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1-Acylamino-1-azadienes as an Alternative to 1-Dimethylamino-1-azadienes in the Preparation of 1,8-Diazaanthracene-2,9,10-triones.

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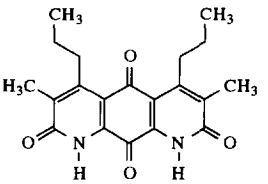
Abstract: Acetylhydrazones of α,β-unsaturated aldehydes behave as 1-azadienes in their reaction with 2,5,8(1*H*)-quinolinetriones, affording 1,8-diazaanthracene-2,9,10-triones, while the corresponding *N*-methyl derivatives are unreactive. In comparison with *N,N*-dimethylhydrazones, acetylhydrazones are less reactive but the yields obtained are similar or higher because of the suppression of side products formed by addition of dimethylamine to the starting quinone.

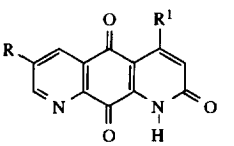
Hetero Diels-Alder reactions[1-5] are gaining widespread acceptance as tools in heterocyclic synthesis. Among the many types of known heterodienes, 1-azadienes are useful starting materials for the preparation of pyridines, quinolines and mono- and diazaanthracenes, among other types of compounds. However, 1-azadienes are less reactive than many other heterodienes due to the combined effects of three factors: a) Low concentration of the reactive species due to *s-cis* - *s-trans* conformational equilibria,[6] imine-enamine tautomerism[7] and isomerization of the diene.[8] b) Loss of the very stable (*ca.* 80 kcal.mol^{-1}) C=N double bond, making the reaction thermodinamically less favourable than other Diels-Alder cycloadditions.[9,10] c) Unsuitable electron density of the diene. The latter factor is crucial and has led to the development of two kinds of 1-azadienes, namely those bearing electron-withdrawing groups on the nitrogen and therefore suitable for "inverse" electron-demand Diels- Alder reactions and those bearing electron-releasing groups on the nitrogen atom, which can be used in "normal" electron-demand reactions. The first class of compounds is represented by the unstable 1-acyl-1-azadienes,[11] their more easily handled 2-cyano derivatives,[10,12] and also by *N*-sulfonyl-1-azadienes.[13] As regards the second type of 1-azadienes, the electron-releasing substituent more commonly employed is the dimethylamino group,[6,14] and thus dimethylhydrazones of α,β-unsaturated aldehydes have been extensively used in heterocyclic syntheses during the last years.[8,15-17] Recently, some 1-(*N*-alky-*N*-acylamino) azadienes have been shown to undergo intramolecular Diels-Alder reactions;[18] 1-*tert*butyldimethyl-silyloxy-1-azadienes are also promising compounds, particularly in that they allow the introduction of substituents in the 2 position of the azadiene system.[19]

During the course of our research into the synthesis of analogues of the natural antifolate antibiotic Diazaquinomycin A **1**[20], we found that monolactam compounds **2**[21] exhibit excellent *in vitro* antitumour activity.[21b,22] Therefore, a more systematic study of this type of diazaquinomycin analogues was planned, using

a synthetic approach based on the hetero Diels-Alder reaction between 2,5,8(1*H*)-quinolinetriones **9** and **10** and 1-azadienes.



1 (Diazaquinomycin A)

