FORMATION OF NOVEL 1:3 ADDUCT IN THE HIGH PRESSURE REACTION OF 2(1H)-PYRIDONES WITH DIMETHYL ACETYLENEDICARBOXYLATE: AN X-RAY CRYSTAL STRUCTURE DETERMINATION

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Abstract——The structure of the 1:3 adduct from 1-(5',5'-dimethylcyclohex-2'-en-1'-on-3'-yl)-2(1H)-pyridone and dimethyl acetylenedicarboxylate was determined, possible mechanism for the reaction being presented.

Knowledge of the volume profile of chemical reaction is now reaching the stage of application in the synthetic laboratory.[1] Indeed, the high pressure strategy has proven extremely useful to surmount the energy barrier imposed by electronic and steric effect in many kinds of addition reactions such as Diels-Alder, Michael, Aldol, and related reactions, particularly when either substrates or products are sensitive to heat and catalysts.[2] However, less attention has been directed on discovery of a new or unusual reaction that does take place only at high pressures.

Previously, we reported[3] on the high pressure Diels-Alder reaction of 2(1H)-pyridones with dimethyl acetylenedicarboxylate (DMAD) that was unsuccessful at ambient pressure.[4] We now describe an X-ray structure determination of the novel 1:3 adduct from 1-(5',5'-dimethylcyclohex-2'-en-1'-on-3'-yl)-2(1H)-pyridone (1)[4b] and DMAD. Reaction of 1 with DMAD in dichloromethane at 15 kbar and ca. 45°C produced the 1:3 adduct (2) along with the 1:1 adduct (3) almost in the same

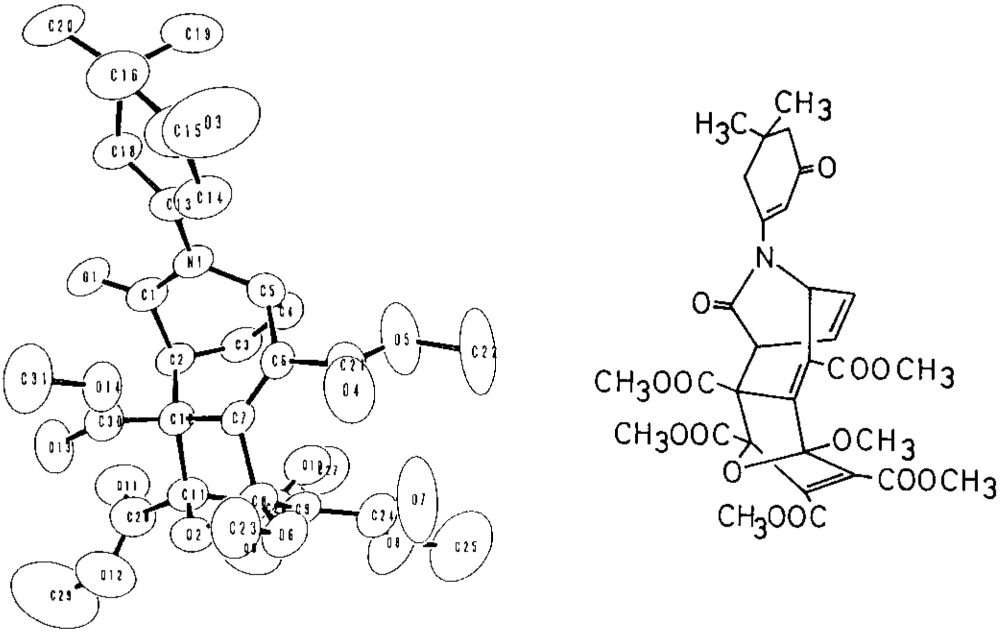
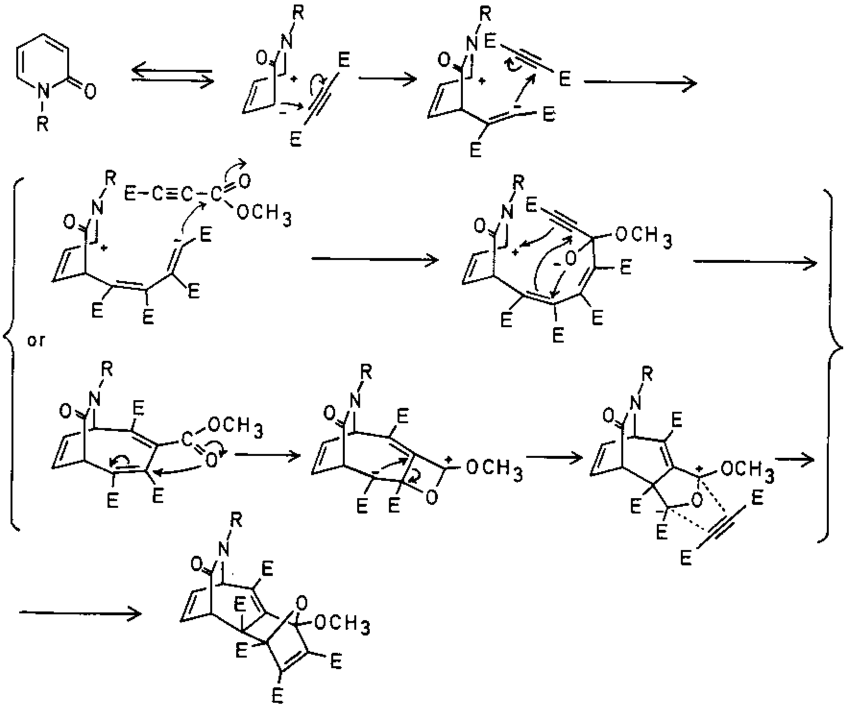
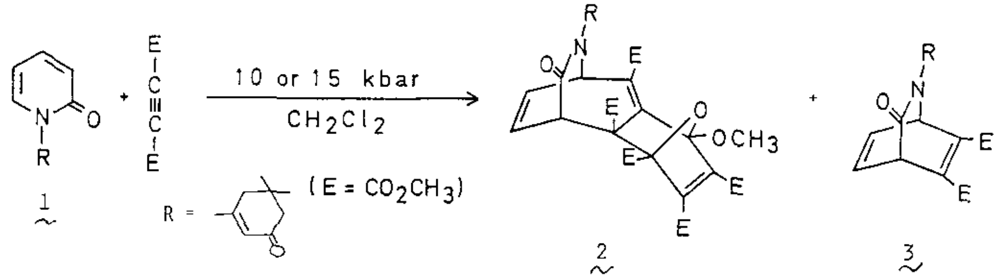


