Reaction of (*E*)-β-Enamino Amides with Dimethyl Acetylenedicarboxylate (DMAD): Formation of Benzene Derivatives, Enamino Esters, and 2-Pyridones

Antonio Nuvole and Giuseppe Paglietti *
Istituto di Chimica Farmaceutica, University of Sassari, Via Muroni 23 A-07100 Sassari, Sardinia-Italy

An investigation of the additions of (*E*)-enamino amides (**1a**—**d**) with DMAD has shown that they are influenced by the stereochemistry of the intermediates and the amine component of the enamine system. In dry acetonitrile (*E*)-benzyl(methyl)amino- (**1b**), (*E*)-pyrrolidin-1-ylamino-(**1c**), and (*E*)-piperidin-1-ylamino- (**1d**) acrylamides, following a known mechanism, yielded tetramethyl benzene-1,2,3,4-tetracarboxylate (**5**), the (*E*)-aminobutenedioates (**6b**—**d**), and the 3,4-bismethoxycarbonylpyridin-2-(1*H*)-one (**8**). Dimethylamino-(**1a**) and morpholin-1-ylamino- (**1e**)-acrylamides, owing to the different nucleophilicity of the β-carbon, formed a zwitterion (**11**) which eliminated propiolamide to give only the (*E*)-aminobutenedioates (**6a**, **e**).

Not only are the reactions of simple enamines with electrophilic reagents well documented in the literature,[1] but there have been numerous reports in the last 15 years on the reactions of enamines with activated olefins. Of these, we are mainly interested in the reactions of cyclic enamines with acetylenic esters to give new heterocycles.[2] Acheson *et al.* have shown that enamines such as di- and tetra-hydropyridine react with the latter esters to give cyclobutapyridines, dienamino diesters,[3–5] di- and tetra-hydroazocines,[5,6] benzene derivatives,[4,5] and cyclobutacyclopentapyrroles.[7] In particular, the reaction of *N*-alkyl or aryl substituted 1,4,5,6-tetrahydronicotinamides with DMAD and methyl propiolate (M.P)[6] provide an interesting example of the reactivity of this type of enamine, the amide group being either eliminated to give methyl aminopropylbenzene, di-, tri-, and tetra-carboxylates,[6] or retained to give 5-carboxamido-1,2,3,4-tetrahydroazocines.[6] We have studied the score and stereochemistry of this latter reaction by treating the *E*-enamino amides (**1a**—**e**) with DMAD and now present our results (Schemes 1, 2, and Table 1).

$R^1R^2NCH{=}CH{-}CONH_2$

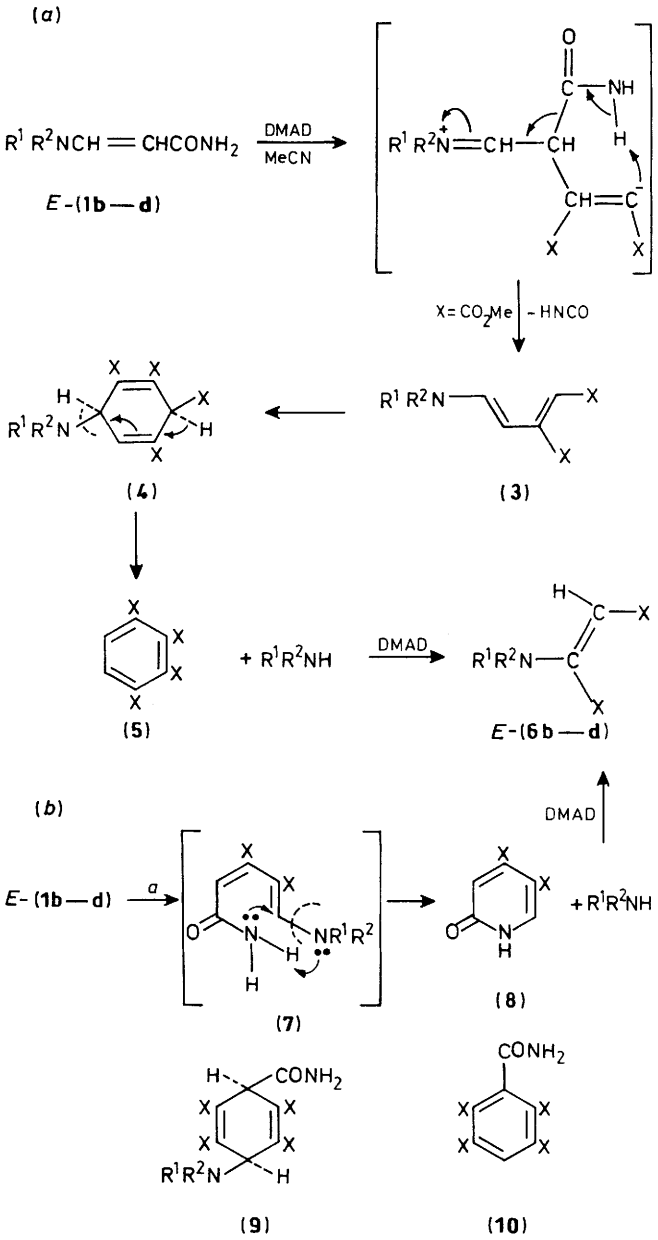
E-(**1a**—**e**)

