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N-ALKYLATION PRODUCTS OF SUBSTITUTED IMIDAZOLES AND DIHYDROPYRIMIDINEDIONES WITH DIBROMOALKANES

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The reactions of N-containing heterocycles with dihaloalkanes were studied. All structures were determined by NMR and mass techniques.

Keywords: N-alkylation, benzimidazole, dihydropyrimidinedione, dibromoalkane, heterocycles, imidazole.

For a long time heterocycles have constituted one of the largest areas of research in organic chemistry. Heterocycles play an important role in biochemical processes and are of interest in biology, pharmacology, microelectronics and optoelectronic material sciences.

The imidazole, benzimidazole, and pyrimidinedione moieties represent important substructures of a wide variety of bioactive compounds [1-4].

In modern microelectronics and optoelectronics, there are signs that the way is paved for the application of new organic materials evolving from the art of molecular design and synthetic chemistry. The possibility of introducing various functionalities into molecules, which is the strong point of organic synthesis, offers a boarder range of optical and electrical properties than for traditional semiconductors [5].

Organic charge-transporting materials required by modern technologies have to exhibit a high enough carrier mobility, a suitable ionization potential, and electron affinity for energy level matching, light absorption, electrochemical stability, good film forming properties, and thermal and morphological stability (no crystallization of amorphous materials should occur).

According to Naito and Miura [6] who examined the relations between thermal properties and thermodynamic parameters, morphologically stable molecular glasses require a high T_g (glass-transition temperature), a low maximum crystal-growth velocity, and a high temperature of maximum crystal growth.

One rather straightforward way to get glass-forming functional molecules is the connection of dyes to "dimeric" twin molecules. In the simplest case, if the electronic structure of each half is to be maintained, the connection is made by an alkyl spacer. Care must be taken that not too much flexibility is introduced, which may reduce T_g. Thus, short spacers like methylene linkages are most suitable.

In the present work, we investigated alkylation of nitrogen heterocycles with dibromoalkanes. The reactions of appropriate imidazoles, benzimidazoles, and dihydropyrimidinediones (**Het**) with dibromoalkanes

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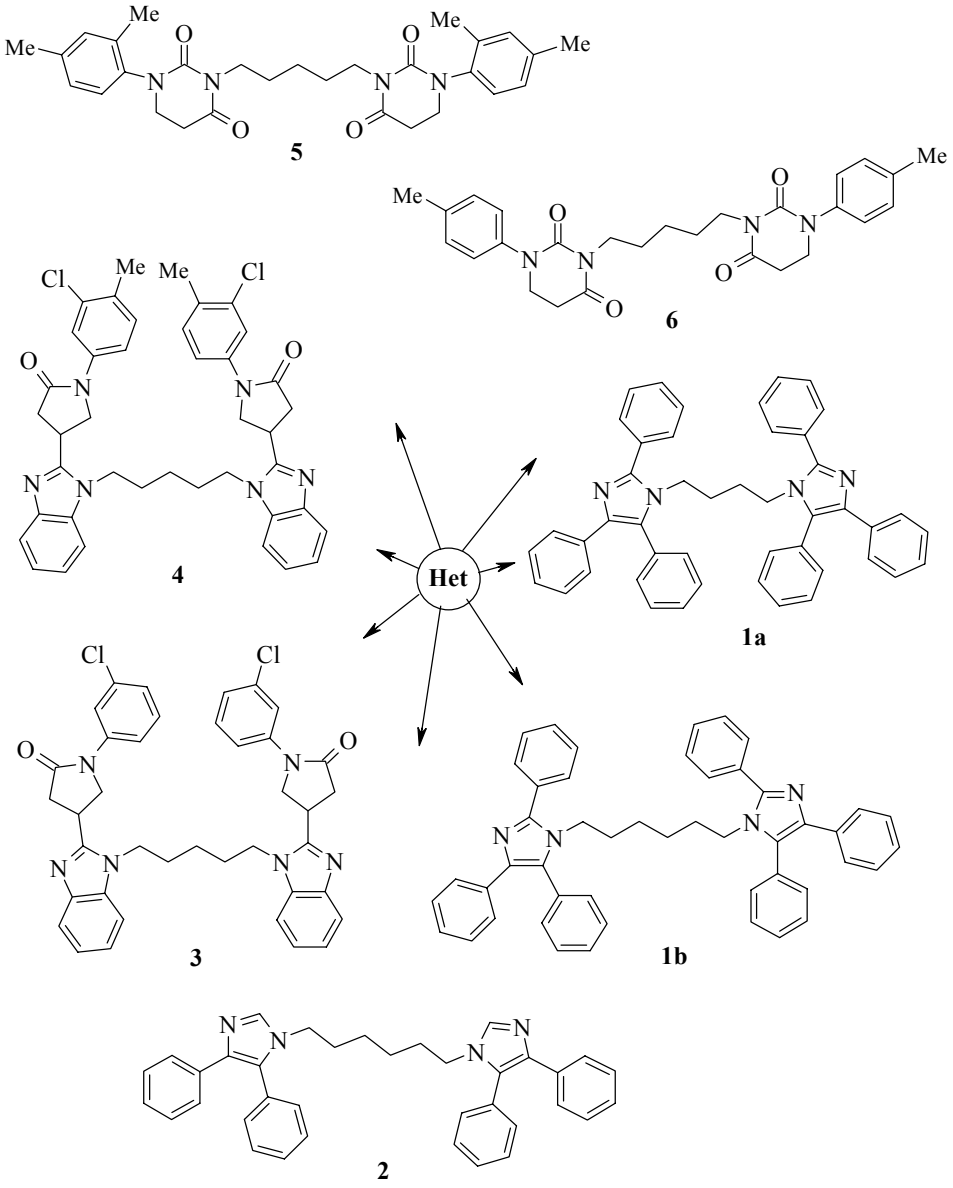
under basic conditions afforded N-substituted bisheterocycles **1-6** with four, five, or six methylene groups. Alkylation was carried out in acetone in the presence of a catalytic amount of tetrabutylammonium iodide. The obtained products were purified by column chromatography or recrystallized from an appropriate solvent.



