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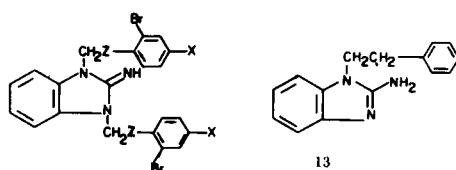
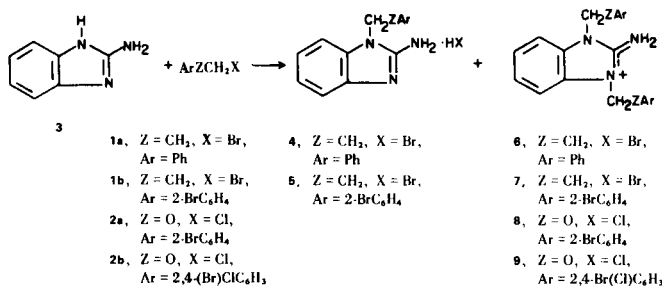
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2-Aminobenzimidazole has been reacted with phenylethyl bromides and phenylloxymethyl chlorides to prepare a number of novel 1,3-bis-substituted quaternary derivatives.

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During the last several years we have been interested in the quaternary derivatives obtained from the reactions of 2-aminopyridines and 2-aminopyrimidines with 2-phenylethyl-, **1**, and phenylloxymethyl halides, **2** (2a-c). In this Note, we are extending these studies to include the quaternary derivatives obtained from 2-aminobenzimidazole, **3**, and the same halides. No reference to the quaternization of **3** are to be found in the literature (3).

When **3** and the highly reactive **2a** or **2b** were dissolved in sulfolane (4) and the mixture kept at ambient temperature, only the bis-alkylated quaternary derivatives, **8** and **9**, respectively, were obtained in 30-50% yield. With the significantly less reactive **1a** or **1b**, **3**, either in sulfolane at ca. 90° or in xylene, under reflux, gave mixtures of **4** and **6** and **5** and **7**, respectively, but in lower yields. Although **8** and **9**, when treated with base gave the stable imino derivatives, **10** and **11**, respectively, all similar attempts to prepare **12** from **7** led to unidentifiable, unseparable mixtures; in contrast, **4** and base readily gave the stable derivative, **13**.



EXPERIMENTAL

The spectra were obtained from the Analytical Department of this Institute as described in the earlier papers (2a-c). The melting points were determined in capillary tubes in an electrically heated oil bath and are uncorrected.

2-Amino-1,3-bis(2-phenylethyl)benzimidazol-3-ium Bromide (**6**).

A mixture of 4.50 g. (0.034 mole) of **3**, 12.80 g. (0.068 mole)

of **1a**, and 40 ml. of sulfolane formed a clear solution at room temperature; no significant reaction was evident after six days under these conditions. The solution was warmed for 24 hours by means of an oil bath maintained at 105-113°, cooled, diluted with 100 ml. of acetonitrile, and refrigerated at -10°. The solid that separated was filtered with suction and air-dried to give 7.0 g. of solid that sintered at 140° and melted at 250-252°. This was recrystallized from 370 ml. of acetonitrile to give 4.18 g. (29% yield) of **6**, m.p. 260-262°; ir (potassium bromide): ν 3310 (w), 3205 (s), 3150 (s), 3050 (s), 1650 (s), 1615 (w), 1590 (s), 1480 (s), 1455 (m), 1445 (m), 1430 (w) cm⁻¹; pmr (DMSO-d₆): δ 2.40-2.60 [m, 4H, (PhCH₂)₂], 4.40 [t (J = 7.5 Hz), 4H, (PhCH₂-CH₂)₂], 7.00-7.50 (m, 14H, 14 Ar-H), 8.50-9.00 [m, 2H, NH₂ (equilibrate with deuterium oxide)].

Anal. Calcd. for C₂₃H₂₄BrN₃: C, 65.40; H, 5.73; N, 9.95. Found: C, 65.35; H, 5.65; N, 9.94.

