Reaction of 1,8-Naphthalenediamine with Dimethyl and Diethyl Acetylenedicarboxylates

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1,8-Naphthalenediamine reacted with dimethyl and diethyl acetylenedicarboxylates, giving rise to tetrahydronaphtho[1,8-*ef*]diazepinones (**2**), dihydroperimidines (**3**) and bis(enamino)fumarates (**4**). The relative yields of **3** and **4** depended on the reaction conditions, while products **2** were always very minor. Products **4**, the yields of which increased considerably in the presence of a large excess of the acetylenes, underwent cyclization at 230 °C leading to quinolinoquinolinediones.

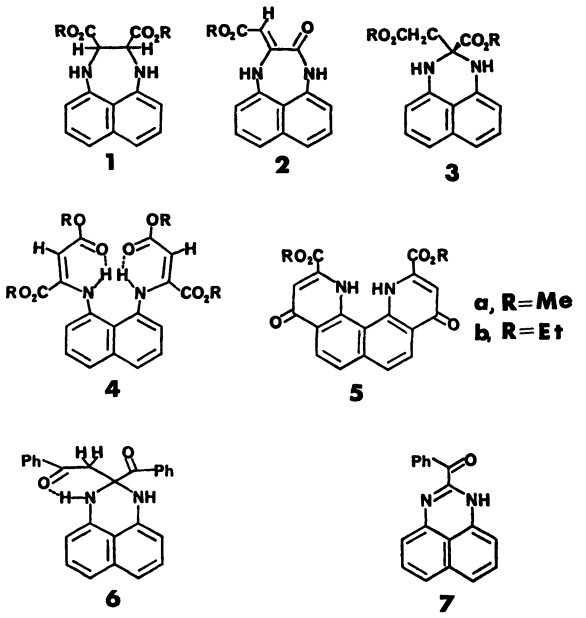
The reaction of amines with acetylenic esters has been investigated in detail.[1] In general, primary monoamines react with acetylenedicarboxylates, giving rise chiefly to the enaminofumarates. In the reaction of aromatic diamines such as *m*-, *p*-phenylenediamines, and 2,2'-biphenyldiamine with dimethyl acetylenedicarboxylate (DMAD), the corresponding bisenamines are formed. Aromatic *vicinal* diamines such as *o*-phenylenediamine and 2,3-naphthalenediamine, however, react with DMAD to give tetrahydroquinoxaline derivatives. On the other hand, in the reaction of 1,8-naphthalenediamine (NDA) with diethyl acetylenedicarboxylate (DEAD), it has been reported that a unique 1 : 1 adduct, 2,3-bis(ethoxycarbonyl)-1,2,3,4-tetrahydronaphtho[1,8-*ef*][1,4]diazepine (**1b**) is formed as a main product, in addition to 3-ethoxycarbonylmethylene-1,2,3,4-tetrahydronaphtho [1,8-*ef*] [1,4] diazepin-2-one (**2b**) which is a product analogous to those from the reactions of *vicinal* diamines.[2]

In connection with the study on the reaction of *peri*-substituted naphthalenes, bis(methoxycarbonyl)tetrahydronaphtho[1,8-*ef*]diazepine (**1a**) was required. Then, the synthesis of **1a** by the reaction of NDA with DMAD was attempted according to the reported method.[2] However, there was found no **1a** in the products, and **2a** was only very minor. The reaction of NDA with DEAD instead of DMAD was also attempted, but the results were similar to those for DMAD, and no **1b** was obtained. We, therefore, have studied the reactions of NAD with DMAD and DEAD in detail.

Results and Discussion

There were found two products besides **2** in the reactions. The products were identified by spectroscopic and elementary analyses as a 1 : 1 adduct, 2-methoxycarbonyl-2-methoxycarbonylmethyl-1,2,3-dihydro-1*H*-perimidine (**3a**) and a 1 : 2 adduct, 2,2'-(1,8-naphthylenediimino)difumarate (**4a**) for the reaction with DMAD, and their ethoxycarbonyl derivatives (**3b**) and (**4b**) for the reaction with DEAD. The spectroscopic data of **2a**, **3a**, and **4a** are summarized in Table 1. Identity of the IR spectrum of **3b** with that of **1b** shown in Ref. 2 indicates that **3b** was erroneously assigned as **1b**, one of the structural isomers of **3b**.