5

6

4

1a

3

1b

2

1a,b Het = 2,4,5-triphenyl-1H-imidazole; **2 Het** = 4,5-diphenyl-1H-imidazole;
3 Het = 4-(1H-benzimidazol-2-yl)-1-(3-chlorophenyl)pyrrolidin-2-one;
4 Het = 4-(1H-benzimidazol-2-yl)-1-(3-chloro-4-methylphenyl)pyrrolidin-2-one;
5 Het = 1-(2,4-dimethylphenyl)dihydropyrimidine-2,4(1H,3H)-dione;
6 Het = 1-(4-methylphenyl)dihydropyrimidine-2,4(1H,3H)-dione.

The structures of **1-6** were confirmed by ^{1}H NMR spectroscopy and mass spectrometry. In the ^{1}H NMR spectra of the synthesized compounds we observed all proton signals of aromatic rings, heterocyclic rings and methylene groups, and did not observe protons of the NH group of heterocyclic rings of the initial compounds.

EXPERIMENTAL

The ^{1}H and ^{13}C NMR spectra were recorded on the Varian Unity Inova-300 (300 and 75 MHz respectively) instrument; chemical shifts are reported in ppm on the δ scale with tetramethylsilane as the internal reference. Mass spectra were determined on the Waters ZQ 2000 spectrometer (ESI, 20 V). Silica gel plates (Silufol UV-254) were used for analytical purposes. Elemental analysis was carried out on the C, H, N Analyzer CE 440, and the melting point was determined on the auto probe analyzer APA 1.

2,4,5-Triphenyl-1-[6-(2,4,5-triphenyl-1H-1-imidazolyl)alkyl]-1H-imidazoles (1a,b) and 4,5-Diphenyl-1-[6-(4,5-diphenyl-1H-1-imidazolyl)hexyl]-1H-imidazole (2) (General Method). To a solution of the corresponding imidazole (10 mmol) in acetone (150 ml), corresponding dihaloalkane (3.3 mmol) and a catalytic amount (~0.1 mmol) of tetrabutylammonium iodide were added. The mixture was stirred to reflux until it became homogenous. Then, of potassium hydroxide (80%) (0.46 g, 6.6 mmol) was added. The reaction mixture was refluxed for 4 h. Then the inorganic components were filtered off. The solvent was evaporated.

