5,12-Diacylated-5,6,11,12-tetrahydrodibenzo[*b*,*f*][1,4]-diazocines and Related Compounds

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Both *N*,*N*'-(*o*-phenylene)diformamide (**1**) and *N*,*N*'-(4-chloro-1,2-phenylene)diformamide (**30**) reacted with α,α-dibromo-*o*-xylene (**2**) in DMF at 95-100° to give 5,6,11,12-tetrahydrodibenzo-[*b*,*f*][1,4]diazocine-5,12-dicarboxaldehyde (**3a**) and the corresponding 2-chloro derivative (**3b**). With potassium hydroxide in ethylene glycol at 110°, **3a** and **3b** were selectively saponified to the 5-carboxaldehyde derivatives (**4**) and either **21a** or **22a**. Reacylation of the latter led to a series of 5,12-unsymmetrically diacylated derivatives, **5-18**. Additionally, **4** was subjected (a) to a base-catalyzed addition to acrylonitrile to give the 12-cyanoethyl derivative (**19**) and (b) alkylation with α-bromotoluene to give the 12-benzyl compound (**20**). Saponification of both carboxaldehyde groups in **3a,b** required potassium hydroxide in ethylene glycol at 135° and gave the *N*,*N*'-unsubstituted heterocycles (**23** and **24**); these were subsequently reacted with several aldehydes to yield the 5,12-methano derivatives (**25-29**).

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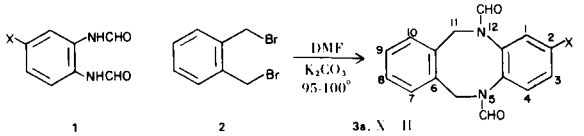
The annulation of *N*,*N*'-(*o*-phenylene)diformamide (**1**) (2) with α,α-dibromo-*o*-xylene (**2**) led to the synthesis of 5,6,11,12-tetrahydrodibenzo[*b*,*f*][1,4]diazocine-5,12-dicarboxaldehyde (**3a**). The central nervous system stimulant activity seen with **3a** was sufficiently interesting to warrant an exploratory synthetic program, and that effort



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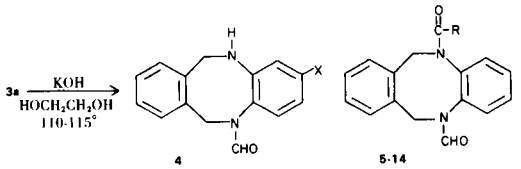
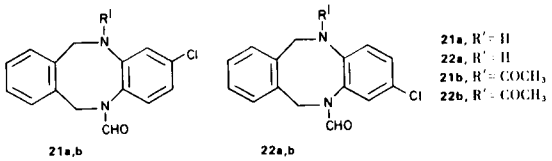
led to the even more potent 5,12-unsymmetrically diacylated derivatives of the same heterocycle. That group of compounds could be prepared only after a procedure was developed that saponified selectively one of the two *N*-carboxaldehyde groups to give **4** (X = H) (3), and when it was found that the latter could be reacylated with phosgene, an acyl chloride, or an acyl anhydride to give derivatives represented by **5-14**. In addition, **5**, treated with ammonia gave the 12-carboxamide (**15**) while **4**, reacted with *n*-propyl isocyanate, gave the 12-*n*-propylcarboxamide (**16**). Finally, nucleophilic displacement of the chlorine atom in **7** by dimethylamine or 4-methylpiperazine gave the 12-(dimethylaminoacetyl)- (**17**) and the 12-(4-methylpiperazine)acetyl- (**18**) derivatives of **4**.

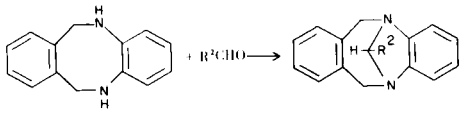


Two additional reactions of **4** were investigated: (a) the base catalyzed addition to acrylonitrile gave the 12-cyanoethyl derivative (**19**) and (b) the alkylation with α-bromotoluene in 2-butanone, employing potassium carbonate as the base, gave the 12-benzyl derivative, **20**.

The selective saponification of **3b** could lead to two isomeric 5-carboxaldehyde derivatives, **21a** and **22a**. The product isolated from that reaction had a broad melting point and was probably a mixture although it appeared to be homogeneous by tlc in three different solvent systems. The 12-acetyl derivative, **21b** or **22b**, had a sharp melting point and, again, was homogeneous by tlc. It was not possible to make precise structure assignments for these derivatives.



Saponification of both carboxaldehyde groups in **3a,b** was effected with potassium hydroxide in ethylene glycol at 135° and gave the *N,N'*-unsubstituted heterocycles (**23** and **24**). Several 5,12-methano derivatives (**25-29**) were prepared from **23** and one aliphatic and several aromatic aldehydes (**4**).



