Pteridines from α-Phenyl-*N,N*-dimethylacetamidine

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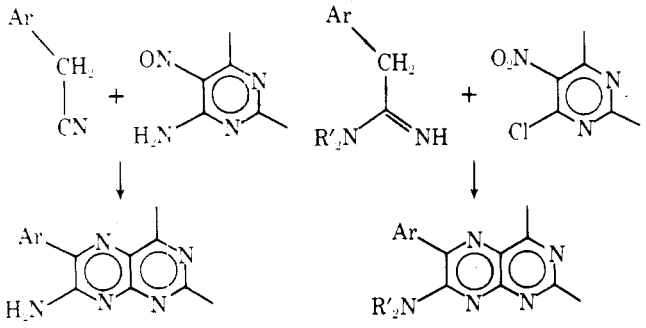
A new synthesis of pteridines from the reaction of chloronitropyrimidines and α-phenyl-substituted amidines is described. It is a useful method for preparing 4-substituted-6-phenyl-7-(*N,N*-dimethylamino)pteridines. The route complements the synthesis of pteridines from nitrosoaminopyrimidines and arylacetonitriles first described by Timmis and Spickett[8] and developed by Pachter and his colleagues[9-11] at Smith, Kline, and French Laboratories. The synthesis and reactions of 4-oxygen-substituted 6-phenyl-7-(*N,N*-dimethylamino)pteridines resulting from reactions of nitrochloropyrimidines and α-phenylamidines are also summarized. The competition between S_NAr displacement and intramolecular cyclization reactions of the pyrimidine precursors is also discussed.

In several previous studies we have reported the use of amidines in preparing benzazocine,[2-4] indole,[5] benzoquinoline,[5] quinoline,[5] isoquinoline,[5,6] quinoxaline,[7] and imidazoquinoxaline[7] ring systems. These reactions involve nucleophilic annelation of a C–C–N fragment from the amidine on appropriate tri- and dinitro aromatic compounds. The reactions occur in two stages: nucleophilic addition or displacement followed by cyclization on the ring or an adjacent substituent.



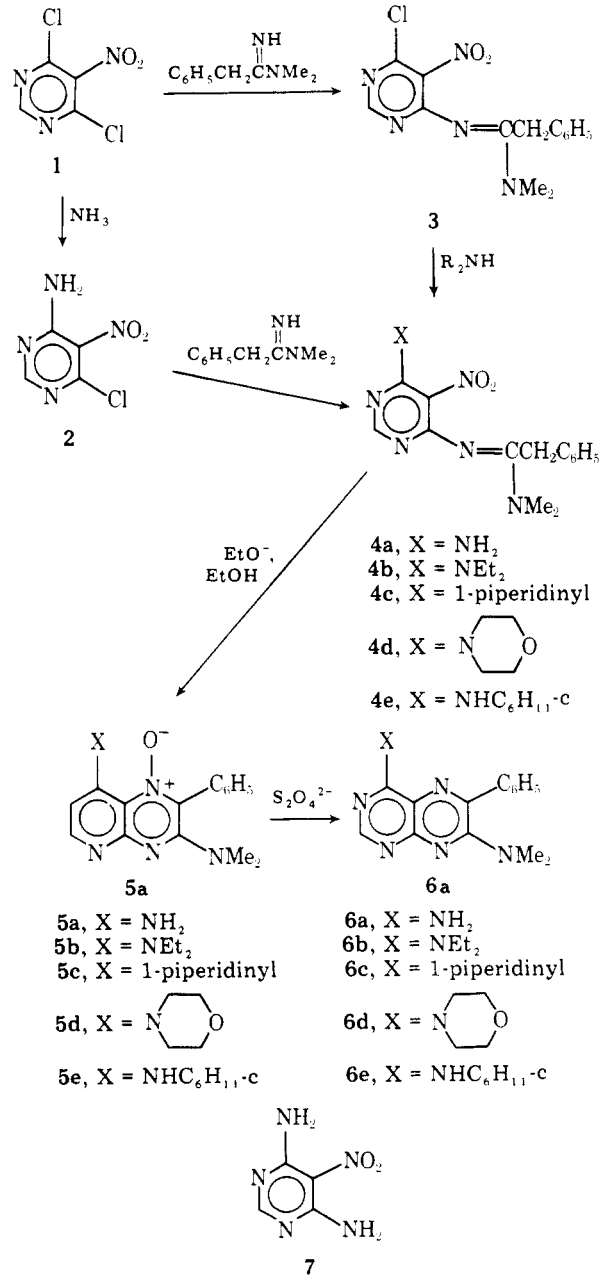
Smith, Kline, and French from amidines

Although pyrimidines are less reactive toward nucleophiles, we expected that amidine annelation on such substrates in an appropriate fashion could lead to pteridine *N*-oxides and provide a new and useful route to pteridines. Such a synthesis complements the route from nitrosoaminopyrimidines and arylacetonitriles first described by Spickett and Timmis[8] and developed by Pachter and his colleagues at Smith, Kline, and French Laboratories.[9-13]

One feature of the amidine preparation makes it particularly useful. Since 7-amino functionality in pteridines prepared from nitrosoaminopyrimidines is derived from the nitrile, only primary amino groups will result at C-7 of the product. The amidine route can lead to 4-amino-7-(*N,N*-dialkylamino)pteridines. These types of compounds, as well as 4-(*N*-substituted)-7-(*N,N*-disubstituted)pteridines, are reported here.

