Synthesis of 1,4-Diaminoazaanthraquinone Derivatives

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Recent reports[1] show that *trans,trans*-1,4-bis[ethoxycarbonylamino]-1,3-butadiene **(1)** behaves as an electron-rich diene in cycloadditions with maleic anhydride, tetracyanoethylene, 1,4-naphthoquinone, 5-hydroxy-1,4-naphthoquinone, dimethyl acetylenedicarboxylate and other dienophiles providing a variety of substituted benzenoid systems. We have also utilized this diene in cycloadditions leading to several 1,4-diaminoazaanthraquinone derivatives related to the 1,4-bis[(aminoalkyl)amino]-9,10-anthracenediones, of current interest in cancer chemotherapy[2-6].

Reaction of 5,8-quinolinedione (**2a**; $Y^1 = Y^2 = CH$, $Y^3 = N$) with the diene **1** in dimethylformamide solution at 80 °C gave the deep-red 1,4-diamino product **4a** ($Y^1 = Y^2 = CH$; $Y^3 = N$).

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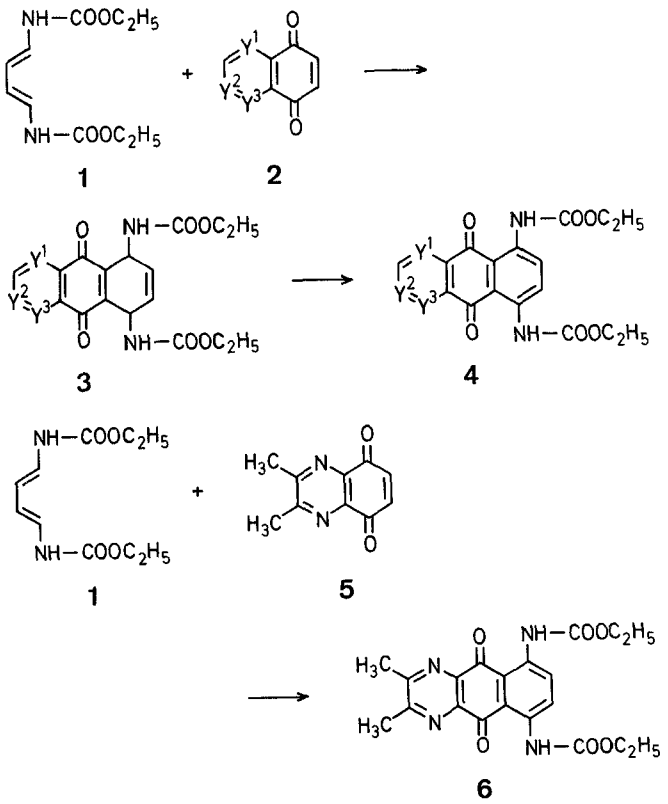
Table. 1,4-Diaminoazaanthraquinone Derivatives

Product No.	Y^1	Y^2	Y^3	Yield [%]	m.p.[a] [°C]	Molecular formula[b]	I.R. (KBr) $\nu_{C=O}$ [cm^{-1}]	^{1}H-N.M.R. ($CDCl_3$, 200 MHz) δ [ppm]	M.S. *m/e* (M^+, 100%)
4a	CH	CH	N	62	256–257°	$C_{19}H_{17}N_3O_6 \cdot 0.5\,H_2O$ (392.4)	1725; 1605	1.39 (2t, 6H, J=7.8 Hz); 4.32 (2q, 4H, J=7.8 Hz); 7.79 (m, 1H); 8.66 (m, 1H); 9.02 (s, 1H); 9.04 (s, 1H); 9.16 (m, 1H)	383
4b	CH	N	CH	56	269–271°	$C_{19}H_{17}N_3O_6$ (383.4)	1725; 1625	1.24 (t, 6H, J=7.8 Hz); 4.17 (q, 4H, J=7.8 Hz); 7.96 (d, 1H, J=5.2 Hz); 8.87 (s, 1H); 8.88 (s, 1H); 9.00 (d, 1H, J=5.2 Hz); 9.44 (s, 1H)	383
4c	N	N	CH	52	240–245° (dec.)	$C_{18}H_{16}N_4O_6$ (384.3)	1730; 1635	1.38 (t, 3H, J=7.8 Hz); 1.39 (t, 3H, J=7.8 Hz); 4.32 (q, 2H, J=7.8 Hz); 4.33 (q, 2H, J=7.8 Hz); 9.11 (s, 2H); 9.77 (s, 1H); 9.79 (s, 1H)	384
6	—	—	—	58	282–284°	$C_{20}H_{20}N_4O_6$ (412.4)	1735; 1635	1.34 (t, 6H, J=7.8 Hz); 2.86 (s, 6H); 4.30 (q, 4H, J=7.8 Hz); 9.04 (s, 2H)	412

[a] All products are crystallized from ethanol/dichloromethane as deep-red, irregular prisms.
[b] Satisfactory microanalyses obtained: C ±0.35, H ±0.05, N ±0.36.



The initial 1:1 cycloadduct **3** was not isolated, apparently undergoing oxidation by atmospheric oxygen to **4** under reaction work-up conditions. Use of 5,8-isoquinolinedione (**2b**; $Y^1=Y^3=CH$; $Y^2=N$) and 2,3-dimethylquinoxalinedione (**5**) in the cycloaddition with **1** gave the corresponding azaanthraquinones **4b** ($Y^1=Y^3=CH$; $Y^2=N$) and **6**, respectively. The physical characteristics of these products are shown in the Table.

5,8-Bis[ethoxycarbonylamino]-1-aza-9,10-anthraquinone (4a; $Y^1=Y^2=CH$, $Y^3=N$); Typical Procedure:

A solution of 5,8-quinolinedione (**2a**; $Y^1=Y^2=CH$, $Y^3=N$; 0.5 g, 0.003 mol), *trans,trans*-1,4-bis[ethoxycarbonylamino]-1,3-butadiene (**1**; 0.6 g, 0.003 mol), and hydroquinone (5 mg) in anhydrous dimethylformamide (7 ml) is kept overnight at 80 °C, stirring being maintained throughout. A deep-red precipitate forms and, after thorough cooling of the reaction mixture (−10 °C), the red product is collected, washed with dry ether, and dried: yield: 0.63 g (62%); m.p. 249–252 °C. It is crystallized from 95% ethanol/dichloromethane as deep-red, irregular prisms; m.p. 256–257 °C.

$C_{19}H_{17}N_3O_6 \cdot 0.5\,H_2O$ (392.4)	calc.	C 58.16	H 4.62	N 10.71
	found	58.11	4.65	10.68

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