

(to whom I am grateful). Unless otherwise mentioned, melting points were determined on a Kofler hot stage and are uncorrected. Infrared (IR) spectra were obtained on a Perkin-Elmer 257 grating spectrometer in Nujol mulls. Proton nuclear magnetic resonance (^1H NMR) spectra were measured on a Varian Associates T-60 instrument, in CDCl_3 . All peak positions were measured in ppm relative to tetramethylsilane (Me_4Si) as an internal standard ($\delta_{\text{Me}_4\text{Si}} = 0$). The J values are recorded in hertz. Yields were based on crystallization from benzene.

Acid Chloride Method. Typical Procedure 1. *N*-Allyl-3-chlorobenzamide (IIe). To a 50-mL dry benzene solution of 3-chlorobenzoyl chloride (17.5 g, 0.1 mol) was added cautiously, with stirring and cooling (ice bath), allylamine (11.4 g, 0.2 mol) in 50 mL of benzene over 0.5 h; the final solution was allowed to stir for 18 h. Workup as usual gave 19.1 g of crude and 15.8 g from benzene. (This procedure was used in the synthesis of the *N*-allyl and *N*-cyclopropyl compounds.)

Typical Procedure 2. *N*-Benzhydrylbenzamide (VIa). Benzoyl chloride (14.1 g, 0.1 mol) in 50 mL of dry benzene was treated likewise, as above, with benzhydrylamine (18.3 g, 0.1 mol) and 15.0 g of triethylamine dissolved in 50 mL of benzene. Workup as usual gave 30.1 g of crude and 26.3 g from acetone-benzene.

Thermal Method. Typical Procedure. *N*-Benzhydryl-4-chlorophenylacetamide (VIII). A mixture of 4-chlorophenylacetic acid (8.5 g, 0.05 mol), benzhydrylamine (9.2 g, 0.05 mol), and 50 mL of *o*-xylene was placed in a 100-mL round-bottomed flask equipped with a reflux condenser and a Dean-Stark apparatus and heated in an electrical heating mantle for 6 h when distillation of water ceased. Workup as usual gave 14.5 g of crude and 13.4 g from acetone-benzene.

Acknowledgment

I thank Mrs. Margaret Adams of the Department of Pure and Applied Chemistry, University of Strathclyde, Glasgow, and the Microanalytical Laboratory, University of Illinois, Urbana, for the microanalyses. I also thank Professor Peter Beak for granting technical facilities.

Registry No. Ia, 15205-35-3; Ib, 88229-12-3; Ic, 88229-13-4; Id, 88229-14-5; Ie, 88229-15-6; If, 88229-16-7; Ig, 88229-17-8; Ih,

39887-35-9; II, 88229-18-9; Ij, 88229-19-0; Ik, 88229-20-3; Il, 88229-21-4; Ila, 88229-22-5; Iib, 88229-23-6; Iic, 39887-14-4; IId, 66896-68-2; Iie, 35306-52-6; Iif, 5866-99-9; Iig, 88229-24-7; Iih, 88229-25-8; III, 88229-26-9; IIIa, 39108-89-9; IIIb, 39108-80-0; IIIc, 5867-01-6; IIId, 88229-27-0; IVa, 724-37-8; IVb, 52745-10-5; Va, 23825-35-6; Vb, 88229-28-1; Vc, 57409-26-4; Vd, 57409-28-6; Ve, 88229-29-2; Vf, 7465-70-5; Vg, 57409-24-2; Vh, 7461-37-2; Vi, 57409-27-5; Vj, 2585-27-5; VIa, 1485-72-9; VIb, 69790-46-1; VIc, 88229-30-5; VIId, 88229-31-6; VIE, 69790-47-2; VIi, 88229-32-7; VIg, 88229-33-8; VIh, 88229-34-9; VIIa, 10254-16-7; VIIb, 88229-35-0; VIIc, 88229-36-1; VIId, 88229-37-2; VIIe, 88229-38-3; VIIf, 88229-39-4; VIIg, 88229-40-7; VIIh, 88229-41-8; VIIi, 88229-42-9; VIIj, 88229-43-0; 3-chlorobenzoyl chloride, 618-46-2; benzoyl chloride, 98-88-4; 4-chlorophenylacetic acid, 1878-68-8; allylamine, 107-11-9; benzhydrylamine, 91-00-9.

