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Δ^2-PYRROLINE-4,5-DIONE, AN AMBIDENT DIENOPHILE IN DIELS-ALDER REACTION[1]

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Abstract— Thermal cycloaddition of activated 1,3-butadienes to benzazepinopyrrolinedione 4 took place to C=O instead of C=C in the enone system, yielding dihydropyrane derivatives. The change of reactivity compared to isoquinolinopyrrolinedione 1 was attributed to the steric hindrance on C=C of the enone due to non-planarity of the aromatic ring and the dioxopyrroline ring.

Enones, as dienophile in Diels-Alder reaction, must be inherently ambident (path A or path B in Chart 1). However, they always give the products following path A (ene-addition), no example of path B reaction (one-addition) having been reported to our knowledge. Although preference of ene-addition over one-addition could be suggested theoretically[2], occurrence of the latter path is still not prohibited, since simple ketones often give the product of one-addition[3]. We now present examples, which we believe the first, of path B reaction of an enone system.

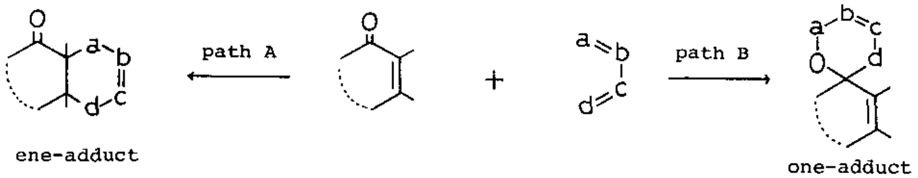


Chart 1

Diels-Alder cycloaddtion of activated butadienes to the Δ^2-pyrroline-4,5-dione (dioxopyrroline) 1 gives, in good yield, an adduct 2 under kinetically controlled conditions[4,5] or an adduct 3 under thermodynamic conditions[5]. Both adducts are the products following path A.

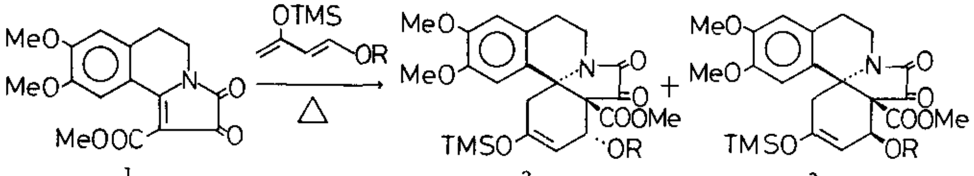


Chart 2

Substituting the dienophile to 4[6] in the above reaction caused dramatic change in the product where path B adduct predominated over path A adduct. For example, heating of 4 with 1,3-bis(trimethylsilyloxy)butadiene at 180°C for 15 min and isolation of the product after silica gel chromatography yielded two adducts, 5[7], mp 202-204°C, and 6, mp 191-195°C, in 4.5 and 39.5% yield, respectively. The minor product 5 was revealed as the <u>cis</u>-<u>exo</u> adduct (thermodynamic product) resulted by path A cycloaddition, on the basis of spectral resembrance (UV, IR, NMR) with the corresponding six-membered ring compound 3 (R=Me)[5]. The major product 6 was the product resulted by path B reaction.

Similar reaction of 4 with 1-methoxy-3-trimethylsilyloxybutadiene resulted in two products, 6 (identical with the compound obtained above) and 7, mp 196-198°C in 33% and 23% yields, both of which were the path B products, no path A product being isolated from this reaction.

