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Synthesis & Anticonvulsant Activity of Some Condensed Imidazoles*†

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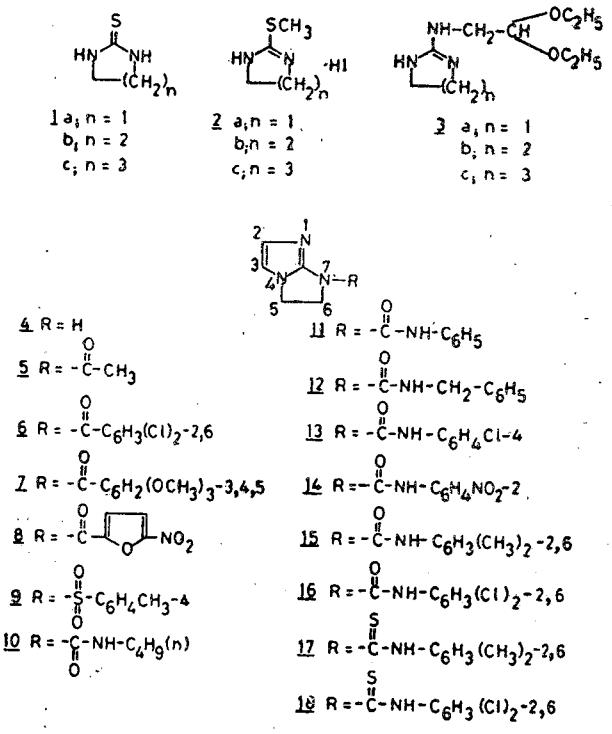
2-Mercapto-4,5-dihydroimidazole (1a), 2-mercapto-3,4,5,6-tetrahydropyrimidine (1b) and 2-mercapto-3,4,5,6-tetrahydro-7*H*-1,3-diazepine (1c) react with methyl iodide to give the corresponding mercaptomethyl derivatives (2a-2c). Reaction of these mercaptomethyl compounds with aminoacetaldehyde diethyl acetal followed by treatment with hydrochloric acid affords 1*H*-2,3-dihydroimidazo[1,2-*a*]imidazole (4), 5,6,7,8-tetrahydroimidazo[1,2-*a*]pyrimidine (19) and 9*H*-5,6,7,8-tetrahydroimidazo[1,2-*a*]-[1,3]-diazepine (22), respectively. These condensed imidazoles have been reacted with aromatic acid chlorides, isocyanates and isothiocyanates. The structure and anticonvulsant activity of these compounds are described.

LEVAMISOLE, a condensed imidazole derivative, has been used extensively in humans and animals for the treatment of nematodal infections[1]. Recently, the drug has been reported to stimulate some aspects of cellular immunity in experimental animals[2-5]. In addition, a number of condensed imidazoles have exhibited hypoglycaemic[6], anorectic[7] and blood platelet aggregation inhibitory activity[8]. In the course of our work on the synthesis of novel heterocycles[9] for pharmacological screening, we have synthesized a number of imidazo[1,2-*a*]imidazole, imidazo[1,2-*a*]pyrimidine and imidazo[1,2-*a*]-1,3-diazepine derivatives. One of the imidazoimidazole derivatives showed interesting anticonvulsant activity. We describe in the present communication the synthesis and anticonvulsant activity of this class of compounds.

Our approach to the synthesis of these condensed imidazoles is as follows: 2-mercapto-4,5-dihydroimidazole (1a), 2-mercapto-3,4,5,6-tetrahydropyrimidine (1b) and 2-mercapto-3,4,5,6-tetrahydro-7H-1,3-diazepine (1c) react with methyl iodide to give the corresponding mercaptomethyl derivatives (2a-2c). Reaction of these with aminoacetaldehyde diethyl acetal affords the guanidines (3a-3c) which on treatment with hydrochloric acid, affords 1H-2,3-dihydroimidazo[1,2-*a*]imidazole (4), 5,6,7,8-tetrahydroimidazo[1,2-*a*]pyrimidine (19) and 9H-5,6,7,8-tetrahydroimidazo[1,2-*a*]-1,3-diazepine (22) respectively.