In order to elucidate the pathway of the reaction, the equimolar ethanol solutions of NDA and DMAD or DEAD were mixed under several reaction conditions. As shown in Table 2, products **2** were very minor under all the reaction conditions adopted here, while the yields of **3** and **4** depended appreciably on the conditions. Main process of the reaction is the formation of 1 : 1 adducts **3**, but the formation of 1 : 2 adducts **4** becomes efficient in the presence of a large excess of the acetylenes (Conditions **A**). The reactions probably proceed through intermediate monoenamines, although they could not be isolated under our experimental conditions. The results indicate that the intermediates undergo cyclization to **3** in preference to **2** in contrast to the analogous intermediates from *vicinal* diamines which cyclize almost exclusively to the corresponding amides like **2**.[1] At room temperature, the intramolecular cyclization of the intermediates was slow enough to compete with the formation of **4** by the reaction with the second acetylene molecule, but it became a sole process at the refluxing temperature of ethanol (Conditions **D**).



The enamine adducts formed in the reaction of primary aromatic amines with acetylenic esters were usually fumarates and underwent cyclization leading to quinolone derivatives.[1] The IR spectrum of **4a** showed two distinctive absorption bands at 1740 and 1680 cm^{-1}, corresponding to a free and a chelated ester group respectively, and a broad band at 3280 cm^{-1} due to hydrogen-bonded N–H. The IR spectrum of **4b** also showed similar bands. These bands indicate that

TABLE 1. SPECTROSCOPIC DATA OF **2a**, **3a**, AND **4a**

Product	^{1}H NMR[a] δ from TMS	^{13}C NMR[a] δ from TMS	IR (KBr) ν_{max}/cm^{-1}	MS, *m/e* (relative int.)	UV (MeOH) λ_{max}/nm (ϵ_{max})
2a	3.703 (s, 3H, OMe), 5.888 (s, 1H, =CH) 6.877 (d, *J*=7.3 Hz, 1H) 7.174 (d, *J*=7.3 Hz, 1H) 7.332 (dd, *J*=7.3 Hz, *J*=8.0 Hz, 1H) 7.350 (dd, *J*=7.3 HZ, *J*=8.0 Hz, 1H) 7.447 (d, *J*=8.0 Hz, 1H) 7.489 (d, *J*=8.0 Hz, 1H) 10.784 (s, 1H, NH), 10.981 (s, 1H, NH) (aromatic protons)	51.19 (OMe), 93.73 (=CH) 114.12, 114.53, 122.65, 123.62, 126.75 (×2) (aromatic CH) 115.28, 133.34, 136.18 (×2) (aromatic *q*.C) 146.82 (=CNH) 159.71 (amide C=O) 169.75 (ester C=O)	3200 (weak, NH) 1670, 1630 (C=O) 1430 (Me) 1280, 1230 (C-O-C) 805, 745	268 (M$^+$, 50.7) 236 (77.5) 208 (47.0) 153 (63.5) 44 (100.0)	404 (3500) 332 (26800) 324 (sh) 229 (41000)
3a	3.093 (s, 2H, CH_2), 3.547 (s, 3H, OMe) 3.687 (s, 3H, OMe), 6.202 (s, 2H, NH) 6.622 (d, *J*=7.3 Hz, 2H) 7.085 (d, *J*=7.5 Hz, 2H) 7.188 (dd, *J*=7.3 Hz, *J*=7.5 Hz, 2H) (aromatic protons)	60.11 (CH_2), 68.10 (OMe) 68.70 (OMe), 85.82 (HNCNH) 122.18, 133.64, 143.66 (aromatic CH) 129.03, 151.19, 156.47 (aromatic *q*.C) 186.77 (C=O), 188.95 (C=O)	3350 (strong, NH) 1720 (C=O), 1600, 1430, 1360 (Me) 1270, 1210 (C-O-C) 810, 760	300 (M$^+$, 14.0) 241 (91.2) 181 (74.2) 149 (100.0)	343 (10900) 330 (10800) 322 (sh) 232 (41400)
4a	3.605 (s, 6H, OMe), 3.646 (s, 6H, OMe) 5.408 (s, 2H, =CH) 6.978 (d, *J*=6.8 Hz, 2H) 7.455 (dd, *J*=6.8 Hz, *J*=8.2 Hz, 2H) 7.786 (d, *J*=8.2 Hz, 2H) 10.262 (s, broad, 2H, NH) (aromatic protons)	67.18 (OMe), 68.90 (OMe) 110.3 (=CH) 138.39, 142.80, 143.24 (aromatic CH) 139.99, 153.20, 153.83 (aromatic *q*.C) 165.10 (=CNH) 181.13 (C=O), 186.14 (C=O)	3280 (broad, NH, chelated) 1740(C=O), 1680 (C=O, chelated), 1610, 1600 (C=C), 1440, 1360 (Me), 1270, 1220 (C-O-C) 820, 760	442 (M$^+$, 6.9) 383 (100.0) 264 (29.4) 205 (53.9)	340 (sh) 329 (15200) 233(31700)

