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2-[2-(2,3-DIHYDROBENZIMIDAZOLYLIDENE)]-AND 2-[2-(2,3-DIHYDROPYRIDO[2,3-*d*]-IMIDAZOLYLIDENE)]-5,5-DIMETHYL-1,3-CYCLOHEXANEDIONES

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The reaction of 2-aminocarbonyl-5,5-dimethyl-1,3-cyclohexanedione with 2,3-diaminopyridine, 1,2-phenylenediamine (and its 4-methyl, 4-nitro, 4-carboxy, and 4-benzoyl derivatives), and 3,3-diaminobenzidine gave the corresponding 2-[2-(2,3-dihydrobenzimidazolylidene)]- and 2-[2-(2,3-dihydropyrido[2,3-d]imidazolylidene)]-5,5-dimethyl-1,3-cyclohexanediones. Their structure was confirmed by ^{1}H NMR spectroscopic data and X-ray analysis.

Keywords: 2-aminocarbonyldimedone, aromatic 1,2-diamines, 2-[2-(2,3-dihydrobenzimidazolylidene)]-5,5-dimethyl-1,3-cylohexanediones.

With the aim of preparing pyrido[3,2-*b*]benzo[*e*][1,4]diazepines, and related to the reaction products of 2,3-diaminopyridine with 2-formyldimedone [1], we have carried out the reaction of 2-aminocarbonyl-5,5-dimethyl-1,3-cyclohexanedione (**2**) with 1,2-phenylenediamine (**1a**), its 4-methyl (**1b**), 4-nitro (**1c**), 4-carboxy (**1d**), and 4-benzoyl (**1e**) derivatives, and with 3,3'-diaminobenzidine (**1f**), and 2,3-diaminopyridine (**1g**). Melting equimolar amounts of the diamine **1a-g** with the amide **2** in the presence of catalytic amounts of *p*-toluenesulfonic acid gave the 2-[2-(2,3-dihydrobenzimidazolylidene]- (**3a-f**) and 2-[2-(2,3-dihydropyrido-[2,3-*d*]imidazolylidene]-5,5-dimethyl-1,3-cyclohexanediones respectively.

A reasonable number of 1,3-cyclohexanediones with a directly added heterocyclic substituent group at position 2 have been recorded in the literature [2-15] but data for 2-benzimidazolyl derivatives is absent.

Previously, 3-(2-benzimidazolyl) derivatives have been obtained only in the 4-hydroxy-2-quinolinone system [16, 17] by the reaction of the corresponding 2-carbethoxy derivatives with *o*-phenylenediamine. With the varied biological activity of benzimidazoles [18] in mind, we have used a series of 4-substituted 1,2-phenylenediamines (**1a-f**) with 2-aminocarbonyldimedone.

The ^{1}H NMR spectra of all of the benzimidazolylidenedimedones **3a-f** show singlet, four-proton signals for $C_{(4)}$ and $C_{(6)}$ of the methylene groups in the dimedone fragment and two-proton, broad singlets for the NH protons in the range 11.5-13.5 ppm. Their IR spectra show typical NH stretching vibrations at frequencies of 3250-3200 cm^{-1}.