The sequence of reactions leading to a series of 4-substituted-6-phenyl-7-(*N,N*-dimethylamino)pteridines, **6**, is outlined in Scheme I. Reaction of commercially available 4,6-dichloro-5-nitropyrimidine, **1** (Aldrich), with ammonia in ethanol yields 4-amino-5-nitro-6-chloropyrimidine, **2**,[14-16] and a trace of the diamino compound **7**. Compound **2** reacts readily with 2 equiv of α-phenyl-*N,N*-dimethylacetamidine to give the substitution product **4a** and 1 equiv of amidine hydrochloride. Compound **2** is not particularly stable, however,[16] and the yield of **4a** is not high (see Experimental Section). Cyclization of **4a** in ethanolic ethoxide gives a good yield of **5a**, however, and upon reduction with dithionite the pteridine **6a** is formed.

Scheme I



4a, X = NH_2
4b, X = NEt_2
4c, X = 1-piperidinyl
4d, X =
4e, X = NHC_6H_{11}-c

5a, X = NH_2
5b, X = NEt_2
5c, X = 1-piperidinyl
5d, X =
5e, X = NHC_6H_{11}-c

6a, X = NH_2
6b, X = NEt_2
6c, X = 1-piperidinyl
6d, X =
6e, X = NHC_6H_{11}-c

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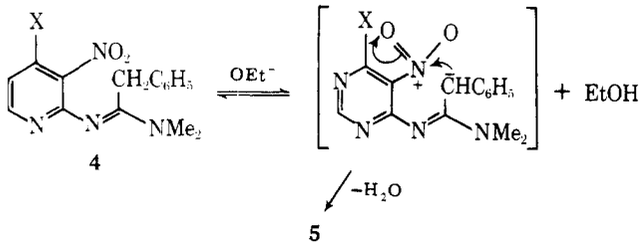
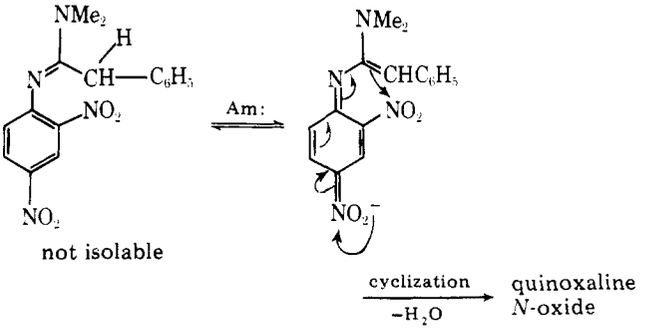
The mechanism for the cyclization step is probably similar to that which we have previously proposed for the formation of quinoxaline *N*-oxides from reaction of halo dinitro aromatic compounds and amidines.[7] Two significant differences are that the initial displacement product **3** is isolable and that strong base is required to cyclize it. Reaction of 1-fluoro-2,4-dinitrobenzene (DNFB) with α-phenyl-*N*,*N*-dimethylacetamidine gives only the cyclic quinoxaline *N*-oxide product even in the absence of added base. Formation of pteridine *N*-oxides **5a–e** probably occurs as follows.



The acidity of the amidine side chain in **4** may in part determine the ease with which cyclization occurs. In an aromatic ring bearing only electron-withdrawing groups (i.e., the product from DNFB and amidine), the amidine methylene is much more acidic. Tautomerization is facile, and rapid cyclization occurs *without added base*.[7] There is another important factor which may contribute to the stability of **4** relative to its dinitrophenyl analogue. The amino group adjacent to the nitro group undergoing attack during cyclization of **4** may reduce the electrophilicity of the nitro group nitrogen sufficiently so that attack occurs only when the nucleophile bears a full negative charge (hence the necessity of added ethoxide).