a) The solvents are DMSO-d_6 for **2a** and acetone-d_6 for **3a** and **4a**.

TABLE 2. RELATIVE YIELDS OF THE PRODUCTS IN THE REACTIONS OF NDA WITH AN EQUIMOLAR AMOUNT OF DMAD OR DEAD IN ETHANOL

Acetylenic diester	Reaction conditions[a]	Product (Relative yield/%)[b]		
DMAD	Conditions **A**	**2a** (1)	**3a** (39)	**4a** (60)
DMAD	Conditions **B**	**2a** (1)	**3a** (70)	**4a** (29)
DMAD	Conditions **C**	**2a** (3)	**3a** (86)	**4a** (11)
DMAD	Conditions **D**	**2a** (0)	**3a** (100)	**4a** (0)
DMAD	Conditions **A**	**2b** (1)	**3b** (78)	**4b** (21)
DMAD	Conditions **C**	**2b** (3)	**3b** (94)	**4b** (3)

a) The reaction conditions are as follows: Conditions **A**, dropwise addition of NDA to the acetylene over 1 h at room temperature; Conditions **B**, similar to Conditions **A** but quick addition; Conditions **C**, dropwise addition of the acetylene to NDA over 1 h at room temperature; Conditions **D**, similar to Conditions **C** but at refuxing temperature of ethanol. b) Based on the molar ratio of the isolated products.

compounds **4** have bis(enamino)fumarate structures with two intramolecular chelates between the N–H and C=O groups. The cyclization of **4a** was attempted by refluxing it in diphenyl ether, and a single product which is slightly soluble in organic solvents was isolated The structure of this product was assigned as 2,11-bis-(methoxycarbonyl) quinolino [7,8-*h*] quinoline - 4,9(1*H*,-12*H*)-dione (**5a**), on the basis of elemental analysis and spectral evidences. Therefore, it was confirmed that **4a** affords a quinolone like other bis(enamino)fumarates. The same is expected to hold for **4b**, although the cyclization was not attempted.

The reaction of NDA with acetylenic esters was found to be quite similar to that with dibenzoylacetylene (DBA). The reaction of NDA with DBA is reported to give a mixture of products consisting of 2-benzoyl-2-phenacyl-2,3-dihydro-1*H*-perimidine (**6**) (9%) and 2-benzoyl-1*H*-perimidine (**7**) (89%).[3] The formation of **7** can be rationalized in terms of loss of one acetophenone molecule from **6**. However, the corresponding perimidines were not formed from **3** under our experimental conditions. It has been reported that two methylene protons of **6** are nonequivalent because of the restricted rotation of the phenacyl group due to the hydrogen-bonding between the N–H and C=O groups.[3] On the other hand, for **3**, the singlet signal for the methylene at around 3 ppm in the ^{1}H NMR spectrum and the strong IR band of the N–H groups at around 3350 cm^{-1} indicated the free rotation of the alkoxycarbonylmethyl group without such chelation. The structural difference between **3** and **6** is very interesting in view of their facility of cyclization, and the chelation in **6** seems to play an important role for its easy conversion to **7**.

Experimental

All melting points were determined on a Mettler FP61 instrument and were uncorrected. ^{1}H NMR and ^{13}C NMR spectra were recorded on a JEOL FX-400 (400.05 MHz for ^{1}H nuclei) and a JEOL FX-90Q (22.50 MHz for ^{13}C nuclei) spectrometer respectively using TMS as an internal standard. Mass, IR and UV spectra were measured with a YHP 595A, a Hitachi 260-30 and a Shimadzu UV-300 apparatus respectively.

Materials. Commercially available NDA was purified by repeated recrystallizations from aqueous ethanol and used immediately after the purification. DMAD and DEAD were purified by distillation under reduced pressure.

