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CYCLOADDITION REACTION OF A NEW PERIPHERAL AZOMETHINE YLID TO SYMMETRICALLY SUBSTITUTED OLEFIN[1)]

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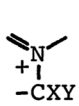
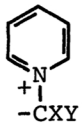
An unusual azomethine ylid 1,3-dipole was generated on the periphery of pyrido[1,2,3-de]quinoxaline ring. This peripheral ylid, anhydro 3H-pyrido[1,2,3-de]quinoxalinium hydroxide, reacted stereoselectively with electron-deficient cis olefins such as dimethyl maleate and N-substituted maleimides giving endo [4+2] cycloadducts as single products. With such a trans olefin as dimethyl fumarate, a mixture of two kinds of the [4+2] cycloadducts, 1-exo-2-endo- and 1-endo-2-exo cycloadduct, was formed. These cycloaddition reactions have possibly proceeded in a concerted manner.

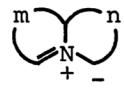
Pyridinium ylid, pyridinium phenacylid as a typical example, undergoes a 1,3-dipolar cycloaddition reaction to electron-deficient acetylenes and olefins to yield indolizine derivatives, bicyclic heterocycles with a ring junction nitrogen atom. The similar cycloaddition reaction may occur by starting with a peripheral azomethine ylid 1,3-dipole which is developed on the periphery of heterocycle with a nitrogen atom at the point of fusion.



Open Chain Ylid



Pyridinium Ylid



Peripheral Ylid

This peripheral ylid bears a rigid configuration of the ylid-forming atoms(carbon-nitrogen-carbon) and therefore may provide more stereochemical informations in its cycloaddition reaction than open chain azomethine ylid and pyridinium ylid. In addition, this cycloaddition reaction could be a simple and useful preparative method of cyclazine derivative[2)]. Only one analogous system, anhydro 3H-[1,2,4]-

triazino[5,6,1-ij]quinoxalinium hydroxide, has been recently synthesized by Tamura and his co-workers[3].

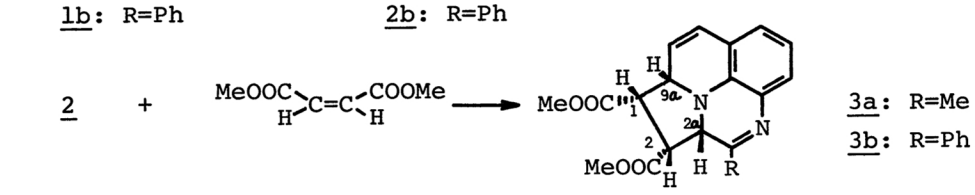
In order to study reactivity and stereochemistry of a peripheral azomethine ylid in the cycloaddition reaction, anhydro 3H-pyrido[1,2,3-de]quinoxalinium hydroxide 2 was generated *in situ* and its cycloaddition reactions to some electron-deficient olefins were investigated here.

The two pyrido[1,2,3-de]quinoxalinium bromides 1a and 1b, the precursors of the ylids 2a and 2b, were synthesized from 8-aminoquinoline and α-bromoketones[2]. The precursors are red crystals and are soluble in water and methanol.

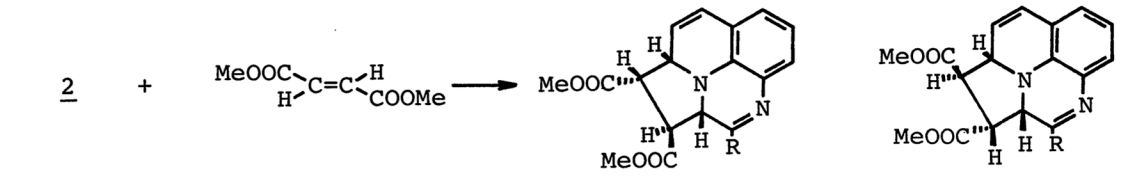
A methanolic solution of 1b and equivalent dimethyl maleate was treated with triethylamine at 0 °C. The methanol was evaporated and the residue obtained was washed with water giving the 1:1 adduct 3b (mp 155-155.5 °C) in 76 % yield.

1a: R=Me
1b: R=Ph

2a: R=Me
2b: R=Ph

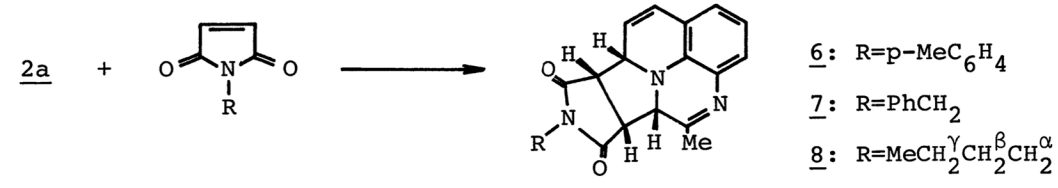


3a: R=Me
3b: R=Ph



4a: R=Me
4b: R=Ph

5a: R=Me
5b: R=Ph



6: R=p-MeC$_6$H$_4$
7: R=PhCH$_2$
8: R=MeCH$_2^{\gamma}$CH$_2^{\beta}$CH$_2^{\alpha}$

The NMR spectrum of 3b indicated that the product would be one of the expected [4+2] cycloadducts. There are eight stereo isomers possible for 3b: each four cis and trans cycloadducts. It was found difficult to make up the trans skeleton with a Dreiding model meaning that these four trans structures would be ruled out for 3b.