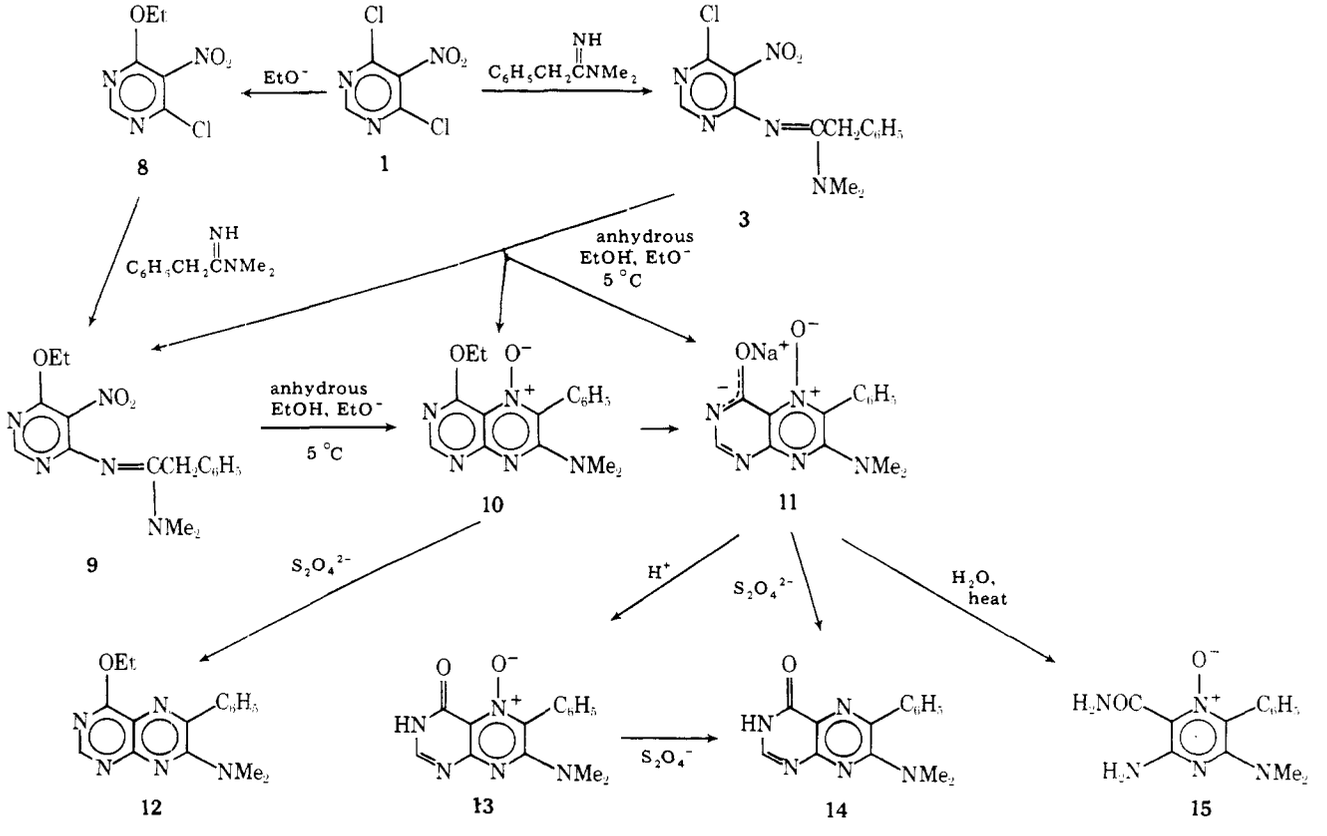
In order to further clarify the way in which formation of pteridine *N*-oxides occurs, we have qualitatively studied the competition between cyclization of and S_NAr displacement of halogen in **3**. The amines used to displace chloride from **3** in the preparation of **4** (Scheme I) were not sufficiently basic to cause cyclization, and no trace of **5** could be found in the product **4**. On the other hand, treating **3** with ethoxide could result in either displacement of chloride or cyclization or both. The results of such a reaction, as well as further transformations to be described, are summarized in Scheme II.



Treatment of **3** with 1 equiv of ethoxide in anhydrous ethanol yields a complex mixture. The composition of this mixture varies depending upon how long the reaction is allowed to stand before workup. After 2 days, the major product is **11**, mixed with sodium chloride which is not easily separated. Acidification of this product yields the pure pteridine *N*-oxide **13** which is easily reduced to pteridine **14** with dithionite. An additional confirmation of structure **11** is the pyrazine *N*-oxide hydrolysis product **15** which results from heating **11** in boiling water for several hours.

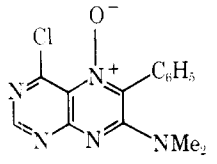
Interestingly, if the reaction of **3** with ethoxide is worked up after only 20 min a good yield of a mixture of the substitution product **9**, the substitution–cyclization product **10**, and the cyclized hydrolysis product **11** is obtained. These products could be separated and purified. Compound **9** is converted to

Scheme II



10 by ethoxide at 5 °C (workup after 20 min), and 10 could be easily reduced to the pteridine 12. Compound 9 was also prepared by reacting 1 with ethoxide to yield 8. Treatment of 8 with amidine gave a good yield of 9, identical in all respects with the product resulting from reaction of 3 and ethoxide. Interestingly, reaction of 3 with 2 equiv of ethoxide at 5 °C yields a mixture of 10 and 11 with no contamination by 9.