25, R^2 = *p*-ClC_6H_4
26, R^2 = *o*-ClC_6H_4
27, R^2 = 3,4,5-$(CH_3O)_3C_6H_2$
28, R^2 = *p*-$[(C_2H_5)_2NCH_2CH_2O]C_6H_4$
29, R^2 = C_2H_5

EXPERIMENTAL

Melting points were determined in capillary tubes in an electrically heated oil bath and are uncorrected. The pmr spectra were obtained on deuteriochloroform or DMSO-d_6 solutions with a Perkin-Elmer R12B spectrophotometer. The ir spectra were obtained on mineral oil mulls or deuteriochloroform solutions on a Perkin-Elmer 621 spectrophotometer. The authors are indebted, respectively, to Dr. M. S. Puar and Mrs. B. Toeplitz of This Institute for these spectra. The microanalyses were performed by Mr. J. F. Alicino and his associates of This Institute.

5,6,11,12-Tetrahydrodibenzo[*b,f*][1,4]diazocine-5,11-dicarboxaldehyde (**3a**).

To 220 g. (1.17 moles) of 65% phenyl formate at 15°was added, in portions, with stirring, during 1.0 hour, a total of 54.0 g. (0.50 mole) of *o*-phenylenediamine. A mildly exothermic reaction produced a temperature rise to 45°. The mixture was stirred for 3 hours at ambient temperature and then diluted with 150 ml. of diisopropyl ether. The solid that separated was filtered, washed with diisopropyl ether, and dried to give 78.4 g. (95% yield) of *N,N'*-(*o*-phenylene)diformamide (**30**), m.p. 163-166° dec. (1).

To 86.0 g. (0.36 mole) of α,α-dibromo-*o*-xylene, 60.0 g. (0.36 mole) of the above **30**, and 1500 ml. of *N,N*-dimethylformamide was added 86.0 g. (0.62 mole) of anhydrous potassium carbonate and the mixture was heated at an internal temperature of 95-100° for 4 hours, filtered, and the filtrate concentrated to dryness *in vacuo*. The residual solid was slurried with 300 ml. of water, filtered, washed, dried, and recrystallized from 1200 ml. of acetonitrile to give 59.0 g. (60% yield) of **3a**, m.p. 217-219°dec.; ir (mull): ν 1670(s), 1580(w), 1490(s), 1485(s), 1450(w), 1445(w), 1420 cm^{-1}; pmr (deuteriochloroform): δ 4.83 [s, 4H, 2 (C*H*$_2$)], 3.0-7.15 (m, 8H, 8 Ar-*H*), 8.45 [s, 2H, 2 (C*H*O)].

Anal. Calcd. for $C_{16}H_{14}N_2O_2$: C, 72.16; H, 5.30; N, 10.52. Found: C, 72.38; H, 5.53; N, 10.63.

N,N'-(4-Chloro-1,2-phenylene)bisformamide (**30**).

The experimental conditions described for **1** (2) gave with 105.0 g. of 63% phenyl formate (0.59 mole) and 35.6 g. (0.25 mole) of 4-chloro-*o*-phenylenediamine 43.5 g. (87% yield) of crude **30**, m.p. 178-180° dec. An analytical sample recrystallized from methanol (80 ml./g.) melted at 184-186° dec.; ir (mull): ν 3250(s), 1690(s), 1595(s), 1530(s), 1480(w), 1440(w), 1410(s) cm^{-1}; pmr (DMSO-d_6): δ 3.34 [s, 2H, 2 (N*H*) (equilibrates with deuterium oxide)], 7.15-8.10 (m, 3H, 3-Ar-*H*), 8.38 [s, 2H, 2 (NHC*H*O)].

Anal. Calcd. for $C_8H_7ClN_2O_2$: C, 48.38; H, 3.57; N, 14.15; Cl, 17.86. Found: C, 48.54; H, 3.70; N, 14.28; Cl, 17.91.

2-Chloro-6,11-dihydrodibenzo[*b,f*][1,4]diazocine-5,12-dicarboxaldehyde (**3b**).

The procedure described for **3a** was followed in the reaction between 58.0 g. (0.22 mole) of α,α-dibromo-*o*-xylene, 40.0 g. (0.2 mole) of **30**, 810 ml. of *N,N*-dimethylformamide, and 58.0 g. (0.4 mole) of anhydrous potassium carbonate to obtain 51.8 g. of crude **3b**, m.p. 205-208° dec.; recrystallization from 775 ml. of acetonitrile gave 42.6 g. (77% yield) of **3b**, m.p. 212-214°; ir (mull): ν 1670(s), 1630(w), 1590(w), 1570(w), 1495(s), 1450(m), 1430(m) cm^{-1}; pmr (deuteriochloroform): δ 4.80 [s, 4H, 2 (C*H*$_2$)], 7.07-7.60 (m, 7H, 7 Ar-*H*), 8.38 [d (J = 2 Hz), 2H, 2 (C*H*O)].

Anal. Calcd. for $C_{16}H_{13}ClN_2O_2$: C, 63.97; H, 4.36; N, 9.70; Cl, 12.10. Found: C, 64.24; H, 4.43; N, 9.47; Cl, 11.89.

6,11-Dihydro-5*H*-dibenzo[*b,f*][1,4]diazocine-5-carboxaldehyde (**4**).