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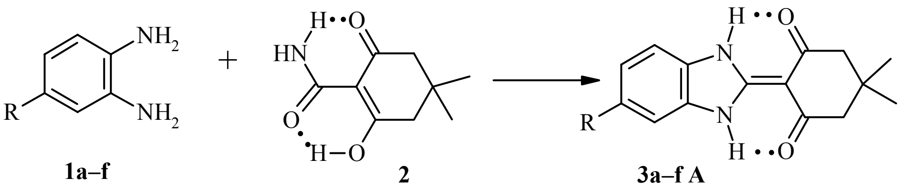
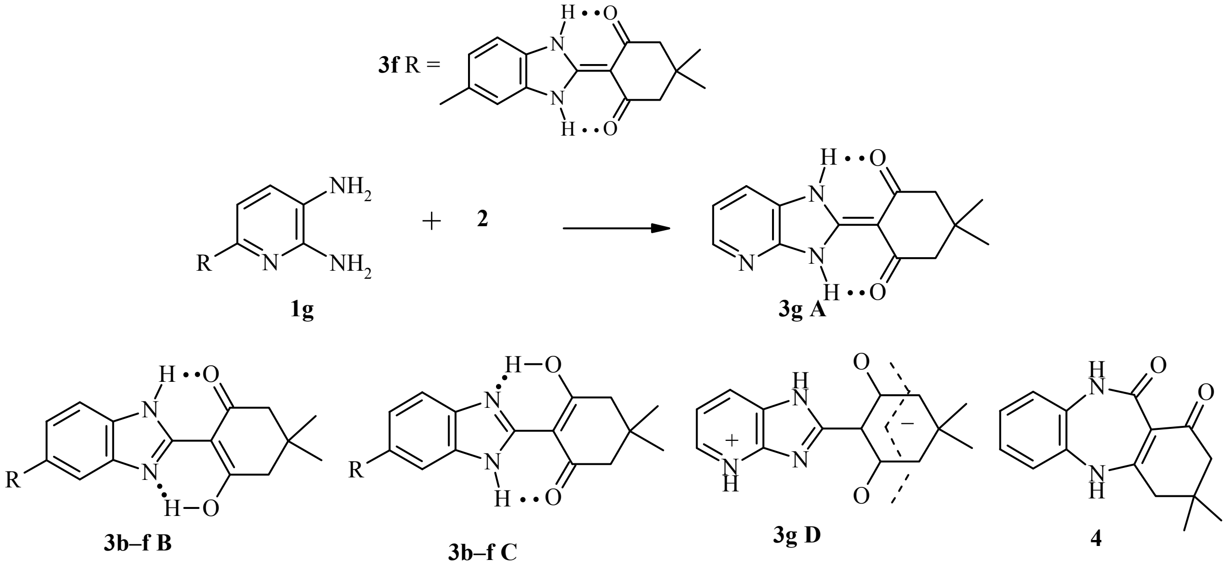


1, 3 a R = H; **b** R = Me; **c** R = NO_2; **d** R = COOH; **e** R = COPh. **1f** R= $C_6H_3(NH_2)_2(3,4)$;



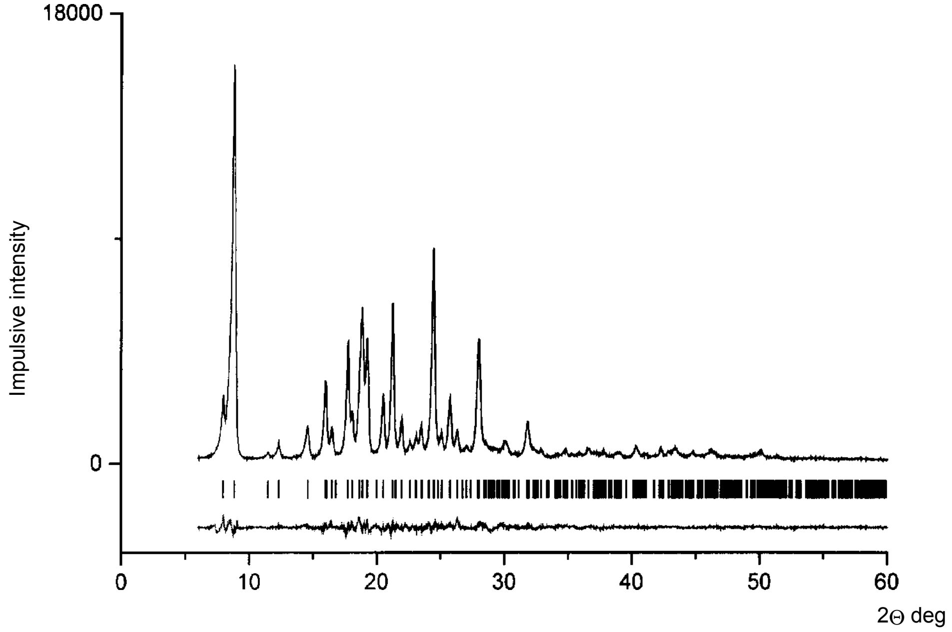


Fig. 1. Experimental (1) and difference (2) profiles after refinement of the crystal structure of the nitrobenzimidazole by the Rietveld method. 3. Calculated position of the diffraction peaks.