Acylation of 4 with acetyl and aromatic acid chlorides gives the N-acyl derivatives (5-8). *p*-Toluenesulphonyl chloride forms the corresponding N-tosyl derivative (9). Reaction with aliphatic and aromatic isocyanates affords the corresponding ureas (10-16). 2,6-Dimethyl- and 2,6-dichlorophenyl-isothiocyanates yield the thioureas (17) and (18) respectively. The imidazo[1,2-*a*]-pyrimidine derivative (19) likewise reacts with 3,4,5-trimethoxybenzoyl chloride to afford the amide (20) and with 2,6-dimethylphenyl isocyanate to form the 2,6-dimethylphenyl carbamoyl derivative (21). Similarly, the imidazo [1,2-*a*]-1,3-diazepine derivative (22) when treated with 3,4,5-trimethoxybenzoyl chloride forms the amide (23) and with 2,6-dimethyl- and 2,6-dichlorophenyl-isocyanates to give the urea derivatives (24) and (25) respectively. Finally, *p*-toluenesulphonyl chloride reacts with (22) to form the N-tosyl derivative



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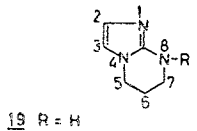
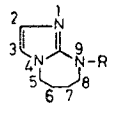


19 R = H

20 R = -C(=O)-C$_6$H$_2$(OCH$_3$)$_3$-3,4,5

21 R = -C(=O)-NH-C$_6$H$_3$(CH$_3$)$_2$-2,6



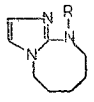
22 R = H

23 R = -C(=O)-C$_6$H$_2$(OCH$_3$)$_3$-3,4,5

24 R = -C(=O)-NH-C$_6$H$_3$(CH$_3$)$_2$-2,6

25 R = -C(=O)-NH-C$_6$H$_3$(Cl)$_2$-2,6

26 R = -S(=O)$_2$-C$_6$H$_4$CH$_3$-4



27 R = -C(=O)-NH-C$_6$H$_3$(CH$_3$)$_2$-2,6

28 R = -C(=O)-NH-C$_6$H$_3$(Cl)$_2$-2,6

29 R = -C(=O)-NH-C$_6$H$_2$(OCH$_3$)$_3$-3,4,5

(26). Imidazoazocine derivatives 27-29 have been reported elsewhere[10].

Biological activities — The anticonvulsant activity of this class of compounds, described in Table 1, shows that the bare skeleton of imidazoimidazole (4) and imidazopyrimidine (19) is devoid of anticonvulsant activity. The aroyl derivatives (6), (7), (20), (23) and (29) as well as the toluenesulphonyl derivatives (9) and (26) are also inactive. Anticonvulsant activity is elicited from ring system 4 upon carbamoylation. Thus butylurea (10) exhibits modest activity against electroshock, but is inactive against chemoshock-induced convulsions. The benzylurea (12) behaves similarly, but is somewhat more potent than 10. Moderate activity against both electroshock and metrazole-induced convulsions appears in phenylurea (11), but the former is lost upon substitution in the *para*-position of the phenyl ring by chlorine or nitro group (13, 14). 2,6-Disubstitution of the phenyl group expands the spectrum of anticonvulsant activity (e.g. 15 and 16) to include seizures induced by electroshock and by chemicals — metrazol and strychnine. Substitution by methyl is favoured over chlorine. Exchange of oxygen atom in the carbamoyl group by sulphur (17, 18) leads to two to five fold reduction in activity against electroshock and to a lesser extent in the other two tests. Expanding the imidazolidine ring in 15 to pyrimidine (21), azepine (24) or azocine (27) leads to deterioration in the anticonvulsant activity. The dichlorophenylureas (25) and (28) represent extreme cases of this attenuation of activity.

The most active compound of the series is 15, having an ED_{50} of 24 mg/kg *p.o.* in protecting against electroshock-induced seizures one hour after oral administration. The duration of action is about 5 hr. It has ED_{50} of 27·9 and 21·6 mg/kg *i.p.* against metrazole and strychnine-induced seizures. However, at 500 mg/kg *p.o.* toxic symptoms (without lethality) in mice were seen. In flaxedil-immobilized cats, hippocampal after discharge is blocked for 40 min at 10 mg/kg *i.v.* but 20 mg/kg *i.v.* is lethal. Comparison of 15 with carbamazepine, a well-known anticonvulsant drug showed it to be 50-75% as active. However its toxicity dissuaded us from further studies.

