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A NOVEL (E)-2-OXOINDOLIN-3-YLIDENEACETONE DIMER

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The dimerization reaction of (E)-2-oxoindolin-3-ylideneacetone(1) is described. The structure and stereochemistry of a novel dimeric product(4) were determined by PMR, CMR analyses and confirmed by X-ray analysis.

Bamfield et al.[1)] have reported an intermolecular Diels-Alder reaction of (E)-2-oxoindolin-3-ylideneacetone(1) to give a dimeric product in nearly quantitative yield by heating 1 at 100° in toluene for 24hr and assigned it planer structure 2.

In this reaction, however, there is another possible regiochemical mode of cycloaddition to give a novel dimer whose formation involves a Diels-Alder reaction between α,β-unsaturated ketone system and exocyclic carbon-carbon double bond.

We now report on the structure of a novel dimeric product of

1 by X-ray crystallography, which gave conclusive evidence for structure 4.

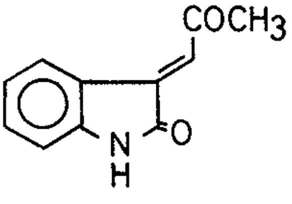
1 was heated at 100° in toluene for 24hr and chromatographic separation on silica gel gave 2(22.5%)[pale yellow prisms(AcOEt), mp 195-198°; $C_{22}H_{18}N_2O_4 \cdot 0.5H_2O$; *m/e* 374($M^+$), 303(base)] and novel dimeric products(29%)[colorless needles(MeOH), mp 256-258°, $C_{22}H_{18}N_2O_4$; *m/e* 374(M^+), 172(base)] as an isomeric mixture, which contained 4 and 5 in a 1:1 ratio as shown in the PMR spectrum (DMSO-d_6)[4; δ 1.67(s, $COCH_3$), 9.98 and 10.72(s, 2xNH): 5; δ 1.63, 9.64 and 10.22].

When 1 was refluxed in acetic acid for 3hr under N_2, the mixture of 4 and 5 was obtained in 41% yield and 2 was not detected.

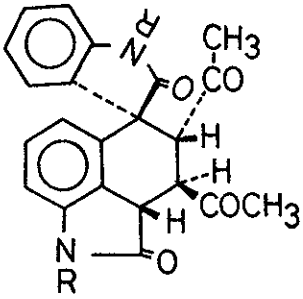
Structure assignments for 2 and 4 were primarily based on PMR and CMR spectroscopic analyses.

Thus, the PMR spectrum(TFA-d_1) of 2 showed the presence of two acetyl methyl(δ 1.84 and 2.68) and the loss of one aromatic proton from the 2-oxoindolin system. Spin-decoupling confirmed the presence of the sequence -CH-CH-CH-[δ 3.62(dd,J=11,12Hz), 3.98 (d,J=12Hz), 4.38(d,J=11Hz)]. Its CMR spectrum(DMSO-d_6) revealed the presence of two acetyl methyl[δ 28.97 and 32.48(q)], three methine[δ 44.83, 45.61 and 60.29(d)] and one new aromatic quaternary carbon[δ 126.17(s)]. Acetylation of 2 afforded N,N-diacetate(3)[mp 235-238°; *m/e* 458(M^+)] and its PMR spectrum($CDCl_3$) showed signals at δ 1.67, 2.62(s, $2xCOCH_3$) and δ 2.68, 2.76(s, $2xNCOCH_3$).

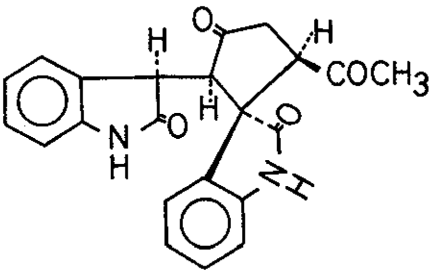
All the above spectral data were fully consistent with the formulation 2.[2)]



1



2 R= H
3 R= COCH$_3$



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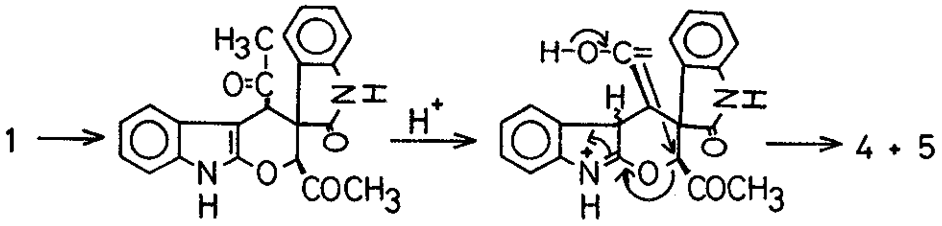

Chart 1

On the other hand, a single isomer 4(mp 267-270°, $C_{22}H_{18}N_2O_4$) was successfully isolated from the diastereoisomeric mixture by silica gel chromatography and recrystallization. Its PMR spectrum in pyridine-d_5 demonstrated that the equilibration of 4 and 5 was reached at the ratio of 38:62 after 5min. The PMR spectrum (TFA-d_1) showed the presence of one acetyl methyl(δ 1.67), -CH-CH- system[δ 4.38 and 4.54(d, J=4Hz)], no loss of aromatic proton from two 2-oxoindolins. Spin-decoupling confirmed the presence of a -CH-CH_2- system[δ 3.25(dd, J=19,9Hz), 3.63(dd, J=19,12Hz), 4.25(dd, J=12,9Hz)].