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Potential Central Nervous System Active Agents. 4. Synthesis of *N*-Isobutylbenzamides

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The preparation and spectral properties (IR, ^1H NMR) are given for 11 *N*-isobutylbenzamides, variously substituted on the acyl part with halo, methoxyl, methyl, or nitro groups, including two new ones. The amides were synthesized by the Schotten-Baumann method in anhydrous benzene.

In the preceding communications (1-3), the synthesis and the spectroscopic data (IR, mass spectra, ^1H NMR) of some

substituted benzamides and phenylacetamides were reported. As part of a general study of the structure-activity relationship in the central nervous system active compounds, 11 *N*-isobutylbenzamides, variously substituted on the acyl part with halo, methoxyl, methyl, or nitro groups, were synthesized by the Schotten-Baumann method in anhydrous benzene. Compounds 4 and 9 are new. The spectroscopic data (IR, ^1H NMR) not hitherto described in the literature are reported in this communication.

The experimental and IR data on all of the compounds are summarized in Table I, and those of the ^1H NMR spectral data

Table I. Experimental and IR Data of *N*-Isobutylbenzamides

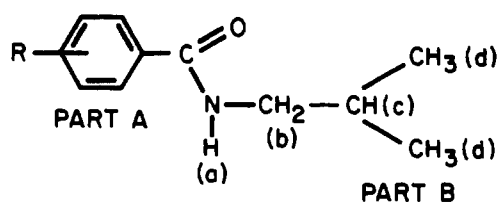
| compd | mol formula | yield, ^a % | mp, °C | | IR, cm ⁻¹ | | | |
|-------|---|--------------------------|----------------------|-----------------------------------|----------------------|---------------|------|----------------------|
| | | | exptl | reported | NH | amide band | | others |
| 1 | C ₁₁ H ₁₅ NO | 72 | 55 ^a | 109-100 (4), 56-57 (5), 55 (6) | 3285 | 1628 | 1535 | 1600 |
| 2 | C ₁₂ H ₁₇ NO | 93 | 88-89 ^a | | 3300 | 1630 | 1528 | 1615 sh ^f |
| 3 | C ₁₂ H ₁₇ NO ₂ | <i>b</i> | 100 ^a | 105-106 (6) | 3310 | 1632 | 1537 | 1612 |
| 4 | C ₁₁ H ₁₄ FNO | 85 | 74 ^c | | 3295 | 1630 | 1534 | 1584 |
| 5 | C ₁₁ H ₁₄ FNO | <i>b</i> | 90-91 ^c | | 3245 | 1620 | 1545 | 1604, 1589 |
| 6 | C ₁₁ H ₁₄ ClNO | 68 | 73 ^d | 74 (5) | 3280 | 1640 | 1533 | 1591 |
| 7 | C ₁₁ H ₁₄ ClNO | 97 | 103 ^d | 96.5 (5), 100-102 (7) | 3295 | 1625 | 1530 | 1594 sh |
| 8 | C ₁₁ H ₁₄ ClNO | <i>b</i> | 94-96 ^d | 104.5 (5) | 3268 | 1640 sh, 1620 | 1548 | 1594 |
| 9 | C ₁₁ H ₁₄ BrNO | 82 | 77 ^d | | 3270 | 1635 | 1530 | 1584 |
| 10 | C ₁₁ H ₁₄ N ₂ O ₃ | 78 | 88-89 ^a | 79.5-80.5 (8) | 3240 | 1628 | 1558 | 1520 |
| 11 | C ₁₁ H ₁₄ N ₂ O ₃ | <i>b</i> | 135-136 ^e | 121.5-122 (8) | 3310 | 1635 | 1545 | 1600, 1515 |

^a From benzene. ^b Quantitative yield. ^c From petroleum ether (60-80 °C). ^d From benzene-petroleum ether. ^e From acetone-benzene. ^f sh = shoulder.

