	H	Ph	165	92
IVA	H	H	H	185	90

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8. The reaction of methylmaleic anhydride acid afforded a mixture of anilic acids (ID and IE) which on treatment with $NaOAc-Ac_2O$ gave in turn a mixture of IID (13%) and IIE (87%) (estimated by pmr spectra).
9. IIA : C, calc. 60.23, obs. 60.26; H, calc. 3.47, obs. 3.71%. IR (cm^{-1}) 1820, 1775, 1750.
   PMR : δ 2.04 (s,3H), 6.48 (d,1H,J=6Hz), 7.73 (d,1H,J=6Hz), 7.3-8.2(4H); CMR,ppm: 21.07, 107, 113.19, 119.51, 125.31, 129.64, 130.46, 136.19, 142.46, 164.75, 167.39, 194.03, 197.88.
   IIB : PMR δ 2.02(s,3H), 6.45(d,1H,J=6Hz), 7.68(d,1H,J=6Hz), 7.6-8.1(3H).
   IIC : PMR δ 2.04(s,3H), 6.45(d,1H,J=6Hz), 7.69(d,1H,J=6Hz), 7.8-8.25(3H).
   IID/E(mixture) : PMR δ 1.97(3H), 2.03(s,3H), 6.48(0.13H), 7.3(0.87H), 8.2(4H).
   IIF : PMR δ 1.87(s,3H), 6.7(s,1H), 7.2-8.2(9H).
   IVA : IR (cm^{-1}) 3450, 2600, 1785, 1715, 1655, 1610.
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