	R^1	R^2	
a	methyl	methyl	
b	benzyl	methyl	
c	pyrrolidinyl	H	3-amino acrylamides
d	piperidinyl	H	
e	morpholinyl	H	

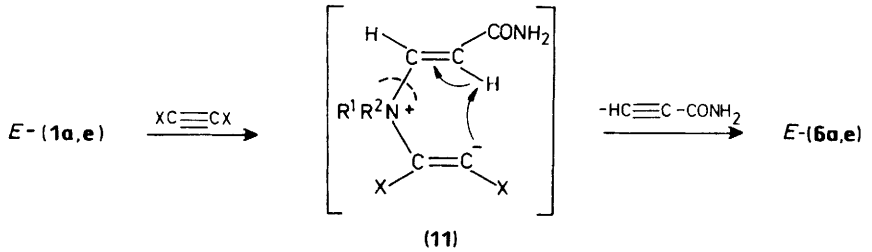
The starting acrylamides *E*-(**1a**—**e**) were obtained in good yield by stereospecific Michael addition of the appropriate amine R^1R^2NH upon the propiolamide and their stereochemistry was deduced as earlier reported.[8,9]

Reactions with DMAD were generally carried out in dry acetonitrile (see Table 1) and an examination of the results shows that it is possible to distinguish between two general cases (**1b**—**d**) and (**1a**, **e**). Compounds (**1b**—**d**) gave the tetracarboxylate (**5**), the *E*-aminobutenedioate *E*-(**6b**—**d**), the pyridone (**8**), and traces of the free amines R^1R^2NH. Compounds (**1a**, **e**) gave only the esters *E*-(**6a**, **e**) and traces of propiolamide.

Isolation of (**5**) and *E*-(**6b**—**d**) and detection of the free amines R^1R^2NH clearly indicate that the dienamine (**3**) (mechanism *a*, Scheme 1), is the key intermediate the stereochemistry of which allows formation of the cycloadduct (**4**). This leads to (**5**) and



Scheme 1. a, [2 + 2] cycloaddition



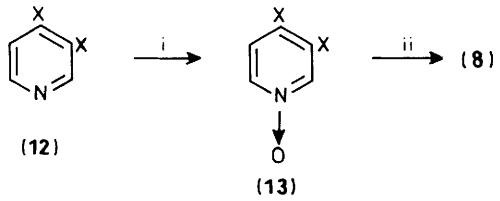
Scheme 2.

E-(**6b**—**d**) in accordance with previous observations[3-6] which prompted the present investigation. The free amine smell detected at the end of each reaction confirms there was insufficient DMAD present to trap all the amines formed in the cycloaddition. On the other hand, isolation of the pyridone (**8**) can be explained by mechanism *b* (Scheme 1), where the di-enaminoamide (**7**), subsequent [2 + 2]cycloaddition followed by ring opening,[10] undergoes ring closure to yield (**8**) in a fashion analogous to formation of lactams by cyclisation of the enamine acrylamide adducts.[11] It seems very likely in the cases examined that this type of cyclisation is dependent on the *E*/*Z* stereochemistry of (**7**) which prevents formation of the possible adducts (**9**) and (**10**).

