Diels–Alder Cycloadditions of 2(1*H*)-Pyridones Having an Electron-withdrawing Group

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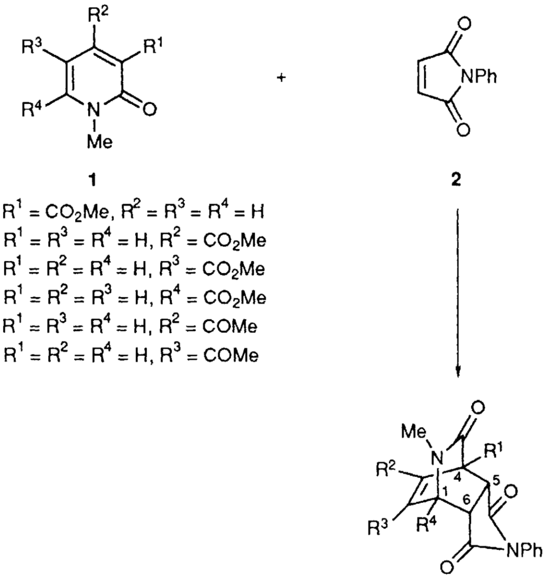
The first examples are presented of Diels–Alder cycloadditions using, as dienes, 2(1*H*)-pyridones substituted by an electron-withdrawing group in the ring.

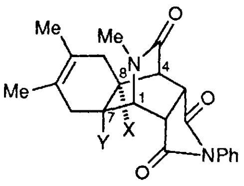
2(1*H*)-Pyridones are classified as aromatic heterocycles, and generally do not undergo efficient Diels–Alder cycloadditions.[1] Nevertheless, the Diels–Alder adducts from the reaction of 2(1*H*)-pyridones with dienophiles have an isoquinuclidine skeleton, and therefore have great potential as synthetic intermediates.[1g] However, there are few publications relating to Diels–Alder cycloadditions of 2(1*H*)-pyridones, possessing electron-withdrawing substituents in the ring, acting as dienes. Herein we report Diels–Alder cycloadditions of 1-methyl-2(1*H*)-pyridones **1a–f**, having a methoxycarbonyl or an acetyl substituent in the ring, with *N*-phenylmaleimide (**2**);[1d,j] these reactions are the first examples of 2(1*H*)-pyridones having an electron-withdrawing group acting as dienes. The Diels–Alder adducts **3b,c,e,f** obtained are potentially valuable synthetic intermediates. They may act as dienophiles leading to richly functionalized, bridged, polycyclic aza-compounds, since they contain an electrophilic group.

A mixture of 2(1*H*)-pyridones **1a–f** and the dienophile **2** (5 equiv.) was heated at 110 °C for 72 h, and the *endo*-adducts **3a–f** were stereoselectively obtained in good yields. The *endo*-stereochemistry of **3a–f** follows from the coupling constant ($J_{1,6}$ = $J_{4,5}$ = 4 Hz). In general, the coupling constants of *endo*-H and *exo*-H coupling with bridgehead protons are 3.5 Hz and under[1d,j] and 3.5–4.5 Hz,[1d,j] respectively, in isoquinuclidine derivatives. Diels–Alder cycloaddition of the adducts **3b and c** with 2,3-dimethylbuta-1,3-diene (1.5 equiv.) in toluene at 110 °C for 72 h produced the corresponding *cis-anti-cis* adducts, **4a** (55%, m.p. 198–200 °C) and **4b** (60%, m.p. 240–242 °C). Treatment of the adducts **3b**



a; R^1 = CO_2Me, R^2 = R^3 = R^4 = H
b; R^1 = R^3 = R^4 = H, R^2 = CO_2Me
c; R^1 = R^2 = R^4 = H, R^3 = CO_2Me
d; R^1 = R^2 = R^3 = H, R^4 = CO_2Me
e; R^1 = R^3 = R^4 = H, R^2 = COMe
f; R^1 = R^2 = R^4 = H, R^3 = COMe

Yield of **3a – f** (%)	M.p., *t*/°C
a; 80	191 – 193
b; 82	166 – 168
c; 80	144 – 146
d; 78	160 – 161
e; 51	222 – 224
f; 55	200 – 201



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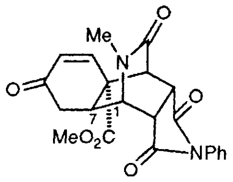
a; X = CO_2Me, Y = H
b; X = H, Y = CO_2Me



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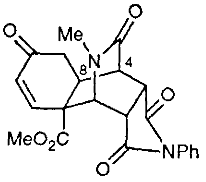

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and **c** with 1-methoxy-3-(trimethylsilyloxy)buta-1,3-diene (Danishefsky's diene) (1.5 equiv.) in toluene at 110 °C for 72 h followed by acidic work-up (trifluoroacetic acid) regio- and stereo-selectively gave the corresponding enone adducts **5** (46%, m.p. 236–238 °C), δ_H (400 MHz; $CDCl_3$) 6.14 (d, J = 10.3 Hz, 1 H, O=CC*H*=CH–) and 6.76 (d, J = 10.3 Hz, 1H, O=CCH=C*H*–) and **6** (44%, m.p. 220–221 °C), δ_H (400 MHz; $CDCl_3$) 6.21 (d, J = 10.3 Hz, 1 H, O=CC*H*=CH–) and 6.72 (d, J = 10.3 Hz, 1 H O=CCH=C*H*–). The *cis-anti*-stereochemistry (C-7 and C-8 positions) was determined from the coupling constant which was *ca.* 0 Hz[1d,j] in the adducts **4a** ($J_{1,7}$ Hz), **4b** ($J_{4,8}$), **5** ($J_{1,7}$), and **6** ($J_{4,8}$), respectively.

All new compounds, **3a–f**, **4a,b**, **5**, and **6** were characterized by IR and ^1H NMR spectroscopy, and gave satisfactory elemental analyses.

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