

Alkaline Condensation of 9,10-Phenanthrenedione with
N,N-Dialkylguanidines. A Novel Synthesis of
2'-(Dialkylamino)spiro[9*H*-fluorene-9,4'-[4*H*]imidazol]-5'(3'*H*)ones

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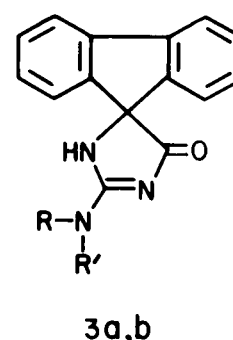
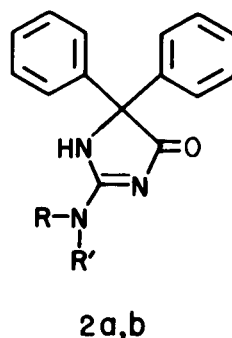
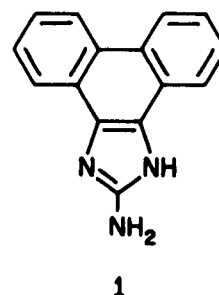
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9,10-Phenanthrenedione was reacted with equimolar amounts of *N,N*-dimethylguanidine or creatine in 0.2 *N* potassium hydroxide in ethanol-water, 7:3 to obtain 2'-(dimethylamino)spiro[9*H*-fluorene-9,4'-[4*H*]imidazol]-5'(3'*H*)one or *N*-(3',5'-dihydro-5'-oxospiro[9*H*-fluorene-9,4'-[4*H*]imidazol]-2'-yl)-*N*-methylglycine, respectively. These products are the first derivatives of this ring system with 2'-amino substituents. Formation of these products accounts for the previously reported absence of fluorescence when 9,10-phenanthrenedione reacts with *N,N*-disubstituted guanidines.

Imidazolidinones or imidazolinones are produced in the alkaline condensation of benzil with equimolar amounts of guanidine, alkylguanidines or *N,N*-dialkylguanidines (1-3). A 1,2-diazaspiro[4.4]nonane ring structure results when the guanidino group of arginine condenses with 1,2-cyclohexanedione (4,5). The rearrangement that accompanies formation of these products resembles the benzilic acid rearrangement (1,2,6). Although 9,10-phenanthrenedione also undergoes this rearrangement (7,8), its reaction in alkaline solution with either guanidine or certain alkylguanidines results in 11-phenanthro[9,10-*d*]imidazol-2-amine (**1**), a fluorescent compound (9,10); however, no fluorescence was observed when *N,N*-dimethylguanidine or creatine was treated with phenanthrenedione (9). This anomaly in reactivity of phenanthrenedione has been investigated, and a novel synthesis has resulted.

Compound **2a** was prepared by a simplified modification of a published procedure (3) as a basis for comparison with the product of equimolar alkaline condensation of 9,10-phenanthrenedione and *N,N*-dimethylguanidine. Comparison of nmr, ir, mass spectra, and analyses supports the conclusion that the latter compound is **3a**, a structural homologue of **2a** (3,11). Other than a difference of two aryl protons, the only significant difference in data is that the frequency of the C=O stretching band in the ir spectrum of **3a** is higher than that of **2a**; on the other hand, the ir spectra of the hydrobromides of **2a** and **3a** are nearly identical. A possible interpretation of these spectra is that ring strain (12) is greater in the imidazoline ring of **3a** than of **2a** (13), but that the difference in strain is eliminated when the C=N bond shifts from its endocyclic position in these compounds to the exocyclic position in

the cations. Nonconjugation of C=O and C=N groups in **3a** is unlikely; when these groups are not conjugated, the frequencies of both the C=O and C=N stretching bands are increased (11,14,15). The homology of **2b** and **3b** is supported by elemental analyses.



a, R = R' = CH₃

b, R = CH₃; R' = CH₂COOH

Thus, whereas benzil and phenanthrenedione react differently with guanidine and certain alkylguanidines, they react similarly with *N,N*-dialkylguanidines. Formation of **3** instead of **1** accounts for the absence of fluorescence (9) when *N,N*-disubstituted guanidines react with phenanthrenedione. Although **3** is a homologue of **2** and other known compounds, condensation of phenanthrenedione with *N,N*-dialkylguanidines is a novel synthesis in that all previous successful syntheses of the ring system of **3** (16) have used either fluorene or fluorenone as a starting material and have produced only 2',5'-diones (hydantoins). No previous synthesis of this ring system with 2'-amino substituents exists.

EXPERIMENTAL (17)

2-(Dimethylamino)-1,5-dihydro-5,5-diphenyl-4*H*-imidazol-4-one (**2a**)

Benzil was added to an equivalent amount of *N,N*-dimethylguanidine in 0.2 *N* potassium hydroxide in ethanol-water, 7:3 at 70°. After 3 days at 5°, the resulting crystalline precipitate (75%) was removed and was recrystallized twice in dimethylformamide to obtain **2a**, m.p. higher than 350° (published m.p. 356-357° (18), 348-349° (3)); mass spectrum *m/e* 279 (*M*⁺); ir (potassium bromide): 3160, 3060 (N-H), 1680 (C=O), and 1612 cm⁻¹ (C-N) (published ir (3) 3107, 3060, and 1675 cm⁻¹); nmr (deuteriotrifluoroacetic acid): δ 3.44 (s, 6H), 7.39 (s, 10H), 11.48 (s, 1H).

