Reactions of 1,1-Diamino-2-nitroethylenes with Dimethyl Acetylenedicarboxylate

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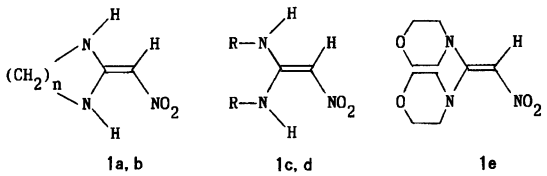
Synopsis. 1,1-Diamino-2-nitroethylenes reacted with dimethyl acetylenedicarboxylate (**2**) to give an electrophilic adduct (dimethyl 2-[(2-imidazolidinylidene)nitromethyl]-2-butenedioate) as well as cyclocondensation products derived from the electrophilic adducts. The reaction of 1,1-dimorpholino-2-nitroethylene with **2** afforded dimethyl 2-(2,2-dimorpholino-1-nitroethenyl)-2-butenedioate or dimethyl 2-(dimorpholinomethylene)-3-(nitroethylene)butanedioate derived from the [2+2] cycloadduct.

1,1-Diamino-2-substituted ethylenes with an electron-withdrawing group, such as a nitro, acyl, or alkoxycarbonyl group, are known to possess only moderate reactivity as enamines, due to the two electron-donating amino groups and an electron-withdrawing group.[1—3] Therefore, 1,1-diamino-2-substituted ethylenes have been used as useful synthetic intermediates for heterocyclic compounds.[4—6] In a previous paper, one of the authors reported that the 1,1-diamino-2-nitroehtylenes reacted with olefins bearing an electron-withdrawing group and aldehydes to give products arising from Michael-type and aldol adducts.[7] The reaction of the 1,1-diamino-2-nitroethylenes with electron-deficient alkynes is also of interest, since it may afford either a [2+2] cycloadduct[8] or an electrophilic adduct.[9] Huang et al., reported that 1,1-diamino-2-aroylethylenes and 2-substituted 1-amino-1-alkylthioethylenes reacted with dimethyl acetylenedicarboxylate to give imidazopyridines[9] and thiazolopyridines[10] via an addition reaction followed by cyclocondensation.

In this paper we report on results concerning the reaction between 1,1-diamino-2-nitroethylenes **1a**—**e** and dimethyl acetylenedicarboxylate (**2**) (Chart 1).

Results and Discussion

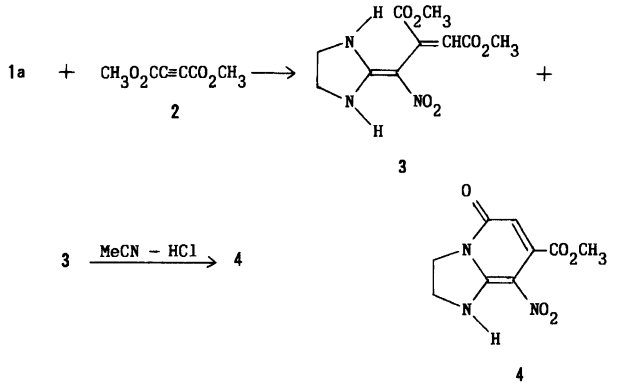
The reaction of **1a** with **2** in methanol gave an electrophilic adduct **3** and its cyclization product **4** in 29 and 42% yields. Isolated **3** gave **4** in an 87% yield upon refluxing for 4 h in acetonitrile containing a catalytic amount of concentrated hydrochloric acid (Eq. 1).



1a, b **1c, d** **1e**

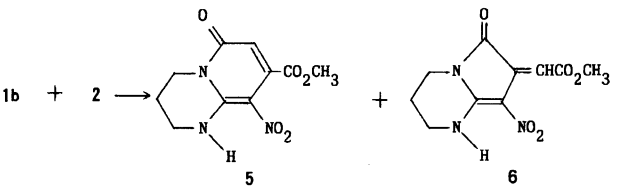
a : $n = 2$ **c** : $R = CH_3$
b : $n = 3$ **d** : $R = PhCH_2$

Chart 1.



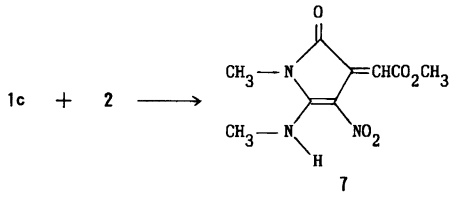
(1)

In the reaction of **1b** with **2** under similar conditions, compounds **5** and **6**, arising from an electrophilic addition followed by cyclocondensation, were obtained in 12—58% and 17—29% yields, respectively (Eq. 2).