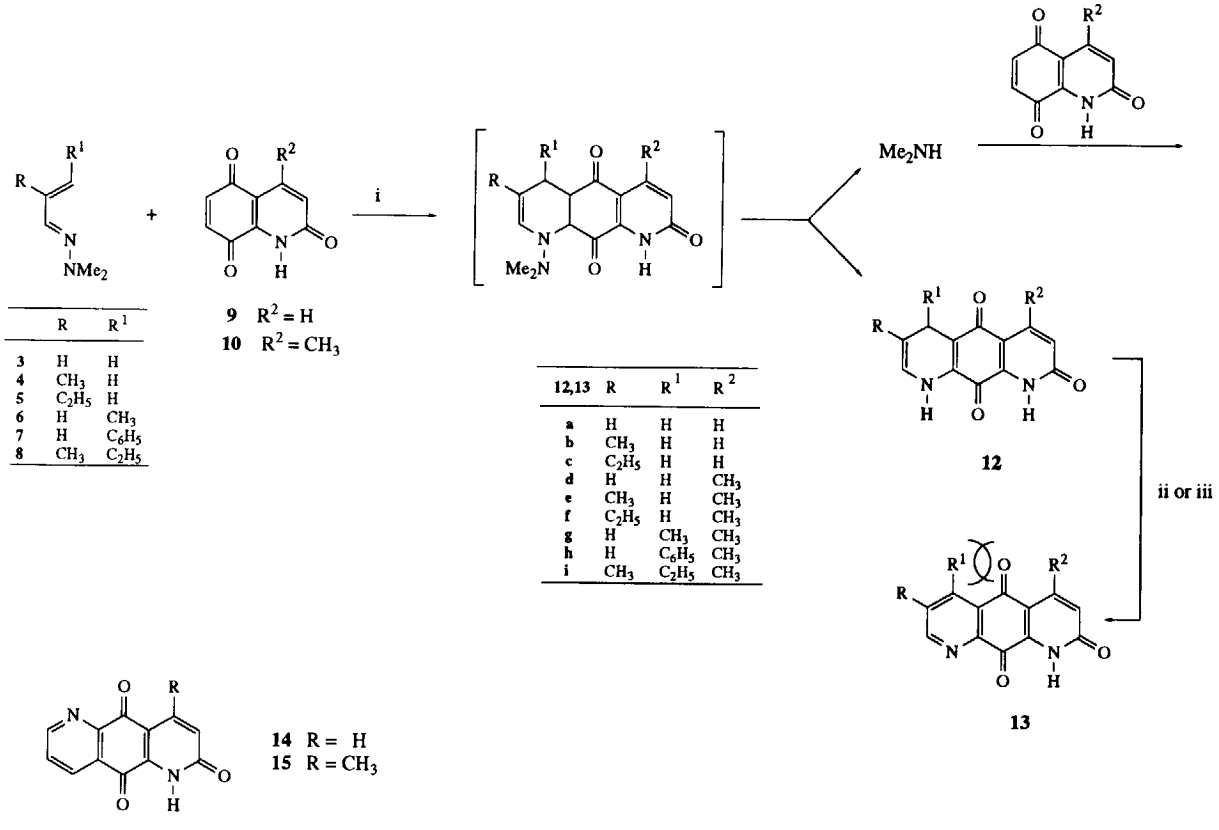


2 R = CH_3, OH
R^1 = H, CH_3

Scheme 1

The 1-dimethylamino-1-azadienes **3-8**, prepared from the corresponding α,β-unsaturated aldehydes using literature procedures,[8] were treated with quinones **9**[23] and **10**.[24] The results obtained in these cycloadditions (Scheme 2) were dependant on the substitution pattern of the azadienes. Thus, compounds **3-5** afforded directly the aromatized adducts **13**, while 1-azadienes **6-8**, bearing substituents on the C_4 position, gave the dihydro derivatives **12**, which could be aromatized in a subsequent step by oxidation with air in refluxing xylene or with manganese dioxide suspended in dichloromethane. The more difficult aromatization of the 5-substituted derivatives **12** can be ascribed to the interaction between the substituent at C_5 and the C_{10} carbonyl group in the planar aromatic structure **13**, which does not exist in the dihydro derivatives. All reactions were completely regioselective, except in the case of the reactions of the less polarized, unsubstituted azadiene **3**, which afforded appreciable amounts of the 1,5-diazaanthracene derivatives **14** (**13a**:**14** = 5:1) and **15** (**13d**:**15** = 4:1). This selectivity was also observed in the reactions of quinone **10** with carbodienes,[25] and can be explained through the combined effects of two factors, namely the electron deficiency created on C_8=O by its conjugation with the C_2=O carbonyl group in the quinone and, on the other hand, the conjugation between C_5=O and the amide nitrogen. These effects leave the C_6=C_7-C_8=O portion of the molecule as an isolated system whose "electrophillic" end is at C_6. In many cases, particularly in the reactions involving quinone **10**, the yields of the cycloadducts were only moderate because of the isolation of substantial amounts of 5-dimethylamino-2,5,8(1*H*)-quinolinetriones (compounds **11**[21a]) due to elimination of dimethylamine from the initial Diels-Alder adduct followed by its addition to the starting quinone. This secondary reaction must be considered as a general problem associated with the use of 1-dimethylamino-1-azadienes with quinones as dienophiles, as shown by our previous observations[21] and those of other workers.[17]

All attempts made to avoid the formation of **11** failed because of the very rapid onset of the cycloaddition, since the dimethylamine could not be eliminated before its addition to **9** or **10**. However, by bubbling an inert gas through the reaction medium, some improvement was achieved in the slower reaction of diene **7** with quinone **10**. Attempts to trap dimethylamine by addition of a Lewis acid also failed because the reaction took a different course, leading to furoquinoline derivatives. Thus, treatment of quinone **10** with diene **7** in the presence of boron trifluoride-ethyl ether afforded **16** as the only product, presumably through a multi-step mechanism involving coordination of the more nucleophillic C_5=O oxygen atom to the Lewis acid, followed by attack of the more nucleophillic end of the diene to the conjugated C_7 position and subsequent 5-*exo-trig* ring closure (Scheme 3). The *cis* stereochemistry of **16** can be deduced from the value of the coupling constant between H-2 and H-3 (J = 7.8 Hz). Formation of related condensed furan systems in the Diels-Alder reactions



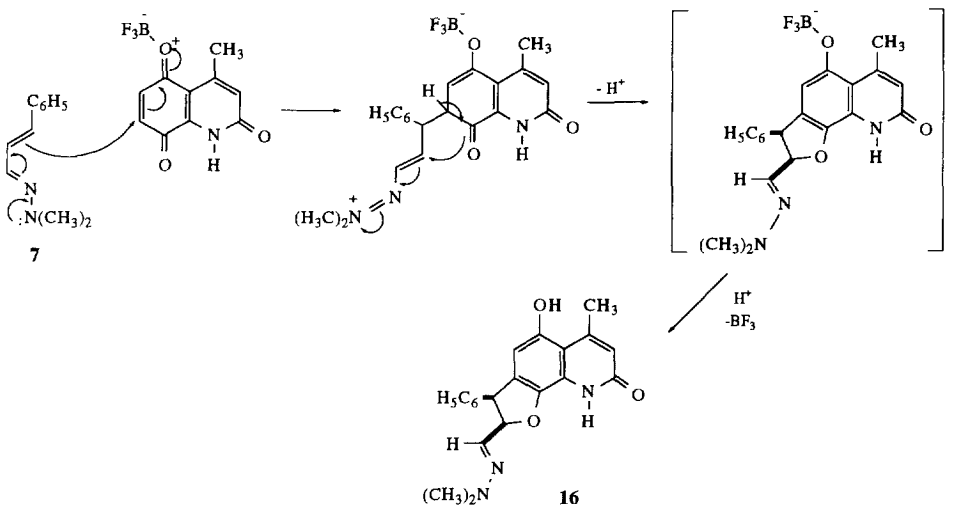
	R	R1
3	H	H
4	CH_3	H
5	C_2H_5	H
6	H	CH_3
7	H	C_6H_5
8	CH_3	C_2H_5