To a solution of 1.80 g. (0.027 mole) of 85% potassium hydroxide in 90 ml. of ethylene glycol at 70° was added 4.80 g. (0.018 mole) of **3a** and the slurry heated to 110° when a solution formed. The solution was maintained at 110-115° for 2 hours, cooled, and poured into 900 ml. of an ice-water mixture. The hydrolysate was extracted with 300 ml. of ether, the ether solution was washed, dried, concentrated, and the residue was recrystallized from 450 ml. of diisopropyl ether to give 2.3 g. (55% yield) of **4**, m.p. 106-108°; ir (mull): ν 3350(s), 3330(s), 1650(s), 1640(s), 1600(m), 1585(m), 1490(s), 1455(m), 1450(m) cm^{-1}; pmr (deuteriochloroform): δ 4.00 [broad s, 1H, N*H* (equilibrates with deuterium oxide)], 4.36 (s, 2H, C*H*$_2$-NH), 5.00 (s, 2H, CH$_2$-NCHO), 6.20-8.10 (m, 8H, Ar-*H*), 8.35 (s, 1H, C*H*O).

Anal. Calcd. for $C_{15}H_{14}N_2O$: C, 75.60; H, 5.92; N, 11.75. Found: C, 75.56; H, 6.09; N, 11.75.

2-Chloro-11,12-dihydrodibenzo[*b,f*][1,4]diazocine-5(6*H*)carboxaldehyde (**21a**) or 3-Chloro-11,12-dihydrodibenzo[*b,f*][1,4]diazocine-5(6*H*)carboxaldehyde (**22a**).

To a solution of 3.60 g. (0.053 mole) of 85% potassium hydroxide in 180 ml. of ethylene glycol and 1 ml. of water, at 50°, was added 10.8 g. (0.036 mole) of **3b**. The temperature was raised to 110° in 0.75 hour, the whole kept for 2.5 hours at 110-115°, cooled, and poured into 600 ml. of an ice-water mixture. Workup as with **4**, gave 6.4 g. of solid, m.p. 128-135°. Recrystallization from 640 ml. of diisopropyl ether gave 4.80 g. of either **21a** or **22a**, m.p. 130-132° (turbid), clearing at 142°. By tlc, in three systems, this material was homogeneous: silica gel plates, one spot, R_f 0.72 (1:1, acetone-benzene); one spot, R_f 0.68 (95:5, ethyl acetate-ethanol); and, one spot, R_f 0.40 (99:1, chloroform-methanol). The following spectral data were obtained with this material: ir (mull): ν 3400 (sharp s), 1660(s), 1625(w), 1600(m), 1580(m), 1495(s), 1470(s), 1450(m), 1440(m), 1420(m) cm^{-1}; pmr (deuteriochlorofrom): δ 4.30 (s, 2H, C*H*$_2$NH), 4.95 (s, 2H, C*H*$_2$NCHO), 6.50-7.20 (m, 7H, 7 Ar-*H*), 8.26 (s, 1H, C*H*O).

Anal. Calcd. for $C_{15}H_{13}ClN_2O$: C, 66.08; H, 4.82; N, 10.37; Cl, 13.00. Found: C, 66.31; H, 4.97; N, 10.57; Cl, 12.79.

5,6,11,12-Tetrahydrodibenzo[*b,f*][1,4]diazocine (**23**).

To a solution of 12.0 g. (0.18 mole) of 85% potassium hydroxide in 180 ml. of ethylene glycol at 90° was added 9.6 g. (0.036 mole) of **3a**; when the slurry was heated to an internal temperature of 130-135°, a solution formed. The solution was maintained at 130-135° for 4.5 hours, and allowed to cool to ambient temperature. The crystalline solid that separated was filtered, washed, and dried to give 6.9 g. of solid, m.p. 188-192°; recrystallization from 400 ml. of absolute ethanol gave 4.5 g. (58% yield) of **23**, m.p. 192-

194° (6); ir (mull): ν 3370(s), 1590(s), 1520(w), 1500(s), 1490(s), 1445(s), 1430(m), 1410(w) cm^{-1}; pmr (DMSO-d_6): δ 4.34 [d (J = 5 Hz), 4H, 2(CH_2)$_2$], 5.03 [broad s, 2H, 2(N*H*) (equilibrates with deuterium oxide)], 6.38-7.40 (m, 8H, 8 Ar-*H*).

Anal. Calcd. for $C_{14}H_{14}N_2$: C, 79.96; H, 6.71; N, 13.33. Found: C, 80.13; H, 6.96; N, 13.54.

2-Chloro-5,6,11,12-tetrahydrodibenzo[*b,f*][1,4]diazocine (**24**).

To a solution of 11.0 g. (0.16 mole) of 85% potassium hydroxide, 180 ml. of ethylene glycol, and 10 ml. of water, at 50°, was added 12.0 g. (0.04 mole) of **3b**. Subsequently, the mixture was heated to 135-140° in 0.5 hour and kept at that temperature for a total of 4.5 hours: after 2.5 hours, a solid began to separate from the reaction mixture. The cooled mixture was filtered, the solid was washed and dried to give 9.0 g. of crude **24**, m.p. 179-183° dec. Recrystallization from 450 ml. of 95% ethanol gave 5.85 g. (65% yield) of **24**, m.p. 182-184° dec. (7); ir (mull): ν 3380(s), 1590(s), 1490(s), 1450(s), 1425(m) cm^{-1}; pmr (DMSO-d_6): δ 4.30 [t, (J = 3 Hz), 4H, 2(CH_2)], 5.10-5.60 [m, 2H, 2(N*H*) (equilibrates with deuterium oxide)], 6.40-7.30 (m, 7H, 7 Ar-*H*).

