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A TETRACYCLOUNDECANE DERIVATIVE OF PYRROLIDINO-BENZOXAZINONE[1]

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Abstract-Conversion of 2-nitrobenzaldehyde by DBU to anthranilic acid (AA,II) and the reaction of the latter with tetracyclo[6.3.0.0^{4,11}.0^{5,9}]undecane-3,6-dione (TCUD,I) to produce a heterocyclic tetracycloundecane derivative of pyrrolidino-benzoxazinone (TCUPB,III) are reported.

In the course of our work on synthesis of heterocyclic clefts, the reaction of 2-nitrobenzaldehyde with tetracyclo[6.3.0.0^{4,11}.0^{5,9}]undecane-3,6-dione (TCUD, I) using DBU as a base, resulted in the formation of two unexpected products, anthranilic acid (II) and an adduct (TCUPB, III).[2]

The formation of anthranilic acid from 2-nitrobenzaldehyde under a variety of basic conditions is well established.[3] However, the reductive effect of DBU under mild conditions, tetrahydrofuran solution at room temperature, is rather interesting. No such extensive reduction of a nitro group has been previously noted in the presence of DBU.[4] The formation of the second product (III) apparently involves a sequence of reactions where the nitrogen of the preformed anthranilic acid links the two wings of TCUD. Oxygen links involving TCUD related systems are known, prominent among which are derivatives of crown ethers[5] and macrocyclic polyether bis-ketals.[6] Such oxa links have been observed and are expected as a result of exo attack of a nucleophile on one carbonyl leaving the alkoxide anion situated comfortably to attack the second carbonyl leading to a furano-hemiacetal.[7] In the present case the most likely route to the formation of the nitrogen bridge is through the intermediacy of an imine (IV) followed by an exo attack of the anthranilate anion and subsequent attack of nitrogen on the second carbonyl.

The structure of III was established by IR, NMR, and MS spectrometric data described below, and was further confirmed by X-Ray,[8] which also shows strong H-bonding between pairs of enantiomers in a

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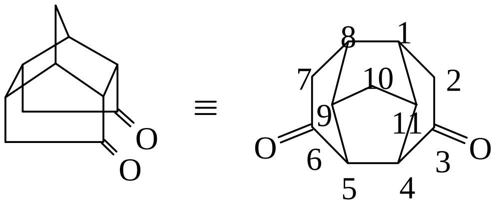
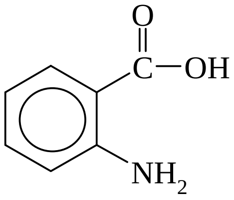
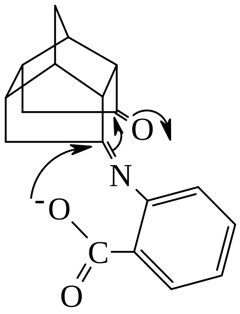