12,13	R	R1	R2
a	H	H	H
b	CH_3	H	H
c	C_2H_5	H	H
d	H	H	CH_3
e	CH_3	H	CH_3
f	C_2H_5	H	CH_3
g	H	CH_3	CH_3
h	H	C_6H_5	CH_3
i	CH_3	C_2H_5	CH_3

Reagents and conditions: i. $CHCl_3$, r.t., 5 min or reflux, 18-24 h. ii. Xylene, reflux, 16-124 h . iii. $CHCl_3$, MnO_2 (excess), r.t.,10 min

Scheme 2

of α,β-unsaturated *N,N*-dimethylhydrazones is not unknown, and has been observed in cases where dienes or dienophiles are very polarized due to the presence of electron-releasing groups in the diene,[26] electron-withdrawing groups in the dienophile[27] or Lewis acid catalysis.[28] An early precedent of this kind of reaction can be found in the addition of ketone acetals to quinones.[29]

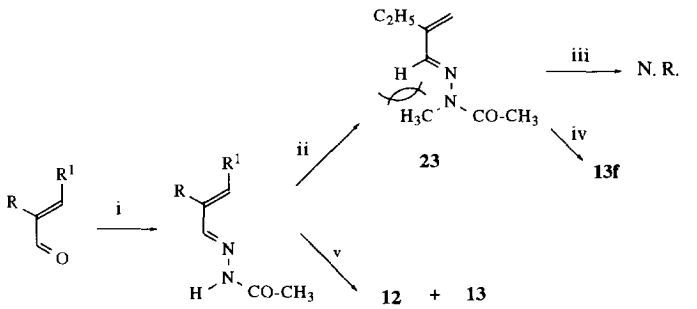


Scheme 3

In an effort to avoid the liberation of strongly nucleophillic species from the Diels-Alder adduct and thus suppress the formation of secondary products **11**, we decided to study the replacement of the dimethylamino moiety of the dienes **3-8** by other electron-releasing groups. Since a few examples are known[18] of intramolecular hetero Diels-Alder reactions of 1-(*N*-alkyl-*N*-acylamino)-1-azadienes in spite of the poorer electron-releasing character of their activating groups, a study of the reactivity of *N*-acetylamino-1-azadienes **17-22** and *N*-methyl-*N*-acetylamino-1-azadiene **23** towards quinones **9** and **10** was carried out. To our knowledge, the only previous intermolecular Diels-Alder reaction of an *N*-acylamino-1-azadiene is the one described by Gilchrist[18] between *N*-benzoylamino-3-methyl-1-azadiene and *N*-phenylmaleimide.

Compounds **17-22** were conveniently prepared by treatment of commercially available α,β-unsaturated aldehydes with acetic acid hydrazide in refluxing ethanol, and compound **23** was obtained by methylation of **19**. An attempt to use **23** as an azadiene with quinone **10** failed, since only unchanged starting materials were recovered after a 7-day reflux in xylene. Limited success was achieved by ultrasound irradiation of the reaction,[30] which allowed the isolation of **13f** in 28 % yield after 5 days at 45 °C. On the other hand, when the *N*-acylaminohydrazones **17-20** or **22** were treated with quinones **9** and **10** in refluxing xylene, mixtures of the desired tricyclic adducts **12** and **13** were obtained, with no traces of secondary products arising from nucleophillic additions to the C_6 position of the starting quinone (Scheme 4). Due to this advantage, the yields of **12** and **13** were often better than the ones obtained from dimethylaminohydrazones, particularly so in the reactions of quinone **10** because in this case the formation of the side product **11** was more significant than when **9** was the starting material (Table 1).

The lower reactivity of the methylated acylhydrazone **23** in spite of the presumably increased electron-releasing ability of its activating group is in contrast with the results described by Gilchrist for intramolecular Diels-Alder reactions of acylhydrazones,[18] and can be attributed to steric inhibition of the coplanarity between the acylamino nitrogen atom and the diene system (Scheme 4).



	R	R^1
17	H	H
18	CH_3	H
19	C_2H_5	H
20	H	CH_3
21	H	C_6H_5
22	CH_3	C_2H_5

Reagents and conditions: i. $CH_3CONHNH_2$, EtOH, reflux, 30 min (5 h for **21**) ii. NaH, xylene, reflux, 30 min, and then ICH_3, reflux, 15 h iii. **10**, xylene, reflux, 7 days iv. **10**, $CHCl_3$, ultrasound, 45 °C, 5 days v. **9** or **10**, xylene (air), reflux, 12-110 h.

Scheme 4

Table 1.- Comparison of the reactions of quinones **9,10** with dimethylaminohydrazones **3-8** and acetohydrazides **17-22**.

Products	Reaction with dimethylhydrazones[a]				Reaction with acetohydrazides			
(**12,13**)	Time	% **11**	% **12**	% **13**	Method[b]	Time, h	% **12**	% **13**
a	5 min	8		81[c]	B	30		71
b	5 min			60	B	50		58
c	30 min			70[d]	B	57		70
d	5 min	14		70[e]	B	60		58
e	5 min	20[f]		48	B	16		84
f	5 min	33		42	A	12		62[g]
g	5 min	35	51		B	96	44	
h	24 h	65	34		A	112	N.R.	
	18 h	44	52[h]					
i	5 min	45	47		A	23	4	54
					B	18	54	25

a. All reactions were carried out at room temperature, except in the preparation of **12h** (80 °C). b. Method A: reflux in xylene; method B: reflux in xylene, with simultaneous bubbling of air. c. The reaction product is a 5:1 mixture of **13a** and **14**. d. According to reference 31. e. The reaction product is a 4:1 mixture of **13d** and **15**. f. According to reference 21b. g. Yield based on unrecovered starting quinone; isolated yield was 52 %. h. With simultaneous bubbling of argon through the reaction.