Anal. Calcd. for $C_{14}H_{13}ClN_2$: C, 68.71; H, 5.36; N, 11.45; Cl, 14.32. Found: C, 68.84; H, 5.61; N, 11.71; Cl, 14.45.

5-Acetyl-5,6,11,12-tetrahydrodibenzo[*b,f*][1,4]diazocine (**31**).

A solution of 2.0 g. (0.01 mole) of **23**, 1.0 g. (0.01 mole) of acetic anhydride, 0.05 g. of *p*-toluenesulfonic acid, and 50 ml. of anhydrous dioxane was heated at an internal temperature of 80° for 2 hours, the solution concentrated *in vacuo*, the residual solid dissolved in 250 ml. of ether, the ether solution washed, dried, and concentrated. The residue, 2.0 g., m.p. 165-167°, was recrystallized from 250 ml. of cyclohexane to give 1.2 g. (48% yield) of **31**, m.p. 167-169°; ir (mull): ν 3330(s), 1635(s), 1590(s), 1515(w), 1485(s), 1445(m), 1400(s) cm^{-1}; pmr (deuteriochloroform): δ 1.95 (s, 3H, CH_3CO), 3.98 [d (J = 15 Hz), 2H, CH_2NH], 4.47 [q (J = 15 Hz, 30 Hz), 2H, CH_2NCO], 6.00-7.50 [m, 9H, 8 Ar-*H* + N*H* (equilibrates with deuterium oxide)].

Anal. Calcd. for $C_{16}H_{16}N_2O$: C, 76.16; H, 6.39; N, 11.10. Found: C, 76.40; H, 6.19; N, 11.09.

12-Acetyl-5,6,11,12-tetrahydrodibenzo[*b,f*][1,4]diazocine-5-carboxaldehyde (**6**).

A solution of 2.40 g. (0.01 mole) of **4**, 25 ml. of acetic anhydride, and 0.1 g. of *p*-toluenesulfonic acid was heated at 90-95° internal temperature for 1 hour, the whole cooled to 50°, and poured on 300 ml. of an ice-water mixture. The precipitate was filtered, washed, and dried to give 2.0 g. of solid, m.p. 163-165°. Recrystallization from 80 ml. of absolute ethanol gave 1.20 g. (42% yield) of **6**, m.p. 165-167°; ir (mull): ν 1665(s), 1650(s), 1590(w), 1575(w), 1500(s), 1460(w), 1450(w) cm^{-1}; pmr (deuteriochloroform): δ 1.80 (s, 3H, CH_3), δ_A 5.84, δ_B 4.12 [q (J_{AB} = 15 Hz) (5) CH_2NCOCH_3], 5.04, 4.56 [AB_q (J_{AB} = 12 Hz), 2H, CH_2NCHO], 6.95-7.52 (m, 8H, 8 Ar-*H*), 8.47 (s, 1H, C*H*O).

Anal. Calcd. for $C_{17}H_{16}N_2O_2$: C, 72.84; H, 5.75; N, 10.00. Found: C, 72.98; H, 5.84; N, 10.22.

The derivatives that were prepared by the procedure described above are listed in Table I along with the relevant physical properties, recrystallization solvents, and analyses.

11,12-Dihydro-12-(trimethylacetyl)dibenzo[*b,f*][1,4]diazocine-5(6*H*)carboxaldehyde (**12**).

To 3.50 g. (0.015 mole) of **4**, 4.0 g. (0.04 mole) of triethylamine, and 125 ml. of anhydrous toluene was added dropwise, with stirring, at ambient temperature, a solution of 3.60 g. (0.03 mole) of trimethylacetyl chloride in 25 ml. of anhydrous toluene. Subsequently, the mixture was stirred for 2 hours at ambient temperature, for 4 hours at an internal temperature of 75-80°, cooled, filtered, and the filtrate concentrated to dryness *in vacuo*. The residue, 4.8 g., m.p. 155-158° was recrystallized from 30 ml. of ethyl acetate to give 2.90 g. (60% yield) of **12**, m.p. 168-170°; ir (deuteriochloroform): ν 1660(s), 1630(s), 1590(s), 1575(s), 1500(s), 1480(s), 1460(s) cm^{-1}; pmr (deuteriochloroform): δ 1.00 [s, 9H, 3(CH_3)], 3.90-6.00 [complex of 3 multiplets, 4H, 2(CH_2)], 6.85-7.50 (m, 8H, 8 Ar-*H*), 8.47 (s, 1H, C*H*O).

Anal. Calcd. for $C_{20}H_{22}N_2O_2$: C, 74.51; H, 6.88; N, 8.64. Found: C, 74.79; H, 7.01; N, 8.94.