2-Amino-1-[2-(2-bromophenyl)ethyl]benzimidazole Hydrobromide (**5**) and 2-Amino-1,3-bis[2-(2-bromophenyl)ethyl]benzimidazol-3-ium Bromide (**7**).

A suspension of 5.50 g. (0.041 mole) of **3**, 11.00 g. (0.041 mole) of **1b**, and 250 ml. of anhydrous xylene was stirred and heated under reflux for 24 hours. At the end of heating and stirring period the hot solution consisted of a two phase system. The mixture was allowed to cool to ambient temperature, the supernatant (see below, for the lower phase) was separated, and concentrated *in vacuo* to give 9.2 g. of an oil. The oil was dissolved in 10 ml. of warm butyronitrile, the solution cooled, the solid that separated was filtered, and air-dried to give 1.30 g. of crude **7**, m.p. 235-240°. Recrystallization from 175 ml. of butyronitrile gave 0.90 g. (4% yield) of pure **7**, m.p. 246-247°; ir (potassium bromide): ν 3430 (m), 3200 (m), 3000 (s), 1650 (s), 1610 (w), 1590 (m), 1510 (w), 1500 (m), 1480 (m), 1465 (m), 1455 (w), 1440 (w), 1430 (w) cm⁻¹; pmr (DMSO-d₆): δ 3.10-3.40 [m, 4H, (PhCH₂)₂], 4.30-4.65 [m, 4H, (PhCH₂CH₂)₂], 7.00-7.70 (m, 12H, 12Ar-H), 8.90-9.10 [m, 2H, NH₂ (equilibrate with deuterium oxide)].

Anal. Calcd. for C₂₃H₂₂Br₃N₃: C, 47.62; H, 3.82; N, 7.24. Found: C, 47.76; H, 4.14; N, 7.26.

The lower phase remaining after separation of the supernatant (see above) slowly crystallized. This was dissolved in 100 ml. of boiling acetonitrile, the hot solution was filtered, and the filtrate cooled to give 1.37 g. of additional crude **7**, m.p. 237-239°; recrystallization from 150 ml. of acetonitrile gave 0.75 g. of pure **7**, m.p. 246-247°, identical in all respects with the **7** described above. The filtrate remaining from the 1.37 g. was kept at ambient temperature for a week, and during that time a mixture of crystalline solids separated. The whole was then refrigerated at 5° overnight and the crystalline material filtered. The major portion consisted of small, yellow rods that could be separated manually from the characteristic opaque white rosettes of **7**. The yellow crystals obtained in this fashion weighed 2.37 g., m.p. 198-200°; recrystallization from 55 ml. of propionitrile gave 1.40 g. (9% yield) of **5**, m.p. 201-203°; ir (potassium bromide): ν 3430 (m), 3200 (s), 1680 (s), 1630 (m), 1500 (m), 1570 (w), 1525 (m), 1485 (m), 1480 (s), 1450 (w) cm⁻¹; pmr (DMSO-d₆): δ 3.18

[t (J = 7 Hz), 2H, PhCH₂], 4.45 [t (J = 7 Hz), 2H, PhCH₂CH₂], 7.00-7.70 (m, 8H, 8Ar-H), 8.76 [s, 2H, NH₂ (equilibrate with deuterium oxide)].

Anal. Calcd. for C₁₅H₁₅Br₂N₃: C, 45.73; H, 3.81; N, 10.57. Found: C, 45.94; H, 3.66; N, 10.58.

2-Amino-(2-phenylethyl)benzimidazole Hydrobromide (**4**) and 2-Amino-1,3-bis(2-phenylethyl)benzimidazole-3-ium Bromide (**6**).