Compound (**5**) was identical with the known tetramethyl benzenetetracarboxylate (**5**).[12] The esters *E*-(**6b**—**d**) were identified by comparison with the known *E*-(**6b**)[8] and *E*-(**6d**)[13] and with *E*-(**6c**) synthesized by an alternative route. The pyridone (**8**) was identical with an authentic specimen obtained by an independent synthesis described later. Surprisingly, in the second general case from the reaction of (**1a**, **e**) we obtained only the esters *E*-(**6a**, **e**). However when samples of the reaction mixture, carefully evaporated under reduced pressure, were examined by i.r. spectroscopy as liquid films an absorption at 2 100 cm^{-1} for an unsymmetrical triple bond was observed. This is good evidence for the displacement of propiolamide through the zwitterion intermediate (**11a**, **e**), a transformation involving a 6-electron transition state giving rise to the *E*-butenedioates (**6a**, **e**) (Scheme 2). Compound (**6a**) was identical with that described in the literature[8] whereas (**6e**) was identical with that obtained by an unambiguous procedure as for (**6c**). The stereochemistry of (**6a**, **e**), was deduced as for the cases above. The high value for the chemical shift of the olefinic proton as reported in the literature[4,8,9,13] suggests that *cis*-addition of DMAD has taken place and that formation of the acetylene derivative from the appropriate olefin often occurs observed under basic catalysis.[14]

At this stage we can conclude that the differing behaviour of (**1a**, **e**) and (**1b**—**d**) may be due to the different nucleophilicity of the β-carbon in (**1a**, **e**) induced by the amine component of the enamine system, as observed in similar reactions with electrophiles.[15] In fact the reaction of morpholine enamino esters with benzyl bromide occurs either with protonation at nitrogen followed by elimination of alkyne or with C-alkylation whereas in some enaminoamides only benzylmorpholine is obtained.[16] Thus in the cases of (**1a**, **e**) the dimethylamino and morpholino species would favour protonation at nitrogen rather than electrophilic attack at the β-carbon.

The previously unknown pyridone (**8**) was identified on the basis of its synthesis by a route (see Scheme 3) earlier described by Boekelheide and Lehn.[17] In our case the diester (**12**) was obtained as described[18] and its *N*-oxide (**13**) was isolated (62%). Although formation of two isomeric pyridones was expected, chromatography of the rearranged product isolated only one, the physical and chemical properties of which were identical with those of the product isolated from the reaction between the



Scheme 3. *Reagents and conditions:* i, 30% H_2O_2 in AcOH; ii, AC_2O, reflux

enamino amides (**1b**—**d**) and DMAD. The ^1H n.m.r. spectrum of (**8**) excludes other possible structures (two sharp singlets for 3-H and 6-H) and its u.v. spectrum is consistent with the structure proposed.

Experimental

M.p.s are uncorrected and were recorded on a Köfler apparatus. U.v. spectra are given for solutions in ethanol and were recorded in nm (log ε) with a Unicam SP 700 and a Perkin-Elmer Lambda 5 spectrometer. I.r. spectra are for Nujol mulls, or liquid films, and were recorded on Perkin-Elmer 297 and 781 instruments. ^1H N.m.r. spectra were recorded in $CDCl_3$ solutions at 60 MHz with TMS as internal standard using a R-24A Perkin-Elmer spectrometer. The alumina used for chromatography was neutral Merck (activity II). Elemental analyses were performed at the Centro di Spettroscopia, Sassari University, and the Laboratorio di Microanalisi (Pharm. Chem. Dept.), University of Padova. Ether refers to diethyl ether throughout.

Propiolamide.—The best yield was obtained using the method of Truce and Tichenor.[19] In this, methyl propiolate (Aldrich) was added to liquid ammonia at −70 °C and the mixture was kept at this temperature for at least 2 h; m.p. 58—61 °C (lit.,[19] 61—62 °C); $\nu_{max.}$(Nujol) 3 340, 3 270, 3 180, 2 100, 1 680, and 1 580 cm^{-1}.