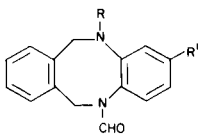
All of the derivatives prepared by the procedure described above are listed in Table II, along with the relevant physical properties, recrystallization solvents, and analyses.

12-Acryloyl-11,12-dihydrodibenzo[*b,f*];1,4]diazocine-5(6*H*)carboxaldehyde (**9**).

To a stirred solution of 3.50 g. (0.015 mole) of **4** and 3.0 g. (0.03 mole) of triethylamine in 125 ml. of anhydrous toluene was added 3.10 g. (0.025 mole) of 3-chloropropionyl chloride in 30 ml. of anhydrous toluene during 1 hour, while maintaining the internal ambient temperature for 6 hours, and then concentrated to dryness *in vacuo*. The residual solid, 9.5 g., m.p. 195-200° dec., was suspended in 50 ml. of cold water, refiltered, and dried to give 3.0

Table I

Substituents in

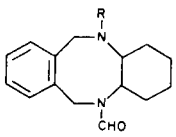


R	R′	M.p. °C	Recrystallization Solvent	Yield %	Analyses Calcd. C	H	N	Found C	H	N
EtCO	H	190-191	95% Ethanol	64	73.43	6.16	9.52	73.32	5.89	9.47
n-PrCO	H	130-132	Isopropyl ether	47	74.03	6.54	9.09	74.06	6.82	9.04
2-PrCO	H	170-172	Isopropyl ether	43	74.03	6.54	9.09	74.23	6.78	9.13
MeCO	Cl	150-152 dec.	2-Propanol	27	64.86	4.82	8.40 (a)	64.63	4.87	8.47

(a) Calcd.: Cl, 11.27; Found: Cl, 11.34.

Table II

R in



	M.p. °C	Recrystallization Solvent	Yield %	Analyses Calcd. C	H	N	Found C	H	N
$CH_3(CH_2)_5CO$	98-100	Isopropyl ether	70	75.38	7.48	7.99	75.49	7.40	7.93
$ClCH_2CO$	183-185	AcOEt	44	64.86	4.82	8.90	64.62	4.49	8.68
PhCO	157-159	PhMe	67	77.17	5.30	8.18	77.26	5.34	8.17

g. of solid, m.p. 198-207° dec. Recrystallization from 70 ml. of toluene gave 2.40 g. (53% yield) of **9**, m.p. 205-207° dec.; ir (mull): ν 1660(s), 1650(s), 1610(m), 1590(m), 1580(m), 1500(s), 1460(m), 1450(m), 1410(s) cm^{-1}; pmr (deuteriochloroform): δ 4.28 [d (J = 15 Hz), 2H, CH_2NCHO], 4.80 [d (J = 12 Hz), 2H, $CH_2NCOCH{:}CH_2$], 5.40-5.80 (m, 2H, $CH{:}CH_2$), 5.80-6.00 (m, 1H, $CH{:}CH_2$), 6.10-7.50 (m, 8H, 8 Ar-*H*), 8.40 (s, 1H, *CHO*).

Anal. Calcd. for $C_{18}H_{16}N_2O_2$: C, 74.95; H, 5.51; N, 9.58. Found: C, 74.66; H, 5.64; N, 9.52.

12-[(Dimethylamino)acetyl]-11,12-dihydrodibenzo[*b,f*][1,4]diazocine-5(6*H*)carboxaldehyde (**17**).

To a suspension of 3.0 g. (0.01 mole) of **7** was added a solution of 10.0 g. (0.22 mole) of anhydrous dimethylamine in 100 ml. of anhydrous benzene, the mixture was stirred at ambient temperature for 66 hours, filtered, and the filtrate concentrated *in vacuo*. The residue was recrystallized from 125 ml. of cyclohexane to give 2.20 g. (68% yield) of **17**, m.p. 115-117°; ir (mull): ν 1670(s), 1640(s), 1590(m), 1500(m), 1455(s) cm^{-1}; pmr (deuteriochloroform): δ 2.08 [s, 6H, 2 (CH_3)], 2.82 (s, 2H, CH_2N)], δ_A 5.77, δ_B 4.23 [q (J_{AB} = 15 Hz) (5), CH_2NCOCH_2], δ_A 5.06, δ_B 4.07 [q (J_{AB} = 14 Hz), 2H, CH_2NCHO), 6.90-7.50 (m, 8H, 8 Ar-*H*), 8.44 (s, 1H, *CHO*).

Anal. Calcd. for $C_{19}H_{21}N_3O_2$: C, 70.56; H, 6.54; N, 12.99; N. E., 323. Found: C, 70.24; H, 6.76; N, 13.12; N. E. ($HClO_4$), 330.

11,12-Dihydro-12-[(4-methyl-1-piperazinyl)acetyl]dibenzo[*b,f*]-[1,4]diazocine-5(6*H*)carboxaldehyde (**18**).