(2)

In the reactions of acyclic 1,1-diamino-2-nitroethylenes **1c** and **1d** with **2**, the former afforded a 2-pyrrolin-5-one derivative **7** in 38% yield (Eq. 3),



(3)

whereas the latter gave a mixture of decomposition products. Such a difference may be attributable to the lower stability of the reaction products of the latter. In contrast with β-nitro enamines, which reacted with **2** to give exclusively [2+2] cycloadducts and its ring cleavage products,[8] the reaction of cyclic and acyclic 1,1-diamino-2-nitroethylenes **1a**, **1b**, and **1c** (except for **1d**) with **2** proved to give exclusively the electrophilic adducts and their cyclocondensation products. The results are listed in Table 1.

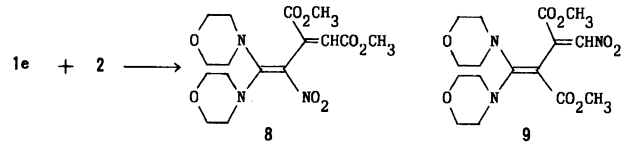
The structure of **3** was confirmed by the presence of the $^{13}CH=$ signal at 121.28 ppm in the ^{13}C NMR spectrum, as well as other spectral data. Compound **4** was

Table 1. Reaction of **1** with Dimethyl Acetylenedicarboxylate

	Solvent	React temp/°C	React time/h	Product	Yield/%		
1a	MeOH	Bp	2	**3**	29	**4**	42
1b	MeOH	R.T.	15	**5**	58	**6**	17
1b	MeCN	Bp	3	**5**	12	**6**	29
1c	MeOH	R.T.	24	**7**	38		
1e	MeOH	Bp	15	**8**	65	**9**	Trace
1e	MeCN	50	0.5	**8**	Trace	**9**	62

formed by a ring closure along with an elimination of methanol from **3**; its structure was confirmed by comparing its spectral data with those of structurally analogous compounds.[10] Compound **4** also reacted with copper(II) acetate to give a Cu complex; its structure proved to be of the N–Cu···O–N type, due to a lack of νNH and $\nu_{as}NO_2$ in the IR spectrum. Compound **6** was an isomer of **5**; a νC=O of its amide carbonyl group in the IR spectrum and its ^{13}C NMR signal was observed in the higher wave-number region and in a lower magnetic field than those of **5**, respectively. From these data, compound **6** was anticipated to possess a five-membered lactam ring. The structure of **7** was also presumed by comparing its spectral data with those of **6**.

1,1-Dimorpholino-2-nitroethylene (**1e**), lacking a hydrogen on the nitrogen, reacted with **2** in methanol to give an electrophilic adduct **8** in 68% yield; the reaction in acetonitrile gave a brownish-red compound **9** in a 62% yield, which was considered to be produced by a [2+2] cycloaddition, followed by a ring opening (Eq. 4).



(4)

Compound **9** was also obtained exclusively from the same reaction in such aprotic solvents as acetone, dichloromethane, and benzene. On the other hand, in the reaction of **1a**, **1b**, and **1c** with **2** in acetonitrile, no adducts corresponding to the compound **9** were isolated. Therefore, the formation of compound **9** from **1e** may be attributed to a specific solvent effect of the aprotic solvents. The results are listed in Table 1. The structure of **8** was also presumed based on an elemental analysis, and comparing its spectral data with **3**. Compound **9** was an isomer of **8**; its νC=C and $\nu_{as}NO_2$ in the IR spectrum were observed in the low wavenumber region of 1554 and 1534 cm^{-1}, compared with 1606 and 1554 cm^{-1} of **8**, similar to that of **1e**, which was observed as an absorption at 1516 cm^{-1}. The UV spectrum showed an intense band at 446 nm (ε 14000), which was red-shifted by 77 nm, compared with that of **8**, which appeared at 369 nm (ε 14000). Such a red-shift of the absorption band may be attributed to a push-pull effect between the electron-donating amino groups and the electron-withdrawing nitro group through the diene.[12] These spectral data appear to support the structure of **9** shown in Eq. 4.

Experimental

The melting points are not corrected. The ^{1}H NMR and ^{13}C NMR spectra were recorded with a Hitachi R-24B or a JEOL GSX-400 instrument using TMS as an internal standard, respectively. The IR and UV spectra were recorded with a Hitachi 270-50 and a Hitachi 124 spectrometer, respectively. Elemental analyses were performed at the Microanalytical Laboratory of Kyoto university. 1,1-Diamino-2-nitroethylene **1** were prepared according to the literature.[1,11]

General Procedure for the Reaction of 1 with Dimethyl Acetylenedicarboxylate (2). A solution containing **1** (2 mmol) and **2** (2.2 mmol) in a solvent (10 ml) was stirred under suitable conditions. After the solvent was removed by a rotary evaporator the residue was separated by fractional crystallization and/or silica-gel column chromatography. The results are summarized in Table 1.