TABLE 1 — ANTICONVULSANT ACTIVITY OF CONDENSED IMIDAZOLES

Compound No.	Anticonvulsant activity in mice		
	E. shock	ED_{50} mg/kg[a] Metrazole	Strychnine
4	O[b]	O[c]	O[c]
6	O[b]	—	—
7	500 p.o.	O[c]	O[c]
9	O[b]	—	—
10	250 p.o.	O[c]	O[c]
11	250 p.o.	>30 i.p.	O[c]
12	71 p.o.	O[c]	O[c]
13	O[b]	>30 i.p.	O[c]
14	O[b]	>30 i.p.	O[c]
15	24 p.o.	27·9 i.p.	21·6 i.p.
16	50 p.o.	30 i.p.	25 i.p.
17	43·5 p.o.	30 i.p.	30 i.p.
18	250 p.o.	>30 i.p.	30 i.p.
19	O[b]	O[c]	O[c]
20	O[b]	O[c]	O[c]
21	150 p.o.	—	—
22	O[b]	O[c]	O[c]
23	O[b]	O[c]	O[c]
24	500 p.o.	—	—
25	O[b]	O[c]	30 i.p.
26	O[b]	—	—
27	250	O[c]	30 i.p.
28	O[b]	O[c]	O[c]
29	O[b]	O[c]	O[c]
Carbamazepine (Tegretol®)	11 p.o.	17·3±4·1 i.p.	17±4·8 i.p.

(a) Obtained by graphical method. (b) Inactive at 250 mg/kg p.o. (c) Inactive at 30 mg/kg i.p.

Representative compounds described in the present communication were tested against a number of bacteria, fungi, protozoa and helminths. None of the compounds possessed any appreciable antibacterial, antifungal, antiamoebic or anthelmintic activity.

Experimental Procedure

M.ps. are uncorrected. UV spectra (λ_{max} in nm, log ϵ in parentheses) were determined in absolute ethanol and were recorded on a Beckman DK 2A spectrophotometer. IR spectra (ν_{max} in cm^{-1}) were taken in nujol and were generally run on a Perkin Elmer 337 infracord spectrophotometer; mass spectra were taken on a Varian Mat CH-7 spectrometer and NMR spectra on a Varian A60 spectrometer; chemical shifts are quoted in δ (ppm) downfield from TMS internal standard. Unless otherwise stated, $CDCl_3$ was used as solvent.

4,5-Dihydro-2-mercaptomethylimidazole (2a) — A slurry of 4,5-dihydro-2-mercaptoimidazole (1a, 204 g) in methanol (500 ml) was treated with methyl iodide (290 g). The reaction mixture was boiled under reflux for 2 hr and concentrated to one-half volume. Addition of ethyl acetate (500 ml) followed by cooling to 0°, afforded a crystalline precipitate which crystallized from methanol-ethyl

and *p*-chlorophenyl isocyanate in 50% yield and recrystallized from methanol-ethyl acetate; m.p. 151° (Found: C, 54·64; H, 4·40; N, 21·12. $C_{12}H_{11}ClN_4O$ requires C, 54·86; H, 4·22; N, 21·33%).

5,6-*Dihydro*-7-(*o-nitrophenylcarbamoyl*)-7*H*-*imidazo*[1,2-*a*]*imidazole* (14) — It was prepared from 4 and *o*-nitrophenyl isocyanate in 64% yield in the manner described for 10 and recrystallized as hydrochloride from methanol-ether, m.p. 207° (Found: C, 46·31; H, 4·19; N, 22·35. $C_{12}H_{11}N_5O_3.HCl$ requires C, 46·53; H, 3·91; N, 22·61%).