Table II. ¹H NMR Spectral Data for the *N*-Isobutylbenzamides^a

| compd | chemical shifts, δ | | | | | | | |
|-------|--|----------|---------------------|----------|--------|--------------------------------------|-------------------------|-------------------------------|
| | aromatic | NH (a) | CH ₂ (b) | <i>J</i> | CH (c) | C(CH ₃) ₂ (d) | <i>J</i> _{c,d} | others |
| 1 | 7.00-8.00 | <i>b</i> | 3.00 t | 6 | 1.73 m | 0.83 d | 6 | |
| 2 | 7.13 (d, 2, <i>J</i> = 8) 7.77 (d, 2, <i>J</i> = 8) | <i>b</i> | 3.23 t | 6 | 1.85 m | 0.92 d | 6 | 2.33 (s, ArCH ₃) |
| 3 | 6.83 (d, 2, <i>J</i> = 8) 7.80 (d, 2, <i>J</i> = 8) | 7.15 br | 3.21 t | 6 | 1.90 m | 0.91 d | 6 | 3.75 (s, ArOCH ₃) |
| 4 | 6.90-7.80 | <i>b</i> | 3.23 t | 6 | 1.85 m | 0.93 d | 6 | |
| 5 | 6.70-8.20 | <i>b</i> | 3.27 t | 6 | 1.95 m | 0.93 d | 6 | |
| 6 | 7.23 m | 6.83 br | 3.13 t | 6 | 1.77 m | 0.91 d | 6 | |
| 7 | 6.80-8.00 | <i>b</i> | 3.18 t | 6 | 1.85 m | 0.92 d | 6 | |
| 8 | 7.25 (d, 2, <i>J</i> = 8) 7.73 (d, 2, <i>J</i> = 8) | <i>b</i> | 3.19 t | 6 | 1.90 m | 0.90 d | 6 | |
| 9 | 7.00-7.80 | 6.68 br | 3.18 t | 6 | 1.87 m | 0.95 d | 6 | |
| 10 | 7.00-8.10 | <i>b</i> | 3.23 t | 6 | 1.90 m | 0.90 d | 6 | |
| 11 | 7.93 (d, 2, <i>J</i> = 8) 8.17 (d, 2, <i>J</i> = 8) | 7.47 br | 3.28 t | 6 | 1.90 m | 0.95 d | 6 | |

^a Symbols: br = broad signal; d = doublet; m = multiplet; s = singlet; t = triplet. ^b Signal occurs in the aromatic region.



| no. | R | no. | R |
|-----|-------|-----|-------------------|
| 1 | H | 7 | 3-Cl |
| 2 | 4-Me | 8 | 4-Cl |
| 3 | 4-OMe | 9 | 2-Br |
| 4 | 3-F | 10 | 2-NO ₂ |
| 5 | 4-F | 11 | 4-NO ₂ |
| 6 | 2-Cl | | |

are given in Table II. Satisfactory elemental analyses ($\pm 0.4\%$ for C, H, N, and halogen, where present) were obtained for all compounds.

These amides have been submitted for biological screening, and the results will be reported elsewhere.

Experimental Section

The reagents used in these experiments were of commercial grade. Melting points were determined on a Kofler hot stage and are uncorrected. Infrared (IR) spectra were obtained on a Perkin-Elmer 257 grating spectrometer in Nujol mulls. Proton nuclear magnetic resonance (¹H NMR) spectra were measured on a Varian Associates T-60 instrument, in CDCl₃. All peak

positions were measured in ppm relative to tetramethylsilane (Me₄Si) as an internal standard ($\delta_{\text{Me}_4\text{Si}} = 0$). The *J* values are recorded in hertz.

Typical Procedure. *N*-Isobutyl-4-methylbenzamide (2). Isobutylamine (7.3 g, 0.1 mol) and 15.0 g of triethylamine in 50 mL of dry benzene were made to react as usual with a solution of 4-methylbenzoyl chloride (15.5 g, 0.1 mol) in 50 mL of benzene (7). Normal workup and crystallization from benzene gave 17.7 g of colorless product.

Acknowledgment

We thank Mrs. Margaret Adams of the Department of Pure and Applied Chemistry, University of Strathclyde, Glasgow, for the microanalyses. We also thank Mr. O. O. Ibe, University of Nigeria, Nsukka, for the proton NMR spectra.

Registry No. 1, 5705-57-7; 2, 88358-24-1; 3, 7464-51-9; 4, 64181-34-8; 5, 88358-25-2; 6, 5397-17-1; 7, 26163-88-2; 8, 7461-33-8; 9, 88358-28-3; 10, 88358-27-4; 11, 2585-25-3; PhCOCl, 98-88-4; 4-MeC₆H₄COCl, 874-60-2; 4-MeOC₆H₄COCl, 100-07-2; 3-FC₆H₄COCl, 1711-07-5; 4-FC₆H₄COCl, 403-43-0; 2-ClC₆H₄COCl, 609-65-4; 3-ClC₆H₄COCl, 618-46-2; 4-ClC₆H₄COCl, 122-01-0; 2-BrC₆H₄COCl, 7154-66-7; 2-O₂NC₆H₄COCl, 610-14-0; 4-O₂NC₆H₄COCl, 122-04-3.