(E)-β-*Enamino Amides* (**1a**—**e**). *General Procedure.*—To propiolamide (10 mmol), in solution or as a suspension in an appropriate solvent (50 ml) was added the secondary amine (R^1R^2NH) (9 mmol), previously dissolved in the same solvent. The mixture was either set aside or heated under reflux as indicated to give a precipitate which was filtered off and recrystallised. Conditions, solvent, m.p., and yields are reported in Table 2, ^1H n.m.r. spectra in Table 3, u.v. and i.r. values in Table 4, and analytical data in Table 5.

Preparation of the Enamino Esters E-(**6c**) *and* E-(**6e**).—(*i*) Equimolar amounts (20 mmol) of DMAD and pyrrolidine in dry ether (20 ml) were stirred for 24 h at room temperature. After evaporation of solvent the residue was induced to

Table 1. Yields of products formed from the reaction of *E*-(**1a**—**e**) with DMAD

Compd.	Reaction time	Solvent temp.	Yields of products isolated (%)
(**1a**)	22 h	*a*	*E*-(**6a**) (73)
(**1a**)	15 days	*c*	*E*-(**6a**) (52)
(**1b**)	24 h	*a*	(**5**) (3), *E*-(**6b**) (22), (**8**) (24), $PhCH_2NHMe$ (43)
(**1c**)	24 h	*a*	(**5**) (14), *E*-(**6c**) (5), (**8**) (8)
(**1c**)	6 h	*a*	(**5**) (10), *E*-(**6c**) (12), (**8**) (10)
(**1d**)	24 h	*a*	(**5**) (6), *E*-(**6d**) (23), (**8**) (22)
(**1d**)	24 h	*b*	(**5**) (16), *E*-(**6d**) (53), (**8**) (24)
(**1e**)	192 h	*b*	*E*-(**6e**) (54)

[a] Dry acetonitrile, reflux. [b] Dry acetonitrile, room temperature. [c] Dry MeOH, room temperature.

Table 2. (*E*)-β-Enamino amides (**1**) from the amine R^1R^2NH and propiolamide

Compd.	Solvent	Reaction time	M.p. (°C) (from)	Yield (%)
(**1a**)	*a*	24 h	122—124 (*e*)	61
(**1b**)	*b*	1 h	118—120 (*g*)	73
(**1c**)	*c*	40 min	199—201 (*f*)	95
(**1d**)	*d*	1 h	143—144 (*d*)	91
(**1e**)	*e*	1 h	150—152 (*e*)	83

[a] Dry ether, room temperature. [b] Refluxing dry benzene. [c] Refluxing dry ether. [d] Ether. [e] Dichloromethane. [f] Ethanol–ether. [g] Ethanol–water.

Table 3. ^1H N.m.r. spectra of *E*-(**1a**—**e**) in $CDCl_3$ at 60 MHz (TMS as internal standard and *J* in Hz)

Compd.	δ H_A[a]	δ H_X[a]	Other resonances
(**1a**)	7.38	4.53	5.50 (2 H, br s, $CONH_2$);[b] 2.81 (6 H, s, 2 × CH_3)
(**1b**)	7.63	4.96	7.45—7.15 (5 H, m, Ph); 5.25 (2 H, br s, $CONH_2$);[b] 4.28 (2 H, s, $PhCH_2$); 2.70 (3 H, s, CH_3)
(**1c**)	7.58	4.41	5.00 (2 H, br s, $CONH_2$);[b] 3.25 [4 H, m, $N(CH_2)_2$–]; 1.90 (4 H, m, $–CH_2–CH_2–$)
(**1d**)	7.35	4.58	5.00 (2 H, br s, $CONH_3$);[b] 3.18 [4 H, m, $N(CH_2)_2$–]; 1.60 (6 H, m, 3 × CH_2)
(**1e**)	7.30	4.70	5.30 (2 H, br s, $CONH_3$);[b] 3.72 [4 H, m, $O(CH_2–)_2$]; 3.17 [4 H, m, $N(CH_2–)_2$]

[a] Centre of doublet with *J* 13 Hz. [b] Exchange with D_2O.

crystallise from light petroleum (b.p. 60—80 °C) to give *E*-(**6c**) (3.2 g, 75%), m.p. 65—66 °C, as a pale yellow dust, δ_H 4.49 (1 H, s, olefinic), 3.88 (3 H, s, CO_2CH_3), 3.58 (3 H, s, CO_2CH_3), 3.4—3.1 [4 H, m, $N(CH_2)_2$], 2.2—1.7 (4 H, s, CH_2CH_2). U.v. and i.r. spectra are reported in Table 4 and analytical data in Table 5.

