

Michael-type Addition of 1,8-Diazabicyclo[5.4.0]undec-7-ene to Dimethyl Acetylenedicarboxylate

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Michael reaction of DBU **1** with dimethyl acetylenedicarboxylate **2** and subsequent intramolecular condensation of the adduct gives a tricyclic derivative **6**; a mechanism for the formation of **6** is proposed and an X-ray crystal structure of **6** is presented.

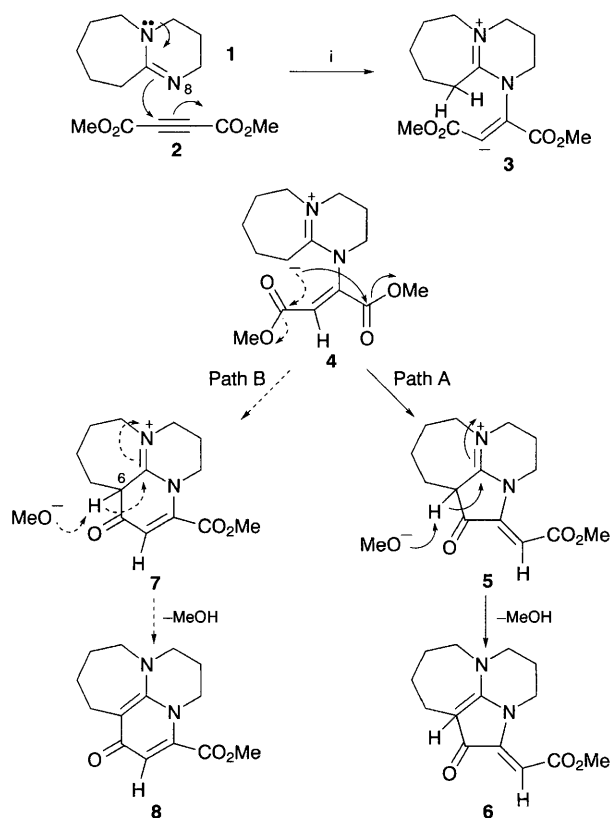
The effectiveness of the bicyclic amidines 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) **1** and 1,5-diazabicyclo[4.3.0]non-5-ene (DBN) as strong non-nucleophilic bases in organic and inorganic chemistry has been widely demonstrated.¹ However, they have recently been found capable of behaving as nucleophiles, under certain conditions, and to react with strong electrophiles such as halogenated phosphanes,² substituted pyrazoles,³ activated alkenes⁴⁻⁶ and the β -ketoester of methyl pheophorbide *a*.⁷ We report here the bifunctional nucleophilic behaviour of DBU in its reaction with dimethyl acetylenedicarboxylate **2**.

In studies related to photosensitizers for the photodynamic therapy of tumours, we have used DBU as a base to tautomerize the isolated double bond in the Diels–Alder cycloadducts of vinyl porphyrins and **2** to the fully conjugated chromophores.⁸ A yellow material is occasionally observed in the chromatographic purification of the rearranged benzoporphyrin derivatives. Since this material shows no electronic absorptions in the visible region (all porphyrins have visible absorptions), we considered that it was not a porphyrin related byproduct. When DBU was added to **2** (1 : 1) in chloroform at room temperature, a golden yellow product was instantly formed with a strong exotherm. After recrystallization (CH_2Cl_2 –hexane), red crystals were obtained (96% yield) and MS and microanalysis indicated

this product to be an adduct of DBU and **2** minus a molecule of methanol. The ^1H NMR spectrum was clean and distinct at 200 MHz, and exhibited two singlets at δ 5.94 (1 H) and 3.33 (3 H) together with 7 completely resolved methylene groups. The connectivity of these methylene signals was correlated by a ^1H – ^1H COSY spectrum to two isolated spin systems with 3 and 4 methylene groups respectively. In combination with its ^{13}C NMR and attached proton experiments, all 14 carbons and 18 hydrogens could be accounted for, and structures **6** and **8** were proposed (Scheme 1). Since spectral analysis was unable to discriminate between these two structures, a single crystal suitable for X-ray analysis was prepared and we have now shown the product to have the unusual structure **6**, as shown in Fig. 1.†

Formation of **6** is initiated by Michael addition of DBU with **2** via N-8 (Scheme 1), affording the quaternary ammonium salt **3**.⁵ Abstraction of the H-6 proton in **3** leads to an intermediate **4** which could react with either ester function to give a five (Path A) or a six (Path B) membered ring (**5** or **7**). Loss of the H-6 proton from the cycloadduct (**5** or **7**) generates the incipient double bond conjugated with the carbonyl to produce the neutral tricyclic product **6** or **8**. Although formation of a six membered ring (Path B) seems to be thermodynamically more favourable the reaction is highly selective and produces only isomer **6**, suggesting that this reaction is similar to typical Michael reactions and is under kinetic control.