2,4,5-Triphenyl-1-[6-(2,4,5-triphenyl-1H-1-imidazolyl)butyl]-1H-imidazole (**1a**). 1.7 g (80% yield), mp 170°C, purified by column chromatography on silica gel; R_f 0.57 (eluent ethyl acetate–hexane, 1:2). ^{1}H NMR spectrum ($CDCl_3$), δ, ppm (*J*, Hz): 7.5-7.1 (30H, m, ArH); 3.56 (4H, t, *J* = 7.2, $2NCH_2$); 0.9-0.8 (4H, m, $2CH_2$). Mass spectrum, *m/z* (*I*, %): 646 $[M + H]^+$ (100). Found, %: C 85.21; H 5.69; N 8.79. $C_{46}H_{38}N_4$. Calculated, %: C 85.42; H 5.92; N 8.66.

2,4,5-Triphenyl-1-[6-(2,4,5-triphenyl-1H-1-imidazolyl)hexyl]-1H-imidazole (**1b**). 1.6 g (70% yield), mp 224-225°C (diethylether). ^{1}H NMR spectrum ($CDCl_3$), δ, ppm (*J*, Hz): 7.7-7.1 (30H, m, ArH); 3.75 (4H, t, *J* = 7.5, $2NCH_2$); 1.2-1.0 (4H, m, $2CH_2$); 0.7-0.5 (4H, m, $2CH_2$). Mass spectrum, *m/z* (*I*, %): 674 $[M + H]^+$ (100). Found, %: C 85.31; H 6.11; N 8.45. $C_{48}H_{42}N_4$. Calculated, %: C 85.43; H 6.27; N 8.30.

4,5-Diphenyl-1-[6-(4,5-diphenyl-1H-1-imidazolyl)hexyl]-1H-imidazole (**2**). 2.1 g (87% yield), mp 233-234°C (ethyl methyl ketone). ^{1}H NMR spectrum ($CDCl_3$), δ, ppm (*J*, Hz): 7.6-7.1 (22H, m, ArH and 2 =CH–); 3.71 (4H, t, *J* = 7.2, $2NCH_2$); 1.5–1.3 (4H, m, $2CH_2$); 1.1-0.9 (4H, m, $2CH_2$). Mass spectrum, *m/z* (*I*, %): 523 $[M + H]^+$ (100). Found, %: C 82.59; H 6.71; N 10.58. $C_{36}H_{34}N_4$. Calculated, %: C 82.72; H 6.56; N 10.72.

Compounds 3, 4 (General Method). To a solution of corresponding benzimidazole (10 mmol) in acetone (30 ml), of 1.5-dibromopentane (0.74, g 3.2 mmol), of potassium carbonate (0.44 g, 3.2 mmol), and a catalytic amount of tetrabutylammonium iodide were added. The mixture was stirred to reflux until it became homogenous. Then, of (80%) potassium hydroxide (0.9 g, 12.8 mmol) was added. The reaction mixture was refluxed for 4 h. Then the inorganic components were filtered off. The solvent was evaporated.

1-(3-Chlorophenyl)-4-[1-(5-{2-[1-(3-chlorophenyl)-2-oxotetrahydro-1H-4-pyrrolyl)-1H-benzo-[*d*]imidazol-1-yl}pentyl)-1H-benzo[*d*]imidazol-2-yl]-2-pyrrolidinone (**3**). 1.16 g (52% yield), mp 182-183°C (ethanol). ^{1}H NMR spectrum ($CDCl_3$), δ, ppm (*J*, Hz): 7.7-7.1 (16H, m, ArH); 4.58 and 4.07 (4H, 2t, *J* = 9.0, $2NCH_2$); 4.2-4.0 (4H, m, $2CH_2N_{het}$); 3.9-3.8 (2H, m, $2CH_{het}$); 3.1-2.9 (4H, m, $2CH_2CO$); 1.9-1.8 (4H, m, $2CH_2$); 1.5-1.4 (2H, m, CH_2). Mass spectrum, *m/z* (*I*, %): 691 $[M + H]^+$ (100), 693 $[M + 2 + H]^+$ (70). Found, %: C 67.59; H 5.41; N 12.28. $C_{39}H_{36}Cl_2N_6O_2$. Calculated, %: C 67.73; H 5.25; N 12.15.