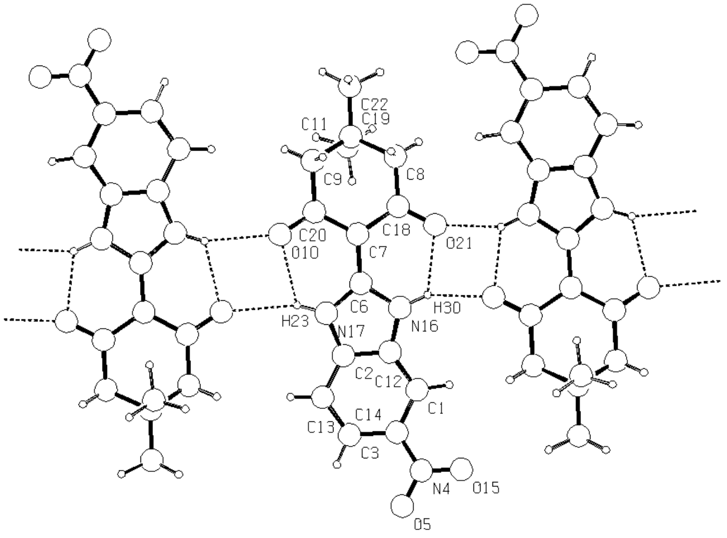


Fig. 2. Hydrogen bonds in the crystal structure of the nitrobenzimidazole **3c**.

The spectroscopic parameters quoted above suggest a preferred symmetric structure **3a-fA** and **3gA** and exclude the diazepine structures of type **4** as well as the presence of other products of monocondensation formed as a result of separation of 1 mol of water in the reaction of the diamines **1** and amide **2**.

For the benzimidazolyl derivatives **3b-f**, besides the tautomeric form **3A**, one should consider the presence of the forms **3B** and **3C** and in the case of **3g** the betaine form **3D** as well. The actual presence of a betaine form in the solid state for compound **3g** would contradict the IR spectroscopic data which shows the absence of $\equiv N^+–H$ bond stretching frequencies.

The X-ray investigation, in fact on the nitrobenzimidazole **3c**, confirmed the presence of the structure **3cA** since each N–H hydrogen atom in the sold state is bound by (found in the field of) two oxygen atoms.

TABLE 1. Crystallographic Data for the Nitrobenzimidazole **3c**

Formula	$C_{15}H_{15}N_3O_4$
M_r	301.30
space group	$P2_1/n$
a, Å	22.185(7)
b, Å	6.355(2)
c, Å	11.093(4)
β, °	115.81(3)
V, Å^3	1407.9(9)
F_{30}	12 (0.010, 270)
Z	4
D_x, g/cm^3	1.421

TABLE 2. Atomic Coordinates in the Crystal Structure of the Nitrobenzimidazole **3c**

Atom	*x*	*y*	*z*	Atom	*x*	*y*	*z*
C1	0.1073(7)	-0.299(2)	0.361(1)	C20	-0.0539(8)	0.527(3)	0.236(1)
C2	0.0712(6)	-0.010(3)	0.456(1)	O21	-0.0454(6)	0.158(2)	-0.007(1)
C3	0.1409(6)	-0.280(3)	0.601(1)	C22	-0.192(1)	0.764(3)	-0.093(2)
N4	0.1937(6)	-0.529(3)	0.512(1)	H23	0.026(4)	0.27(1)	0.461(7)
O5	0.2292(5)	-0.582(3)	0.626(1)	H24	0.106(3)	-0.01(1)	0.657(7)
C6	0.0110(7)	0.182(2)	0.275(2)	H25	-0.138(3)	0.41(1)	-0.136(6)
C7	-0.0339(8)	0.342(3)	0.184(2)	H26	-0.066(3)	0.77(1)	0.111(6)
C8	-0.1068(6)	0.478(4)	-0.055(1)	H27	-0.220(3)	0.51(1)	0.080(6)
C9	-0.0992(8)	0.691(3)	0.139(2)	H28	-0.231(3)	0.38(1)	-0.062(6)
O10	-0.0313(6)	0.552(2)	0.358(1)	H29	-0.218(3)	0.69(1)	-0.189(7)
C11	-0.1955(7)	0.436(4)	0.029(2)	H30	0.025(3)	-0.02(1)	0.149(6)
C12	0.0737(7)	-0.108(3)	0.346(1)	H31	0.107(3)	-0.36(1)	0.280(7)
C13	0.1084(6)	-0.087(3)	0.586(1)	H32	0.168(3)	-0.34(1)	0.688(6)
C14	0.1447(7)	-0.381(3)	0.490(1)	H33	-0.075(3)	0.60(1)	-0.053(7)
O15	0.1976(6)	-0.619(4)	0.421(1)	H34	-0.124(3)	0.76(1)	0.178(7)
N16	0.0358(6)	0.009(3)	0.236(1)	H35	-0.165(3)	0.31(1)	0.088(7)
N17	0.0353(6)	0.172(2)	0.411(1)	H36	-0.226(3)	0.83(1)	-0.062
C18	-0.0614(7)	0.315(3)	0.039(1)	H37	-0.161(3)	0.88(1)	-0.101(7)
C19	-0.1498(7)	0.594(3)	0.005(2)				