5,6-*Dihydro*-7-(2′,6′-*dimethylphenylcarbamoyl*)-7*H*-*imidazo*[1,2-*a*]*imidazole* (15) — This compound (15) was prepared from 4 and 2,6-dimethylphenyl isocyanate in 76% yield in the manner described for 10, converted into the HCl salt which recrystallized from methanol-ethyl acetate, m.p. 210°; IR: 1670 (-C = O), 3280 (-NH) (Found: C, 57·59; H, 6·16; N, 18·95. $C_{14}H_{16}N_4O.HCl$ requires C, 57·43; H, 6·95; N, 19·14%).

5,6-*Dihydro*-7-(2′,6′-*dichlorophenylcarbamoyl*)-7*H*-*imidazo*[1,2-*a*]*imidazole* (16) — It was prepared from 4 and 2,6-dichlorophenyl isocyanate in the manner described for 10 and recrystallized as hydrochloride from methanol-ethyl acetate; m.p. 216° (Found: C, 43·16; H, 3·61; N, 16·78. $C_{12}H_{10}Cl_2N_4O.HCl$ requires C, 43·30; H, 3·32; N, 16·80%).

5,6-*Dihydro*-7-(2′,6′-*dimethylphenylthiocarbamoyl*)-7*H*-*imidazo*[1,2-*a*]*imidazole* (17) — This compound was prepared from 4 and 2,6-dimethylphenyl isothiocyanate in 36% yield and recrystallized from ether-*n*-hexane to afford (17), m.p. 134° (Found: C, 61·84; H, 6·17; N, 20·22; M^+ 272. $C_{14}H_{16}N_4S$ requires C, 61·75; H, 5·92; N, 20·58; mol. wt 272).

5,6-*Dihydro*-7-(2′,6′-*dichlorophenylthiocarbamoyl*)-7*H*-*imidazo*[1,2-*a*]*imidazole* (18) — It was prepared from 4 and 2,6-dichlorophenyl isothiocyanate in 19% yield and recrystallized from methylene chloride-ether; m.p. 208-210° (Found: C, 46·13; H, 3·61; N, 17·53. $C_{12}H_{10}Cl_2N_4S$ requires C, 46·02; H, 3·22; N, 17·89%).

5,6,7,8-*Tetrahydro*-*imidazo*[1,2-*a*]*pyrimidine* (19) — This compound was prepared from 2b (21·9 g) and aminoacetaldehyde diethyl acetal (12 g) in the manner described for 4 and recrystallized from methylene chloride-ether; 6·5 g; 62%; m.p. 106-9°; UV: 215 (3·90); IR: 3200 (-NH); NMR: 1·98 (complex *m*, 2H, $-CH_2$ at C-6), 3·52 (*t*, 2H, $-CH_2$- at C-7), 3·80 (*t*, 2H, $-CH_2$- at C-7), 5·60 (*s*, 1H, -NH); 6·48 (*d*, 1H, aromatic proton), 6·62 (*d*, 1H, aromatic proton) (Found: C, 58·52; H, 7·69; N, 34·31; M^+ 123. $C_6H_9N_3$ requires C, 58·51; H, 7·37; N, 34·12%; mol. wt 123).

5,6,7,8-*Tetrahydro*-8-(3′,4′,5′-*trimethoxybenzoyl*)-*imidazo*[1,2-*a*]*pyrimidine* (20) — It was prepared from 19 (6·2 g) and 3,4,5-trimethoxybenzoyl chloride (12 g) in the manner described for 5 and recrystallized as hydrochloride from methanol-ethyl acetate, 3·5 g (20%), m.p. 250-51° (Found: C, 54·30; H, 6·05; N, 11·84. $C_{16}H_{19}N_3O_4.HCl$ requires C, 54·31; H, 5·70; N, 11·88%).

8-(2′,6′-*Dimethylphenylcarbamoyl*)-5,6,7,8-*tetrahydro*-*imidazo*[1,2-*a*]*pyrimidine* (21) — This compound was prepared from 19 and 2,6-dimethylphenyl isocyanate in 80% yield. The product was converted to the hydrochloride which recrystallized from methanol-ethyl acetate; m.p. 196-98° (Found: C, 55·68; H, 6·65; N, 17·25. $C_{15}H_{18}N_4O.HCl.H_2O$ requires C, 55·46; H, 6·52; N, 17·25%).

