High-pressure Cycloaddition of 2(1*H*)-Pyridones with Dimethyl Acetylenedicarboxylate

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Summary Reaction of dimethyl acetylenedicarboxylate with the 2(1*H*)-pyridones (**1**) at 10—15 kbar pressure and 60—70 °C gives the bicyclic adducts (**2**), some of which are unobtainable under atmospheric pressure in moderate yields.

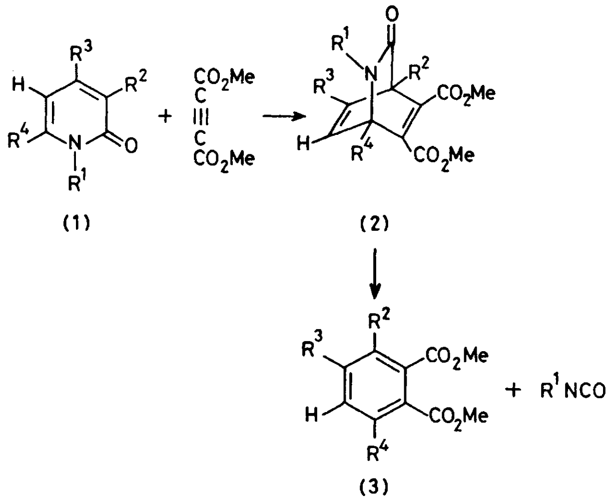
EARLY attempts to bring about Diels–Alder reactions with 2(1*H*)-pyridones failed, but adducts have been obtained with some dienophiles such as dimethyl acetylenedicarboxylate,[1–3] maleic anhydride,[3] maleimides,[4] and benzyne.[3] Success in the isolation of bicyclic adducts from dimethyl acetylenedicarboxylate and a variety of 2(1*H*)-pyridones depends on the steric and electronic effects of the substituents present in the ring.[2]

We now describe the effects of 10—15 kbar hydrostatic pressure on some of these reactions as this procedure can sometimes overcome the energy barrier imposed by steric and electronic effects when the reaction proceeds with a

TABLE[a]

Pyridone	Pressure /kbar	Time /h	Temp. /°C	Yield[b] of (2) /%	Yield of (2) previously reported/%
(1a)	10	12	70	16	0[c]
	15	16	60	22	
(1b)	15	15	60	40	0[d]
(1c)	10	35	60	22	36[d,e]
	15	19	60	20	
(1d)	15	21	60	16	0[d]
(1e)	15	48	60	15	8[d,f] (0)[g]

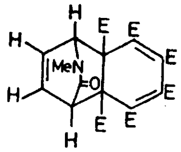
[a] All new compounds analysed correctly for C, H, and N, and were separated by silica gel t.l.c. [b] Yields were not optimised but were >90% based on the 2(1*H*)-pyridone consumed. [c] See R. M. Acheson and P. A. Tasker, *J. Chem. Soc. (C)*, 1967, 1542. [d] See ref. 2. [e] Extended reaction in neat dimethyl acetylenedicarboxylate at 80 °C; (**2c**) was produced in trace quantities only after 72 h. [f] Reaction at 80 °C for 170 h. [g] See U. Heep, *Tetrahedron*, 1975, **31**, 77.



SCHEME

a; R^1 = Me, R^2 = R^3 = R^4 = H
b; R^1 = R^2 = Me, R^3 = R^4 = H
c; R^1 = Me, R^2 = H, R^3 = Ph, R^4 = H
d; R^1 = Me, R^2 = R^3 = H, R^4 = OMe
e; R^1 = OMe, R^2 = H, R^3 = R^4 = Me

net volume contraction.[5] Our results are summarised in the Table along with those previously reported for experiments carried out at atmospheric pressure. At room temperature for 1 week, significant combination did not occur, but at 60—70 °C, adducts were obtained and reactions were carried out on a gram scale. It is clear that the use of high pressure enables adducts to be prepared which are not available by conventional thermal methods. The adducts (**2**), when refluxed with xylene, cleaved to the corresponding phthalic esters (**3**) (Scheme). Self-condensation of dimethyl acetylenedicarboxylate to hexamethyl benzenehexacarboxylate also occurs, as it does at atmospheric pressure,[1] but was inhibited considerably by the addition of a trace of hydroquinone. Treatment of the pyridone (**1a**) with 2 equiv. of the acetylenic ester in the absence of hydroquinone gave a 4% yield of a 1:3 molar adduct, identified as a mixture of the *exo* and *endo* adducts (**4**) from its ^{1}H and ^{13}C n.m.r. spectra.



(4)

E = CO_2Me

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[1] R. M. Acheson and N. F. Elmore, *Adv. Heterocyclic Chem.*, 1978, **23**, 263, and papers cited therein.

[2] G. P. Gisby, S. E. Royall, and P. G. Sammes, *J.C.S. Chem. Comm.*, 1979, 501, and papers cited therein.

[3] P. S. Mariano, P. L. Huesman, R. L. Beamer, and D. Dunaway-Mariano, *Tetrahedron*, 1978, **34**, 2617, and references cited therein.

[4] K. Somekawa, T. Watanabe, and S. Kumamoto, *Nippon Kagaku Kaishi*, 1978, 412, and papers cited therein.

[5] For recent examples of high-pressure organic reactions see: G. Jenner, H. Abdi-Oskoui, and J. Rimmelin, *Bull. Soc. chim. France*, 1979, II-33; J. Jurczak, M. Chmielewski, and S. Filipek, *Synthesis*, 1979, 41; J. A. Gladysz and Y. S. Yu, *J.C.S. Chem. Comm.*, 1978, 599; K. Matsumoto, Y. Ikemi-Kono, and T. Uchida, *ibid.*, p. 543, and references cited in these papers.