Synthesis, Structure and Properties of 5,5-Diphenyl-2,3,5,6-tetrahydroimidazo-[2,1-*b*]-imidazoline-3,6-dione

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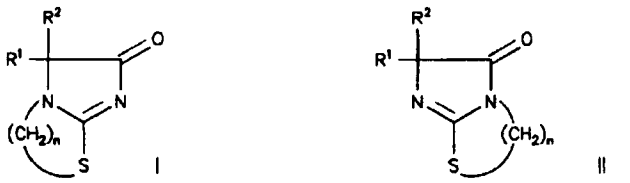
Cyclization of *N*-[(5,5-diphenyl)-4-oxo-2-imidazolidinyl]glycine (**3**) yielded 5,5-diphenyl-2,3,5,6-tetrahydroimidazo[2,1-*b*]imidazoline-3,6-dione (**6**) or its acetyl derivative **5** depending on the method used. The stabilities of **5** and **6** in acidic or alkaline solutions were examined. The crystal structure of the hydrolysis products **7**, **8** of **5** and **6** were solved by X-ray analysis.

Synthese, Struktur und Eigenschaften von 5,5-Diphenyl-2,3,5,6-tetrahydroimidazo-[2,1-*b*]-imidazolin-3,6-dion

Die Zyklisierung von *N*-[(5,5-diphenyl)-4-oxo-2-imidazolidinyl]glycin (**3**) ergab 5,5-diphenyl-2,3,5,6-tetrahydroimidazo[2,1-*b*]imidazolin-3,6-dion **6** oder sein Acetylderivat abhängig von der verwendeten Methode. Die Stabilität von **5** und **6** wurden in säurem oder alkalischem Milieu untersucht. Die Kristallstrukturen der Hydrolyseprodukte **7**, **8** von **5** und **6** wurden mittels Röntgenstrukturanalyse untersucht.

5,5-Diphenylhydantoin (DPH) is known as the antiepileptic drug phenytoin. This inspired us to the synthesis of annelated hydantoin derivatives of



R¹, R² = Ph R¹, R² = (un)substituted ArCH=

Scheme 1

types **I** and **II** (Scheme 1) as compounds with potential anticonvulsive properties [1,2]. Preliminary pharmacological tests reveal that some of the newly obtained compounds are biologically active, especially those of type **II** [R^1, R^2 = (un)substituted ArCH=] which show some anxiolytic, analgesic, antidepressant, and anticonvulsive properties [3,4]. Since an important feature in the action of antiepileptic drugs is the ability to form hydrogen bonds with specific proteins within the receptors [5-8], continuing our studies on structure/activity correlation we decided to prepare fused hydantoin derivatives in which the S atom is isosterically substituted by N. With such a modification an additional H-bonding group is introduced in the skeleton of the examined imidazoimidazoline.

Thus, as an extension of our search for new anticonvulsants, we studied two groups of imidazoimidazoline derivatives: the present paper deals with diphenylimidazoimidazoline derivatives; arylidene-imidazoimidazoline derivatives were described previously [9].

Results and discussion

As the starting substance in the synthesis of the diphenylimidazoimidazoline derivatives, 5,5-diphenyl-2-thiohydantoin **1** (DPTH) (Scheme 2) was reacted with glycine *via* its *S*-methylated derivative **2**. The obtained glycine derivative **3** was stable in the acidic medium and underwent esterification to **4**. X-ray analysis established the proposed structure **4**.

Upon refluxing **3** with acetic anhydride, cyclization to the bicyclic product **5** occurred; this was confirmed by physicochemical and spectral analysis (EI-MS, ^{1}H-NMR, ^{13}C-NMR).

$M^{+\bullet}$ at m/z = 333 and the fragment ion with m/z = 291 formed by loss of ketene indicated that the obtained structure was the bicyclic monoacetylated compound. The ^{1}H-NMR spectrum showed signals at 4.58 ppm (CH_2) and 2.72 ppm (CH_3). In the ^{13}C-NMR spectrum apart from aliphatic carbon signals (CH_3: 24.42 ppm and CH_2: 51.66 ppm), C=O signals at 161.60, 167.78, 170.17 ppm, characteristic of three C=O groups were present. The down-field shifted signal at 186.87 ppm was assigned to the C=N group. According to our experience [2], it indicated an 1,2-annelated derivative of DPTH (type **I**, Scheme 1) with conjugated C=O and C=N groups.