Dimethyl 2-[(2-Imidazolidinylidene)nitromethyl]-2-butenedioate (3): Compound **3** was obtained as white crystals by fractional recrystallization from ethanol. Mp 195—196 °C; IR (KBr) 3368m, 3268m, 1734vs, 1714vs, 1622s, 1582vs, 1546s, and 1344vs cm^{-1}; UV (EtOH) λ/nm ($10^{-4}\varepsilon$) 342 (1.0); ^{1}H NMR (DMSO-d_6) δ=3.70 (m, 10H), 6.07 (s, 1H), and 8.60 (br, 2H); ^{13}C NMR (DMSO-d_6) δ= 43.50 (NCH_2CH_2N), 51.49 (OCH_3), 51.86 (OCH_3), 106.19 (=CNO_2), 121.28 (=CH), 138.08 (=$\underline{C}(CO_2CH_3)$), 159.08 (C-(N)N), 165.31 (C(O)O), and 166.23 (C(O)O). Found: C, 44.26; H, 4.71; N, 15.36%. Calcd for $C_{10}H_{13}N_3O_6$: C, 44.28; H, 4.83; N, 15.49%.

Methyl 8-Nitro-1,2,3,5-tetrahydro-5-oxoimidazo-[1,2-*a*]pyridine-7-carboxylate (4): Compound **4** was isolated as yellow crystals by silica-gel column chromatography (MeCN) from the filtrate of **3**. Mp 200—201 °C; IR (KBr) 3376m, 1724vs, 1682vs, 1622vs, 1572vs, and 1346vs cm^{-1}; UV (EtOH) λ/nm ($10^{-4}\varepsilon$) 259 (0.6), 303 (0.4), and 366 (1.7); ^{1}H NMR (DMSO-d_6) δ=3.82 (s, 2H), 4.03 (m, 4H), 5.78 (s, 1H), and 9.54 (br, 1H); ^{13}C NMR (DMSO-d_6) δ=43.41 (NCH_2), 43.84 (NCH_2), 52.84 (OCH_3), 106.88 (=CH), 109.46 (=CNO_2), 141.01 (=$\underline{C}(CO_2CH_3)$), 151.93 (=C-(N)N), 159.05 (O=CN), and 165.63 (C(O)O). Found: C, 45.21; H, 3.61; N, 17.57%. Calcd for $C_9H_9N_3O_5$: C, 45.19; H, 3.79; N, 17.56%.

The isolated **3** (2 mmol) was refluxed in 10 ml of acetonitrile containing a drop of concentrated hydrochloric acid for 4 h to give **4** in an 87% yield. Cu complex of **4**; Mp 264—266 °C (decomp); IR (KBr) 1722vs, 1680vs, 1600vs, and 1324vs cm^{-1}.

Methyl 1, 3, 4, 6- Tetrahydro- 9- nitro- 6- oxo- 2*H*-pyrido[1,2-*a*]pyrimidine-8-carboxylate (5): Compound **5** was obtained as yellow crystals by silica-gel column chromatography (dichloromethane–acetone 5 : 1). Mp 177—178 °C; IR (KBr) 3224m, 1740vs, 1694vs, 1592s, 1580vs, and 1342vs cm^{-1}; UV (EtOH) λ/nm ($10^{-4}\varepsilon$) 256 (0.6), 305 (0.4), and 382 (1.8); ^{1}H NMR (DMSO-d_6) δ=2.13 (m, 2H), 3.66 (m, 2H), 3.87 (s, 3H), 4.05 (m, 2H), 5.88 (s, 1H),

and 10.24 (br, 1H); ^{13}C NMR (DMSO-d_6) δ=18.01 (CH_2), 38.62 (NCH_2), 39.37 (NCH_2), 52.33 (OCH_3), 105.59 (=CH), 110.59 (=CNO_2), 140.99 (=$\underline{C}(CO_2CH_3)$), 149.70 (=C(N)N), 159.24 (O=CN), and 165.41 (C(O)O). Found: C, 47.36; H, 4.36; N, 16.51%. Calcd for $C_{10}H_{11}N_3O_5$: C, 47.44; H, 4.37; N, 16.59%.