It seems clear from the reactions summarized in Scheme II that 9 and 10 are converted to 11 by ethoxide and/or water. Since no cyclized product which contains chlorine, i.e., 16, can



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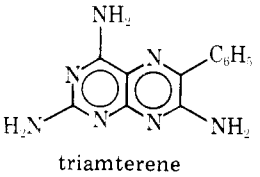
be isolated, it is possible to conclude that S_NAr displacement by ethoxide occurs before cyclization. This is not necessarily true, however, since the chlorine in 16 may be much more susceptible to nucleophilic attack than that in 3 because of the adjacent activating *N*-oxide moiety. Thus, 16, if formed by a rapid cyclization, could even more rapidly be converted to 10. A detailed quantitative study of the rate of conversion of 9 to 10 as well as 3 to 9 and 10 would answer this question. Although the reactions were carried out in anhydrous ethanol, hydroxide ion must eventually form from the elimination–aromatization to the *N*-oxides 5. This hydroxide is probably the nucleophile responsible for formation of 11. Another possibility is contamination by small amounts of water, although considerable attention was given to carrying out these reactions under anhydrous conditions.

Compounds similar to 6, 12, and 14 have substantial diuretic activity,[17,18] and we expect that the pteridines reported here will also be diuretics. There is still considerable interest in



triamterene

developing potassium-sparing diuretics like triamterene. We will report the results of biological testing elsewhere.

Experimental Section

All melting points are uncorrected. ^1H NMR spectra were run on JEOL C-60 HL and MH-100 spectrometers with Me_4Si as an internal reference. Visible and ultraviolet spectra were recorded on a Perkin-Elmer Model 402 UV-visible spectrophotometer. Infrared spectra were recorded on a Perkin-Elmer Model 237 B infrared spectrophotometer. Mass spectra were obtained on a Perkin-Elmer RMU-6D mass spectrometer. Elemental analyses were cross-checked by Galbraith Laboratories, Inc., Knoxville, TN, G. I. Robertson Laboratories, Florham Park, NJ, and Integral Microanalytical Laboratories, Inc., Raleigh, NC, and the analytical laboratories at the University of Rouen.

Compound 1 was obtained from Aldrich Chemical Co., and it was used without further purification. α-Phenyl-*N*,*N*-dimethylacetamidine was prepared as described previously.[4]

Preparation of 3. A solution of 3.07 g (0.018 mol) of α-phenyl-*N*,*N*-dimethylacetamidine in 20 mL of dry chloroform was added in small portions to a rapidly stirred solution of 1.83 g (0.0095 mol) of 4,6-dichloro-5-nitropyrimidine in 20 mL of dry chloroform. After 5 days at room temperature, the chloroform was removed with a rotary evaporator, and the resulting oily solid was extracted with four small portions of dry ether (~5 mL each time). This ether was again filtered and evaporated, yielding an oil. About 4 mL of dry ethanol was added to the oil, and the product which rapidly crystallized was filtered off and then washed with dry ethanol. Concentration of the ethanolic filtrate yielded a second crop of crystals (total yield 1.67 g, 55%), mp 72–73 °C. The ^1H NMR spectrum ($CDCl_3$) shows absorptions at δ 2.95 (3 H, s, NCH_3), 3.10 (3 H, s, NCH_3), 4.25 (2 H, s, $CH_2C_6H_5$), 7.25 (5 H, m, C_6H_5), and 8.45 (1 H, s, pyrimidine H). Anal. Calcd for $C_{14}H_{14}N_5O_2Cl$: C, 52.59; H, 4.41; N, 21.90. Found: C, 52.57; H, 4.42; N, 21.89.

Table I. Chemical Shifts (δ) in $CDCl_3$ and Elemental Analyses of 4b–e

	pyrimidine H	$N(CH_3)_2$	$CH_2C_6H_5$	C_6H_5	amine moiety
4b	8.21 s	2.95 s	4.10 s	7.25 s	1.15 (3 H, t), 3.40 (4 H, q)
4c	8.25 s	3.00 s	4.10 s	7.30 s	1.65 (6 H, s), 3.50 (4 H, s)
4d	8.30 s	3.00 s	4.15 s	7.35 s	3.55–3.75 (8 H, m)
4e	8.20 s	3.05 s	4.05 s	7.35 s	1.2–2.1 (10 H, m), 4.2 (1 H, m)

	theoretical, %			found, %		
	C	H	N	C	H	N
4b	60.66	6.78	23.58	60.62	6.73	23.85
4c	61.94	6.56	22.81	61.85	6.64	23.47
4d	58.37	5.98	22.69			
4e	62.81	6.84	21.97	62.17	6.85	22.38