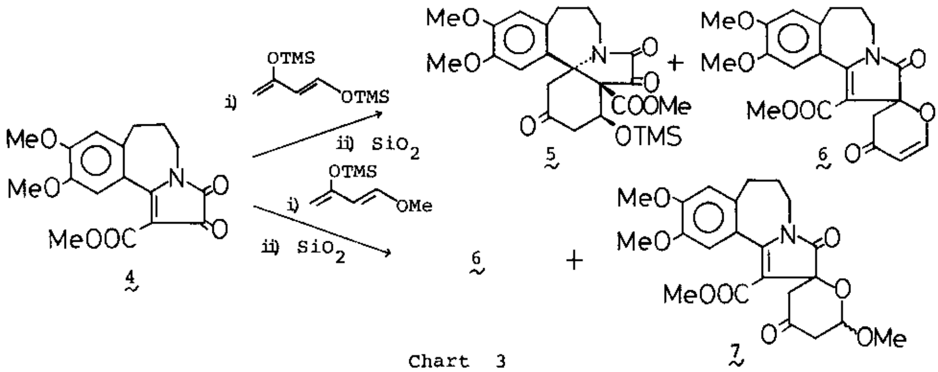
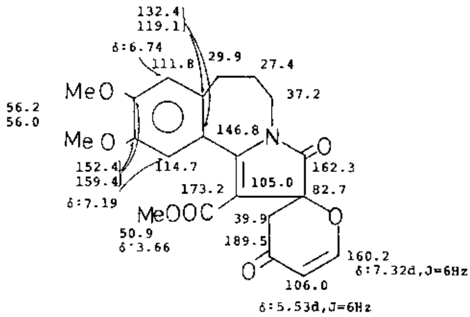


Chart 3

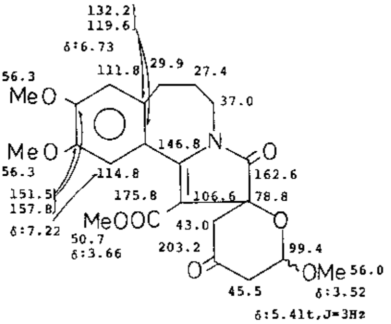


6

$C_{21}H_{21}NO_7$

IR: 1735, 1680, 1675 cm^{-1}

UV. 246(ε=17400), 288(ε=10300)
348(ε=10400)



7

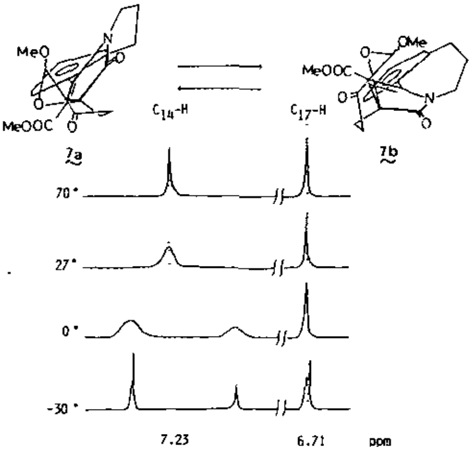
$C_{22}H_{25}NO_8$

IR. 1735, 1725, 1685 cm^{-1}

UV: 242(ε=15500), 285(ε=6900),
337(ε=11000)

The structures of 6 and 7 were elucidated mainly by spectroscopic means which allowed full determination of their structures: elementary analyses together with high resolution MS confirmed their formulas, UV indicated the presence of a conjugated system which is similar to that of the original dioxopyrroline, IR suggested disapperance of a five membered-ring ketone, and ^{1}H-NMR and ^{13}C-NMR unambigously established their functional groups.

The ^{1}H-NMR spectra of 6 and 7 showed interesting behaviours. C_{14}-H of the both compounds showed appreciable broadening at room temp., which changed to a sharp singlet at 70°C and to a clean doublet at -30°C. This phenomenon indicates that the compounds exist in equilibrium between two conformational isomers (for example, 7a and 7b for 7).



Signal pattern of aromatic protons of 7 in $CDCl_3$
(omitted two OMe's in benzene ring)

As suggested from the configuration of the products, the above unusual Diels-Alder reaction is obviously due to non-planarity of the aromatic ring with dioxopyrroline ring in the dienophile 4, thus the aromatic ring causing steric hindrance for approaching the dienes to dioxopyrroline by path A. On the contrary, in the six-membered ring congener 1 the aromatic ring is almost coplanar with the dioxopyrroline ring. In fact, UV spectra of 1 and 4 showed appeciable difference in the intensity at the longest wave-length.

