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FORMATION OF NOVEL 1:3 MOLAR ADDUCTS IN THE HIGH PRESSURE REACTION OF 2(1H)-PYRIDONES WITH DIMETHYL ACETYLENEDICARBOXYLATE[1]

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Abstract---The high pressure (10-15 kbar) reaction of N-substituted 2(1H)-pyridones possessing bulky groups such as cyclohexenyl, isopropyl, and phenyl with dimethyl acetylenedicarboxylate each yielded only one isomer of a 1:3 molar adduct along with a 1:1 adduct while N-methyl- and N-benzyl-2(1H)-pyridones each gave isomeric mixtures of 1:3 molar adducts together with a 1:1 molar adduct. The formation of these 1:3 molar adducts is discussed.

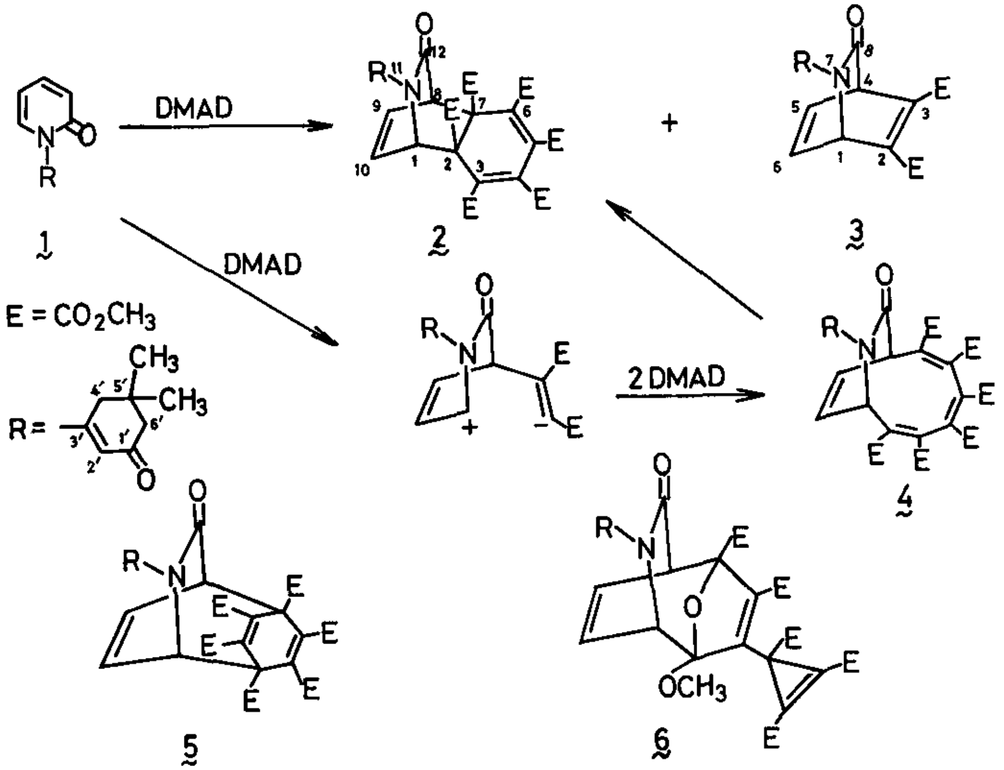
We have reported[2] a successful synthesis of the isoquinuclidienone system by the high pressure Diels-Alder reaction of 2(1H)-pyridones with dimethyl acetylenedicarboxylate (DMAD), which failed at ambient pressure.[3,4] Further studies have now shown that 1:3 molar adducts are formed along with 1:1 molar adducts when substituents are absent from the ring carbons of a 2(1H)-pyridone. This is the subject of the present report.

Reaction of 1-(5,5-dimethyl-3-cyclohex-2-en-1-onyl)-2(1H)-pyridone (**1**; R=dimedonyl) with DMAD[5] in dichloromethane at 15 kbar and 46 °C resulted in the formation of a 1:3 molar adduct (**2**; R=dimedonyl)[6] along with the 1:1 adduct (**3**; R=dimedonyl)[7] in almost the same ratio. The structure of **2** (R=dimedonyl) was deduced from a comparison of its ^{1}H and ^{13}C n.m.r. spectra with those of **3** (R=dimedonyl). The main differences in the ^{1}H spectra are that the resonances for the 1-H and 8-H of **2** are at significantly lower field than the 1-H and 4-H of **3**, and that the 4'-methylene group of **2** appears as an AB system while that of **3** is a singlet. The methylene assignments in these compounds are based on those of Mariano et al.,[8] but it is possible that the 4'- and 6'-resonances should be interchanged. This does not however alter the conclusion that the proton arrangements in 2 and 3 must be very similar indeed, but that the environment round what corresponds to the the bridgehead protons of 3 is different in 2. The ^{13}C n.m.r. spectrum confirms the structural relationship, and shows that in addition to the corresponding resonances for 3, 2 possesses two sp^2 and two sp^3 C atoms not bonded to hydrogen, and four ester groups. This permits us to form one additional ring in reacting 1 across the 2,5-positions to give 2. Separate experiments showed that 2 was not formed from 3, and nor was 2 formed from 1 and hexamethyl benzenehexacarboxylate,[9] a self-condensation product of DMAD under the reaction conditions. Although other formulations such as 5 and 6 cannot be rigorously excluded the most probable structure for 2 is as shown. Analogous 1:1 and 1:3 molar adducts[10] have been obtained (Table) from 1-isopropyl- and 1-phenyl-2(1H)-pyridones while the 1-methyl and 1-benzyl-2(1H)-pyridones gave the 1:3 molar adducts as mixtures of isomers. No 1:3 molar adducts were obtained from 6-methoxy-1-methyl-, 1,3-dimethyl- and 4,6-dimethyl-1-phenyl-2(1H)-pyridones, probably because of steric hindrance. The 1:3 molar adducts could be formed by a stepwise Michael type addition of DMAD to the pyridone to yield a large ring compound 4 followed by a disrotatory intramolecular cyclisation[11] leading to an exo or endo product, or a mixture. The two conformational isomers would be possible in the structure 4 when R is not bulky.

