

ON THE CRYSTAL STRUCTURE OF THE DIELS-ALDER ADDUCT OF THE HYDROGENATED
LACTAMS OBTAINED BY REDUCTIVE PHOTOCYCLIZATION OF N-CYCLOHEX-1-ENYL-
BENZAMIDE

Takeaki Naito and Ichiya Ninomiya*

Kobe Women's College of Pharmacy, 4-19-1 Motoyamakita, Higashinada,
Kobe 658, Japan

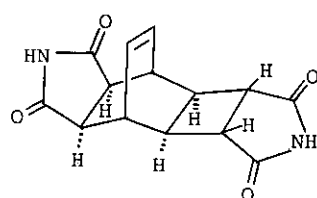
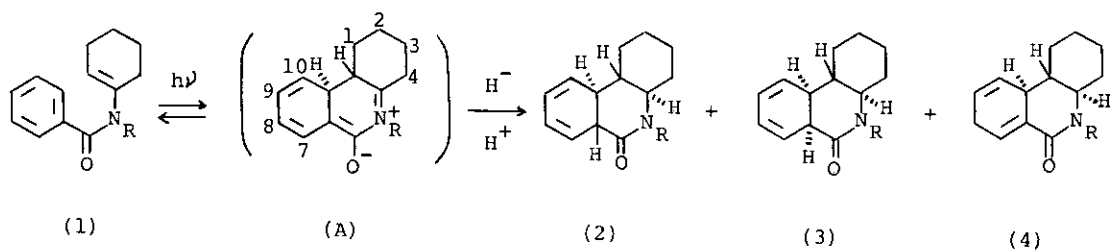
Mitsunobu Doi and Masatoshi Inoue

Osaka College of Pharmacy, 2-10-65 Kawai, Matsubara, Osaka 580, Japan

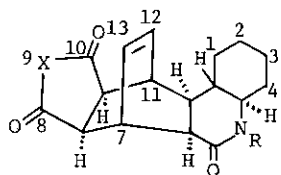
Abstract — The stereostructure of the Diels-Alder adduct (5) of the hydrogenated lactam (3) with maleic anhydride was unequivocally established by X-ray analysis, thus confirmed the stereochemical course of reductive photocyclization of the enamide (1).

In the previous papers^{1,2}, we have reported the formation of three hydrogenated lactams (2), (3), and (4) by reductive photocyclization of the N-cyclohex-1-en-ylbenzamide (1). Diels-Alder reaction of these lactams provided important information for the proposal of their stereostructures. The lactam (2) with conjugated diene moiety afforded the adduct (5) by the Diels-Alder reaction with maleic anhydride in a boiling toluene as a result of the preceding isomerization of (2) into (3) while the another lactam (3) gave similar Diels-Alder adducts (5) and (6) by the reaction with maleic anhydride and N-phenylmaleimide respectively.

Recently, Pettit et al.³ have reported X-ray analysis of mitindomide (7) which is known to have high activity against several of the U.S. National Cancer Institute's key experimental tumor systems and unequivocally established its stereostructure (7) as shown in Chart. Although interpretation of the spectral data², particularly the ¹H-NMR spectra, of the adducts (5) and (6) gave results consistent with their structures, unequivocal assignment of the stereochemistry required an X-ray crystal structure determination of at least one of these compounds (5) and (6) with potential biological importance.



mitindomide (7)



X=O : (5)

X=NPh: (6)

R=CH₂Ph

Chart

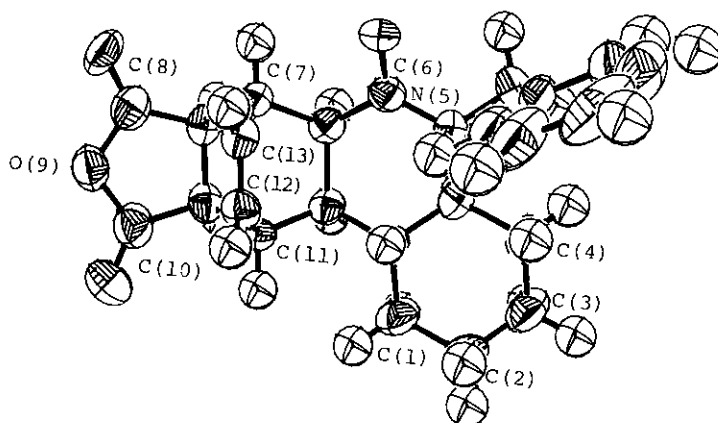


Figure: X-ray structure of (5)

The adduct (5), $C_{24}H_{25}NO_4$, molecular weight=391.45, was crystallized from ethanol in the monoclinic, space group $P2_1/c$, $a=7.085(2)$, $b=10.941(3)$, $c=26.592(11)\text{\AA}$, $\beta=102.82(4)^\circ$, $V=2010(1)\text{\AA}^3$, $Z=4$. A total of 2971 unique reflections having $F_o > 0$ were measured on a Rigaku AFC-5 diffractometer using Cu-K α radiation. The structure was solved by the direct method using the program MULTAN 78 and refined by the block diagonal least squares method to $R=0.0967$. The molecular structure of (5) so derived is depicted in Figure, proving the stereostructure deduced from the previous analysis².

Consequently, coupled with the previous data obtained by chemical means and spectral analysis^{1,2}, the stereostructures of two hydrogenated lactams (2) and (3) are definitely represented as shown in Chart, therefore providing concrete evidence of the stereochemical course of reductive photocyclization of the enamide (1) as follows: upon irradiation, the photochemical electrocyclic ring closure of 6 π -electron system in the enamide (1) would occur to give a 10a/10b-trans cyclic intermediate (A), which would then be subjected to reduction of the iminium moiety from α -side attack of a hydride reagent to yield three hydrogenated lactams (2), (3), and (4), all having the 4a/10b-trans and 10a/10b-trans stereochemistries.

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