Upon performing the cyclization of **3** in the presence of DCC, the major product **6** with m.p. 269–270 °C, R_F (D) = 0.12 was obtained and identified on the basis of spectral data (EI-MS, ^{1}H-NMR, ^{13}C-NMR). MS showed $M^{+\bullet}$ at m/z = 291. The ^{1}H- and ^{13}C-NMR spectra contained signals for CH_3 the (1.07 ppm; 18.51 ppm) and CH_2 (3.45 ppm; 56.17 ppm) groups of ethanol, since **6** crystallized with 0.5 molecule of ethanol, as was confirmed by elemental analysis. In the reaction of **6** with acetic anhydride, the acetylated compound **5** arises, which can be easily converted to **6** by mild hydrolysis (EtOH; NH_3aq). The structure of **6** (and consequently of **5**) was proved by X-ray analysis [10].

Compounds **5** and **6** were examined in respect of their stabilities under alkaline and acidic conditions. In alkaline medium (at elevated temp.) they were converted to the glycine derivative **3**, whereas in acidic medium both were cleaved to the N1-acylated structures **7** and **8**, respectively. While **7** is relatively stable under acidic conditions, **8** is converted to the DPH **10** upon heating in dil. HCl. Depending on the crystallization conditions, the hydrochloride of **8** crystallized either with 0.5 water molecule or with one acetic acid molecule.

The different behaviour of **5** and **6** upon acidic and alkaline hydrolysis seems noteworthy. Because routine methods for identification of the products did not allow a determination of that mechanism, X-ray analyses of **8** and **7** were performed as the only way to confirm their structures. The molecular

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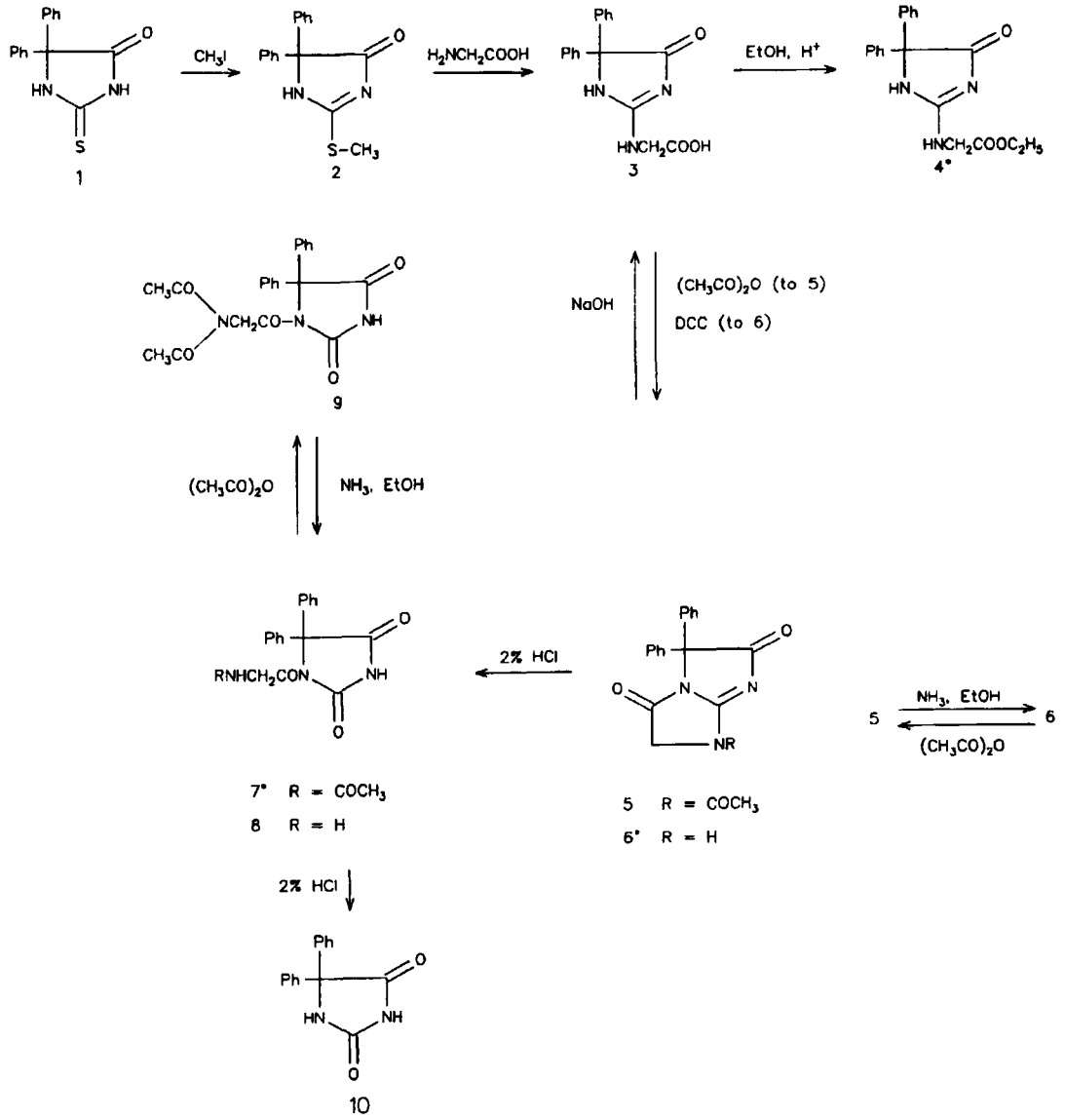
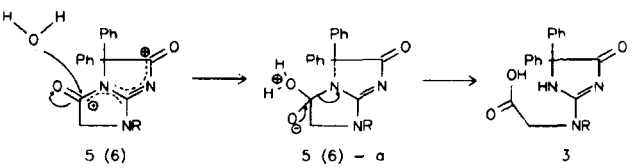