The procedure described above for **17** was utilized to prepare **18** in 34% yield, m.p. 115-117°, after recrystallization from cyclohexane; ir (deuteriochloroform): ν 1670(s), 1490(m), 1450(m) cm^{-1}; pmr (deuteriochloroform): δ 2.30-3.35 (m, 13H, $CH_2N(CH_2)_4NCH_3$), δ_A 5.90, δ_B 4.36 (5) [q (J_{AB} = 15 Hz)], δ_A 5.20, δ_B 4.85 [q (J_{AB} = 15 Hz), 2H, CH_2NCHO], 7.10-7.60 (m, 8H, 8 Ar-*H*), 8.64 (s, 1H, *CHO*).

Anal. Calcd. for $C_{22}H_{26}N_4O_2$: C, 69.81; H, 6.93; N, 14.81; N. E., 189. Found: C, 69.93; H, 6.95; N, 15.02; N. E. ($HClO_4$), 195.

11,12-Dihydro-12-formyl[*b,f*][1,4]diazocine-5(6*H*)carbonyl Chloride (**5**).

To a solution of 3.50 g. (0.015 mole) of **4** and 4.0 g. (0.04 mole) of triethylamine in 125 ml. of anhydrous toluene was added dropwise and with stirring at 5-10°, a solution of 2.0 g. (0.02 mole) of phosgene in 20 ml. of anhydrous toluene. Subsequently, the mixture was stirred at 5-10° for 0.5 hour, and then at ambient temperature for 2 hours. The solid remaining following the concentration *in vacuo* was resuspended in 25 ml. of cold water, the whole was filtered and dried to give 4.20 g. of solid, m.p. 188 190° dec. Recrystallization from 100 ml. of ethyl acetate gave 2.90 g. (70% yield) of **5**, m.p. 190-192° dec.; ir (mull): ν 1730(s), 1665(s), 1595(m), 1580(m), 1500(s), 1460(s) cm^{-1}; pmr (deuteriochloroform): δ_A 5.47, δ_B 4.45 [(q, J_{AB} = 15 Hz), 2H, CH_2NCOCl] (5), 4.85 [d (J = 4 Hz), 2H, CH_2NCHO], 7.00-7.55 (m, 8H, 8 Ar-*H*), 8.45 (s, 1H, *CHO*).

Anal. Calcd. for $C_{16}H_{13}ClN_2O_2$: C, 63.97; H, 4.36; N, 9.32; Cl, 11.81. Found: C, 63.93; H, 4.32; N, 9.43; Cl, 11.80.

11,12-Dihydryo-12-formyldibenzo[*b,f*][1,4]diazocine-5(6*H*)carboxamide (**15**).

A suspension of 1.50 g. (0.005 mole) of **5** in 50 ml. of 3.5 *N* absolute ethanolic ammonia was stirred in a stoppered pressure bottle at ambient temperature for 72 hours and then concentrated to dryness *in vacuo*. The residual material was leached with 25 ml. of water, filtered, and dried to give 1.3 g. of solid, m.p. 253-255° dec. Recrystallization from 80 ml. of acetonitrile gave 0.90 g. (64% yield) of **15**, m.p. 258-260° dec.; ir (mull): ν 3440(s), 3360(m), 3330(m), 3290(m), 3205(m), 1650(s), 1590(s), 1500(m), 1465(m), 1455(m), 1425(s) cm^{-1}; pmr (DMSO-d_6): δ 4.90 [s, 4H; 2 (CH_2)], 6.00 [s, 2H, NH_2 (equilibrates with deuterium oxide)], 7.25 [d (J = 6 Hz), 8H, 8 Ar-*H*], 8.57 (s, 1H, *CHO*).

Anal. Calcd. for $C_{16}H_{15}N_3O_2$: C, 68.31; H, 5.37; N, 14.88. Found: C, 68.49; H, 5.37; N, 14.78.

11,12-Dihydro-12-formyl-*N*-(*n*-propyl)dibenzo[*b,f*][1,4]oxazocine-5(6*H*)carboxamide (**16**).

To a solution of 3.0 g. (0.013 mole) of **4** in 50 ml. of anhydrous toluene was added, dropwise and with stirring, at ambient temperature, a solution of 4.0 g. (0.05 mole) of *n*-propylisocyanate in 30 ml. of anhydrous toluene. Following the addition, the stirring was continued for one hour, the mixture heated for 3 hours at 75-80°, concentrated to dryness *in vacuo*, and the residue recrystallized from 75 ml. of cyclohexane to give 1.40 g. (33% yield) of **16**, m.p. 55-57°; ir (mull): ν 3350(m), 1665(s), 1590(m), 1575(m), 1510(s), 1490(s), 1450(s) cm^{-1}; pmr (deuteriochloroform): δ 0.060-2.20 (m, 7H, $CH_3CH_2CH_2$), 3.30, 3.00 [q (J_{AB} = 6 Hz), 2H, CH_2NCHO], 4.15-4.65 [m, 1H, N*H* (equilibrates with deuterium oxide)], 4.88 (s, 2H, CH_2NHCO), 7.10-7.60 (m, 8H, 8 Ar-*H*).

Anal. Calcd. for $C_{19}H_{21}N_3O_2$: C, 70.56; H, 6.54; N, 12.99. Found: C, 70.74; H, 6.83; N, 13.06.

12-Formyl-11,12-dihydrodibenzo[*b,f*][1,4]diazocine-5(6*H*)propanenitrile (**19**).

