454. *Some Potential Chelating Agents derived from Benziminazole.*

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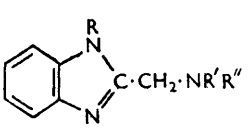
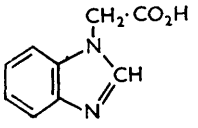
2-Methylamino(and dimethylamino)methylbenziminazole, 1-methyl-2-methylamino(and dimethylamino)methylbenziminazole, 1-benziminazolylacetic acid, (2-benziminazolylmethyl)amine-*NN*-diacetic acid, (1-methyl-2-benziminazolylmethyl)amine-*NN*-diacetic acid, and 2-2′-pyridyl-1-benziminazolylacetic acid have been prepared as potential chelating agents.

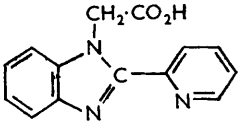
Since 2-aminomethylbenziminazole (I; R = R′ = R″ = H) forms a series of stable metal complexes,[1] several new derivatives of benziminazole, some of which contain the grouping $:N\cdot CH_2\cdot CH_2\cdot NH_{2-n}(CH_2\cdot CO_2H)_n$ ($n = 1$ or 2) characteristic of " complexones," have been prepared for examination as complexing agents.



(I)



(II)



(III)

2-Aminomethyl-1-methylbenziminazole (I; R = Me, R′ = R″ = H) was prepared from *N*-methyl-*o*-phenylenediamine (modified preparation) and ethyl aminoacetate hydrochloride following Lane's method for the preparation of 2-aminomethylbenziminazole itself.[2]

2-Dimethylaminomethylbenziminazole (I; R = H, R′ = R″ = Me) was best prepared from 2-chloromethylbenziminazole [3] and dimethylamine. 1-Methyl-2-methylaminomethylbenziminazole (I; R = R′ = Me, R″ = H) and 2-dimethylaminomethyl-1-methylbenziminazole (I; R = R′ = R″ = Me) were similarly prepared from 2-chloromethyl-1-methylbenziminazole and methylamine or dimethylamine, respectively.

1-Benziminazolylacetic acid (II) was readily obtained from benziminazole and chloroacetic acid under alkaline conditions, but attempts to extend this reaction to the preparation of 2-2′-pyridyl-1-benziminazolylacetic acid (III) were unsuccessful. However, this compound was prepared by hydrolysing the ester obtained by condensing 2-2′-pyridylbenziminazole [4] with methyl bromoacetate in the presence of anhydrous potassium carbonate.

(2-Benziminazolylmethyl)amine-*NN*-diacetic acid (I; R = H, R′ = R″ = $CH_2\cdot CO_2H$) was obtained by the hydrolysis of its dimethyl ester which resulted from the condensation

[1] Irving and Weber, *J.*, 1958, in the press.
[2] Lane, *J.*, 1957, 3313.
[3] Bloom and Day, *J. Org. Chem.*, 1939, **4**, 14.
[4] Leko and Vlajinac, *Bull. Soc. Chim. roy. Yougoslavie*, 1930, **1**, 3.

of 2-chloromethylbenziminazole[3] with dimethyliminodiacetate. The 1-methyl-derivative and its dimethyl ester were prepared similarly. (1-Methyl-2-benziminazolylmethyl)amine-*NN*-diacetic acid was also obtainable directly from 2-aminomethylbenziminazole and chloroacetic acid, but it has not proved possible to introduce a third $CH_2 \cdot CO_2H$ group in position 1 of the heterocyclic ring.

Experimental

N-Methyl-o-phenylenediamine.—The following procedure is based upon kinetic studies of the interaction of methyl iodide and *o*-phenylenediamine reported by Brown and Le Roi Nelson.[5] *o*-Phenylenediamine (35 g., 0·32 mole), methyl iodide (10·6 g., 0·16 mole), and methanol (400 ml.) were heated under reflux for 2 hr., then allowed to cool; more methyl iodide (10·6 ml., 0·16 mole) was added, and heating under reflux continued for a further 12 hr. Most of the methanol was distilled off, and the residue poured on crushed ice (1000 g.), basified with potassium hydroxide, and extracted with ether. The extracts were dried (K_2CO_3), the solvent removed under reduced pressure, and the residue fractionated in a vacuum. *N*-Methyl-*o*-phenylenediamine was obtained as a pale lemon-coloured oil, b. p. 116—120°/8 mm. (32 g., 82%), which, soon darkened.