We have also found that DBU reacts with other activated triple bonds, such as methyl propiolate and methyl cyanofornate, but so far no products have been characterized from these complex reaction mixtures. The reaction of DBN with **2** is also strongly exothermic and gives an as yet intractable unidentified red mixture. The conformational rigidity of the five membered ring undoubtedly hinders a transformation similar to that of **4** to **5**.



Scheme 1, Reagents and conditions: i, DBU; **2** = 1 : 1, CHCl_3 , room temp., 2 min

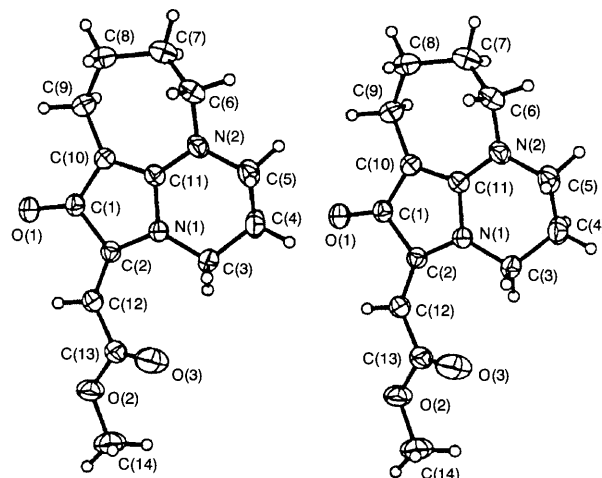


Fig. 1 X-Ray structure of **6**. The five-membered ring is planar, the six-membered ring has an envelope-like conformation, and the seven-membered ring adopts a distorted chair conformation. Important bond lengths (Å): C(2)–C(12) 1.339(2), C(10)–C(11) 1.390(2).

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Footnote

† *Crystal data* for **6**: Red prism, $C_{14}H_{18}N_2O_3$, $M = 262.31$, triclinic, space group $P\bar{1}$ (No. 2), $a = 12.066(1)$, $b = 12.946(2)$, $c = 9.0900(8)$ Å, $\alpha = 103.695(9)$, $\beta = 103.828(8)$, $\gamma = 101.68(1)^\circ$, $V = 1288.1(3)$ Å³, $Z = 4$ (two molecules in the asymmetric unit), $D_c = 1.190$ g cm⁻³. The final unit cell parameters were obtained by least-squares analysis on the setting angles for 25 reflections with $110.5 \leq 2\theta \leq 114.60^\circ$. The intensities of three standard reflections were measured every 200 reflections throughout the data collection: no decay correction was necessary. Data were corrected for Lp and absorption (azimuthal scans for three reflections, relative transmission factors 0.86–1.00). The structure was solved by direct methods. Non-hydrogen atoms were refined with anisotropic thermal parameters and hydrogen atoms were refined with isotropic thermal parameters. An isotropic Zachariasen type I secondary extinction correction was applied,

the final value of the extinction coefficient being $5.68(6) \times 10^{-5}$. The refinement converged at $R = 0.041$ and $R_w = 0.038$ for 4303 independent reflections with $I \geq 3\sigma(I)$. Calculations were performed using the TEXSAN structure analysis package (Molecular Structure Corporation, 1985 & 1992). Atomic coordinates, bond lengths and angles, and thermal parameters have been deposited at the Cambridge Crystallographic Data Centre. See Information for Authors, Issue No. 1.

References

- 1 I. Hermez, *Adv. Heterocycl. Chem.*, 1987, **42**, 83.
- 2 R. Reed, R. Réau, F. Dahan and G. Bertrand, *Angew. Chem., Int. Ed. Engl.*, 1993, **32**, 399.
- 3 H. Lammers, P. Cohen-Fernandes and C. L. Habraken, *Tetrahedron*, 1994, **50**, 805.
- 4 L. L. McCoy and D. Mal, *J. Org. Chem.*, 1981, **46**, 1016.
- 5 M. Perbost, M. Lucas, C. Chavis and J.-L. Imbach, *J. Heterocycl. Chem.*, 1993, **30**, 627.
- 6 R. D. Chambers, A. J. Roche, A. S. Batsanov and J. A. K. Howard, *J. Chem. Soc., Chem. Commun.*, 1994, 2055.
- 7 L. Ma and D. Dolphin, *Tetrahedron*, in press.
- 8 V. S. Pangka, A. R. Morgan and D. Dolphin, *J. Org. Chem.*, 1986, **51**, 1094.