5,6,7,8-*Tetrahydro*-9*H*-*imidazo*[1,2-*a*]-[1,3]-*diazepine* (22) — It was prepared from 2c (68 g) and aminoacetaldehyde diethyl acetal (32·25 g) in the manner described for 4. The product was recrystallized from methylene chloride and *n*-hexane to afford 22 (30 g; 90%), m.p. 119-20°; UV: 218 (3·90); IR: 3240 (-NH); NMR: 1·80 (*m*, 4H, $-CH_2$- at C-6, C-7); 3·05 (*m*, 2H, $-CH_2$- at C-8); 3·80 (*t*, 2H, CH_2 at C-5); 5·25 (*s*, -NH); 6·55 (*s*, 2H, aromatic protons) (Found: C, 60·93; H, 8·33; N, 30·48; M^+ 137. $C_7H_{11}N_3$ requires C, 61·28; H, 8·08; N, 30·63; mol. wt 137·18).

5,6,7,8-*Tetrahydro*-9-(3,4,5-*trimethoxybenzoyl*)-9*H*-*imidazo*[1,2-*a*]-[1,3]-*diazepine* (23) — It was prepared from 22 (7 g) and 3,4,5-trimethoxybenzoyl chloride (12 g) in 72% yield in the manner described for 5 and the base crystallized from methylene chloride-*n*-hexane; m.p. 194-95° (Found: C, 61·53; H, 6·65; N, 12·35; M^+ 331. $C_{17}H_{21}N_3O_4$ requires C, 61·62; H, 6·39; N, 12·68%; mol. wt 331).

9-(2,6-*Dimethyl phenylcarbamoyl*)-5,6,7,8-*tetrahydro*-9*H*-*imidazo*[1,2-*a*]-[1,3]-*diazepine* (24) — It was prepared from 22 (1·4 g) and 2,6-dimethylphenyl isocyanate (1·5 g) in the manner described for 10 and recrystallized from methylene chloride-*n*-hexane in 40% yield; m.p. 138° (Found: C, 67·36; H, 7·27; N, 19·53; M^+ 284. $C_{16}H_{20}N_4O$ requires C, 67·58; H, 7·09; N, 19·71%; mol. wt 284·35).

9-(2,6-*Dichlorophenylcarbamoyl*)-5,6,7,8-*tetrahydro*-9*H*-*imidazo*[1,2-*a*]-[1,3]*diazepine* (25) — It was prepared from 22 and 2,6-dichlorophenyl isocyanate in 66% yield and crystallized from methylene chloride-*n*-hexane; m.p. 110° (Found: C, 52·08; H, 4·68; N, 17·49. $C_{14}H_{14}Cl_2N_4O$ requires C, 51·70; H, 4·34; N, 17·23%).

5,6,7,8-*Tetrahydro*-9-(*p-toluenesulphonyl*)-9*H*-*imidazo*[1,2-*a*]*imidazole* (26) — It was prepared from 22 (1·4 g) and *p*-toluenesulphonyl chloride (1·9 g) in the presence of pyridine (1 g) in dioxane (80 ml) by the procedure described for 9. The base was recrystallized from methylene chloride-isopropanol-*n*-hexane in 25% yield; m.p. 166-68° (Found: C, 58·06; H, 6·18; N, 14·37; M^+ 291. $C_{14}H_{17}N_3O_2S$ requires C, 57·72; H, 5·88; N, 14·43%; mol. wt 291·30).

Pharmacological experiments — Compounds were administered orally (*p.o.*) in 0·2% agar suspension or parenterally (*i.p.*) to CF male mice for evaluation of anticonvulsant activity. Protection against seizures at 500 mg/kg *p.o.* and against chemoshock, strychnine and pentylene tetrazol (Metrazol®) was also examined. ED_{50} doses were calculated and used as a basis of comparison[11]. The results are given in Table 1.

Acknowledgement

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acetate to give 2a as hydroiodide; 444·6 g (90%); m.p. 142-44° (Found: C, 19·92; H, 3·35; N, 11·52. $C_4H_8N_2S.HI$ requires C, 19·68; H, 3·29; N, 11·48%).