Preparation of 4a. This compound was prepared from the known 4-amino-5-nitro-6-chloropyrimidine[14–16] by a procedure similar to that used for the preparation of 3 from 1. The yellow crystalline product was obtained in 25% yield (0.51 g) from 1.25 g of pyrimidine starting material. It was recrystallized from a mixture of benzene and petroleum ether; mp 155–156 °C. The ^1H NMR spectrum ($CDCl_3$) shows absorptions at δ 3.15 (6 H, s, $N(CH_3)_2$), 4.15 (2 H, s, $CH_2C_6H_5$), 7.35 (2 H, br s, NH_2), 7.50 (5 H, br s, C_6H_5), and 8.40 (1 H, s, pyrimidine H). Anal. Calcd for $C_{14}H_{16}N_6O_2$: C, 55.99; H, 5.36; N, 27.98. Found: C, 55.79; H, 5.78; N, 26.40. (It should be noted that we have occasionally had some difficulty in obtaining accurate analytical data for nitrogen from some laboratories on compounds where the values exceed 25%).

In addition to isolating **4a**, an insoluble compound was obtained by filtering the hot solution of **4a** in the recrystallization step. This compound (0.140 g) had a melting point and IR and ^1H NMR spectra identical with those of a sample of 4,6-diamino-5-nitropyrimidine.

Preparation of 4b–e. Compound 3 (0.0015 mol) was dissolved in 10 mL of chloroform and cooled to 0–5 °C in an ice bath. A solution of 0.0031 mol of the amine in 5 mL of chloroform was added very slowly. After 24 h at room temperature, the solvent was removed under vacuum. The remaining yellow solid was washed with ethanol. The crude products were purified by recrystallization from ethanol. All of the compounds **4b–4e** were obtained in 70–80% yield. The melting points are as follows: **4b**, 101–102 °C; **4c**, 133–134 °C; **4d**, 173–175 °C; **4e**, 133–135 °C. The ^1H NMR spectra and elemental analyses are summarized in Table I.

Preparation of 5a–e. A freshly prepared solution of sodium ethoxide in ethanol (3.1 mL, 0.43 M) was added dropwise to a solution of **4a–e** (0.013 mol) in 50 mL of dry ethanol at room temperature. After 5 days, the solvent was removed under vacuum. About 4 mL of dry ethanol was added to the residue, and after the solution was permitted to stand for a few minutes, the yellow crystals which formed were filtered off. These were recrystallized from a benzene–petroleum ether mixture to give yields of **5** ranging from 60 to 80%. The melting points of the products are as follows: **5a**, 221–222 °C; **5b**, 169–170 °C; **5c**, 228–229 °C; **5d**, 237–238 °C; **5e**, 222–223 °C. The ^1H NMR spectra and elemental analyses are summarized in Table II.

Preparation of 6a–e. A mixture of **5** (0.0039 mol) and sodium dithionite (0.013 mol) in 20 mL of 50% aqueous ethanol was heated at ~100 °C for 2 h. The ethanol was then removed on a rotary evaporator, and the yellow crystals which remained in the aqueous mixture were filtered off. Extraction of the aqueous solution with chloroform and evaporation of this solvent gave an additional amount of **6**. The crude product was recrystallized from ethanol–water, providing **6a–e** in approximately 50% yield. The melting points of the products are as follows: **6a**, 220–221 °C; **6b**, an oil which could not be recrystallized; **6c**, 157–158 °C; **6d**, 173–174 °C; **6e**, 175–176 °C. The ^1H/NMR spectra and elemental analyses are summarized in Table III.

Preparation of 8. A freshly prepared solution of sodium ethoxide in ethanol (27.6 mL, 0.43 M) was added dropwise at 0 °C to a stirring

Table II. Chemical Shifts (δ) in $CDCl_3$ and Elemental Analyses of 5a–e

	pteridine aromatic H	$N(CH_3)_2$	C_6H_5	amine moiety
5a	8.40 s	2.85 s	7.50 s	6.45 (1 H, br s), 9.30 (1 H, br s)
5b	8.35 s	2.90 s	7.45 s	1.30 (6 H, t), 3.65 (4 H, q)
5c	8.45 s	2.90 s	7.50 s	1.70 (6 H, br s), 3.65 (4 H, br s)
5d	8.45 s	2.90 s	7.45 s	3.80 (8 H, br s)
5e	8.45 s	2.85 s	7.50 s	1.2–2.1 (10 H, m), 4.15 (1 H, m), 10.1 (1 H, br s, N*H*)

	theoretical, %			found, %		
	C	H	N	C	H	N
5a	59.57	4.99	29.77	58.46	4.84	28.91
5b	63.89	6.55	24.83	63.97	6.85	23.96
5c	65.13	6.32	23.98	65.84	6.38	23.94
5d	61.35	5.72	23.85	62.07	5.84	24.18
5e	65.92	6.63	23.06	65.28	6.84	22.78