(*ii*) In a similar manner, reaction of morpholine and DMAD (20 mmol) yielded *E*-(**6e**) (3.92 g, 86%) as pale yellow prisms, m.p. 48—50 °C (ether); δ_H 4.75 (1 H, s, olefinic), 3.85 (3 H, s, CO_2CH_3), 3.75—3.55 [4 H, m, $O(CH_2)_2$], 3.60 (3 H, s, CO_2CH_3), and 3.25—2.95 [4 H, m, $N(CH_2)_2$].

Reaction of (E)-3-(N,N-*Dimethylamino*)*acrylamide* (**1a**) *with DMAD.*—(*i*) Compound (**1a**) (1.27 g, 11 mmol) and DMAD (1.58 g, 11 mmol) in dry acetonitrile (20 ml) were heated under reflux for 24 h and then evaporated to provide an oily residue. This was extracted with ether and the extract evaporated to yield *E*-(**6a**) (1.52 g, 73%) as pale yellow leaflets, m.p. 81—82 °C (lit.,[8] 83—84.5 °C). U.v., i.r., and ^1H n.m.r. spectral data were identical with an authentic sample described in the literature.[8]

(*ii*) Compound (**1a**) (1.5 g, 13.15 mmol) and DMAD (1.7 ml) in dry MeOH (30 ml) were kept for 15 days. Periodically a sample of the reaction mixture was withdrawn and evaporated under reduced pressure and the i.r. spectrum of the residue recorded (thick film). Absorption (2 100 cm^{-1}) characteristic of propiolamide was often observed but its isolation was not attempted. Evaporation of solvent and work-up of the mixture gave an oil which when chromatographed on alumina using ether as eluant gave *E*-(**6a**) (1.27 g) identical with the sample prepared above.

Reaction of (E)-3-(N-*Benzyl*-N-*methylamino*)*acrylamide* (**1b**) *with DMAD.*—A mixture of (**1b**) (2 g, 10.5 mmol) and DMAD (1.42 g, 10.4 mmol) in dry acetonitrile (50 ml) was refluxed for 24 h during which time it turned from yellow-orange to red and finally dark green. Evaporation of the solvent gave an amine-smelling residue which was chromatographed on silica gel using ether and then ether–methanol (99:1) as eluant. The ether fractions gave (**5**) (0.1 g, 3%) and *E*-(**6b**) (0.52 g, 23%). The ether–methanol fractions gave (**8**) (0.54 g, 24%) and starting amine (0.87 g, 43%). Compound (**5**), m.p. 131—133 °C (MeOH) (lit.,[12] 131—133 °C), $\nu_{max.}$ 1 730 cm^{-1} strong; δ_H 8.0 (2 H, s, ArH), 3.9 (12 H, s, 4 × CO_2CH_3). *E*-(**6b**) Was identical (u.v., i.r., n.m.r., and m.p.) with an authentic sample previously described.[4] Compound (**8**) was identical (physical and spectroscopic properties) with a sample described later.

Reaction of (E)-3-(*Pyrrolidin*-1-*yl*)*acrylamide* (**1c**) *with DMAD.*—(*i*) A mixture of (**1c**) (1.5 g, 10.7 mmol) and DMAD (1.52 g, 10.7 mmol) in dry acetonitrile (75 ml) was refluxed for 24 h. Solvent was evaporated to yield an oil, strongly smelling of pyrrolidine. This oil was slightly soluble in ether and concentration of the ethereal solution yielded (**5**) (0.21 g, 6.5%). The insoluble residue was dissolved in a small amount of dichloromethane and chromatographed on silica gel (100 ml).