1-(3-Chloro-4-methylphenyl)-4-[1-(5-{2-[1-(3-chloro-4-methylphenyl)-2-oxotetrahydro-1H-3-pyrrolyl)-1H-benzo[*d*]imidazol-1-yl}pentyl)-1H-benzo[*d*]imidazol-2-yl]-2-pyrrolidinone (**4**). 1.34 g (61% yield), mp 99–100°C (from ethanol). ^{1}H NMR spectrum ($CDCl_3$), δ, ppm (*J*, Hz): 7.8–7.2 (14H, m, ArH); 4.59 and 4,09 (4H, 2t, *J* = 9.0, $2NCH_2$); 4.2–4.0 (4H, m, $2CH_2N_{het}$); 3.9–3.6 (2H, m, $2CH_{het}$); 3.1–2.9 (4H, m, $2CH_2CO$); 2.34 (6H, s, $2CH_3$); 1.9–1.8 (4H, m, $2CH_2$); 1.6–1.4 (2H, m, CH_2). Mass spectrum, *m/z* (*I*, %): 719 $[M + H]^+$ (100), 721 $[M + 2 + H]^+$ (80). Found, %: C 68.65; H 5. 78; N 11.42. $C_{41}H_{40}Cl_2N_6O_2$. Calculated, %: C 68.42; H 5.60; N 11.68.

Compounds 5, 6 (General Method). To a solution of corresponding pyrimidinedione (10 mmol) in acetone (30 ml), of 1.5-dibromopentane (0.74 g, 3.2 mmol), of potassium carbonate (2 g, 14.5 mmol), and a catalytic amount of tetrabutylammonium iodide were added. The mixture was stirred to reflux until it became

homogeneous. Then, of potassium hydroxide (80%) (0.9 g, 12.8 mmol) was added. The reaction mixture was refluxed for 4 h. Then the inorganic components were filtered off. The solvent was evaporated.

1-(2,4-Dimethylphenyl)-3-{5-[1-(2,4-dimethylphenyl)-2,4-dioxohexahydro-3-pyrimidinyl]pentyl}-hexahydro-2,4-pyrimidinedione (**5**). 0.6 g (30% yield), mp 175-176°C (ethanol). ^{1}H NMR spectrum ($CDCl_3$), δ, ppm (*J*, Hz): 7.1-7.0 (6H, m, ArH); 3.82 (4H, t, *J* = 7.3, $2CH_2N_{het}$); 3.7-3.4 (4H, m, $2NCH_2$); 2.81 (4H, t, *J* = 7.3, $2COCH_2$); 2.32 (6H, s, $2CH_3$); 2.18 (6H, s, $2CH_3$); 1.7–1.6 (4H, m, $2CH_2$); 1.4-1.3 (2H, m, CH_2). Mass spectrum, *m/z* (*I*, %): 505 $[M + H]^+$ (100). Found, %: C 68.82; H 6.97; N 11.34. $C_{29}H_{36}N_4O_4$. Calculated, %: C 69.02; H 7.19; N 11.10.

1-(4-Methylphenyl)-3-{5-[1-(4-methylphenyl)-2,4-dioxohexahydro-3-pyrimidinyl]pentyl}hexahydro-2,4-pyrimidinedione (**6**). 1.34 g (46.5% yield), mp 179-180°C (ethanol). ^{1}H NMR spectrum ($CDCl_3$), δ, ppm (*J*, Hz): 7.3-7.1 (8H, m, ArH); 3.81 (4H, t, *J* = 7.2, $2CH_2N_{het}$); 3.9-3.7 (4H, m, $2NCH_2$); 2.84 (4H, t, *J* = 7.3, $2COCH_2$); 2.34 (6H, s, $2CH_3$); 1.7–1.5 (4H, m, $2CH_2$); 1.4–1.3 (2H, m, CH_2). Mass spectrum, *m/z* (*I*, %): 477 $[M + H]^+$ (100). Found, %: C 67.92; H 6.49; N 11.50. $C_{27}H_{32}N_4O_4$. Calculated, %: C 68.05; H 6.77; N 11.76.

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