solution of **1** (2.50 g, 0.0129 mol) in 20 mL of dry ethanol. After 24 h the sodium chloride was filtered off and the remaining ethanol was removed on a rotary evaporator. The remaining white solid was purified by sublimation to give white crystals, mp 46–47 °C, in ~20% yield. The ^1H NMR spectrum ($CDCl_3$) shows absorptions at δ 1.45 (3 H, t, OCH_2CH_3), 4.65 (2 H, q, OCH_2CH_3), and 8.75 (1 H, s, pyrimidine H). Anal. Calcd for $C_6H_6N_3ClO_3$: C, 35.22; H, 2.95; N, 20.54. Found: C, 35.24; H, 2.93; N, 20.68.

Preparation of 9. Compound **9** was prepared from **8** in the same manner as compound **3** was prepared from **1**, except that the reaction mixture was refluxed for 24 h. The yield of product, mp 107–108 °C, was ~60%. The ^1H NMR spectrum shows absorptions at δ 1.35 (3 H, t, OCH_2CH_3), 3.00 (6 H, br s, $N(CH_3)_2$), 4.20 (2 H, s, $CH_2C_6H_5$), 4.50 (2 H, q, OCH_2CH_3), 7.30 (5 H, s, C_6H_5), and 8.40 (1 H, s, pyrimidine H). Anal. Calcd for $C_{16}H_{19}N_5O_3$: C, 58.35; H, 5.81; N, 21.26. Found: C, 58.08; H, 5.62; N, 20.99.

Preparation of 10, 11, 12, 13, and 14. A solution of sodium ethoxide in ethanol (4.6 mL, 0.43 M) was added dropwise to a solution of **3** (0.32 g, 0.001 mol) in 10 mL of ethanol at 5 °C. The reaction was kept at 5 °C during the addition. After 15 min at this temperature, the solvent was removed under vacuum and the remaining solid was washed with a small portion of dry ethanol. The resulting mixture of **10** and **11** could be separated by extracting the mixture with chloroform which dissolves **10**, leaving **11**. Evaporation of the chloroform provided crude **10** which was recrystallized from distilled water to give 0.135 g (43%) of yellow crystals, mp 195–196 °C. The residue which did not dissolve in chloroform (crude **11** and sodium chloride) was dissolved in water and acidified with 0.5 M HCl to pH 3–4. The acidic solution was extracted four times with small portions of chloroform. The chloroform was then removed under vacuum to yield the crude pteridine *N*-oxide **13** which was recrystallized from ethanol to give 0.045 g (16%) of pure **13**, mp 270–275 °C dec.

The ^1H NMR spectrum ($CDCl_3$) of **10** shows absorptions at δ 1.50 (3 H, t, OCH_2CH_3), 2.90 (6 H, s, $N(CH_3)_2$), 4.60 (2 H, q, OCH_2CH_3), 7.50 (5 H, s, C_6H_5), and 8.65 (1 H, s, pteridine aromatic H). Anal. Calcd for $C_{16}H_{17}N_5O_2$: C, 61.73; H, 5.50; N, 22.49. Found: C, 61.51; H, 5.51; N, 22.29.

The ^1H NMR spectrum (Me_2SO-d_6) of **13** shows absorptions at δ 2.70 (6 H, s, $N(CH_3)_2$), 7.45 (5 H, s, C_6H_5), 8.10 (1 H, s, pteridine aromatic H), and 12.10 (1 H, br, s, NH). In $CDCl_3$ these absorptions appear at δ 2.85, 7.45, 8.35, and 12.20, respectively.

When the reaction time exceeds 2 h, **3** yields **11**, contaminated only by a trace of **10**. Compound **10** can also be prepared by reaction of **9** with ethoxide. A solution of sodium ethoxide in ethanol (0.9 mL, 0.43 M) was added dropwise to a solution of **9** (0.115 g, 0.035 mol) in 5 mL of ethanol at 5 °C. After 3 h, the ethanol was removed under vacuum, and the solid residue was washed with ethanol and recrystallized from water to yield 60 mg of **10**. This product is identical in all respects with **10** prepared from **3**. If the reaction is allowed to stand for more than 3 h, increasing amounts of **11** are obtained.

Both **13** and **10** were easily reduced by dithionite to the corresponding pteridines **14** and **12**. These reductions were performed in the same fashion as described for reduction of the derivatives **5a–e**.