Cis configuration of the olefinic hydrogens in the maleate is most likely retained in the cycloadduct since the ylid 2b gave a mixture of two [4+2] cycloadducts from the reaction with dimethyl fumarate and since neither of them was identical with 3b. Unfortunately coupling constants among the hydrogens on the reaction sites (J_{1-9a}=7.5 and J_{2-2a}=6.5 Hz) do not tell the stereochemistry of 3b. The estimated coupling constants (J_{1-9a} and J_{2-2a}) show little difference between the structural models for endo and exo [4+2] cycloadducts.

The structure of 3b was determined as an endo [4+2] cycloadduct on the basis of the chemical shifts of two ester methyls which are shielded by the fused benzene ring showing their signals in higher fields (δ 3.22 and 3.34 ppm) than those of the starting maleate (δ 3.79 ppm). Similarly the endo [4+2] cycloadduct 3a (mp 131-134 °C) was obtained as a single product from the ylid 2a and dimethyl maleate.

On the other hand, dimethyl fumarate gave a mixture of two kinds of products, 4b and 5b, from the reaction with the ylid 2b. Resemblance of the NMR spectrum to that of 3b and dehydrogenation of the mixture with chloranil into a single product, 3-phenyl-1,2-bis(methoxycarbonyl)indolizino[3,4,5,6-cde]quinoxaline[2], led to a conclusion that the two products, 4b and 5b, were both the [4+2] cycloadducts. Stereochemical determination was made on the basis of consideration for the chemical shifts of each ester methyl in 4b and 5b. Thus, 4b and 5b were assigned to be the 1-endo-2-exo- and 1-exo-2-endo [4+2] cycloadduct, respectively. The another mixture, 4a and 5a, was afforded from the ylid 2a in fair yield.

Table. Cycloadducts of Anhydro 3H-Pyrido[1,2,3-de]quinoxalinium Hydroxides 2 to Electron-deficient Olefins

Olefins	Products	Mp (°C)	Yield (%)	$\nu_{C=O}$ (cm^{-1})	Chemical Shifts (δ ppm) 1-MeO	2-MeO
MeOOC, H, C=C, COOMe, H	3a	131-4	45	1745, 1725	3.34	3.38
	3b	155-5.5	76	1745, 1735	3.22	3.34
MeOOC, H, C=C, H, COOMe	4a	Mixture	51	1725, 1720	-	-
	5a				3.72	3.40
	4b	Mixture	86	1735, 1715	3.18	3.40
	5b			1700	3.72	3.40
N-R Maleimide	6	190-1	95	1700	2.25 (p-Me)	
	7	160.5-2	100	1695	4.21 (CH_2)	
	8	163-5	84	1685	3.00, 0.7, 0.9, 0.93(α,β,γ, Me)	

Both N-(p-tolyl)maleimide and N-benzylmaleimide easily cycloadded at 0 °C to the ylid 2a giving the respective [4+2] cycloadducts, 6 (mp 190-191 °C) and 7 (mp 160.5-162 °C), in almost quantitative yields. They were found to be endo [4+2] cycloadducts from the NMR investigation.

A satisfactory evidence for the endo structure was provided from the cycloaddition reaction with N-butylmaleimide. The cycloadduct 8 (mp 163-165 °C) showed a very interesting NMR spectrum in which the signals for three methylenes and a methyl in the starting maleimide (α 3.49; β 1.57; γ 1.30; Me 0.93 ppm) shifted to higher fields in the cycloadduct 8 (α 3.00; β ca. 0.7; γ ca. 0.9; Me 0.66 ppm). This inequality of the shift values can be explained only by a location of the butyl group in the shielding zone of the fused benzene ring. The largest shift of the β methylene is consistent with the endo structure.

Thus, dimethyl maleate and some N-substituted maleimides reacted stereoselectively with the peripheral azomethine ylid 2 giving the endo [4+2] cycloadducts as the single products. They are probably through an endo approach in which the unsaturated moieties in the olefins interacted with the conjugated system in the ylid. Two kinds of interactions are possible in case of dimethyl fumarate and it is believed the two interactions actually competed each other giving the two [4+2] cycloadducts.

REFERENCES

1. Part 4 of the series "Peripheral Conjugate Systems". For the part 3, H. Shimoharada, S. Ikeda, S. Kajigaeshi, and S. Kanemasa, *Chem. Lett.*, 1977, 1237.
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