Figure 1. Structure of 2. Selected bond lengths (Å). C(1)-C(2) 1.533(7), C(2)-C(3) 1.490((7), C(3)-C(4) 1.318(8), C(4)-C(5) 1.495(7), C(5)-C(6) 1.540(7), C(6)-C(7) 1.319(7), C(7)-C(8) 1.558(7), C(8)-C(9) 1.533(8), C(9)-C(10) 1.334(8), C(10)-C(11) 1.538(8), C(11)-C(12) 1.594(7), C(12)-C(2) 1.557(7), C(1)-N(1) 1.364(6), N(1)-C(5) 1.480(6).



Scheme 2



Scheme 1

ratio (36% yield).[5] Since an inspection of ^{1}H- and ^{13}C-nmr spectra did not permit structural determination, an X-ray analysis has been performed.[6] The crystal structure *analysis clearly shows the tetracyclic* structure (*Fig.* 1). Surprisingly, **2** is quite stable to heat and had a discrete melting point. Controlled experiments have shown that **2** was not formed from **3** and DMAD at high pressure.

Analogous 1:3 adducts have been obtained, albeit in lower yields from 1-isopropyl- and 1-phenyl-2-(1H)-pyridones whereas the 1-methyl- and 1-benzyl-2(1H)-pyridones afforded the 1:3 adducts as mixtures (from ^{1}H- and ^{13}C-nmr spectra) of the possible stereoisomers.[3b] No 1:3 adducts were obtained when substituents are present on the ring carbons of a 2(1H)-pyridone, presumably because of steric hindrance.

Although mechanistic considerations are still premature, formation of **2** can be explained by either of the routes shown in Scheme 2.

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5. **2**: IUPAC name is 10-(5',5'-dimethylcyclohex-2'-en-1'-on-3'-yl)-6-methoxy-2,3,4,5,8-penta(methoxycarbonyl)-10-aza-14-oxatetracyclo[7.2.2.$1^{3,6}$.$0^{2,7}$]-tetradec-4,7,12-trien-11-one; mp 147-150°C; ^{1}H-nmr($CDCl_3$) δ 1.07, 1.12(3H, s), 2.28(2H, s), 2.45, 2.95(2H, ABq, J=18Hz), 3.65(6H, s), 3.76, 3.84, 3.98, 4.02(12H, s), 4.43(1H, dd, J=2.0 and 6.8Hz), 5.21(1H, dd, J=2.0 and 4.5Hz), 5.87(1H, s), 5.95-6.60(2H, m) ; ^{13}C-nmr($CDCl_3$, 22.49MHz) δ 27.5, 28.6(q), 33.6(s), 42.3, 50.7(t), 48.0(d), 57.0(d), 52.7, 53.1, 53.2, 55.9(q), 59.3(s), 83.8(s), 113.2(s), 116.7, 131.5(d), 122.7(d), 129.3(s), 137.2, 139.2, 140.0(s), 159.2(s), 160.2, 161.0, 164.6, 165.2, 168.6(s), 199.2(s); ir(KBr) 1650, 1700, 1735 cm^{-1}; ms m/z 643(M^+).
6. Crystal data for **2**: $C_{31}H_{33}NO_{14}$, monoclinic, space group $P2_{1/n}$, a=22.766(5), b=10.768(4), c=13.01(4)Å, β=94.71(1)°, Z=4, D_x=1.345Mg/m^3. Intensities were measured up to 2θ=127° on Rigaku AFC-5 diffractometer with graphite-monochromated Cu-K_α (1.5418Å) radiation. The structure was solved by the direct method (MULTAN 78) and refined by the block-diagonal least-square method(HBLS) to R=0.081 (R_w=0.073) for 3943 reflections with $F_o > 3\sigma(F_o)$. The details will be reported in a forthcoming paper.

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