To a solution of 7.0 g. (0.03 mole) of **4** in 25 ml. of acrylonitrile, cooled to -15°, was added, dropwise, during 0.33 hour, 0.3 ml. of Triton B. Although the external cooling bath was retained, about 0.5 hour after the addition was completed, a spontaneous rise in temperature to 5° was observed. When the temperature began to decline, the cooling bath was removed, the mixture was allowed to warm to ambient temperature, and, finally, was heated under reflux for 3 hours. The cooled mixture was diluted with 250 ml. of chloroform, the chloroform solution was filtered, the filtrate was concentrated *in vacuo*, and the residue extracted with 3-100 ml. portions of boiling diisopropyl ether. The extracts were concentrated to give 3.0 g. of solid, m.p. 138-142°; recrystallization from 50 ml. of ethyl acetate gave 1.70 g. (20% yield) of **19**, m.p. 149-151°; ir (mull): ν 2250(w), 1660(s), 1630(w), 1595(s), 1570(w), 1495(s), 1445(s), 1420 cm^{-1}; pmr (deuteriochloroform): δ 2.47 [t (J = 6 Hz), 2H, CH_2CH_2CN), 4.26 (s, 2H, CH_2NCH_2), 4.88 (s, 2H, CH_2NCHO), 6.80-7.70 (m, 8H, 8 Ar-*H*), 8.46 (s, 1H, C*H*O).

Anal. Calcd. for $C_{18}H_{17}N_3O$: C, 74.19; H, 5.88; N, 14.42. Found: C, 73.85; H, 5.71; N, 14.66.

12-Benzyl-6,11-dihydrodibenzo[*b,f*][1,4]diazocine-5(6*H*)carboxaldehyde (**20**).

A mixture of 1.30 g. (0.01 mole) of anhydrous potassium carbonate, 2.40 g. (0.01 mole) of **4**, 1.70 g. (0.01 mole) of α-bromotoluene, and 50 ml. of Reagent grade 2-butanone was heated and stirred under reflux for 44 hours, cooled, and diluted with 15 ml. of water. The 2-butanone layer was separated, dried, concentrated to dryness *in vacuo*, and the residual oil dissolved in 100 ml. of ether. The ether solution was washed, dried, and concentrated to give 2.80 g. of solid, m.p. 120-125°. Recrystallization from 50 ml. of 2-propanol gave 1.30 g. (40% yield) of **20**, m.p. 135-137°; ir (mull): ν 1675(s), 1590(s), 1500(s), 1490(s), 1460(m), 1445(s), 1440(s), 1415(m) cm^{-1}; pmr (deuteriochloroform): δ 4.34, 4.44 [2s, 4H, 2 (CH_2N-Ar)], 4.83 (s, 2H, CH_2NCHO), 6.50-7.50 (m, 8H, 8 Ar-*H*), 8.52 (s, 1H, C*H*O).

Anal. Calcd. for $C_{22}H_{20}N_2O$: C, 80.45; H, 6.14; N, 8.53. Found: C, 80.65, H, 6.19; N, 8.31.

13-(*p*-Chlorophenyl)-6,11-dihydro-5,12-methanodibenzo[*b,f*][1,4]-diazocine (**25**).

A mixture of 2.50 g. (0.012 mole) of **4**, 2.00 g. (0.014 mole) of *p*-chlorobenzaldehyde, and 80 ml. of anhydrous xylene was heated under reflux for 6 hours and then concentrated to dryness *in vacuo*. The residue, 3.5 g., was recrystallized from 75 ml. of 95% ethanol to give 2.30 g. (58% yield) of **25**, m.p. 157-159°; ir (mull): ν 1590(w), 1480(s), 1465(s), 1440(m), 1430(m) cm^{-1}; pmr (deuteriochloroform): δ 4.85, 4.40 [AB_q (J = 18 Hz), 4H, 2 (CH_2)], 5.30 (s, C*H*Ph), 6.70-7.80 (m, 12H, 12 Ar-*H*).

Anal. Calcd. for $C_{21}H_{17}ClN_2$: C, 75.79; H, 5.15; N, 8.42. Found: C, 75.93; H, 5.07; N, 8.34.

The above precedure was also employed for the preparation of three related derivatives, **26**, **27**, **28** and **29**.

13-(*o*-Chlorophenyl)-6,11-dihydro-5,12-methanodibenzo[*b,f*][1.4]-diazocine (**26**).

This compound was prepared in 78% yield, m.p. 164-166°, after recrystallization from diisopropyl ether; ir (deuteriochloroform): ν 1590(w), 1560(w), 1420(m) cm^{-1}; pmr (deuteriochloroform): δ 4.97, 4.48 [AB_q (J = 18 Hz), 4H, 2-(CH_2)], 5.67 (s, 1H, C*H*Ph), 6.65-7.60 (m, 12H, 12 Ar-*H*).

Anal. Calcd. for $C_{21}H_{17}ClN_2$: C, 75.79; H, 5.15; N, 8.42. Found: C, 75.97; H, 5.30; N, 8.38.

6,11-Dihydro-13-(3,4,5-trimethoxyphenyl)-5,12-methanodibenz-[*b,f*][1,4]diazocine (**27**).