Reaction of NDA with DMAD. Ethanol solutions of NDA (1.1 g, 7.0 mmol, 10 ml) and DMAD (1.0 g, 7.0 mmol, 10 ml) were mixed under stirring by the several ways described in Table 2. The mixture was left in a refrigerator (*ca.* −10 °C) overnight, from which **2a** and **4a** precipitated. On treatment of the precipitate with $CHCl_3$ at room temperature, **2a** and **4a** were separated as an undissolved product and a dissolved one respectively. Recrystallization of the undissolved product from ethanol gave pure **2a** as silky red needles; mp>300 °C. Found: C, 67.00; H, 4.55; N, 10.26%. Calcd for $C_{15}H_{12}O_3N_2$: C, 67.16; H, 4.51; N, 10.44%. Recrystallization of the dissolved product from ethanol gave pure **4a** as yellow-brown needles; mp 146 °C. Found: C, 59.66; H, 5.10; N, 6.12%. Calcd for $C_{22}H_{22}O_8N_2$: C, 59.73; H, 5.01; N, 6.33%.

From the concentrated mother liquor kept in a refrigerator for a week, **3a** was obtained as a massive precipitate. Recrystallization of the precipitate from ethanol gave pure **3a** as white needles; mp 99 °C. Found: C, 63.79; H, 5.43; N, 9.09%. Calcd for $C_{16}H_{16}O_4N_2$: C, 63.99; H, 5.37; N, 9.33%.

The spectroscopic data of **2a**, **3a**, and **4a** are shown in Table 1. The yields of **2a**, **3a**, and **4a** were as follows respectively: Conditions **A**, 0.01 g (0.53%), 0.39 g (18.6%), and 0.90 g (29.1%); Conditions **B**, 0.01 g (0.53%), 0.81 g (38.5%), and 0.51 g (16.5%); Conditions **C**, 0.05 g (2.7%), 1.35 g (64.2%), and 0.25 g (8.1%); Conditions **D**, 0 g (0%), 1.70 g (80.9%), and 0 g (0%).

Reaction of NDA with DEAD. The reaction was carried out in the same manner as that with DMAD by using 1.1 g (7.0 mmol) of NDA and 1.2 g (7.0 mmol) of DEAD. Sparingly soluble **2b** precipitated from the reaction mixture. Recrystallization of the precipitate from ethanol gave pure **2b** as red silky needles; mp>300 °C. Found: C, 67.24; H, 5.07; N, 9.59%. Calcd for $C_{16}H_{14}O_3N_2$: C, 68.08; H, 5.00; N, 9.92%. ^{13}C NMR (DMSO-d_6) 14.16 (CH_3), 59.82 (OCH_2), 94.51 (=CH), 114.14, 114.65, 122.67, 123.69, 126.77(doubled) (aromatic CH), 115.15, 133.46, 136.30, 136.34 (aromatic *q*.C), 146.89 (=CNH), 159.93 (CONH), 169.46 (CO_2Et). ^{1}H NMR (DMSO-d_6) δ 1.299 (t, J=7.0 Hz, 3H, CH_3), 4.243 (q, J=7.0 Hz, 2H, OCH_2), 6.009 (s, 1H, =CH), 6.963 (d, J=7.3 Hz, 1H), 7.239 (d, J=7.3 Hz, 1H), 7.387 (dd, J=7.8, 8.1 Hz, 1H), 7.392 (dd, J=7.3, 8.1 Hz, 1H) 7.494 (d, J=8.1 Hz, 1H), 7.546 (d, J=7.8 Hz, 1H) (aromatic protons), 10.841 (s, 1H, NH), 11.038 (s, 1H, NH).

The concentrated mother liquor left in a refrigerator for a week gave a massive precipitate of **3b**. On recrystallization from ethanol, pure **3b** was obtained as white needles; mp 80 °C. Found: C, 65.73; H, 6.11; N, 8.46%. Calcd for $C_{18}H_{20}O_4N_2$: C, 65.84; H, 6.14; N, 8.53%. ^{13}C NMR (acetone-d_6) δ 30.26 ($2CH_3$), 60.11 (CH_2CO), 77.37, 77.83 (OCH_2), 85.74 (HNCNH), 122.15, 133.58, 143.58 (aromatic CH), 129.19, 151.13, 156.58 (aromatic *q*.C), 186.24, 188.19 (C=O). ^{1}H NMR (acetone-d_6) δ 1.039 (t, J=7.1 Hz, 3H, CH_3), 1.254 (t, J=7.1 Hz, 3H, CH_3), 3.079 (s, 2H, CH_2), 4.015 (q, J=7.1 Hz, 2H, OCH_2), 4.168 (q, J=7.1 Hz, 2H, OCH_2), 6.179 (s, 2H, NH), 6.621 (d, J=7.4 Hz, 2H), 7.083 (d, J=8.3 Hz, 2H), 7.188 (dd, J=7.4, 8.3 Hz, 2H) (aromatic protons).