2-*Mercaptomethyl*-3,4,5,6-*tetrahydropyrimidine* (2b) — This compound (2b) was prepared from the pyrimidine derivative (1b) and methyl iodide in 92% yield in the manner described for 2a and recrystallized as hydroiodide from methanol-ethyl acetate; m.p. 148-49° (Found: C, 23·58; H, 4·67; N, 10·50. $C_5H_{10}N_2S.HI$ requires C, 23·26; H, 4·30; N, 10·86%).

2-*Mercaptomethyl*-3,4,5,6-*tetrahydro*-7*H*-1,3-*diazepine* (2c) — A suspension of 1c (70 g) in methanol (350 ml) was treated with methyl iodide (78 g) and the reaction mixture boiled under reflux for 4 hr. It was allowed to stand at room temperature for 16 hr and concentrated to one-half volume and ethyl acetate (500 ml) added. The crystalline precipitate formed was recrystallized from methanol-ether to afford 2c; 125 g (84%); m.p. 128-30° (Found: C, 26·85; H, 5·13; N, 10·33. $C_6H_{12}N_2S.HI$ requires C, 26·48; H, 4·82; N, 10·30%).

5,6-*Dihydro*-7*H*-*imidazo*[1,2-*a*]*imidazole* (4) — A solution of 2a (288 g) in isopropanol (600 ml) was treated with aminoacetaldehyde diethyl acetal (266 g). The reaction mixture was boiled under reflux for 13 hr, solvent distilled off and the crude hydroiodide treated with conc. hydrochloric acid (280 ml) and heated at 100° for 1 hr. It was allowed to stand at room temperature overnight. The excess of hydrochloric acid was distilled off. The residual gum was taken up in methanol (500 ml), rendered alkaline with 60% aq. NaOH and extracted with methylene chloride. The organic extract was dried (Na_2SO_4) and the solvent distilled off. The residue (229 g) was chromatographed on a column of neutral alumina (2·5 kg) using chloroform as the solvent. That fraction which eluted with the same solvent was recrystallized to afford 4; 109 g (80%), m.p. 122-25°. UV: 215 (3·88); IR: 3205 (-NH); NMR (DMSO-d_6): 3·86 (*s*, 4H, $-CH_2-$ at C-5 and C-6), 5·40 (*s*, 1H, -NH); 6·55 (*s*, 2H, aromatic proton) (Found: C, 54·83; H, 6·70; N, 38·65; M^+ 109. $C_5H_7N_3$ requires C, 55·03; H, 6·47; N, 38·51%; mol. wt 109).

7-*Acetyl*-5,6-*dihydro*-7*H*-*imidazo*[1,2-*a*]*imidazole* (5) — A solution of 4 (16·35 g) in chloroform (120 ml) was treated with acetyl chloride (11·8 g) and triethyl amine (15·1 g). The reaction mixture was stirred for 1 hr at room temperature and then boiled under reflux for 3 hr. The solvent was distilled off. The residue was triturated with water (15 ml) and extracted with methylene chloride. The extract was dried (Na_2SO_4) and the solvent evaporated to dryness. The residue (22 g) was dissolved in chloroform (200 ml) and chromatographed on a column of alumina (500 g) to afford 5 after recrystallization from methylene chloride-*n*-hexane; 15·1 g (66%), m.p. 123-24°; IR: 1680 (-C = O); NMR: 2·56 (*s*, 3H, $-COCH_3$); 3·92-4·60 (complex *m*, 4H, $-CH_2-$ at C-5 and C-6), 6·80 (*s*, 2H, aromatic protons) (Found: C, 55·97; H, 6·22; N, 27·54. $C_7H_9N_3O$ requires C, 55·61; H, 6·00; N, 27·80%).

7-(2',6'-*Dichlorobenzoyl*)-5,6-*dihydro*-7*H*-*imidazo*-[1,2-*a*]*imidazole* (6) — This compound (6) was prepared from 4 and 2,6-dichlorobenzoyl chloride in 26% yield. The product was recrystallized from *n*-hexane to afford 6, m.p. 175° (Found: C, 50·84; H, 3·36; N, 14·92; M^+ 281, 283. $C_{12}H_9Cl_2N_3O$ requires C, 51·08; H, 3·22; N, 14·90%; mol. wt 282).

