DIELS-ALDER CYCLOADDITION OF 2(1*H*)-PYRIDONES HAVING TWO ELECTRON-WITHDRAWING GROUPS WITH ELECTRON DEFICIENT DIENOPHILE

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Abstract- The first examples are presented of Diels-Alder cycloadditions of 2(1*H*)-pyridones having two electron-withdrawing groups on the ring, with electron deficient dienophiles, and the adducts obtained may act as dienophiles leading to richly functionalized, bridged, and polycyclic aza-compounds, under high pressure conditions.

2(1*H*)-Pyridones are classified as aromatic heterocycles, and generally do not undergo efficient Diels-Alder cycloaddition. Nevertheless, the Diels-Alder adducts from the reactions of 2(1*H*)-pyridones with dienophiles have an isoquinuclidine skeleton, and therefore have potential as synthetic intermediates.[1h] Recently we reported the first examples of Diels-Alder cycloadditions using, as dienes, 2(1*H*)-pyridones substituted by an electron-withdrawing group on the ring, with electron deficient dienophiles.[1l] Furthermore, the *endo* Diels-Alder adducts obtained may act as dienophiles leading to bridged and polycyclic aza-compounds.[1l] Although inverse-electron-demand [2+4] cycloadditions of 1,3-disulfonyl-2(1*H*)-pyridones with electron rich dienophiles were reported only by Posner and his co-worker,[2] there are few publications relating to [4+2] cycloadditions of 2(1*H*)-pyridones possessing two electron-withdrawing groups on the ring, with electron deficient dienophiles. Herein we wish to report Diels-Alder cycloaddition of 1-methyl-2(1*H*)-pyridones (**1a-d**) having two methoxycarbonyl groups on the ring, with *N*-

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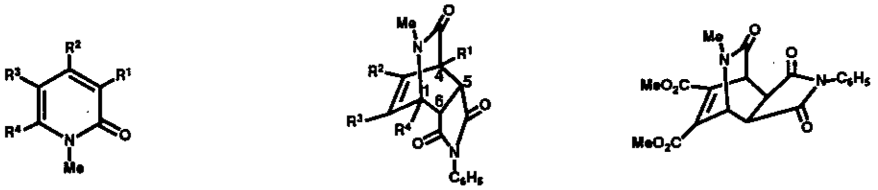
Dedicated to Prof. E. C. Taylor on the occasion of his 70th birthday.

phenylmaleimide (**2**), and these reactions are the first examples of [4+2] cycloadditions of 2(1*H*)-pyridones substituted by two electron-withdrawing groups, with electron deficient dienophiles. The Diels-Alder adducts (**3a-d**) obtained are potentially valuable synthetic intermediates. In fact, the compounds (**3dn** and **3dx**) act as dienophiles under high pressure conditions[3] leading to bridged and polycyclic aza-compounds (**4a** and **4b**), which are unobtainable under atmospheric pressure conditions.



1a-e **3a-c, dn,e** **3dx** : mp 225-226°C

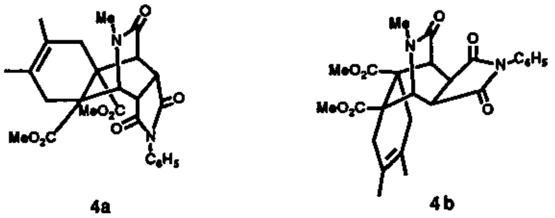
1a : $R^1 = R^3 = CO_2Me$, $R^2 = R^4 = H$
1b : $R^1 = R^2 = H$, $R^3 = R^4 = CO_2Me$
1c : $R^1 = R^3 = H$, $R^2 = R^4 = CO_2Me$
1d : $R^1 = R^4 = H$, $R^2 = R^3 = CO_2Me$

mp, °C
3a : 238-240
3b : 186-188
3c : 92-94
3dn : 90-93

Scheme 1

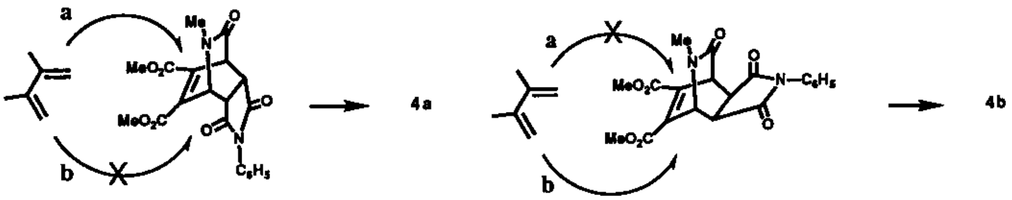
A mixture of 2(1*H*)-pyridones (**1a-c**) and the dienophile (**2**) (5 equiv.) was heated at 110°C for 72 h, and the *endo* adducts (**3a-c**) were stereoselectively obtained in 23, 71, and 17 % yields, respectively. However, the same reaction of **1d** with **2** afforded a mixture of the *endo* [**3dn**(43%)] and the *exo* [**3dx**(33%)] adducts. The stereochemistry of the *endo* **3a-dn** ($J_{1,6}=J_{4,5}=$ 4 Hz) and the *exo* **3dx** ($J_{1,6}=J_{4,5}=$ 2 Hz) adducts follows from the coupling constants. In general, the coupling constants of *endo*-H and *exo*-H coupling with bridgehead protons are 3.5 Hz and under[1d,k,l,m] and 3.5-4.5 Hz,[1d,k,l,m] respectively, in isoquinuclidine derivatives (Scheme 1).

Diels-Alder cycloadditions of the adducts (**3dn** and **3dx**) with 2,3-dimethylbuta-1,3-diene (**5**) (3 equiv.) under high pressure conditions (10 Kbar, 70°C, 48 h, methylene dichloride) stereoselectively afforded the corresponding *cis-anti-cis* adducts [**4a** (54% ; mp 177-179°C) and **4b** (96% ; mp 230-232°C)] (Scheme 2).



Scheme 2

Considering that the adducts (**4a** and **4b**) were stereoselectively obtained, the *cis-anti-cis* stereochemistry of **4a,b** was deduced from the basis of steric factor ; the diene (**5**) attacked from less hindered side[11] of the *endo* adduct (**3dn**) (upper side a) and the *exo* adduct (**3dx**) (under side b), respectively (Scheme 3).



Scheme 3

The structures of **3a-d** and **4a,b** were confirmed by ir and ^{1}H-nmr spectroscopy and gave satisfactory elemental analyses.

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