Table 4. I.r. (Nujol) and u.v. (EtOH) spectroscopic data

Compd.	$\lambda_{max.}$/nm (ε)	$\nu_{max.}$/cm^{-1}
E-(**1a**)	282 (4.55)	3 425, 3 330, 3 160, 1 640, 1 620, 1 550
E-(**1b**)	288 (4.42)	3 460, 3 300, 3 140, 1 660, 1 635, 1 565
E-(**1c**)	286 (4.47)	3 340, 3 140, 1 650, 1 630, 1 560
E-(**1d**)	287 (4.44)	3 340, 3 140, 1 650, 1 630, 1 560
E-(**1e**)	282 (4.26)	3 340, 3 140, 1 650, 1 630, 1 560
E-(**6c**)	288 (4.38)	1 734, 1 680, 1 560
E-(**6e**)	282 (4.22)	1 738, 1 645, 1 580

Table 5. Analytical data

Compd.	% Found C	% Found H	% Found N	Molecular Formula	% Required C	% Required H	% Required N
(**1a**)	52.5	8.9	24.6	$C_5H_{10}N_2O$	52.6	8.8	24.5
(**1b**)	69.8	7.4	14.9	$C_{11}H_{14}N_2O$	69.4	7.2	14.7
(**1c**)	59.5	8.7	19.8	$C_7H_{12}N_2O$	59.9	8.6	20.0
(**1d**)	62.0	9.2	18.2	$C_8H_{14}N_2O$	62.3	9.2	18.2
(**1e**)	53.6	7.6	17.9	$C_7H_{12}N_2O$	53.8	7.7	17.9
(**6c**)	56.4	7.3	6.1	$C_{10}H_{15}NO_4$	56.3	7.1	6.6
(**6e**)	52.6	6.5	6.0	$C_{10}H_{15}NO_5$	52.4	6.6	6.1

The initial yellow band gave (**5**) as yellow crystals (0.29 g, 7.6%) and *E*-(**6c**) (5.13%) (1:1). A second band eluted with ether gave (**8**) (0.17 g, 7.5%). An equimolar mixture of pure (**5**) and *E*-(**6c**), prepared as described earlier was dissolved in $CDCl_3$ and its n.m.r. ^1H spectrum recorded. The latter was identical with that of the *1:1 mixture*.

(*ii*) Equimolar amounts (7.1 mmol) of (**1c**) and DMAD in dry acetonitrile (50 ml) were refluxed for 6 h. Solvent was evaporated under reduced pressure to give a residue smelling of pyrrolidine. The mixture was extracted with ether to leave (**1c**) (70 mg). Chromatography of the extract through neutral alumina using ether as eluant, yielded successively DMAD, a mixture (0.18 g) of (**5**) and *E*-(**6c**) (1:5), a mixture (70 mg) of (**5**) and *E*-(**6c**) (2:1), and (**5**) (0.1 g). Further elution with 2% EtOH–chloroform gave (**8**) (0.15 g) and more (**1c**) (0.33 g). The overall yields were (**5**) (10%), *E*-(**6c**) (12%), and (**8**) (10%).

Reaction of (E)-3-(*Piperidin*-1-*yl*)*acrylamide* (**1d**) *with DMAD*.—(*i*) Equimolar amounts (2.6 mmol) of (**1d**) and DMAD in dry acetonitrile (20 ml) were refluxed for 24 h to give a deep red solution. Removal of solvent gave a residue (0.85 g), smelling of piperidine, which was dissolved in a little ether–dichloromethane (99:1) and chromatographed through neutral alumina, with the same solvent as eluant. A yellow band yielded oily crystals (0.18 g) and a mixture of (**5**) (5%) and *E*-(**6d**) (23%) (1:4). This was chromatographed on silica gel using toluene and toluene–ether to give *E*-(**6d**) as colourless prisms, m.p. 85—88 °C (lit.,[13] 88—90 °C), u.v. and ^1H n.m.r. data identical with those reported in the literature.[13] Further elution of the alumina column with 20% EtOH–chloroform yielded (**8**) (0.12 g, 22%).

(*ii*) The experiment above was repeated at room temperature for 24 h. The amine-smelling residue was chromatographed through silica gel, eluting with ether–dichloromethane (10:0.1), to give as the main fraction oily crystals (0.54 g) of a mixture of (**5**) (16%) and *E*-(**6d**) (5%) (1:4). The crystals were washed with ether to yield compound (**5**). A brown-orange band on the top of the column was eluted with dichloromethane to afford a solid (0.22 g) which was again chromatographed through silica gel (dichloromethane) to yield (**8**) (0.13 g, 24%).