TABLE 3. Hydrogen bonds in the Crystal Structure of the Nitrobenzimidazole **3c**

Bond*	*l*, Å	Bond*	*l*, Å	Bond*	*l*, Å
N16···O21	2.68(2)	H30···O21	2.10(6)	N16–H30···O21	121(5)
N16···O21^{i}	2.85(2)	H30···O21^{i}	2.01(8)	N16–H30···O21^{i}	152(6)
N17···O10	2.76(2)	H23···O10	2.21(6)	N17–H23···O10	118(5)
N17···O10^{ii}	3.13(2)	H23···O10^{ii}	2.27(8)	N17–H23···O10^{ii}	160(6)

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* Symmetry notations: (i) -*x*, -*y*, -*z*; (ii) -*x*, 1-*y*, 1-*z*.

EXPERIMENTAL

IR spectra were recorded on a Specord 75-IR instrument for suspensions in vaseline oil and in hexachlorobutadiene. The ^{1}H NMR spectra were recorded on a Bruker WH-90/DS spectrometer (90 MHz) or on a Varian-BB Mercury (200 MHz) for solutions in $CDCl_3$ or DMSO-d_6 with HMDS internal standard

The diamines used came from the Acros and Maybridge companies.

2-[2-(5H- (3a), 5-Methyl- (3b), 5-Nitro- (3c), 5-Carboxy- (3d), and 5-Benzoyl- (3e) 2,3-Dihydrobenzimidazolylidene)]-5,5-dimethyl-1,3-cyclohexanediones, Bis[2,3-dihydro-2-(5,5-dimethyl-1,3-cyclohexanedion-2-ylidene)-5-benzimidazolyl (3f), and 2-[2-(2,3-Dihydropyrido[2,3-*d*]-imidazolylidene)]-5,5-dimethyl-1,3-cyclohexanedione (3g). A mixture of 2-aminocarbonyldimedone **2** (4 mmol), the corresponding diamine **1** (4 mmol) (in the case of **1f**, 2 mmol), and a catalytic amount of *p*-toluenesulfonic acid in a broad test tube was fused in an oil bath (bath temperature 200°C) for 25-35 min. The initial frothing ended with the formation of an oily melt which rapidly solidified. It was recrystallized twice with the addition of activated carbon.

3a. Yield 48%; mp 249-250°C (ethanol–DMF, 10:1). IR spectrum, ν, cm^{-1}: 1625-1615, 1565, 1550; 3200-3180. ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 1.1 (6H, s, $2CH_3$); 2.44 (4H, s, $2CH_2$); 7.36 (4H, m, C_6H_4); 11.91 (2H, br. s, 2NH). Found, %: C 70.32; H 6.53; N 10.94. $C_{15}H_{16}N_2O_2$. Calculated, %: C 70.32; H 6.71; N 10.97.

3b. Yield 64%; mp 274-275°C (ethanol–DMF, 10:1). IR spectrum, ν, cm^{-1}: 1624, 1580-1560; 3200. ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 1.11 (6H, s, $2CH_3$); 2.44 (7H, s, $2CH_2$, CH_3); 7.22 (3H, m, C_6H_3); 12.72 (2H, br. s, 2NH). Found, %: C 70.88; H 6.60; N 10.19. $C_{16}H_{18}N_2O_2$. Calculated, %: C 71.09; H 6.71; N 10.36.