A solution of 9.00 g. (0.068 mole) of **3**, 25.6 g. (0.14 mole) of **1a**, and 25 ml. of sulfolane was heated at ca. 90° for 6 hours, then cooled, the semisolid mass agitated mechanically with 50 ml. of acetonitrile, the solid filtered, resuspended in 10 ml. of fresh acetonitrile, and refiltered. The air-dried solid at this point weighed 12.30 g., it sintered at 160° and melted over the range 175-205°. The solid was added to 365 ml. of boiling water, the stirred suspension was boiled for 5 minutes, and then filtered through a coarse sintered glass funnel. The filtered, air-dried solid weighed 2.25 g. and was identified as crude **6**, m.p. 153-260°. A crystalline solid separated from the cooled aqueous filtrate and this was shown to be 2.73 g. of additional crude **6**, m.p. 254-260°. The combined 4.98 g., recrystallized from 270 ml. of acetonitrile gave 3.58 g. (12% yield) of pure **6**, m.p. 260-262°, identical in all respects with the product described above.

The aqueous filtrate from the 4.98 g. above was concentrated to dryness *in vacuo* to give 6.31 g. of residual solid; a sample, dried at 56° (1 mm) sintered at 188° and melted at 205-207° (turbid) and clear at 209-210°. The ir spectrum and analytical data supported the conclusion that this was hydrate of **4**.

Anal. Calcd. for C₁₅H₁₆BrN₃·1.5 H₂O: C, 52.17; H, 5.55; Br, 23.15; N, 12.17. Found: C, 51.76; H, 5.11; Br, 23.46; N, 12.14.

The solid, 6.28 g. was recrystallized from 240 ml. of butyronitrile to give 4.80 g. (22% yield) of anhydrous **4**, m.p. 206-208°; ir (potassium bromide): ν 3260 (s), 3100 (s), 1655 (s), 1620 (m), 1585 (m), 1520 (m), 1490 (w), 1475 (m), 1470 (m), 1445 (m) cm⁻¹; pmr (DMSO-d₆): δ 2.80-3.20 (m, 2H, PhCH₂), 4.24-4.55 (m, 2H, PhCH₂CH₂), 7.00-7.50 (m, 8H, 8Ar-H).

Anal. Calcd. for C₁₅H₁₆BrN₃: C, 56.62; H, 5.07; N, 13.20. Found: C, 56.49; H, 4.92; N, 13.16.

A mixture of 0.51 g. (0.0016 mole) of **4**, 25 ml. each of chloroform and water, and 0.44 g. (0.0032 mole) of potassium carbonate was agitated for 1 hour at ambient temperature, the chloroform layer separated, the aqueous layer extracted with 25 ml. of chloroform, the combined chloroform solutions washed, dried, and concentrated gave 0.38 g. of solid, m.p. 116-118°. Recrystallization from 25 ml. of toluene gave 0.24 g. (63% yield) of **13**, m.p. 120-122°; ir (potassium bromide): ν 3360 (s), 3160 (s), 1675 (s), 1630 (s), 1610 (m), 1595 (m), 1590 (m), 1540 (s), 1490 (m), 1480 (s), 1470 (s), 1455 (s), 1445 (s), 1435 (s), 1425 (m) cm⁻¹; pmr (deuteriochloroform): δ 3.12 [t (J = 5 Hz), 2H, PhCH₂], 4.03 [s, 2H, NH₂ (equilibrates with deuterium oxide)], 4.20 [t (J = 5 Hz), 2H, PhCH₂CH₂], 6.75-7.70 (m, 9H, Ar-H).

Anal. Calcd. for C₁₅H₁₅N₃: C, 75.92; H, 6.37; N, 17.64. Found: C, 75.94; H, 6.51; N, 17.62.

2-Amino-1,3-bis[(2-bromophenoxy)methyl]benzimidazol-3-ium Chloride (**8**) and 2-Imino-1,3-bis[(2-bromophenoxy)methyl]benzimidazole (**10**).

A solution initially of 15.00 g. (0.068 mole) of **2a**, 4.50 g. (0.034 mole) of **3**, and 40 ml. of sulfolane became solid after several hours at ambient temperature. After 24 hours, the mixture was diluted with 40 ml. of 2-propanol, the whole refrigerated at 5°, the solid filtered, washed with 2-propanol, triturated with anhydrous ether, and air-dried to give 7.70 g. of solid, m.p. 229-230° dec. Recrystallization from 715 ml. of 90% ethanol gave

5.50 g. (31% yield) of **8**, m.p. 236-237°; ir (mull): ν 3370 (w), 1668 (s), 1607 (s), 1479 (s), 1462 (s), 1439 (s) cm⁻¹; pmr (DMSO-d₆): δ 6.30 [s, 4H, (PhOCH₂)₂], 7.00-8.00 (m, 14H 12Ar-H, NH₂).