5,6-*Dihydro*-7-(3',4',5'-*trimethoxybenzoyl*)-7*H*-*imidazo*-[1,2-*a*]*imidazole* (7) — It was prepared from 4 and 3,4,5-trimethoxybenzoyl chloride in 60% yield in the manner described for 5. The product was recrystallized from ethyl acetate to afford 7; m.p. 164-65° (Found: C, 59·41; H, 5·74; N, 14·18; M^+ 303. $C_{15}H_{17}N_3O_4$ requires C, 59·39; H, 5·65; N, 13·86%; mol. wt 303·3); hydrochloride, m.p. 259-60° (from methanol-ethyl acetate) (Found: C, 53·30; H, 5·74; N, 12·70. $C_{15}H_{17}N_3O_4.HCl$ requires C, 53·02; H, 5·34; N, 12·37%).

5,6-*Dihydro*-7-(5'-*nitro*-2'-*furoyl*)-7*H*-*imidazo*[1,2-*a*]-*imidazole* (8) — It was prepared from 4 and 5-nitro-2-furancarboxylic acid chloride in dioxane in 22% yield in the manner described for 5. The product (8) was recrystallized from chloroform-*n*-hexane; m.p. 128° (Found: C, 48·12; H, 3·33; N, 22·17; M^+ 248. $C_{10}H_8N_4O_4$ requires C, 48·39; H, 3·25; N, 22·58%; mol. wt 248·20).

5,6-*Dihydro*-7-(*p*-*toluenesulphonyl*)-7*H*-*imidazo*-[1,2-*a*]*imidazole* (9) — A solution of 4 (3·3 g) in dry dioxane (130 ml) was treated with pyridine (4 g) and *p*-toluenesulphonyl chloride (6 g). The reaction mixture was boiled under reflux for 20 hr. The solvent was distilled off and the residue triturated with ice to give a crystalline product which recrystallized from methylene chloride-ether to afford 9, as hydrochloride; 2·7 g (30%), m.p. 148° (Found: C, 48·14; H, 4·74; N, 13·74; Cl, 11·41. $C_{12}H_{13}N_3O_2S.HCl$ requires C, 48·08; H, 4·70; N, 14·02; Cl, 11·83%).

5,6-*Dihydro*-7-(*n*-*butylcarbamoyl*)-7*H*-*imidazo*[1,2-*a*]-*imidazole* (10) — A solution of 4 (7·6 g) in dry dioxane (75 ml) was treated with *n*-butyl isocyanate (7·5 g). The reaction mixture was boiled under reflux for 4 hr. The solvent was distilled off, the residue treated with isopropanolic hydrogen chloride and the crystalline product formed recrystallized from methylene chloride-ether to afford 10 as hydrochloride, 6 g (30%), m.p. 138-40° (Found: C, 48·88; H, 7·30; N, 22·87. $C_{10}H_{16}N_4O.HCl$ requires C, 49·07; H, 7·00; N, 22·90%).

5,6-*Dihydro*-7-*phenylcarbamoyl*-7*H*-*imidazo*[1,2-*a*]-*imidazole* (11) — It was prepared from 4 and phenyl isocyanate in 76% yield in the manner described for 10 and recrystallized from methylene chloride-ether; m.p. 145° (Found: C, 63·32; H, 5·53; N, 24·79. $C_{12}H_{12}N_4O$ requires C, 63·14; H, 5·30; N, 24·55%).

5,6-*Dihydro*-7-(*benzylcarbamoyl*)-7*H*-*imidazo*[1,2-*a*]-*imidazole* (12) — This compound (12) was prepared from 4 and benzyl isocyanate in 80% yield in the manner described for (10). The product was converted to its hydrochloride which recrystallized from isopropanol, m.p. 182° (Found: C, 56·20; H, 5·77; N, 20·17. $C_{13}H_{14}N_4O.HCl$ requires C, 56·01; H, 5·42; N, 20·10%).

5,6-*Dihydro*-7-(*p*-*chlorophenylcarbamoyl*)-7*H*-*imidazo*[1,2-*a*]*imidazole* (13) — It was prepared from 4

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