Scheme 2: Asterisks indicate that structures have been confirmed by X-ray analysis.

structures of **7** and **8** in the solid state are shown in Figs. 1 and 2, respectively, the legends of which list selected bond lengths, bond angles and torsional angles. The final positional parameters with equivalent temp. factors of all non-H atoms are listed in Table 1 for both molecules. In the light of the crystallographic results, only N1-acylated hydrolysis products (DPH derivatives) were confirmed. The sp^3 hybridization of the endocyclic N3 atom was verified by localization of the respective H atom from the electron density distribution map. It is also in accordance with the bond lengths values of C2=O2 [1.193(5)Å and 1.210(4)Å for **7** and **8**, respectively] and C2-N3 [1.386(6)Å and 1.367(5)Å for **7** and **8** respectively]. The acyl substituents at N1 possess similar configurations in both molecules, as follows immediately from the corresponding torsional angle values (legends to Figs. 1 and 2). The independent part of the structure of **7** consists of one main molecule linked to its neighbours by N8-H8...O4 (-+x/ 1/2+y/ 1/2-z) = 2.893(6)Å intermolecular H-bonds. On the other hand, **8** exists in the solid in the form of discrete ions $C_{17}H_{16}O_3N_3^+$ (with positively charged N8) and Cl^-. Both ions are connected by H-bonds, also incorporating an acetic acid molecule. Three H-bonds were found: N3-H3....Cl = 3.171(3)Å, N8-H81...Cl (1-x,1/2+y,1/2-z) = 3.141(2)Å and N8-H82...01' = 2.814(4)Å. The overall geometry of the hydantoin rings in both molecules is consistent with that of many related structures [12].