Anal. Calcd. for C₂₁H₁₈Br₂ClN₃O₂: C, 46.79; H, 3.39; N, 7.80; Cl, 6.58. Found: C, 46.82; H, 3.66; N, 7.79; Cl, 6.76.

A mixture of 2.57 g. (0.0048 mole) of **8**, 50 ml. each of chloroform and water, and 2.00 g. (0.014 mole) of potassium carbonate was agitated at ambient temperature for 1.25 hours, the chloroform layer separated, the aqueous layer extracted with 50 ml. of chloroform, the combined chloroform solutions washed, dried, and concentrated to give 2.23 g. of solid, m.p. 144-150°. Recrystallization from 70 ml. of absolute ethanol gave 1.56 g. (65% yield) of **10**, m.p. 159-161°; ir (potassium bromide): ν 3360 (w), 3070 (w), 1660 (s), 1498 (s), 1475 (s), 1430 (s), 1388 (s) cm⁻¹; pmr (deuteriochloroform): δ 5.83 [s, 4H, (PhOCH₂)₂], 6.70-7.70 (m, 13H, 12Ar-H, NH).

Anal. Calcd. for C₂₁H₁₇Br₂N₃O₂: C, 50.14; H, 3.41; Br, 31.78; N, 8.35. Found: C, 50.42; H, 3.69; Br, 31.71; N, 8.50.

2-Amino-1,3-bis[(2-bromo-4-chlorophenoxy)methyl]benzimidazol-3-ium Chloride, (**9**) and 2-Imino-1,3-bis[(2-bromo-4-chlorophenoxy)methyl]benzimidazole (**11**).

The reaction was carried out as with **8** above between 1.00 g. (0.0075 mole) of **3**, 1.91 g. (0.0075 mole) of **2b**, and 5 ml. of sulfolane and gave 2.28 g. of crude **9**, m.p. 233-234° dec.; recrystallization from 200 ml. of 95% ethanol gave 1.11 g. (49% yield) of **9**, m.p. 235-236° dec.; ir (mull): ν 3365 (w), 1666 (s), 1606 (s), 1477 (s) cm⁻¹; pmr (DMSO-d₆): δ 6.43 [s, 4H (PhCH₂-O)], 7.20-7.90 (m, 12H, 10Ar-H, NH₂).

Anal. Calcd. for C₂₁H₁₆Br₂Cl₃N₃O₂: C, 41.48; H, 2.65; Cl, 17.47; N, 6.91. Found: C, 41.75; H, 2.93; Cl, 17.70; N, 6.99.

The 2-imino derivative, **11**, was obtained by the same procedure employed to prepare **10**; the yield was 70%, m.p. 199-201°; ir (mull): ν 3355 (w), 1660 (s), 1614 (w), 1562 (w), 1493 (s), 1465 (s), 1430 (s) cm⁻¹; pmr (deuteriochloroform): δ 5.77 [s, 4H, (PhCH₂O)₂], 7.00-7.54 (m, 11H, 10Ar-H, NH).

Anal. Calcd. for C₂₁H₁₅Br₂Cl₂N₃O₂: C, 44.09; H, 2.90; Br, 27.94; N, 7.35. Found: C, 44.39; H, 2.91; Br, 27.76; N, 7.05.

REFERENCES AND NOTES

(1) To whom all correspondence should be addressed.

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with phenacyl bromide and obtained 1,3-bis-(phenacyl)-5,6-dimethylbenzimidazol-3-ium bromide.

(4) D. E. Portlock, M. J. Kane, J. A. Bristol and R. E. Lyle, *J. Org. Chem.*, **38**, 2351 (1973) have utilized sulfolane as the solvent for preparing pyridinium derivatives.