Anal. Calcd. for C₁₇H₁₇N₃O: C, 73.10; H, 6.13; N, 15.04. Found: C, 73.29; H, 6.14; N, 15.18.

Hydrobromide of **2a**

Compound **2a** was recrystallized from ethanolic hydrogen bromide to obtain **2a**·HBr; ir (potassium bromide): 2984 (N-H), 1780 (C-O), and 1695 cm⁻¹ (C=N).

Anal. Calcd. for C₁₇H₁₈BrN₃O: C, 56.68; H, 5.04; Br, 22.18; N, 11.66. Found: C, 55.94; H, 4.96; Br, 22.94; N, 11.83 (19).

N-(4,5-Dihydro-4-oxo-5,5-diphenyl-1*H*-imidazol-2-yl)-*N*-methylglycine (**2b**)

Benzil and creatine were condensed in the same manner and recrystallized from ethanol-water to obtain **2b** (93%), m.p. 245°.

Anal. Calcd. for C₁₈H₁₇N₃O₃: C, 66.86; H, 5.30; N, 13.00. Found: C, 67.01; H, 5.58; N, 13.27.

2'-(Dimethylamino)spiro[9*H*-fluorene-9,4'-[4*H*]imidazol]-5'(3'*H*)-one (**3a**)

N,N-Dimethylguanidine sulfate (13.6 g.) was added to 140 ml. of 1 *N* potassium hydroxide in ethanol, and the resulting precipitate of potassium sulfate was removed by filtration. After the addition of 60 ml. of water, the solution (0.2 *N* potassium hydroxide) was heated to 70°, and 9,10-phenanthrenedione (20.8 g.) was added. After 6 days at room temperature, the reaction mixture was acidified to pH 6 with hydrochloric acid, and the precipitated solid was washed with water, collected, and dried (12.6 g., 45%). One crystallization of this product from ethanol yielded **3a**, m.p. 310-311°; mass spectrum *m/e* 277 (*M*⁺); ir (potassium bromide): 3200 (N-H), 1713 (C=O), and 1610 cm⁻¹ (C=N); nmr (deuteriotrifluoroacetic acid): δ 3.38, 3.45 (d, 6H), 7.1-7.7 (m, 8H), 11.29 (s, 1H).

Anal. Calcd. for C₁₇H₁₅N₃O: C, 73.63; H, 5.45; N, 15.15. Found: C, 73.76; H, 5.32; N, 15.25.

Hydrobromide of **3a**

Compound **3a** was recrystallized from ethanolic hydrogen bromide to obtain **3a**·HBr; ir (potassium bromide): 2980 (N-H), 1776 (C=O), and 1697 cm⁻¹ (C=N).

Anal. Calcd. for C₁₇H₁₆BrN₃O: C, 57.00; H, 4.50; Br, 22.31; N, 11.73. Found: C, 57.18; H, 4.81; Br, 22.23; N, 11.88.

N-(3',5'-Dihydro-5'-oxospiro[9*H*-fluorene-9,4'-[4*H*]imidazol]-2'-yl)-*N*-methylglycine (**3b**)

9,10-Phenanthrenedione and creatine were condensed in the same manner and recrystallized from ethanol-water to obtain **3b** (31%), m.p. 194-196°.

Anal. Calcd. for C₁₈H₁₅N₃O₃: C, 67.28; H, 4.71; N, 13.08. Found: C, 67.56; H, 4.89; N, 12.80.

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- (13) The structural homology of **2** and **3** is not three-dimensional because the phenyl groups of **2** are not coplanar with the imidazole ring. See K. Lempert, J. Nyitrai, K. Zauer, A. Kálmán, G. Argay, A. J. M. Duisenberg, and P. Sohár, *Tetrahedron*, **29**, 3565 (1973).
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is 1*H*-phenanthro[9,10-*d*]imidazol-2-ol, the 2-hydroxy analogue of **1**, is under investigation.

(17) Ir spectra were recorded on a Perkin-Elmer Model 421 spectrophotometer. Mass spectra were obtained by means of a Hitachi Perkin-Elmer RMV-7 spectrometer. Nmr spectra were recorded on a Varian T-60 spectrometer with trimethylsilane as internal standard by Dr. S. Mannen. Microanalytical, ir, and mass spectral data were supplied by Dr. W. C. Alford and associates of

the Section of Microanalytical Services, NIAMD. Melting points were determined with a Kofler hot-stage microscope and are uncorrected.

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(19) Although there are minor discrepancies in the analyses of C and Br, this preparation from an analytically pure sample of **2a** was considered adequate for an ir spectrum.