2-Aminomethyl-1-methylbenziminazole (I; R = Me, R′ = R″ = H).—A mixture of finely ground ethyl aminoacetate hydrochloride (38·4 g., 0·25 mole) and freshly distilled *N*-methyl-*o*-phenylenediamine (32 g., 0·25 mole) was heated in a stream of nitrogen at 180—200° (oil-bath) for 3 hr. After being cooled, the residue was taken up in dilute hydrochloric acid, boiled with metal-free sugar-charcoal, and filtered. The filtrate was taken almost to dryness, and the residue triturated with ethanol, pale blue crystals separating. After repeated recrystallisation from hot ethanol *2-aminomethyl-1-methylbenziminazole dihydrochloride* was obtained as colourless crystals, m. p. 257—259° (31 g., 50%) (Found: C, 46·4; H, 5·8; N, 17·9; Cl, 30·3. $C_9H_{11}N_3$,2HCl requires C, 46·2; H, 5·6; N, 17·95; Cl, 30·3%).

1-Methyl-2-methylaminomethylbenziminazole (I; R = R′ = Me, R″ = H).—2-Chloromethyl-1-methylbenziminazole (7·5 g., 0·045 mole) [6] was added in small quantities to a solution of 9·8 ml. of 33% methylamine (2·8 g., 0·09 mole) in ether (50 ml.), the temperature being kept below 15°. After the initial reaction had subsided the mixture was kept at 35° for 3 hr. and then stored overnight at room temperature. Ether (150 ml.) was then added, the mixture cooled below 0°, and the precipitated methylamine hydrochloride collected. The filtrate was then saturated with dry hydrogen chloride. *1-Methyl-2-methylaminomethylbenziminazole dihydrochloride* was collected, washed with ether, and recrystallised from ethanol, from which it separated as colourless needles, m. p. 186—187° (3·2 g., 29%) (Found: C, 48·4; H, 6·0; N, 17·1; Cl, 28·6. $C_{10}H_{13}N_3$,2HCl requires C, 48·4; H, 6·1; N, 16·9; Cl, 28·6%).

2-Dimethylaminomethyl-1-methylbenziminazole (I; R = R′ = R″ = Me).—This was prepared similarly. The *dihydrochloride* crystallised from ethanol as long white needles, m. p. 244° (3·5 g., 32%) (Found: C, 50·1; H, 6·6; N, 15·8; Cl, 27·1. $C_{11}H_{15}N_3$,2HCl requires C, 50·4; H, 6·5; N, 16·0; Cl, 27·05%).

1-Benziminazolylacetic Acid (II).—Chloroacetic acid (13·5 g., 0·125 mole) was dissolved in water (25 ml.) and neutralised with sodium hydroxide (5 g., 0·125 mole) in water (80 ml.). Benziminazole (9 g., 0·075 mole) was added, and the stirred solution heated to 80—90°. An almost saturated solution of sodium hydroxide (5 g., 0·125 mole) was added dropwise at such a rate that the pH of the solution was maintained for as long as possible between the change points of phenolphthalein and thymolphthalein. Towards the end of the reaction the mixture was allowed to become more alkaline, and when all the sodium hydroxide had been added heating was continued for 0·5 hr. at 80—90°. After being cooled, the solution was acidified with concentrated hydrochloric acid to pH 2—3, and the solid which separated was collected, washed with water and recrystallised thrice from boiling water. *1-Benziminazolylacetic acid* formed crystals, m. p. 285—290° (7·5 g., 57%) (Found: C, 61·6; H, 4·6; N, 16·0. $C_9H_8O_2N_2$ requires C, 61·4; H, 4·6; N, 15·9%).

2-2′-Pyridyl-1-benziminazolylacetic Acid (III).—A finely ground mixture of 2-2′-pyridylbenziminazole (9·7 g., 0·05 mole) [4] and anhydrous potassium carbonate (13·8 g., 0·1 mole) was heated with methyl bromoacetate (15·3 g., 0·1 mole) under reflux for 8 hr. and then at a higher

[5] Brown and Nelson, *J. Amer. Chem. Soc.*, 1953, **73**, 24.
[6] Hughes and Lions, *Proc. Roy. Soc. N.S. Wales*, 1938, **71**, 209.