In conclusion, we have shown that acetylhydrazones of α,β-unsaturated aldehydes are suitable dienes for the hetero Diels-Alder reaction with 2,5,8(1*H*)-quinolinetriones. Although their reactions require harsher conditions, they compare favourably with the corresponding dimethylhydrazones in that side products arising from the addition of dimethylamine to the starting quinone are avoided, allowing for a simpler and more efficient purification of the final products. With some exceptions, the yields of the adducts **12** and **13** are normally maintained or improved.

EXPERIMENTAL

All reagents were of commercial quality (Aldrich, Merck, SDS, Probus) and were used as received except for acetohydrazide, which was recrystallized from ethanol prior to use. Solvents (SDS, Scharlau) were dried and purified using standard techniques. The expression "petroleum ether" refers to the fraction boiling at 40-60 °C. Reactions were monitored by thin layer chromatography, on aluminium plates coated with silica gel with fluorescent indicator (Scharlau Cf 530). Separations by flash chromatography were performed on silica gel (SDS 60 ACC, 230-400 mesh and Scharlau Ge 048). Melting points were measured with a Reichert 723 hot stage microscope, or in open capillary tubes using a Büchi inmersion apparatus, and are uncorrected. Reactions under ultrasound irradiation were performed with a Branson 450 ultrasound probe, using the pulsed mode (pulse duration, 0.2 to 0.3 s), with output values between 30 and 40 Watt. Ultraviolet-visible spectra were obtained on 10^{-4} M methanolic solutions using a Shimadzu UV-2100 spectrophotometer. Infrared spectra were recorded on Perkin-Elmer 577 and Perkin-Elmer Paragon 1000 spectrophotometers, with solid compounds compressed into KBr pellets and liquid compounds placed between two NaCl disks. NMR spectra were obtained on Bruker AC-250 (250 MHz for ^{1}H, 63 MHz for ^{13}C) and Varian VXR-300 (300 MHz for ^{1}H, 75 MHz for ^{13}C) spectrometers with $CDCl_3$, DMSO-d_6 and pyridine-d_5 as solvents. Exchangeable assignments are marked with * and **. Elemental analyses were determined by the Servicio de Microanálisis, Universidad Complutense, on a Perkin-Elmer 2400 CHN microanalyzer.

1-Dimethylamino-1-azabutadienes. General Procedure:

The method described by Waldner[7] was employed for their preparation. Previously unreported[7,32] spectral data are given below and in Table 2.

Trans-Crotonaldehyde dimethylhydrazone (**6**). ^{1}H-NMR ($CDCl_3$, 250 MHz) δ: 7.01 (d, 1H, J = 8.8 Hz, H-1); 6.20 (ddd, J_{23} = 15.4 Hz, J_{21} = 8.8 Hz, J_{24} = 1.5 Hz, H-2); 5.82 (m, 1H, H-3); 2.81 (s, 6H, NMe_2); 1.84 (dd, 3H, J_{43} = 13.3 Hz, J_{42} = 1.5 Hz, H-4).

Trans-Cinnamaldehyde dimethylhydrazone (**7**). ^{1}H-NMR ($CDCl_3$, 250 MHz) δ: 7.42 (dd, 2H, $J_{2'3'}$ = 8.1 Hz, $J_{2'4'}$ = 1.2 Hz, H-2',6'); 7.31 (t, 2H, J = 8.1 Hz, H-3',5'); 7.21 (tt, 1H, $J_{4'3'}$ = 7.8 Hz, $J_{4'2'}$ = 1.2 Hz, H-4'); 7.14 (d, 1H, J = 8.7 Hz, H-1); 6.96 (dd, 1H, J_{21} = 8.7 Hz, J_{23} = 15.6 Hz, H-2); 6.62 (d, 1H, J = 15.9 Hz, H-3); 2.92 (s, 6H, NMe_2).

N-Alkenylideneacetohydrazides; General Procedure:

A solution of the suitable α,β-unsaturated aldehyde (5.1 mmol) and acetohydrazide (378 mg, 5.1 mmol) in EtOH (25 ml) was refluxed for 30 min (5 h in the case of **21**). The solvent was evaporated and the residue was used for the next step with no further purification. Analytical samples were obtained by recrystallization from petroleum ether. NMR data of compounds **17-22** are collected in Tables 3 and 4. Other data follow:

Table 2.- ^{13}C-NMR Data ($CDCl_3$, 62.9 MHz) of dimethylhydrazones **3-8**

Cmpd.	C-1	C-2	C-3	NMe_2	R^1	R^2
3	135.70*	135.80*	116.76	42.73		
4	136.91	142.56	115.25	42.75	17.61	
5	136.58	148.27	113.57	42.73	23.85 (CH_2) 13.86 (CH_3)	
6	136.93	130.28*	130.08*	42.97		18.08
7	135.18	131.62	127.36*	42.62		137.14 (C-1'), 128.50 (C-3',5') 127.25 (C-4')*, 126.09 (C-2',6')
8	140.58	133.80	134.97	42.91	11.51	20.48 (CH_2), 12.84 (CH_3)

N'-(2-propenylidene)acetohydrazide (**17**): Yield, 67 %. Mp, 106-108 °C. IR (KBr): 3186 (NH), 1670 (CO) cm^{-1}. Anal. Calcd. for $C_5H_8N_2O$: C, 53.55; H, 7.19; N, 25.01. Found: C, 53.74; H, 7.49; N, 24.83.