This compound was prepared in 63% yield, m.p. 204-206°, after recrystallization from absolute ethanol; ir (mull): ν 1585(s), 1500(s), 1480(m), 1460(s), 1455(s), 1435(m), 1420(m), 1405(s) cm^{-1}; pmr (deuteriochloroform): δ 3.88 [s, 9H, 3 (CH_3O)], 4.95, 4.55 [AB_q (J = 18 Hz), 4H, 2 (CH_2)], 5.40 (s, 1H, C*H*Ph), 6.75-7.60 (m, 10H, 10 Ar-*H*).

Anal. Calcd. for $C_{24}H_{24}N_2O_3$: C, 74.19; H, 6.23; N, 7.20. Found: C, 74.43; H, 6.41; N, 7.33.

13-[*p*-[2-(Diethylamino)ethoxy]phenyl]-6,11-dihydro-5,12-methanodibenzo[*b,f*][1,4]diazocine (**28**).

This compound was prepared in 51% yield, m.p. 120-122°, after recrystallization from diisopropyl ether: ir (mull): ν 1610(s), 1585(m), 1505(s), 1490(s), 1470(s), 1460(s), 1430(s) cm^{-1}; pmr (deuteriochloroform): δ 1.04 [t (J = 7 Hz), 6H, 2 (CH_3)], 2.40-3.00 [m, 6H, 3 (CH_2N)], 4.00 [t (J = 7 Hz), 2H, OCH_2], 4.89, 4.50 [AB_q (J = 12 Hz), 4H, 2 (CH_2)], 5.36 (s, 1H, C*H*Ph), 6.70-7.70 (m, 12H, 12 Ar-*H*).

Anal. Calcd. for $C_{27}H_{31}N_3O$: C, 78.42; H, 7.56; N, 10.16; N. E. 207. Found: C, 78.64; H, 7.55; N, 10.11; N. E. ($HClO_4$), 203.

6,11-Dihydro-13-ethyl-5,12-methanodibenzo[*b,f*][1,4]diazocine (**29**).

This compound was prepared in 8% yield, m.p. 142-144°, after recrystallization from hexane; ir (deuteriochloroform): ν 1490(m), 1470(s), 1435(m) cm^{-1}; pmr (deuteriochloroform): δ 0.96 [t J = 6 Hz), 3H, CH_3], 1.50 [t (J = 6 Hz), 2H, CH_2CH_3], 4.00-4.20 (m, 1H, C*H*), 4.64, 4.28 [AB_q (J_{AB} = 13 Hz), 4H, 2 (CH_2N)], 6.80-7.30 (m, 8H, 8 Ar-*H*).

Anal. Calcd. for $C_{11}H_{18}N_2$: C, 81.57; H, 7.25; N, 11.22. Found: C, 81.46; H, 7.48; N, 11.37.

REFERENCES AND NOTES

(1) To whom all correspondence should be addressed.

(2) H. L. Yale, *J. Org. Chem.*, **36**, 3238 (1971), prepared this compound for the first time by the reaction of *o*-phenylenedianime with phenyl formate.

(3) N. J. Harper and J. M. Sprake, *J. Chem. Soc. (C)*, 882 (1969), prepared the 5,12-bis-*p*-toluenesulfonyl derivative related to **3** by the reaction of *N,N'*-(*o*-phenylene)di-*p*-toluenesulfonamide with **2**. Cleavage of the *p*-toluenesulfonyl substituent required 50% hydrobromic acid in glacial acetic acid, at 50°, and this procedure was not selective since it led to the isolation of only 5,6,11,12-tetrahydrodibenzo[*b,f*][1,4]diazocine.

(4) N. J. Harper and J. M. Sprake (3) have prepared several derivatives of this type with aryl, furyl, and pyridyl aldehydes; they reported that ketones, *e.g.*, acetone, acetophenone, and cyclohexanone did not react with the heterocycle. While it is reasonable to speculate that spatial requirements are critical, these authors reported an 80% yield of methano derivative from the reaction of the heterocycle with salicylaldehyde, and we have found that *o*-chlorobenzaldehyde gave a 78% yield of product.

(5) The notation employed here is that of L. M. Jackman and S. Sternhell, "Applications of Nuclear Magnetic Resonance Spectroscopy in Organic Chemistry," Pergamon Press, Elmsford, N. Y., 2nd Ed., 1969, pp. 129-130, for a two-spin system. The difference between the chemical shifts in cps (ν_{AB}) for the non-equivalent

$C\begin{matrix}HA\\HB\end{matrix}$ protons was derived from the equation $\nu_{AB} = \sqrt{(1\text{-}4)(2\text{-}3)}$ and the actual values of ν_A and ν_B could then be obtained by adding or substracting, respectively, $\nu_{AB}/2$ from the center of the AB quartet. The ν_A and ν_B were then converted to ppm and these values listed as δ_A and δ_B.

(6) N. J. Harper and J. M. Sprake (3) reported a m.p. of 190-192°.

(7) A. Saunders and J. M. Sprake, *J. Chem. Soc. (C)*, 1161 (1970), reported a m.p. of 180-181°.