That the steric hidrance is a factor which influences the pathway of Diels-Alder reaction of enones was shown by the following examples. In Diels-Alder reaction of the dioxopyrroline 8 with activated butadienes, ene-adduct (path A product) predominates when R=H or Me, while one-adduct (path B product) predominates when R=Et, i-Pr, or CH_2COOEt. Apparently inhibition of taking coplanarity of phenyl and dioxopyrroline ring due to restricted rotation is prohibiting path A approach of the diene to the dienophile. Details will be discussed later.

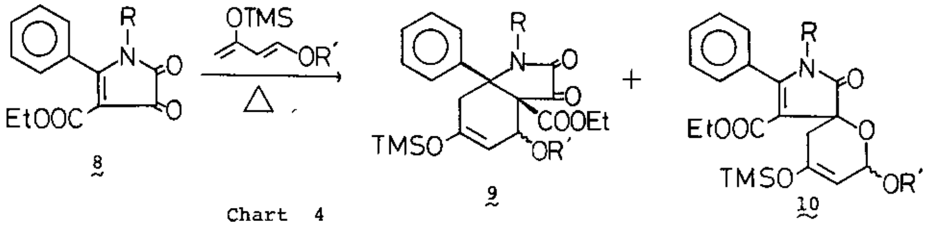
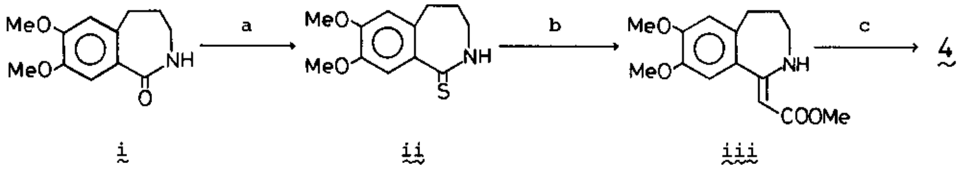


Chart 4

REFERENCES AND NOTES

1. Dioxopyrrolines XXV. Part XXIV: ref. 5.
2. K. N. Houk, "Pericyclic Reactions" ed. by A. P. Marchand and R. E. Lehr, Chapt. 4, 1977, Academic Press , New York.
3. S. B. Needleman and M. C. Chang Kuo, Chem. Rev., 1962, 62, 405. Recently examples of Lewis acid mediated cyclocondensation of siloxydienes with aldehyde including cinnamaldehyde are reported: S. Danishefsky, J. F. Kerwin Jr., and S. Kobayashi, J. Am. Chem. Soc., 1982, 104, 385; S. Danishefsky, N. Kato, D. Askin, and J.F. Kerwin, ibid., 1982, 104, 360; E. R. Larson and S. Danishefsky, Tetrahedron Lett., 1982, 23, 1975.
4. T. Sano, J. Toda, N. Kashiwaba, Y. Tsuda, and Y. Iitaka, Heterocycles, 1981, 16, 1151.
5. Y. Tsuda, T. Ohshima, T. Sano, and J. Toda, Heterocycles, 1982, 18,
6. The benzazepinopyrrolinedione 4, mp 258-261°C, was prepared from the benzazepinone i (T. Fushimi, H. Ikuta, H. Irie, K. Nakadachi, and S. Uyeo, Heterocycles, 1979, 12, 1131) as follows.



a: P_2S_5, b: 1. $BrCH_2COOMe$, 2. $KHCO_3$, 3. PPh_3, t-BuOK, c: $(COCl)_2$

7. 5, UV(EtOH): λ_{max} 238(ε=10800), 282nm(ε=7100). IR(KBr): 1770, 1750, 1725, 1720cm^{-1}. ^{1}H-NMR($CDCl_3$): δ 6.91(1H, s), 6.56(1H, s), 4.92(1H, t, J= 3 Hz), 3.87, 3.84(each 3H, s), 3.08(3H, s), 0.27(9H, s).

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