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Synthesis of Some Schiff Bases

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Six new Schiff bases having the ONNO donor system have been synthesized from the condensation of biacetyl monoxime, benzil, *o*-vanillin, 9,10-phenanthrenequinone, ethanalamine, 1,3-diaminopropan-2-ol, and ethylenediamine. Their characterization has been based on their physical, analytical, and spectral data.

The amine was added to the stirred solution of the ketone in dry benzene at room temperature. The reaction mixture was then boiled under reflux for 1 h. The water formed in the reaction mixture was then distilled off azeotropically with benzene. Evaporation of the remaining solvents at reduced pressure gave the desired Schiff bases in good yields. Their physical, analytical, and spectral data are included in Tables I and II.

Table I. Physical Data^a

| Schiff base | formula | yield, % | color | mp, °C |
|------------------------------------|---|-------------|---------------|-----------|
| 1 B-ENOL-H ₂ | C ₁₈ H ₂₀ N ₂ O ₂ | 80 | colorless | oil |
| 2 BAM-ENOL-H ₂ | C ₆ H ₁₁ N ₂ O ₂ | 77 | cream | 112 |
| 3 PQ-ENOL-H ₂ | C ₁₈ H ₁₈ N ₂ O ₂ | 60 | yellow | 250 |
| 4 BB-EN | C ₃₂ H ₂₈ N ₄ | 84 | orange-yellow | 154 |
| 5 <i>o</i> -VAN-EN-H ₂ | C ₁₈ H ₂₀ N ₂ O ₄ | 80 | dark yellow | 165 |
| 6 <i>o</i> -VAN-DAP-H ₃ | C ₁₉ H ₂₂ N ₂ O ₅ | 73 | dark yellow | 125 |

^a B-ENOL-H₂ = Schiff base from benzil and ethanalamine. BAM-ENOL-H₂ = Schiff base from biacetyl monoxime and ethanalamine. PQ-ENOL-H₂ = Schiff base from 9,10-phenanthrenequinone and ethanalamine. BB-EN = Schiff base from benzil and ethylenediamine. *o*-VAN-EN-H₂ = Schiff base from *o*-vanillin and ethylenediamine. *o*-VAN-DAP-H₃ = Schiff base from *o*-vanillin and 1,3-diaminopropan-2-ol.

Registry No. 1, 67414-71-5; 2, 88635-65-8; 3, 84838-94-8; 4, 79403-78-4; 5, 41349-57-9; 6, 88635-66-9; benzil, 134-81-6; biacetyl monoxime, 57-71-6; 9,10-phenanthrenequinone, 84-11-7; *o*-vanillin, 148-53-8; 2-aminoethanol, 141-43-5; 1,2-ethanediamine, 107-15-3; 1,3-diamino-2-propanol, 616-29-5.

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Table II. Spectral Data

| Schiff base | IR (Nujol mull), cm ⁻¹ | | NMR (CDCl ₃) ^a | | UV (CHCl ₃), nm |
|-------------|------------------------------------|--------------------|---------------------------------------|---------------------------------|--|
| | $\nu(\text{OH})$ | $\nu(\text{N-OH})$ | $\delta(-\text{N-CH}_2-)$ | $\delta(-\text{CH}_2-\text{O})$ | |
| 1 | 3390 | 1630 | 2.80 t | 3.60 t | 220 (680), 260 (700), 305 (1700) |
| 2 | 3410 | 1620 | 2.86 | 3.70 t | 210 (160), 240 (720), 325 (1600) |
| 3 | 3410 ($\nu(\text{N-OH})$ 3360) | 1615 | 3.65 t | 3.33 t | 211 (500), 254 (430), 301 (4956), 334 (1810), 351 (1950), 400 (291) |
| 4 | | 1650, 1550 | 3.30-3.60 m | | 215 (560), 255 (600), 310 (1700), 402 (800) |
| 5 | 3400 | 1628 | 3.70-3.87 m | | 223 (580), 263 (625), 310 (1630), 368 (1610), 400 (700), 420 (440) |
| 6 | 3420 | 1632 | 3.68-3.84 m | | 226 (585), 248 (600), 262 (620), 294 (1500), 299 (1600), 368 (1560), 418 (520) |

^a m = multiplet; d = doublet; s = singlet; b = broad.