Reaction of (E)-3-(*Morpholin*-1-*yl*)*acrylamide* (**1e**) *with DMAD*.—Compound (**1e**) (0.5 g, 3.2 mmol) and DMAD (0.454, 3.2 mmol) in dry acetonitrile were kept at room temperature for 8 days with t.l.c. and i.r. monitoring of the reaction. After this time an aliquot of the mixture was carefully evaporated under reduced pressure and the residue subjected to i.r. (liquid film) analysis. The spectrum showed absorption at 2 100st cm^1 (HC≡C) and 3 450, 3 320, and 3 100 (NH_2) cm^{-1} (eliminated propiolamide). Removal of solvent yielded a thick yellow-orange oil, which when taken up in dry ether gave pale yellow crystals and a gummy solid (0.51 g). The u.v. spectra of both showed the same chromophore at 286 nm and t.l.c. showed that crystal spots were still present in the solid and in the mother liquors. Treatment of the solid and crystals with dry ether, chloroform, and methanol yielded *E*-(**6e**) (0.39 g) which was identical with an authentic sample described earlier. Chromatography of the ether mother liquor through neutral alumina (1% MeOH–dichloromethane), yielded more *E*-(**6e**) (0.1 g). The overall yield was 54%.

Dimethyl Pyridine-3,4-*dicarboxylate* (**12**).—A mixture of pyridine-3,4-dicarboxylic acid (Aldrich) (5 g, 30 mmol) suspended in dry MeOH (25 ml) and conc. hydrochloric acid (10 ml) was heated under reflux overnight. Solvent was evaporated, the residue made alkaline with solid sodium carbonate, and the mixture extracted with chloroform. The organic extracts were dried (Na_2SO_4) and evaporated to give the ester (**12**) (3.07 g, 52%) as an oil, $\nu_{max.}$(neat) 1 740 cm^{-1}; δ_H 8.89 (1 H, s, 2-H), 8.66 (1 H, d, *J* 5 Hz, 6-H), 7.37 (1 H, d, *J* 5 Hz, 5-H), and 3.85 (6 H, s, 2 × CO_2CH_3); $\lambda_{max.}$(EtOH) 268 and 212 nm.

Dimethyl Pyridine-3,4-*dicarboxylate* N-*Oxide* (**13**).—Compound (**12**) (2.8 g, 4.3 mmol) in glacial acetic acid (25 ml), and 30% aqueous hydrogen peroxide (15 ml), were stirred overnight at 50—60 °C. Solvent was removed under reduced pressure, the residue made alkaline with 10% sodium hydrogen carbonate solution (excess), and the mixture extracted with chloroform. Evaporation of solvent gave whitish leaflets of (**13**) (1.88 g, 62%), m.p. 110—112 °C (chloroform–ether) (Found: C, 51.1; H, 4.4; N, 6.7. $C_9H_9NO_5$ requires C, 51.2; H, 4.3; N, 6.6%); $\nu_{max.}$ 1 740, 1 720, and 1 610 cm^{-1}; $\lambda_{max.}$ 290 (4.12) and 229 nm (4.05); $\delta_H(CDCl_3)$ 8.18 (1 H, s, 2-H), 8.12 (1 H, dd, *J* 7 and 2, 6-H), 7.56 (1 H, d, *J* 7, 5-H), 3.82 (3 H, s, CO_2CH_3), and 3.84 (3 H, s, CO_2CH_3).

Rearrangement of Compound (**13**) *with Acetic Anhydride: Dimethyl* 1,2-*Dihydro*-2-*oxopyridine*-3,4-*dicarboxylate* (**8**).—A solution of compound (**13**) (1.14 g, 5.39 mmol) in acetic anhydride (10 ml) was refluxed overnight. Solvent was removed under reduced pressure, the residue taken up with water, and the mixture extracted with chloroform. Evaporation of the extract gave a mixture (1.2 g) of (**8**) and (**13**). Chromatography through silica gel eluting with ether yielded (**8**) (0.14 g, 12%), m.p. 148—150 °C (chloroform–ether) (Found: C, 50.2; H, 4.3; N, 6.4. $C_9H_9NO_5 \cdot 0.25H_2O$ requires C, 50.1; H, 4.2; N, 6.5%); $\lambda_{max.}$ 302 (3.66) and 261 nm (4.16); $\nu_{max.}$ 3 200—2 500br, 1 740, 1 660, and 1 615 cm^{-1}; δ_H 9.5 (1 H, br, NH), 8.10 (1 H, s, 6-H), 6.50 (1 H, s, 3-H), 3.80 (3 H, s, CO_2CH_3), and 3.90 (3 H, s, CO_2CH_3). Elution with acetone gave a mixture (50 mg) of (**8**) and (**13**) (1:1) and further (**13**) (0.73 g).