N'-(2-Methyl-2-propenylidene)acetohydrazide (**18**): Yield, 90 %. Mp, 106-108 °C. IR (KBr): 3180 (NH), 1700 (CO) cm^{-1}. Anal. Calcd. for $C_6H_{10}N_2O$: C, 57.12; H, 7.99; N, 22.20. Found: C, 57.44; H, 7.74; N, 22.60.

N'-(2-Ethyl-2-propenylidene)acetohydrazide (**19**): Yield, 94 %. Mp, 74-76 °C. UV-VIS, λ_{max} (ε): 261 (17240) nm. IR (KBr): 3160 (NH), 1690 (CO) cm^{-1}. Anal. Calcd. for $C_7H_{12}N_2O$: C, 59.97; H, 8.62; N, 19,98. Found: C, 59.90; H, 8.41; N, 19.60.

N'-(2-Butenylidene)acetohydrazide (**20**): Yield, 95 %. Mp, 110-112 °C. IR (KBr): 3200 (NH), 1670 (CO) cm^{-1}. Anal. Calcd. for $C_6H_{10}N_2O$: C, 57.12; H, 7.99; N, 22.20. Found: C, 56.81; H, 7.76; N, 22.26.

Table 3.- ^{1}H-NMR Data (250 MHz, $CDCl_3$) of Compounds **17-23**

	H-1	H-2	H-3	$COCH_3$	R	R^1	R^3
17	7.50(d, *J*=9.2)	6.43 (m)	5.60 (m)	2.27 (s)			10.12 (s)
18	7.53 (s)		5.36 (m)	2.26 (s)	1.90 (s)		10.28 (s)
19	7.51 (s)		5.27 (m)	2.18 (s)	2.26(q, *J*=7.4)		10.91 (s)
					1.02 (t, *J*=7.4)		
20	7.62(d, *J*=8.0)	6.24	(m, 2H)	2.36 (s)		1.95 (d, *J* = 4.6)	10.77 (s)
21	7.69 (m)	6.88	(m, 2H)	2.33 (s)		7.46 (dd,*J*=7.7;1.7;H-2',6')	
						7.37 (t, *J* = 8.5; H-3',5')	
						7.33 (m, H-4')	
22	7.44 (s)		5.78	2.26 (s)	1.81 (s)	2.23 (q, *J* = 7.5)	
			(t, *J*=7.3)			1.01 (t, *J* = 7.5)	10.16 (s)
23	7.37 (s)		5.38 (m)	2,35 (s)	2.38 (m)	1.03 (t, *J* = 7.5)	3.25 (s)
					1.16 (t, *J*=7.4)		

N'-(3-Phenyl-2-propenylidene)acetohydrazide (**21**): Yield, 56 %. Mp, 154-156 °C. IR (KBr): 3180 (NH), 1680 (CO) cm^{-1}. Anal. Calcd. for $C_{11}H_{10}N_2O$: C, 70.19; H, 6.42; N, 14.88. Found: C, 69.80; H, 6.28; N, 14.53.

N'-(2-Methyl-2-pentenylidene)acetohydrazide (**22**): Yield, 93 %. Mp, 109-111 °C. IR (KBr): 3190 (NH), 1680 (CO) cm^{-1}. Anal. Calcd. for $C_8H_{14}N_2O$: C, 62.33; H, 9.09; N, 18.18. Found: C, 62.60; H, 8.82; N, 18.46.

Table 4.- ^{13}C-NMR Data (62.9 MHz, $CDCl_3$) of Compounds **17-23**

	C-1	C-2	C-3	$COCH_3$	R	R^1	R^3
17	146.33	133.61	124.62	174.54			
				20.32			
18	147.19	140.92	122.51	174.61	17.10		
				20.34			
19	147.18	146.84	120.78	174.90	23.55 (CH_2)		
				20.52	12.44 (CH_3)		
20	146.78	138.32	128.39	174.50		18.63	
				20.29			
21	146.25	139.34	124.76	174.21		135.81 (C-1'), 127.00 (C-2',6')	
				20.30		128.92 (C-3',5'), 129.14 (C-4')	
22	149.28	141.80	132.28	174.56	13.65	21.70 (CH_2)	
				20.19		11.16 (CH_3)	
23	141.63	147.42	119.99	173.15	23.93 (CH_2)		27.35
				21.61	12.60 (CH_3)		

***N'*-(2-Ethyl-2-propenylidene)-*N*-methylacetohydrazide 23**

A solution of compound **19** (100 mg, 0.71 mmol) in dry xylene (30 ml) was added to NaH (8.25 mmol, from 33 mg of a commercial 60 % suspension in mineral oil, washed twice with dry petroleum ether). The suspension was refluxed for 30 min and was then cooled. After addition of methyl iodide (50 mg, 3.5 mmol), the reaction was refluxed for 15 h and filtered while hot. The solid was washed with xylene (2 x 10 ml). The combined organic layers were evaporated *in vacuo* and the residue was chromatographed on silica gel, eluting with $CHCl_3$, to yield 86 mg (78 %) of the methylated hydrazide **11**. The analytical sample was recrystallized from petroleum ether. Mp 61-63 °C. UV-VIS, λ_{max} (ε): 263 (11850) nm. IR (KBr): 1680 (CO) cm^{-1}. Anal. Calcd. for $C_8H_{14}N_2O$: C, 62.30; H, 9.15; N, 18.16. Found: C, 62.63; H, 9.45; N, 18.43. NMR data of **23** can be found in Tables 3 and 4.