Rather unexpected and different behaviour of **5** and **6** under alkaline or acidic conditions prompted us to discuss both reaction mechanisms. Under alkaline conditions the hydrolytic attack (Scheme 3) on the lactam carbonyl atom (C-3) of the annelated ring with partial charge +0.29e occurred. It



Scheme 3

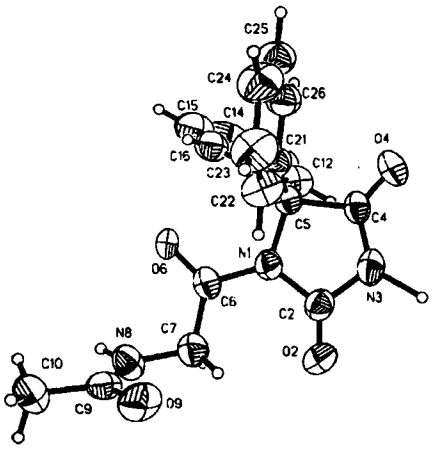


Fig. 1: View of the molecule **7**. Selected bond lengths [Å]: N(1)-C(2) 1.411(5), C(2)-N(3) 1.386(6), C(2)-O(2) 1.139(5), N(1)-C(6) 1.392(6); Selected bond angles [°]: C(5)-N(1)-C(2) 11.2(3), C(5)-N(1)-C(6) 122.7(3), C(6)-N(1)-C(2) 126.1(4); Selected torsional angles [°]: C(5)-N(1)-C(6)-O(6) 3.9(7), C(5)-N(1)-C(6)-C(7) 175.4(4), N(1)-C(6)-C(7)-N(8) 171.6(4).

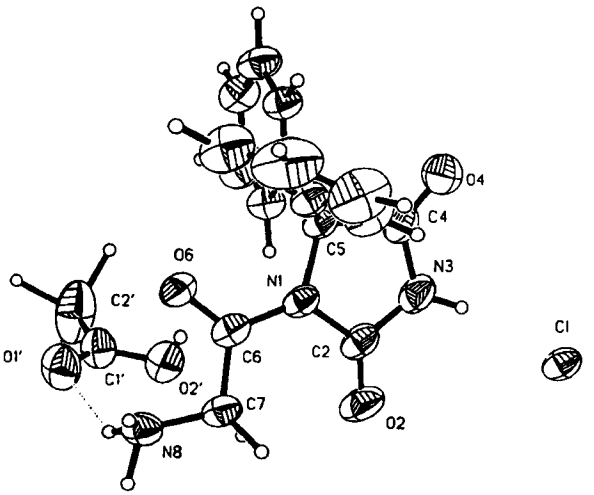
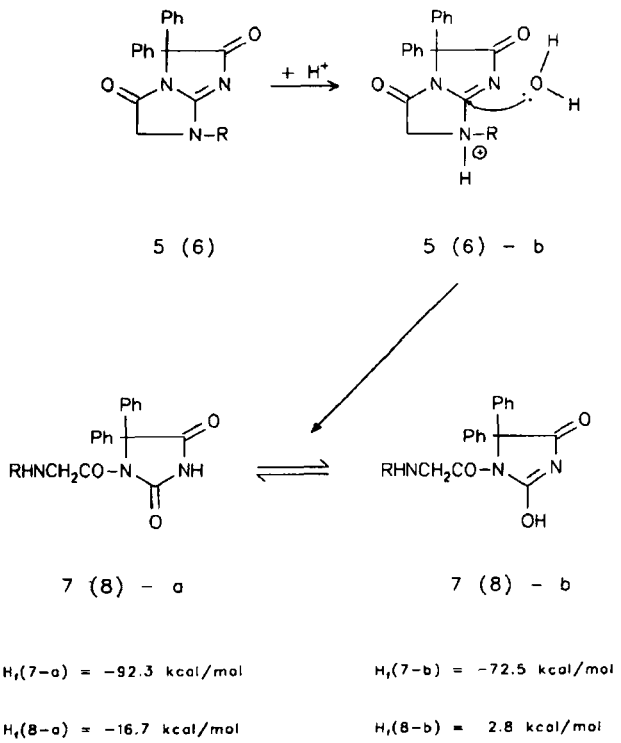


Fig. 2: Independent part of structure **8** with intermolecular H-bonds marked by dotted lines. Selected bond lengths [Å]: N(1)-C(2) 1.393(3), C(2)-N(3) 1.367(5), C(2)-O(2) 1.210(4), N(1)-C(6) 1.389(4); Selected bond angles [°]: C(5)-N(1)-C(2) 111.8(2), C(5)-N(1)-C(6) 122.9(2), C(6)-N(1)-C(2) 125.2(2); Selected torsional angles [°]: C(5)-N(1)-C(6)-O(6) 10.6(4), C(5)-N(1)-C(6)-C(7) 169.3(2), N(1)-C(6)-C(7)-N(8) 179.2(2).