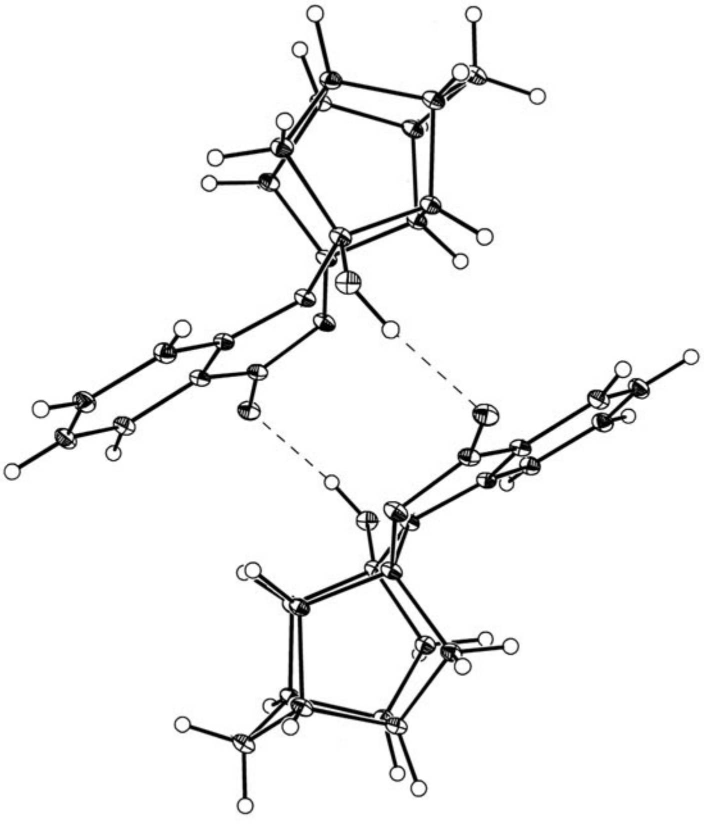
I



II

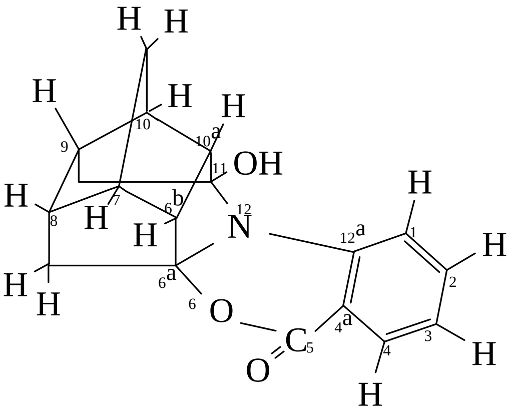


IV



V

dimeric form (V). ^{1}H and ^{13}C spectra (DMSO-d$_6$, 300 MHz and 75 MHz) show the presence of 17 protons and 18 different carbon atoms. Assignments are shown in Figure 1, and are based on one-dimensional and two-dimensional NMR(COSY, HMQC, HMBC). The absence of carbon-13 absorptions above 200 ppm and the presence of signals at 98.2 and 102.6 instead, indicated the conversion of both carbonyl groups of TCUD to sp^3 carbons each holding two electronegative atoms. The signal at 162.6 ppm confirms the presence of an ester carbonyl carbon. The preservation of three sets of CH_2 is asserted by HNMR (δ: 1.66, $C^{12}\underline{H}_2$; 1.81, C^9H_2; 2.04, C^3H_2) and carbon-13 DEPT experiment. The presence of an exchangeable O–H is shown by a singlet at 6.52 ppm which experiences a large up-field shift in $CDCl_3$ (δ: 3.02 ppm), an indication of strong H-bonding and large solvent effect in DMSO.



III

Position	^{13}C (δ: ppm)	^1H (δ: ppm)	Position	^{13}C (δ: ppm)	^1H (δ: ppm)
1	114.7	7.44	6b	57.7	2.60
2	134.9	7.55	7:10 methano	35.5	1.66
3	118.8	6.93	7 & 10	45.6, 46.1	2.51
4	129.9	7.77	8 & 9	41.5, 41.7	2.21
4a	112.5	---	9:11 methano	38.4	2.04
5	162.6	---	10a	53.4	2.80
6a:8 methano	37.7	1.81	11	98.2	---
6a	102.6	---	12a	146.1	---
			C^{11}-O-$\underline{H}$	---	3.02($CDCl_3$) 6.52(DMSO)

Figure 1[^{1}HNMR and ^{13}CNMR Assignments (DMSO-d_6)]

The IR spectrum of III shows the absence of: 1) multiple carbonyl absorptions around 1730 cm^{-1}which are characteristic of the dione system in TCUD; 2) the nitro absorptions around 1530 and 1330 cm^{-1} ; 3) the two absorptions characteristic of anthranilic acid at 3379 and 3473 cm^{-1} (-NH_2). The presence of an O–H and of an anthranilate carbonyl is indicated by an absorption at 3362 cm^{-1} and at 1694 cm^{-1} respectively. The MS spectrum (EI) shows the molecular mass of III (295.0) as the most abundant, an indication of its stability (mp 280°C). The stability is also manifested in the high resistance to reaction with acids or bases, in contrast to bis-ketals which are normally acid labile.[5] It should be added that product III was obtained independently through a reaction of anthranilic acid and TCUD in the presence of DBU in THF as a solvent.

Experimentally, the reaction of 2-nitrobenzaldehyde(1.66 g, 10 mmol) and TCUD(0.83 g, 5 mmol) in dry THF(10 mL) was run with DBU(1.5 mL) for 48 h at rt. The gum resulting from dilution with water was soaked with 5% HCl (25 mL) and the resulting precipitate was filtered and the filtrate extracted with CH_2Cl_2 which on evaporation yielded III(20 mg). Further extraction of the filtrate with ether gave anthranilic acid (15 mg), the identity of which was established by comparison with an authentic sample. A direct method of preparing III consists of a reaction of TCUD (0.52 g, 3 mmol) with anthranilic acid (0.41 g, 3 mmol) in dry THF (10 mL) and DBU (1 mL) for 48 h at rt. Work up according to the above procedure yielded 0.1g of III (mp 280°C, from CH_2Cl_2/MeOH).

ACKNOWLEDGEMENTS

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REFERENCES AND NOTES

1. A proposed name is : 6b,7,8,9,10,10a-hexahydro-11-hydroxy-6a:8,7:10,9:11-trismethanoisoindolo[2, 1-*a*][3, 1]benzoxazin-5-one.
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8. Detailed X-Ray analysis of this compound along with other products obtained from the aldol reaction will be reported separately.