Diels-Alder Reactions Between Dimethylhydrazones 3-8 and Quinones 9 and 10; General Procedure:

To a solution of quinone **9** (20 to 30 mg, 0.11 to 0.17 mmol) or **10** (125 to 200 mg, 0.66 to 1.06 mmol) in $CHCl_3$ (5 ml for **9**, 80 ml *per* 100 mg of **10**) was added the suitable diene (1 to 1.1 equiv). The solution was stirred at room temperature for 5 min (hydrazones **3-6** and **8**) or was refluxed for 24 h with simultaneous

bubbling of argon and periodical additions of fresh solvent (hydrazone **7**). The residue from the evaporation of the solvents was chromatographed on silica gel, eluting with ethyl acetate (reactions starting with **3-5**, leading to **13d-f**), or alternatively eluting with a gradient from neat CH_2Cl_2 to 6:4 CH_2Cl_2-AcOEt (reaction starting with **6-8**, leading to **12g-i**). Compounds **13a** and **13d** were obtained as mixtures with their regioisomers **14** and **15**, respectively (see footnotes to table 1). Column chromatography (silica gel, ethyl acetate) of these mixtures allowed the isolation of **13a** and **13d**. Data for compounds **12**, **14** and **15** are given below. Data for compounds **13** are in Tables 5 and 6 (see below).

5,8-Dihydro-4,5-dimethyl-1*H*-1,8-diazaanthracene-2,9,10-trione (**12g**). Mp 301-303 °C. IR (KBr): 3660-3040 (NH); 1660, 1650 (CO) cm^{-1}. ^{1}H-NMR (300 MHz, d_5-pyridine) δ: 8.77 (d, 1H, J = 3.6 Hz, H-8); 6.54 (dd, 1H, J_{78} = 4.0 Hz, J_{76} = 7.8 Hz, H-7); 6.54 (d, 1H, J = 1.2 Hz, H-3); 4.85 (m, 1H, H-6); 3.50 (m, 1H, H-5); 2.55 (d, 3H, J = 1.2 Hz, C_4-CH_3); 1.02 (d, 3H, J = 6.6 Hz, C_5-CH_3) ppm. Anal. Calcd. for $C_{14}H_{12}N_2O_3$: C, 65.62; H, 4.69; N, 10.92. Found: C, 65.28; H, 4.62; N, 10.83.

5,8-Dihydro-4-methyl-5-phenyl-1*H*-1,8-diazaanthracene-2,9,10-trione (**12h**). Mp 206-208 °C. IR (KBr): 3600-3100 (NH), 1660, 1655, 1650 (CO) cm^{-1}. ^{1}H-NMR (300 MHz, d_5-pyridine) δ: = 10.40 (d, 1H, J = 4.0 Hz, H-8); 7.69 (dd, 2H, $J_{2'3'}$ = 8.0 Hz, $J_{2'4'}$ = 1.0 Hz, H-2',6'); 7.41 (t, 2H, J = 8.0 Hz, H-3',5'); 7.25 (tt, 1H, $J_{4'3'}$ = 7.8 Hz, $J_{4'2'}$ = 1.1 Hz, H-4'); 6.70 (m, 1H, H-7); 6.70 (d, 1H, J = 1.0 Hz, H-3); 5.17 (m, 1H, H-6); 5.11 (m, 1H, H-5); 2.46 (d, 1H, J = 1.0 Hz, C_4-CH_3) ppm. ^{13}C-NMR (75 MHz, d_5-pyridine): δ = 183.56 (C-9); 177.48 (C-10); 162.23 (C-2); 150.85 (C-4); 148.28 (C-1'); 139.77 (C-8a)*; 138.10 (C-9a)*; 128.90 (C-2',6'); 128.82 (C-3',5'); 127.14 (C-3)**; 126.88 (C-7)**; 124.41 (C-4'); 114.84 (C-4a); 112.66 (C-10a); 107.21 (C-6); 37.66 (C-5); 22.47 (C_4-CH_3) ppm. Anal. Calcd. for $C_{19}H_{14}N_2O_3$: C, 71.69; H, 4.43; N, 8.80. Found: C, 71.36; H, 4.29; N, 8.41.

5-Ethyl-5,8-dihydro-4,6-dimethyl-2*H*-1,8-diazaanthracene-2,9,10-trione (**12i**). Mp 220-223 °C. IR (KBr): 3640-3060 (NH); 1650 (CO) cm^{-1}. ^{1}H-NMR (300 MHz, d_5-pyridine) δ: 6.65 (br. s, 1H, H-8); 6.65 (d, 1H, J = 1.2 Hz, H-3); 6.10 (dd, 1H; J_{78} = 4.5 Hz, J_{al} = 1.2 Hz, H-7); 3.65 (t, 1H, J = 4.5 Hz, H-5); 2.62 (d, 3H, J = 1.2 Hz, C_4-CH_3); 1.73 (d, 3H, J = 1.2 Hz, C_6-CH_3); 1.56 (dq, 2H, J = 7.5 Hz, and 4.5 Hz, C_5-CH_2CH_3); 0.81 (t, 3H, J = 7.5 Hz, C_5-CH_2CH_3) ppm. ^{13}C-NMR (75 MHz, d_5-pyridine): δ = 183.08 (C-9); 175.79 (C-10); 160.83 (C-2); 152.03 (C-4); 137.11 (C-8a)*; 136.33 (C-9a)*; 127.76 (C-3); 119.49 (C-7); 115.46 (C-6); 114.93 (C-4a); 111.51 (C-10a); 36.43 (C-5); 25.56 (C_5-CH_2CH_3); 22.53 (C_4-CH_3); 18.68 (C_6-CH_3); 9.27 (C_5-CH_2CH_3) ppm. Anal. Calcd. for $C_{16}H_{14}N_2O_3$: C, 68.15; H, 5.01; N, 9.93. Found: C, 67.97; H, 5.34; N, 10.11.