Table III. Chemical Shifts (δ) in $CDCl_3$ and Elemental Analyses of 6a–e

	pteridine aromatic H	$N(CH_3)_2$	C_6H_5	amine moiety
6a	8.60 s	3.00 s	7.55 (m, 3 H), 7.80 (m, 2 H)	6.55 (br s)
6b	8.55 s	3.00 s	7.40 (m, 3 H), 7.70 (m, 2 H)	1.35 (6 H, t), 4.00 (4 H, q)
6c	8.50 s	2.95 s	7.40 (m, 3 H), 7.70 (m, 2 H)	1.70 (6 H, s), 4.15 (4 H, s)
6d	8.55 s	3.00 s	7.45 (m, 3 H), 7.65 (m, 2 H)	3.85 (4 H, m), 4.35 (4 H, m)
6e	8.60 s	2.95 s	7.50 (m, 3 H), 7.75 (m, 2 H)	1.2–2.2 (10 H, m), 4.20 (1 H, br s), 6.60 (N*H*, br s)

	theoretical, %			found, %		
	C	H	N	C	H	N
6a	63.15	5.29	31.56	62.90	5.17	31.35
6b	67.06	6.87	26.07			
6c	68.24	6.62	25.13	68.91	6.90	25.40
6d	64.27	5.99	24.98	64.25	6.22	25.54
6e	68.94	6.94	24.12	68.60	6.80	24.41

Crude **12** was recrystallized from a mixture of benzene–petroleum ether to give a 50% yield of pure product, mp 105–106 °C. Crude **14** was recrystallized from water to also yield 50% of pure product, mp 275 °C dec. Compound **14** could also be prepared by treating crude **11**, contaminated by NaCl, with dithionite.

The ^1H NMR spectrum ($CDCl_3$) of **12** shows absorptions at δ 1.60 (3 H, t, OCH_2CH_3), 3.10 (6 H, s, $N(CH_3)_2$), 4.85 (2 H, q, OCH_2CH_3), 7.70 (3 H, m, C_6H_5), 7.95 (2 H, m, C_6H_5), and 8.95 (1 H, s, pteridine aromatic proton). Anal. Calcd for $C_{16}H_{17}N_5O$: C, 65.07; H, 5.79; N, 23.71. Found: C, 65.36; H, 6.03; N, 22.70.

The ^1H NMR spectrum ($CDCl_3$) of **14** shows absorptions at δ 3.10 (6 H, s, $N(CH_3)_2$), 7.60 (3 H, m, C_6H_5), 7.90 (2 H, m, C_6H_5), 8.45 (1 H, s, pteridine aromatic H), 12.90 (1 H, br, NH). Anal. Calcd for $C_{14}H_{13}N_5O$: C, 62.91; H, 4.90; N, 26.20. Found: C, 62.88; H, 4.70; N, 26.08.

Hydrolysis of 11 to 15. A suspension of compound **11** (0.30 g, 0.001 mol) in water (25 mL) was refluxed for 6 h. The reaction was cooled to room temperature, and the resulting yellow crystals were filtered off. Concentration of the filtrate provided a second crop of crystals for a total yield of 20% (0.055 g) of pure **15**, mp 193–197 °C. Anal. Calcd for $C_{13}H_{15}N_5O_2$: C, 57.12; H, 5.54; N, 25.63. Found: C, 56.76; H, 5.33; N, 24.84. The mass spectrum of this product shows a parent peak at *m/e* 273 as well as strong absorptions at *m/e* 258, 241, 229, and 213. The ^1H NMR spectrum (Me_2SO-d_6) shows absorptions at δ 2.64 (6 H, s, $N(CH_3)_2$), 7.44 (5 H, m, C_6H_5), 7.88 (2 H, br s, $ArNH_2$), and 9.84 (2 H, br s, $CONH_2$).

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Registry No.—**1**, 4316-93-2; **2**, 4316-94-3; **3**, 69352-36-9; **4a**, 69331-05-1; **4b**, 69352-35-8; **4c**, 69331-06-2; **4d**, 69331-07-3; **4e**, 69331-08-4; **5a**, 69331-09-5; **5b**, 69352-34-7; **5c**, 69331-10-8; **5d**, 69331-11-9; **5e**, 69331-12-0; **6a**, 69331-13-1; **6b**, 69331-14-2; **6c**, 69331-15-3; **6d**, 69352-33-6; **6e**, 69331-16-4; **7**, 2164-84-3; **8**, 54851-36-4; **9**, 69331-17-5; **10**, 69331-18-6; **11**, 69331-19-7; **12**, 69331-20-0; **13**, 69331-19-7; **14**, 69331-21-1; **15**, 69331-22-2; α-phenyl-*N,N*-dimethylacetamidine, 56776-16-0; diethylamine, 109-89-7; piperidine, 110-89-4; morpholine, 110-91-8; cyclohexylamine, 108-91-8.