temperature until reaction, as indicated by the evolution of carbon dioxide, had ceased (4 hr.). The brown resin was taken up in methanol (5 × 50 ml.) and separated from inorganic salts. The solvent was removed on the water-bath, and the residue fractionated *in vacuo*. Methyl 2-2′-pyridyl-1-benziminazolylacetate (7·5 g.), which distilled as a pale yellow oil at 80—100°/1 mm., was hydrolysed by hot aqueous 0·3N-barium hydroxide (150 ml.) for 1 hr. on the water-bath. The exactly equivalent amount of 2N-sulphuric acid was then added, and barium sulphate removed by centrifugation of the hot mixture. The centrifugate was evaporated to dryness, and the residue taken up in aqueous ethanol. *2-2′-Pyridyl-1-benziminazolylacetic acid* recrystallised from aqueous ethanol as white needles, m. p. 240° (subl.) (1 g., 8%) (Found: C, 66·1; H, 4·5; N, 16·7. $C_{14}H_{11}O_2N_3$ requires C, 66·4; H, 4·4; N, 16·6%).

(2-Benziminazolylmethyl)amine-NN-diacetic Acid (I; R = H, R′ = R″ = $CH_2{\cdot}CO_2H$).—(a) *From 2-aminomethylbenziminazole and chloroacetic acid.* 2-Aminomethylbenziminazole dihydrochloride (7·1 g., 0·03 mole) [2] in water (30 ml.) was neutralised with potassium hydroxide (3·37 g., 0·06 mole) in water (30 ml.). A solution of chloroacetic acid (9·9 g., 0·105 mole) in water (100 ml.), neutralised with potassium hydroxide (5·9 g., 0·105 mole), was added, and the mixture heated at 80—90° and shaken continuously while an almost saturated solution of potassium hydroxide (5·9 g., 0·105 mole) was added dropwise under the same conditions as in the preparation of (II), and the mixture was finally heated to boiling for 1·5 hr. After being cooled the solution was acidified to pH 3 with concentrated hydrochloric acid. The *diacetic acid* which separated was collected, well washed with water, and recrystallised thrice from boiling water, from which it separated as colourless crystals (4·5 g., 55%), m. p. 212° [Found: C, 55·0; H, 5·1; N, 16·0%; *M* (by titration), 261·7. $C_{12}H_{13}O_4N_3$ requires C, 54·8; H, 5·0; N, 16·0%; *M*, 263·2. Calc. for $C_{14}H_{15}O_6N_3$ (2-benziminazolylmethylamine-1 : *N* : *N*-triacetic acid): C, 52·3; H, 4·7; N, 13·1%; *M*, 321·3].

(b) *From 2-chloromethylbenziminazole and iminodiacetic ester.* An immediate reaction took place when the benziminazole (2·5 g., 0·015 mole) [3] was added to a solution of the ester (5 g., 0·03 mole) [7] in ethanol (10 ml.), accompanied by the separation of the hydrochloride of iminodiacetic ester. After being kept at room temperature for 0·5 hr. the mixture was heated on a water-bath (2 hr.) to complete the reaction, then filtered; dimethyl iminodiacetate hydrochloride remaining in the filtrate was removed by adding ether, cooling to below 0°, and filtration. The solvent was then evaporated, and the residue fractionally distilled *in vacuo*. Dimethyl (2-benziminazolylmethyl)amine-*NN*-diacetate (b. p. 110—120°/*ca.* 1 mm.) was hydrolysed as described above and gave the free acid (2 g., 45%), m. p. 212—214° after recrystallisation from hot water, identical with the previous specimen [Found: N, 15·9%; *M* (by titration), 262·5].

(1-Methyl-2-benziminazolylmethyl)amine-NN-diacetic Acid (I; R = Me, R′ = R″ = $CH_2{\cdot}CO_2H$).—2-Chloromethyl-1-methylbenziminazole (3·25 g., 0·018 mole) [6] was treated with a solution of dimethyl iminodiacetate (5·8 g., 0·036 mole) [7] in ethanol (10 ml.), and the product worked up as described in the previous preparation. *(1-Methyl-2-benziminazolylmethyl)amine-NN-diacetic acid* formed very pale yellow crystals, m. p. 186—188°, from hot water (2·2 g., 55%) (Found: C, 56·3; H, 5·6; N, 15·0. $C_{13}H_{15}O_4N_3$ requires C, 56·3; H, 5·45; N, 15·15%).

The authors are indebted to the Medical Research Council for generous financial assistance to one of them (O. W.).

INORGANIC CHEMISTRY LABORATORY, OXFORD. [*Received, December 19th*, 1958.]

[7] Dubsky, *Ber.*, 1917, **50**, 1694.