1*H*-1,5-Diazaanthracene-2,9,10-trione (**14**). ^{1}H-NMR (250 MHz, $CDCl_3$) δ: 8.95 (m, 1H, H-6); 8.61 (m, 1H, H-8); 8.21 (d, 1H, J = 9.7 Hz, H-4); 7.51 (m, 1H, H-7); 6.73 (d, 1H, J = 9.7 Hz, H-3) ppm.

4-Methyl-1*H*-1,5-diazaanthracene-2,9,10-trione (**15**). ^{1}H-NMR (250 MHz, d_6-DMSO) δ: 8.94 (d, 1H, J = 4.6 Hz, H-6); 8.41 (d, 1H, J = 7.9 Hz, H-8); 7.70 (dd, 1H, J = 7.9 and 4.8 Hz, H-7); 6.50 (s, 1H, H-3); 2.58 (s, 3H, C_4-CH_3) ppm.

(±) *cis*-2-(Dimethylhydrazonomethyl)-3-phenyl-5-hydroxy-6-methylfuro[3,2-*h*]quinolin-8-one 16.

A solution of quinone **10** (217 mg, 1.15 mmol) and BF_3-Et_2O complex (358 mg, 2.52 mmol) in dry $CHCl_3$ (130 ml) was treated with 219 mg (1.63 mmol) of hydrazone **7**. The solution was refluxed for 10 h, and an additional amount of **7** (296 mg, 1.69 mmol) was then added. Reflux was continued for additional 5 h and the cooled reaction mixture was washed with water (2 x 15 ml), dried over Na_2SO_4 and evaporated. The residue

was evaporated and chromatographed on silica gel, eluting with a gradient from neat CH_2Cl_2 to 1:1 CH_2Cl_2-AcOEt, to yield 292 mg of recovered **7** and 400 mg (75 %) of compound **16**. Mp 125-127 °C (AcOEt). IR (NaCl): 3450 (OH, NH), 1655 (C=O), 1640 (C=N) cm^{-1}. ^{1}H-NMR (300 MHz, d_5-pyridine) δ: 2.63 (d, 3H, J = 1.2 Hz, C_6-CH_3); 2.78 (s, 6H, NMe_2); 4.94 (d, 1H, J = 7.8 Hz, H-3); 5.47 (dd, $J_{2,3}$ = 7.8 Hz, $J_{2,CH=N}$ = = 6.0 Hz, H-2), 6.69 (d, 1H, J = 1.2 Hz, H-7), 6.94 (d, 1H, J = 5.9 Hz, CH=N), 7.01 (s, 1H, H-4), 7.27 (m, 1H, H-4'), 7.33 (t, 2H, J = 7.0 Hz, H-3',5'), 7.37 (dd, 2H, $J_{2',3'}$ = 1.5 Hz, $J_{2',4'}$ = 7.0 Hz, H-2',6'), 11.85 (br. s, 1H. NH) ppm. ^{13}C-NMR (75 MHz, $CDCl_3$): δ = 22.68 (C_6-CH_3), 42.38 (NMe_2), 53.01 (C-3); 92.60 (C-2); 107.93 (C-5a); 112.63 (C-4); 121.88 (C-7); 127.43 (C-1'); 128.65 (C-3'); 128.75 (C-9a); 129.17 (C-2'); 129.64 (C-3a); 130.52 (C-4'); 131.10 (CH=N); 139.11 (C-9b); 142.96 (C-5); 148.51 (C-6); 162.38 (C-8) ppm. Anal. Calcd. for $C_{21}H_{23}N_3O_3$: C, 69.02; H, 6.34; N, 11.49. Found: C, 68.85; H, 5.98; N, 11.15

Diels-Alder Reactions Between Quinones 9,10 and Acetohydrazides 17-23. General Procedure:

Method A (for hydrazides **19**, **21**, **22**): A solution of quinone **10** (75 to 141 mg, 0.39 to 0.74 mmol) and the suitable acetylhydrazone (1.1 equiv) in xylene (20 ml) was refluxed for 12 to 110 h. The solvent was evaporated *in vacuo* and the residue was chromatographed on silica gel, eluting with ethyl acetate to give compound **13f**, or with a gradient from dichloromethane to ethyl acetate to give **12g** and **13g**. Compound **21** decomposed, and no reaction products could be isolated.

Method B (for hydrazides **17**, **18**, **20-23**): A solution of quinone **10** (50 to 75 mg, 0.26 to 0.39 mmol) and the suitable acetylhydrazone (1.1 equiv) in xylene (20 ml) was refluxed for 16 to 96 h with simultaneous bubbling of air through the solution and periodical additions of fresh xylene. Workup and purification as above gave compounds **13d-g** and **13i**. The same procedure was followed in the reactions between quinone **9** and dienes **17-19**, yielding **13a-c**.

Method C (for hydrazide **23**): A solution of quinone **10** (28 mg, 0.15 mmol) and the methylated acetylhydrazone **23** (28 mg, 0.18 mmol) in chloroform (2 ml) was placed in a bath at 45 °C and irradiated with ultrasound for 5 days. Evaporation of the solvent and column chromatography on silica gel, eluting with ethyl acetate, afforded 17 mg of recovered **23** and 11 mg of compound **13f** (28 %, 71 % based on unrecovered **23**).

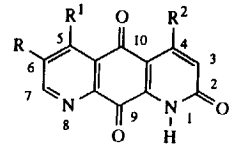
Oxidation of Compounds 12g-i to 1,8-Diazaanthracene-2,9,10-triones 13g-i. General Procedures:

Method A : To a solution of dihydro derivatives **6** (0.063 to 0.097 mmol) in $CHCl_3$ (10 ml) was added solid activated manganese dioxide (5 eq.). The black suspension was stirred at room temperature for 10 min, and was filtered through a plug of silica gel. The solvent was evaporated, giving the following yields of pure aromatic compounds **13**: **13g**, 88 %; **13h**, 83 %; **13i**, 94 %.