Table. Reactions of 2(1H)-pyridones with DMAD

2(1H)-Pyridone R	Pressure kbar	Temperature °C	Time h	% Yield[a] of Adducts 2	3
Dimedonyl	15	46	72	36	36
i-Pr	10	35	106	3	4
Ph	10	40	72	20	10
Me	10	70	12	4	14
$PhCH_2$	10	35	120	4	6

[a] Not optimised.



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4. Successful examples with other dienophile: H. Tomisawa, H. Hongo, R. Fujita, H.

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5. This reaction failed under normal pressure: ref. 3c.
6. Yield 36 %; m.p. 153 °C; m/e 643 (M^+), i.r. 1650, 1700, 1735 cm^{-1}; ^{1}H-n.m.r.($CDCl_3$) 1.07, 1.12(s, 6H, $C\underline{H}_3$), 2.28(s,2H, 6'-$C\underline{H}_2$), 2.45, 2.95(ABq, J=18 Hz, 4'-$C\underline{H}_2$), 3.65(s, 6H), 3.76, 3.84, 3.98, 4.02(s, 12H), 4.43(dd, J=2, 6.8 Hz, H-1), 5.21(dd, J=2, 4.5 Hz, H-8), 5.87(s, 1H, H-2'), 5.95-6.6(m, 2H, H-9,10); ^{13}C-n.m.r.($CDCl_3$) 27.4, 28.6(q. $\underline{C}H_3$), 33.5(s, C-5'), 42.3(t, C-6'), 50.7(t, C-4'), 48.0, 56.9(d, C-1,8), 52.7, 53.0, 53.2, 53.7, 55.8(q, $O\underline{C}H_3$), 59.3, 83.7(s, C-2,7), 116.6, 131.4(d, C-9,10), 122.6(C-2'), 113.1, 129.1, 137.1, 139.8(s, C-3, 4, 5, 6), 159.1(C-1), 160.1, 160.9, 164.5, 165.1, 167.9, 168.4(s, O$\underline{C}$=O and N$\underline{C}$=O), 199.1(s, C-3').
7. Yield 36 %; pale yellow oil; m/e 359 (M^+), 194($C_6H_4E_2$); i.r. 1650, 1715 cm^{-1}; ^{1}H-n.m.r.($CDCl_3$) 1.03(s, 6H, $C\underline{H}_3$), 3.76(s, 6H, $OC\underline{H}_3$), 2.20(s, 2H, 6'-$C\underline{H}_2$), 2.66 (s, 2H, 4'-CH_2), 4.69(dd, J=2, 5 Hz, H-1), 5.80(dd, J=2, 4.8 Hz, H-4), 5.92(s, 1H, H-2'), 6.7-7.2(m, 2H, H-5,6); ^{13}C-n.m.r.($CDCl_3$) 28.1, 28.5(q, $\underline{C}H_3$), 33.6(s, C-5'), 41.5, 50.4(t, C-6', 4'), 53.0(br q, $O\underline{C}H_3$), 56.7, 58.3(d, C-1, 4, J=153, 156 Hz), 112.4(d, C-2', J=163 Hz), 135.1, 136.4(d, C-5, 6), 140.3, 145.1(s, C-2, 3), 157.2(s, C-1'), 162.9, 164.2, 168.2(s, O$\underline{C}$=O and N$\underline{C}$=O), 199.1(s, C-3').
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9. Non-annelated arenes normally do not undergo cycloadditions except at high pressure and high temperature: W. Jarre, D. Bieniek, and F. Korte, Angew. Chem. Int. Ed., **14**, 181 (1975).
10. New compounds have been adequately characterized by spectroscopic (i.r., ^{1}H and ^{13}C n.m.r., and mass) and elemental analyses.
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