References

1 J. Szmuszkovicz, *Adv. Org. Chem.*, 1963, **14**, 1; K. Blaha and O. Cervinka, *Adv. Heterocycl. Chem.*, 1966, **6**, 146; E. A. Cook, 'Enamines: Synthesis, Structure and Reactions,' Marcel Dekker, New York, 1969.

2 S. F. Dyke, 'The Chemistry of Enamines,' Cambridge University Press, 1973; D. N. Reinhoudt, *Adv. Heterocycl. Chem.*, 1987, **21**; P. W. Hickmott, *Tetrahedron*, 1982, **38**, 2050; *ibid.*, p. 3363; *ibid.*, 1984, **40**, 2989.

3 R. M. Acheson, N. D. Wright, and P. A. Tasker, *J. Chem. Soc., Perkin Trans. 1*, 1972, 1918.

4 R. M. Acheson and G. Paglietti, *J. Chem. Soc., Perkin Trans. 1*, 1979, 591.

5 R. M. Acheson and G. Paglietti, *J. Chem. Res.*, 1981, (*S*), 306; (*M*), 3537.

6 R. M. Acheson, G. Paglietti, and P. A. Tasker, *J. Chem. Soc., Perkin Trans. 1*, 1974, 2496.

7 R. M. Acheson, A. R. D. Knott, D. J. M. Lucas, P. A. Tasker, and G. Paglietti, *J. Chem. Soc., Perkin Trans. 1*, 1980, 81.

8 R. Huisgen, K. Herbig, A. Siegl, and H. Hubner, *Chem. Ber.*, 1966, **99**, 2526.

9 J. E. Dolfini, *J. Org. Chem.*, 1965, **30**, 1298.

10 M. V. George, S. K. Khetan, and R. K. Gupta, *Adv. Heterocycl. Chem.*, 1976, **19**, 279; E. Winterfeldt, *Angew. Chem., Int. Ed. Engl.*, 1967, **6**, 423 and references cited therein.

11 A. A. El-Barbary, S. Carlsson, and S. O. Laweson, *Tetrahedron*, 1982, **38**, 405.

12 H. Bamford and J. L. Simonsen, *J. Chem. Soc.*, 1910, 1904; L. Fieser and M. Peters, *J. Am. Chem. Soc.*, 1932, **54**, 4347.

13 R. Huisgen and K. Herbig, *Liebigs Ann. Chem.*, 1965, **688**, 98.

14 V. Jager, in Houben-Weyl, 'Methoden der Organische Chemie; Alkine, Di-und Polyine, Allene, Kumulene,' George Thieme Verlag, Stuttgart, 1977 and literature cited therein.

15 P. Houdewind and U. K. Pandit, *Tetrahedron Lett.*, 1974, 2359; M. S. Manhas, J. W. Brown, U. K. Pandit, and P. Houdewindt, *Tetrahedron*, 1975, **31**, 1325; S. A. G. de Graaf and U. K. Pandit, *ibid.*, 1973, **29**, 2141, 4263; *ibid.*, 1974, **30**, 1115; U. K. Pandit and S. A. G. de Graaf, *Chem. Commun.*, 1972, 659.
16 C. B. Kanner and U. K. Pandit, *Tetrahedron*, 1982, **38**, 3597.
17 V. Boekelheide and W. L. Lehn, *J. Org. Chem.*, 1961, **26**, 428.
18 A. Kirpal, *Monatsh. Chem.*, 1899, **20**, 177.
19 W. B. Truce and G. J. W. Tichenor, *J. Org. Chem.*, 1972, **37**, 2391.

Received 8*th June* 1988; *Paper* 8/02302F