Method B: A solution of the suitable dihydro derivative **12** (0.1 to 0.3 mmol) in xylene (60 ml) was refluxed in an oil bath at 160 °C, while a stream of air was bubbled through the solution, for 25 h (**13g**), 124 h (**13h**), or 58 h (**13i**), with periodical (*ca.* 12 h) additions of fresh xylene to make up for the amounts lost through evaporation. On completion of the aromatization, the solution was evaporated and the residue was purified by column chromatography on silica gel, eluting with ethyl acetate. The yields obtained were: **13g**, 90 %; **13h**, 70 %; **13i**, 95 %.

Data for compounds **13** can be found in Tables 5 and 6.

Table 5.- Data for Compounds **13**



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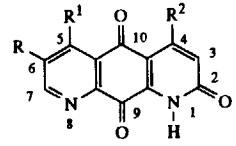
Comp.	Mp, °C	Analysis, calculated (found)			IR (KBr), cm^{-1}	^{1}H-NMR, ppm[a,b]						
		C	H	N		C_7-H	C_6-H	C_5-H	C_3-H	R	R^1	R^2
13a	226-228	63.77	2.67	12.39	3423 (NH)	9.08 (dd)	7.78 (dd)	8.57 (dd)	6.94 (d)			8.13 (d)
		(63.41)	(3.05)	(12.09)	1645 (C=O)	*J* = 4.7, 1.8	*J* = 7.9, 4.6	*J* = 7.9, 1.8	*J* = 9.6			*J* = 9.7
13d	> 300	65.06	3.36	11.67	3445 (NH)	9.08(dd)	7.80 (dd)	8.58 (dd)	6.75 (s)			2.71 (d)
		(64.82)	(3.75)	(11.28)	1644 (C=O)	*J* = 4.8, 1.5	*J* = 8.1, 4.8	*J* = 7.8, 1.5				*J*=1.2
13f[c]	225-227	67.16	4.51	10.44	3420 (NH)	8.90(s)		8.36(s)	6.72(s)	2.89 (q, *J*=9.1)		2.71(s)
		(66.87)	(4.53)	(10.21)	1655, 1636 (C=O)					1.38(t, *J*=9.1)		
13g	> 300	66.20	3.96	11.02	3440 (NH)	8.85	7.53 (d)		6.72 (d)	2.86(s)		2.68 (d)
		(66.57)	(4.24)	(11.45)	1655 (C=O)	(d, *J*=5.1)	*J*=4.9		(*J*=1.2)			(*J*=1.2)
13h	285-288	72.14	3.82	8.85	3430 (NH)	8.94 (d)	7.50 (d)		6.62 (d)	7.42(m, 2H)		2.44 (d)
		(71.95)	(3.99)	(8.52)	1660, 1650, 1640	*J*=4.5	*J*=4.5		(*J*=1.2)	7.22(m, 3H)		*J*=1.2
					(C=O)							
13i	190-193	68.14	5.00	9.93	3440 (NH)	8.74(s)			6.69(s)	3.20 (q, *J*=6.2)	2.51(s)	2.66(d)
		(67.85)	(5.34)	(10.11)	1655 (C=O)					1.31 (t, *J*=6.0)		*J*=1.2

[a]Data for compounds**13b**, **13c** and **13e** can be found in references 21 and 31. b. At 250 or 300 MHz, in $CDCl_3$, except in the case of compound **13a** (d_6-DMSO).
[c]An additional NMR signal (br. s, δ = 9.78), due to an NH, was observed.

Table 6.- ^{13}C-NMR Data for Compounds **13**



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Cmpd.[a,b]	C_2	C_3	C_4	C_{4a}	C_5	C_6	C_7	C_{8a}	C_9	C_{9a}	C_{10}	C_{10a}	R	R^1	R^2
13a	162.16	128.71	147.87	115.95	135.96	129.37	154.27	146.92	180.19	141.99	176.43	134.52			
13b	160.91	128.24	134.95	115.86	135.90	140.42	155.53	144.74	179.31	139.25	176.11	129.37	19.14		
13c	160.93	128.29	133.77	115.89	135.29	141.93	154.97	146.28	179.41	139.27	176.13	129.61	26.55 (CH_2) 14.55 (CH_3)		
13d	160.26	129.23	151.91	115.73	135.60	130.76	154.82	146.06	180.59	140.22	176.62	130.72			22.77
13f	160.06	128.07	151.78	115.16	133.92	144.18	154.89	146.47	180.93	140.14	176.39	130.51	26.59 (CH_2) 14.20 (CH_3)		21.07
13g	160.45	128.78	151.58	119.24	152.02	132.81	153.31	147.85	c	139.00	c	129.26		29.26	22.82
13h	160.17	128.84*	151.72	117.08	152.69	132.03	153.42	147.30	181.43	138.75	176.88	128.78*	c ($C_{1',4'}$)	128.67 ($C_{3',5'}$) 127.84 ($C_{2',6'}$)	21.07
13i	160.51	128.64*	151.82	117.46	154.76**	140.00	154.85**	145.86	183.66	138.72	177.16	128.89*	17.26	23.52 (CH_2) 13.14 (CH_3)	17.26

a. All spectra were obtained in $CDCl_3$, except in the case of compound **13a** (d_6-DMSO); interchangeable assignments are marked with * and **

b. Data for compound **13e** can be found in reference 21b. c. Signal not detected

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