Further, its CMR data in DMSO-d_6 revealed the presence of one acetyl methyl[δ 29.23(q)], three methine[δ 43.14, 55.09 and 59.90 (d)] and in pyridine-d_5 one ring methylene[δ 39.16(t)] essential for structural evidence.

Although the gross structure of 4 was deduced from these spectroscopic data, the more detailed structure and stereochemistry were established unambigously by single crystal X-ray crystallographic analysis.

The crystal belongs to the triclinic space group $P\bar{1}$ with the lattice parameters; a=12.561(8), b=8.857(6), c=8.644(6)Å, α=80.39 (4), β=103.72(4), γ=107.28(4)°. *Two molecules are contained in* a unit cell.

Intensity data were measured on a Philips PW 1100 four-circle diffractometer using Cu Kα radiation monochromated by a graphite plate. The 2θ-θ scanning technique was used with the scan speed of 0.1°/sec. in θ. A total of 1707 independent reflexions was observed within the 2θ range of 120°. The structure was solved

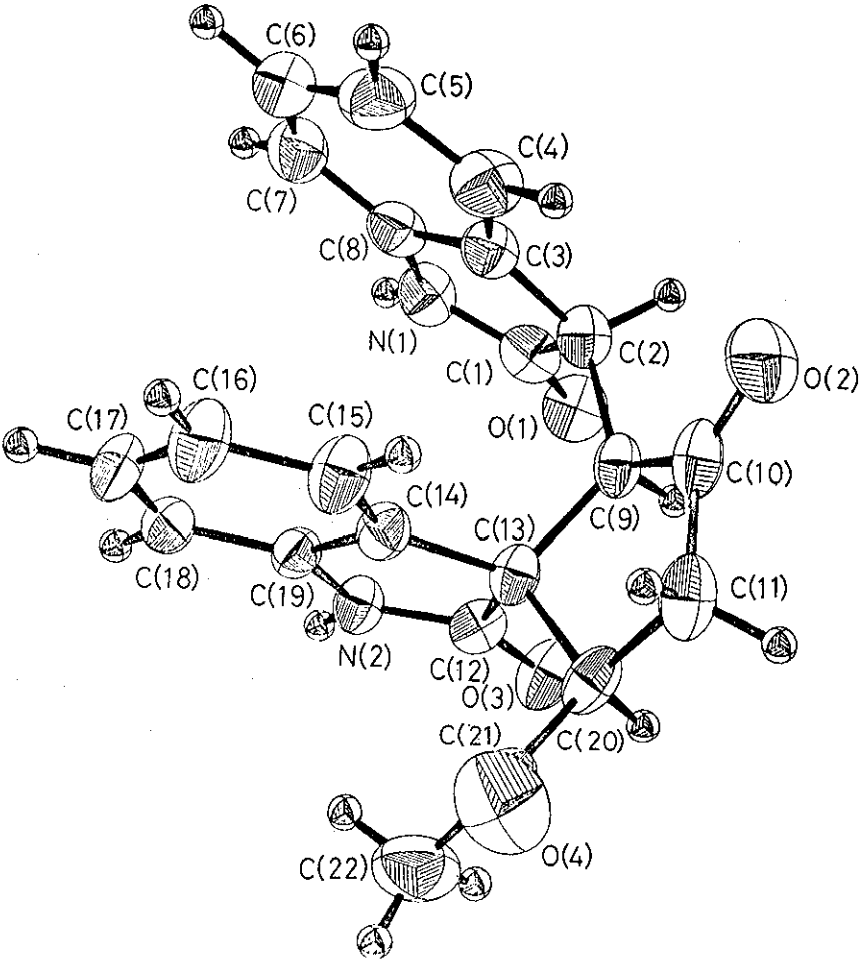

Fig. 1. ORTEP drawing of the structure of 4.

by the direct method. All the 28 non-hydrogen atoms were located on a E-map and successive several cycles of block-diagonal least-squares refinement established the molecular structure as shown in Fig. 1.

Hydrogen atoms were located on a difference electron density map and the R-index was reduced to 0.05 after refinements assuming anisotropic thermal vibrations for non-hydrogen atoms and isotropic ones for hydrogen atoms.

As is seen in Fig. 1, the stereochemistry about the C(2)-C(9) bond is *threo* configuration and the two substituents of cyclopentanone ring at C(9) and C(20), a 2-oxoindolin and an acetyl groups, are on the same side of the ring.

The molecule adopts a folded conformation. The C(2)-C(3) bond turns to gauche-gauche direction with respect to the C(9)-C(13) and C(9)-C(10) bonds and the two 2-oxoindolin rings come close to each other. The two rings stack at the dihedral angle of 21.2° and the mean separation of the two 2-oxoindolin rings is 3.32Å.

The reaction mechanism for the formation of 4 can be proposed in Chart 1.

It should be pointed out that the first step of the formation of 4 is rationalized in terms of a Diels-Alder reaction between α,β-unsaturated ketone system and the exocyclic carbon-carbon double bond of 1.

REFERENCES

1 P.Bamfield, A.W.Johnson and A.S.Katner, J.Chem.Soc.(C), 1966, 1028.

2 Recently, the structure of a Diels-Alder adduct of 2-oxoindolin-3-ylideneacetophenone with ethyl vinyl ether was determined to have the same skeleton as 2 by X-ray analysis. G.Tacconi, A.C.Piccolini, P.P.Righetti, E.Selva and G.Desimoni, J.Chem.Soc.Perkin I, 1976, 1248.

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