Methyl 1, 2, 3, 4, 6, 7- Hexahydro- 8- nitro- 6- oxopyrrolo[1,2-*a*]pyrimidine-7-ylideneacetate (6): Compound **6** was separated as yellow crystals by silica-gel column chromatography (dichloromethane–acetone 5 : 1) from **5**. Mp 166—168 °C; IR (KBr) 3292m, 1750vs, 1718vs, 1670vs, 1638vs, 1532vs, and 1316vs cm^{-1}; UV (EtOH) λ/nm ($10^{-4}\varepsilon$) 358 (1.6); ^{1}H NMR (DMSO-d_6) δ=2.05 (m, 2H), 3.60 (m, 4H), 3.69 (s, 3H), 6.90 (s, 1H), 9.90 (br, 1H); ^{13}C NMR (DMSO-d_6) δ=18.57 (CH_2), 36.83 (NCH_2), 40.34 (NCH_2), 51.95 (OCH_3), 105.46 (=CNO_2), 115.75 (=CH), 126.33 (=$\underline{C}$(CO)), 152.99 (=C(N)N), 161.79 (O=CN), and 166.84 (C(O)O). Found: C, 47.46; H, 4.21; N, 16.51%. Calcd for $C_{10}H_{11}N_3O_5$: C, 47.44; H, 4.37; N, 16.59%.

Methyl 1-Methyl-2-methylamino-3-nitro-5-oxo-2-pyrrolin-4-ylideneacetate (7): Compound **7** was obtained as yellow crystals by silica-gel column chromatography (dichloromethane–acetone 4 : 1). Mp 154—155 °C; IR (KBr) 3130w, 1760vs, 1722s, 1664vs, 1646vs, 1538s, and 1320vs cm^{-1}; UV (EtOH) λ/nm ($10^{-4}\varepsilon$) 232 (1.3) and 363 (1.6); ^{1}H NMR ($CDCl_3$) δ=3.45 (d, J=6 Hz, 3H), 3.48 (s, 3H), 3.82 (s, 3H), 7.20 (s, 1H), and 10.3 (br, 1H); ^{13}C NMR (DMSO-d_6) δ=28.71 (NCH_3), 31.40 (NCH_3), 51.78 (OCH_3), 113.43 (=CNO_2), 116.37 (=CH), 124.95 (=$\underline{C}$(CO)), 156.65 (=C(N)N), 163.17 (O=CN), and 166.71 (C(O)O). Found: C, 44.79; H, 4.50; N, 17.44%. Calcd for $C_9H_{11}N_3O_5$: C, 44.81; H, 4.59; N, 17.42%.

Dimethyl 2-(2,2-Dimorpholino-1-nitroethenyl)-2-butenedioate (8): Compound **8** was separated as yellow crystals by silica-gel column chromatography (dichloromethane–acetone 3 : 1). Mp 178—179 °C; IR (KBr) 1726s, 1712vs, 1606m, 1554vs, and 1328s cm^{-1}; UV (EtOH) λ/nm ($10^{-4}\varepsilon$) 291 (0.8) and 369 (1.4); ^{1}H NMR ($CDCl_3$) δ=3.42 (s, 3H), 3.50 (s, 3H), 3.68 (m, 8H), 3.86 (m, 8H), and 6.09 (s, 1H); ^{13}C NMR ($CDCl_3$) δ=50.09 (NCH_2), 50.83 (NCH_2), 51.56 (OCH_3), 53.01 (OCH_3), 65.44 (OCH_2), 65.54 (OCH_2), 109.04 (=CNO_2), 116.48 (=CH), 142.77 (=C), 165.66 (=C(N)-N), 165.66 (C(O)O), and 167.45 (C(O)O). Found: C, 49.75; H, 6.03; N, 10.85%. Calcd for $C_{16}H_{23}N_3O_8$: C, 49.86; H, 6.01; N, 10.90%.

Dimethyl 2- (Dimorpholinomethylene)- 3- (nitro methylene)butanedioate (9): Compound **9** was obtained as brownish-red crystals by silica-gel column chromatography (dichloromethane–acetone 3 : 1). Mp 165—166 °C; IR (KBr) 1724vs, 1662vs, 1554vs, 1534vs, and 1316vs cm^{-1}; UV (EtOH) λ/nm ($10^{-4}\varepsilon$) 247 (1.3), 303 (1.0), and 446 (1.4); ^{1}H NMR ($CDCl_3$) δ=3.49 (s, 3H), 3.52 (s, 3H), 3.60 (m, 8H), 3.79 (m, 8H), and 6.80 (s, 1H); ^{13}C NMR ($CDCl_3$) δ=50.69 (NCH_2), 50.80 (NCH_2), 51.46 (OCH_3), 53.24 (OCH_3), 65.95 (OCH_2), 66.22 (OCH_2), 84.57 ($\underline{C}$=C-(N)N), 123.36 (=$CHNO_2$), 144.68 ($\underline{C}$=CNO_2), 166.64 (=C-(N)N), 169.04 (C(O)O), and 170.96 (C(O)O). Found: C, 49.80; H, 5.91; N, 10.86%. Calcd for $C_{16}H_{23}N_3O_8$: C, 49.86; H, 6.01; N, 10.90%.

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