Removal of the solvent from the residual ethanol solution gave a mass which was chromatographed over silica gel. Elution of the column with a mixture (9 : 1) of petroleum ether (boiling range, 30—70 °C) and ether gave **4b** and **2b** as the first and the second eluted compounds respectively. Pure **4b** was obtained by recrystallization from ethanol as yellow needles; mp 92 °C. Found: C, 62.49; H, 6.03; N, 5.58%. Calcd for $C_{26}H_{30}O_8N_2$: C, 62.64; H, 6.07; N, 5.62%. ^{13}C NMR (acetone-d_6) δ 29.93, 30.80 (CH_3), 76.31, 78.37 (OCH_2), 110.28 (=CH), 138.92, 142.85, 143.33 (aromatic CH), 140.60, 153.16, 154.12 (aromatic *q*.C), 165.63 (=CNH), 180.75, 185.89 (C=O). ^{1}H NMR (acetone-d_6) δ 0.879 (t, J=7.1 Hz, 6H, $2CH_3$), 1.232 (t, J=7.1 Hz, 6H, $2CH_3$), 4.041 (q, J=7.1 Hz, 4H, $2OCH_2$), 4.111 (q, J=7.1 Hz, 4H, $2OCH_2$), 5.385 (s, 2H, 2=CH), 6.955 (d, J=6.8 Hz, 2H), 7.432 (dd, J=6.8, 8.4 Hz, 2H), 7.763 (d, J=8.4 Hz, 2H) (aromatic protons), 10.239 (s, broad, 2H, 2NH).

UV, IR, and mass spectra of **2b**, **3b**, and **4b** are similar to those of **2a**, **3a**, and **4a** respectively. The yields of **2b**, **3b**, and **4b** were as follows respectively: Conditions **A**, 0.01 g (0.51%), 0.81 g (35.2%), and 0.41 g (11.7%); Conditions **C**, 0.04 g (2.0%), 1.60 g (69.6%), and 0.08 g (2.3%).

Preparation of 5a. A mixture of **4a** (0.3 g, 0.7 mmol) and diphenyl ether (5 ml) was heated at 230 °C for 30 min. The precipitated product was filtered and treated with ether to give **5a** (0.15 g, 58% yield) as pale yellow foils, which is sparingly soluble in usual organic solvents; mp>300 °C. Found: C, 62.65; H, 3.73; N, 7.16%. Calcd for $C_{20}H_{14}O_6N_2$: C, 63.50; H, 3.73; N, 7.40%. ^{1}H NMR (DMSO-d_6) δ 4.066 (s, 6H, $2OCH_3$), 6.278 (s, broad, 2H, NH), 7.290 (s, 2H, 2=CH), 7.801 (d, J=8.2 Hz, 2H), 8.140 (d, J=8.2 Hz, 2H) (aromatic protons). IR (KBr) ν_{max} 1735 (ester C=O), 1610 (ring C=O), 1540, 1515 (C=C), 1440, 1350 (CH_3), 1215 (C–O–C) cm^{-1}. UV (methanol) λ_{max} (ε_{max}) 393 (13300), 374 (10700), 330 (sh), 322 (12700), 307 (sh), 278 (sh), 271 (sh), 249 (19700), 235 (20600), 221 (sh), 216 (37300) nm.

References

1) M. V. George, S. K. Khetan, and R. K. Gupta, "Advances in Heterocyclic Chemistry" ed by A. R. Katritzky and A. J. Boulton, Academic Press, New York (1976), Vol. 19, pp. 279—371, and the references cited therein.

2) Y. Iwanami, *Nippon Kagaku Zasshi* **83**, 597 (1962).

3) S. Lahiri, M. P. Mahajan, R. Prasad, and M. V. George, *Tetrahedron* **33**, 3159 (1977).