should be noted that C-6 also possesses an identical charge but as an element of a more stable ring (with longer conjugated bonds) and more sterically hindered by the two phenyl groups was undisturbed by hydrolysis. The interpretation of that process was affirmed by the formation of **3**. On the other hand, under acidic conditions the amidine part of the molecule is presumably initially protonated to **5-b** (or **6-b**) (Scheme 4). Now hydrolytic attack occurs at C-8 of the bicyclic structures **5** and **6**. Thus the bicyclic moiety is cleaved to N1-substituted DPH amino-imino tautomers **7-a** and **7-b** (or **8-a** and **8-b**), although crystallographically only **7-a** and **8-a** tautomers were detected (Figs. 1 and 2). The value for the heat of formation (H_f in kcal/mol) calculated for both tautomers (PM3-MNDO method from MOPAC.6 [11]), indi-

Tab. 1: Non-hydrogen fractional atomic coordinates of **7** and **8** ($\times 10^4$) and equivalent temperature factors ($Å^2 \times 10^3$); U_{eq} defined as 1/3 for the trace of the orthogonalized U_{ij} tensor.

Molecule **7**					Molecule **8**				
	x	y	z	U_{eq}		x	y	z	U_{eq}
N1	772(3)	6184(3)	2501(2)	43(1)	N1	7943(1)	3854(2)	5700(2)	40(0.4)
C2	1955(4)	5613(4)	2717(3)	48(1)	N3	7922(2)	5021(3)	7130(2)	51(0.4)
O2	3017(3)	5656(3)	2325(3)	67(1)	N8	9287(1)	1991(3)	4470(2)	47(0.4)
N3	1657(4)	4968(3)	3486(3)	52(1)	O2	9183(1)	4474(3)	7027(2)	63(0.4)
C4	408(4)	5144(3)	3837(3)	44(1)	O4	6535(2)	5235(3)	6799(2)	68(1)
O4	-62(4)	4736(3)	4540(2)	59(1)	O6	7759(1)	2709(3)	4133(2)	50(0.4)
C5	-319(4)	5943(4)	3194(3)	44(1)	C2	8440(2)	4448(3)	6664(2)	45(0.4)
C6	593(5)	6874(4)	1739(3)	48(1)	C4	7101(2)	4834(3)	6557(2)	49(1)
O6	-502(4)	7258(3)	1594(3)	53(1)	C5	7049(2)	4024(3)	5536(2)	38(0.4)
C7	1804(5)	7119(4)	1131(3)	55(1)	C6	8224(2)	3099(3)	4997(2)	40(0.4)
N8	1431(5)	7711(3)	301(3)	56(1)	C7	9130(2)	2774(3)	5340(2)	44(0.4)
C9	1274(4)	7267(4)	-542(3)	48(1)	CL	8822(.4)	6453(1)	9387(1)	46(0.4)
O9	1518(4)	6318(3)	-672(3)	68(1)	O1′	8876(2)	3723(3)	2604(2)	70(1)
C10	814(6)	7976(5)	-1329(4)	68(1)	O2′	8965(2)	5400(2)	3778(2)	59(1)
C21	-1503(4)	5343(4)	2764(3)	47(1)	C1′	8799(2)	5000(4)	2782(3)	54(1)
C22	-1426(5)	4841(5)	1895(4)	61(1)	C2′	8512(1)	6142(2)	1962(2)	103(2)
C23	-2496(6)	4249(6)	1560(5)	76(1)	C11	6604(1)	5047(2)	4625(2)	39(0.4)
C24	-3659(6)	4163(5)	2091(5)	73(2)	C12	5756(1)	5054(2)	4197(2)	48(1)
C25	-3741(5)	4632(5)	2957(4)	64(1)	C13	5341(2)	6089(4)	3450(3)	59(1)
C26	-2661(5)	5213(4)	3304(4)	55(1)	C14	5774(2)	7108(3)	3114(3)	56(1)
C11	-675(5)	6945(4)	3765(3)	47(1)	C15	6624(2)	7133(3)	3555(3)	54(1)
C12	55(6)	7214(5)	4553(4)	65(1)	C16	7039(2)	6107(3)	4308(3)	46(1)
C13	-210(7)	8130(5)	5070(5)	84(2)	C21	6665(2)	2529(3)	5510(2)	41(.4)
C14	-1203(6)	8795(3)	4790(4)	90(2)	C22	6285(2)	1792(3)	4556(3)	51(1)
C15	-1950(6)	8541(3)	4011(4)	83(2)	C23	5984(2)	406(4)	4569(4)	67(1)
C16	-1702(6)	7616(4)	3489(4)	63(1)	C24	6060(3)	-247(5)	5512(5)	86(1)
					C25	6419(3)	473(5)	6452(4)	83(1)
					C26	6727(2)	1866(4)	6467(3)	62(1)