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1,9-Disubstituted Phenalenes. 4.[1] Preparation and Properties of 1,9-Dihetero-Substituted Phenalenyl Cations

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The synthesis of new 1,9-dihetero-substituted (OR, SR, NR_2) phenalenes and phenalenyl cations is reported and their ^1H and ^{13}C NMR and UV/Vis spectra together with their redox potentials are discussed. Shifts of the ^{13}C resonances of the ring atoms of the cations indicate a close relationship with the parent compound phenalenyl. This can also be seen from the existence of the free radical and the anionic species, which can be generated electrochemically.

The odd alternant hydrocarbon phenalenyl and some of its 1-substituted derivatives are known to exist in three different oxidation states: plus, zero, minus.[3] Recently Haddon pointed out the prospect of intermolecular charge transfer in solids of carbon-centered free radicals and of phenalenyl in particular.[4] Since the parent compound is rather unstable toward dimerisation,[5] the influence of hetero substituents on the redox properties of the carbon skeleton should be of interest. 1- and 1,3-substituted derivatives are not well suited for this kind of investigation because they are either rather reactive, as in the case of 1-phenalenes,[3a,c] or may behave more like 1,8-trimethinecyanine-bridged naphthalenes.[3b,d,6] Only 1,9 substitution allows conjugation over the carbon skeleton as a whole.[3d]

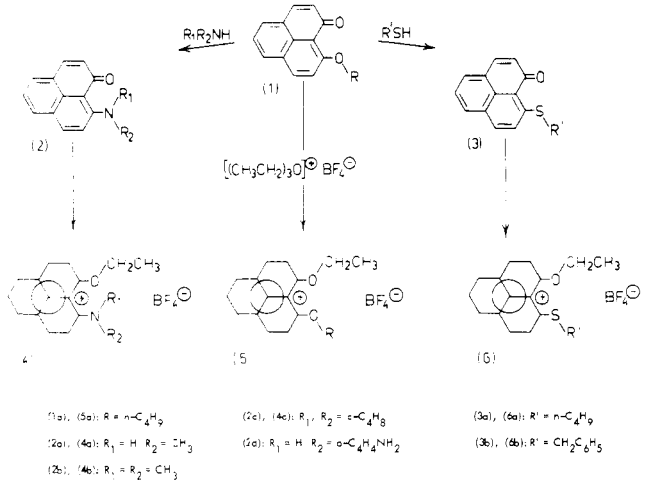
In preceding papers of this series we reported synthetic methods for the preparation of a variety of 1,9-dihetero-substituted phenalene derivatives.[7] As important intermediates in this chemistry, 1,9-disubstituted phenalenium ions have been found to be very stable cations, thus showing the same behavior as their parent compound phenalenyl.[8] Earlier results already showed that phenalenium ions have very low and reversible redox potentials, thus representing quite a unique class of nearly planar carbon-based free radicals,[8b] in contrast to other reduction products of carbonium ions which easily tend to dimerize, as for instance tropylium ions.[9] We therefore decided to further investigate the charge distribution and redox properties of 1,9-dihetero-substituted phenalenium ions.

Results

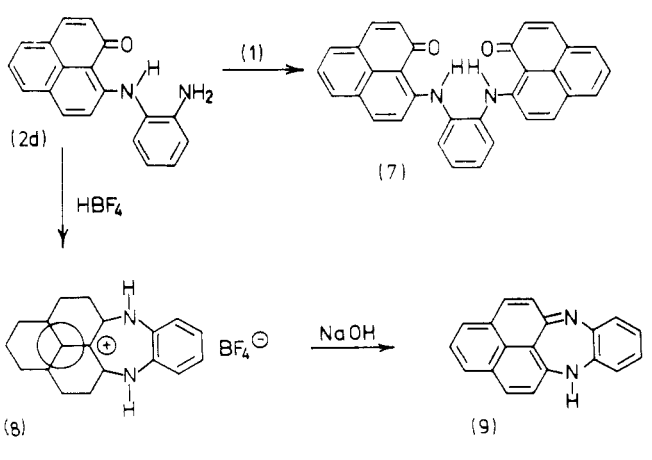
In a general reaction 9-hetero-substituted 1-phenalenones can be alkylated at the oxygen on 1 position by Meerwein's salt (Scheme I). Thus 9-butoxy-1-phenalenone (**1a**) and its N (**2**), and S (**3**) derivatives form 1,9-disubstituted phenalenium tetrafluoroborates (**4–6**).

Nucleophilic substitution of the alkoxy group by primary amines gives 9-amino-1-phenalenones (**2a,b**), in which a second substitution is normally prevented by the strong intramolecular hydrogen bond.[7] It is therefore possible to react **1** with *o*-phenylenediamine to give **2d.** At higher temperature **2d** reacts with a further molecule of **1** to form **7** (Scheme II).[10] However, in the presence of acid and above 120 °C, the internal cyclization of the diamine occurs preferentially to give 8. Treatment of the 1,5-diazepinium ion (8) with aqueous

Scheme I



Scheme II



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