3c. Yield 29%; mp 345-346°C (DMF). IR spectrum, ν, cm^{-1}: 1630, 1612. 1570-1550; 3200. ^{1}H NMR spectrum (DMSO-d$_6$), δ, ppm: 1.08 (6H, s, $2CH_3$); 2.38 (4H, s, $2CH_2$); 7.88 (1H, d, *J* = 8 Hz, C_6H_3); 8.27 (1H, dd, *J* = 8 Hz, *J* = 2 Hz, C_6H_3); 8.66 (1H, d, *J* = 2 Hz, C_6H_3); 11.49 (2H, br. s, 2NH). Found, %: C 59.61; H 5.05; N 13.86. $C_{15}H_{15}N_3O_4$. Calculated, %: C 59.79; H 5.02; N 13.95.

3d. Yield 51%; mp 360-362°C (pyridine–DMF, 10:1). IR spectrum, ν, cm^{-1}: 1625-1615, 1565, 1550, 1515; 3200-3180. ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 1.02 (6H, s, $2CH_3$); 2.33 (4H, s, $2CH_2$); 7.83 (2H, m, C_6H_3); 8.34 (1H, s, C_6H_3); 12.9 (1H, br. s, COOH); 13.21 (2H, br. s, 2NH). Found, %: C 63.75; H 5.25; N 9.19. $C_{16}H_{16}N_2O_4$. Calculated, %: C 63.99; H 5.37; N 9.33.

3e. Yield 63%; mp 290-291°C (pyridine). IR spectrum, ν, cm^{-1}: 1640, 1620, 1590, 1550, 1535; 3220. ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 1.11 (6H, s, $2CH_3$); 2.44 (4H, s, $2CH_2$); 7.28-8.02 (8H, m, C_6H_5, C_6H_3); 12.94 (2H, s, 2NH). Found, %: C 73.13; H 5.50; N 7.70. $C_{22}H_{20}N_2O_3$. Calculated, %: C 73.32; H 5.59; N 7.77.

3f. Yield 35%; mp 376-378°C (acetic acid). IR spectrum, ν, cm^{-1}: 1615, 1570; 3300-3200. ^{1}H NMR spectrum (DMSO-d$_6$), δ, ppm: 1.02 (12H, s, $4CH_3$); 2.41 (8H, s, $4CH_2$); 7.74 (6H, m, $2C_6H_3$); 13.13 (4H, br. s, 4NH). Found, %: C 70.40; H 5.81; N 10.83. $C_{30}H_{30}N_4O_4$. Calculated, %: C 70.57; H 5.92; N 10.97.

3g. Yield 51%; mp 300-301°C (pyridine). IR spectrum, ν, cm^{-1}: 1628, 1612, 1556; 3200 cm^{-1}. ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 1.09 (6H, s, $2CH_3$); 2.44 (4H, s, $2CH_2$); 7.24 (1H, dd, *J* = 7.5, *J* = 4.5 Hz, C_5H_3N); 7.86 (1H, dd, *J* = 7.5, *J* =1.5 Hz, C_5H_3N); 8.38 (1H, dd, *J* =4.5 Hz, *J* = 1.5 Hz, C_5H_3N); 12.99 (2H, br. s, 2NH). Found, %: C 65.15; H 5.73; N 16.11. $C_{14}H_{15}N_3O_2$. Calculated, %: C 65.36; H 5.88; N 16.33

X-ray Structural Investigation. The nitrobenzimidazole **3c** was separated as a yellowish colored powder. The unit cell parameters (Table 1) were determined using the TREOR90 program [19] for the positions of 30 peaks with the measurements made in a Guinier chamber in the range 0-50° and using CuKα_1 radiation. The space group $P2_1/n$ was selected based on conditions of systematic extinction. Collection of diffraction data for solution and refinement of the structure was carried out on a Philips X'pert laboratory θ-2θ diffractometer with a PW 3056/00 goniometer using CuKα radiation (Ni filter, 40 kV/mA) with stepwise scanning in the range 6-60° 2θ in 0.02° steps and calculation time 15 s for each step. The structure was solved by a systematic search method [20] and refined using the Rietveld method with the MRIA program [21] to values of R_p = 6.0%, R_{wp} = 8.9%, and R_{exp} = 3.2% (Fig. 1). The atomic coordinates are given in Table 2. In the refinement process the boundaries of the available bond lengths were applied. The overall thermal factor U_{iso} for the non-hydrogen atoms was refined to 0.093(2) Å. For the hydrogen atoms the value U_{iso} = 0.05 Å^2 was fixed.

The crystal packing of the nitrobenzimidazole molecule is characterized as an infinite linear network (Fig. 2) forming centrosymmetric hydrogen bonds on both sides of the molecule (Table 3).

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