

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

Akinori Kubo*, Tatsuya Nakai, and Toshikazu Nozoye

Meiji College of Pharmacy, Nozawa, Setagaya, Tokyo, Japan

Akiko Itai and Yoichi Iitaka

Faculty of Pharmaceutical Sciences, University of Tokyo

Hongo, Bunkyo, Tokyo, Japan

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 regio-chemical 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.

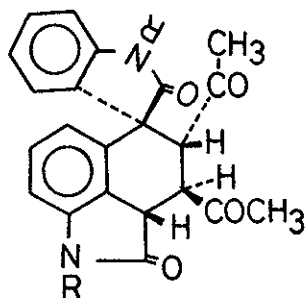
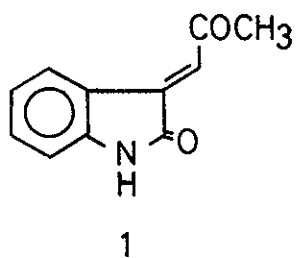
1 was heated at 100° in toluene for 24hr and chromatographic separation on silica gel gave 2(22.5%) [pale yellow prisms(AcOEt), mp 195-198°; $C_{22}H_{18}N_2O_4 \cdot 0.5H_2O$; m/e 374(M^+), 303(base)] and novel dimeric products(29%) [colorless needles(MeOH), mp 256-258°, $C_{22}H_{18}N_2O_4$; m/e 374(M^+), 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, COCH₃), 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 N₂, 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(CDCl₃) showed signals at δ 1.67, 2.62(s, 2xCOCH₃) and δ 2.68, 2.76(s, 2xNCOCH₃).

All the above spectral data were fully consistent with the formulation 2.²⁾



2 R=H

3 R=COCH₃

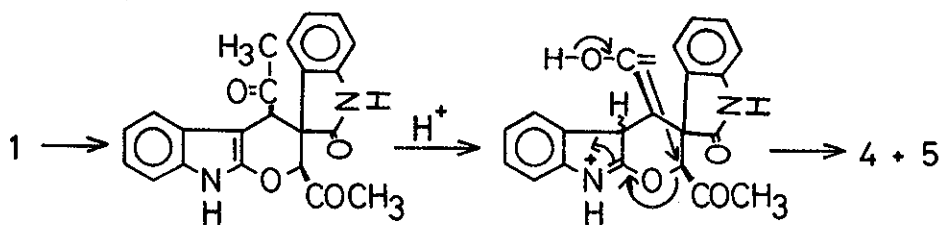
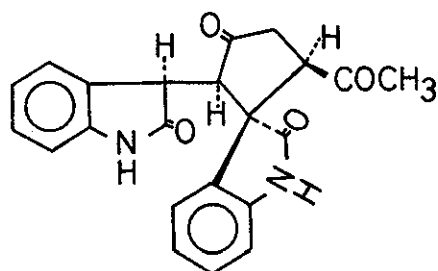


Chart 1

On the other hand, a single isomer 4 (mp 267-270°, C₂₂H₁₈N₂O₄) 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-CH₂- 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 unambiguously 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, $\alpha=80.39(4)$, $\beta=103.72(4)$, $\gamma=107.28(4)$ °. Two molecules are contained in a unit cell.

Intensity data were measured on a Philips PW 1100 four-circle diffractometer using Cu K α 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

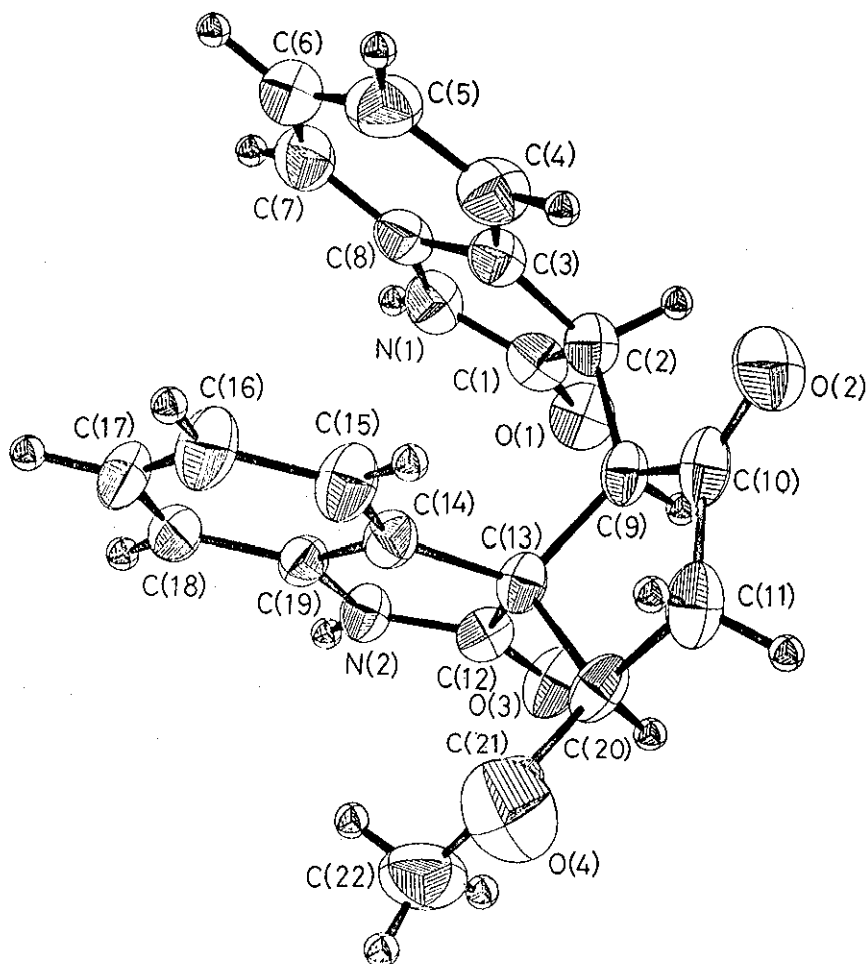


Fig. 1. ORTEP drawing of the structure of 4.

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 3.32\AA .

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

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- 2 Recently, the structure of a Diels-Alder adduct of 2-oxo-indolin-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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