Scheme 4

cate tautomers **7-a** and **8-a** to be thermodynamically more stable. The respective values of H_f are given in Scheme 4 for comparison (quantum chemical semi-empirical calculations were performed for the positively charged ion of **8**).

Reaction of **7** and **8** with acetic acid anhydride yielded the diacetylated compound **9** whose structure was assigned on the basis of MS, ^{1}H- and ^{13}C-NMR spectral analysis. In the MS of **9** $M^{+\bullet}$ was found at m/z = 393. In its ^{1}H-NMR spectrum both acetyl groups gave identical signals–six protons singlet at δ = 2.22 ppm and in ^{13}C-NMR signals at 25.90 ppm (CH_3) and 173.33 ppm (C=O). Additionally in the ^{1}H-NMR the signals at 12.53 ppm (exchangeable with D_2O) similar to those for compounds **7** (12.40 ppm) and **8** (11.80 ppm) assigned the N-1 substituted hydantoin derivative [13]. The second acetyl group at N-8 can be easily cleaved, converting **9** to compound **7**.

Crystallographic data are deposited at Cambridge Structure Database under no. ...

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Experimental Part

Melting points: Kofler hot stage microscope, uncorrected.– IR spectra: Specord 80 IR (Carl Zeiss, Jena) KBr.– ^{1}H-NMR and ^{13}C-NMR: Bruker VM 300 or Varian Gemini 200, δ [ppm] TMS as internal standard.– MS: Finnigan MAT CH 7A (170 °C, EI) 70 eV m/z(%); direct inlet.– TLC: silica GF_{254} precoated TLC plates. Developing systems A: $CHCl_3$:2-propanol:NH_3aq. 9:11:2; B: $CHCl_3$:acetone 1:1; C: toluene:acetone 20:1.5; D: $CHCl_3$:AcOEt 1:1.

N-[(5,5-Diphenyl)-4-oxo-2-imidazolidinyl]glycine (**3**)

a. A suspension of 5,5-diphenyl-2-methylmercapto-4-oxo-imidazoline (2.82 g, 0.01 mol) and glycine (0.83 g, 0.011 mol) in acetic acid (30 ml) was refluxed for 10 h. The solution was left at room temp. overnight and was then poured into a large volume of water. The precipitated product was recrystallized from ethanol: m.p. 259–260 °C, yield 2.44 g (79%).– R_F (A) 0.12.– $C_{17}H_{15}N_3O_3$ (309.3) Calc. C 66.0 H 4.89 N 13.6 Found C 66.1 H 4.78 N 13.4.– IR: 3400, 3250 (NH), 1770 (C=O), 1704 (br., C=N).– ^{1}H-NMR ([D$_6$]DMSO): 4.04 (s, 2H, CH_2), 7.36 (m, 10H, aromatic), 7.77 (br.s., 1H, N*H*CH_2), 9.21 (br.s., 1H, NH).– MS: 309 (16, $M^{+\bullet}$), 291 (12, $(M - H_2O)^{+\bullet}$), 280 (9), 264 (13), 44 (100).

b. A solution of **6** (1.0 g; 3.2 mmol) in 15 ml ethanol and 3 ml of 10% NaOH was refluxed. The reaction was monitored by TLC. After about 2h the spot of **6** had disappeared. Ethanol was evaporated *in vacuo*. The residue was acidified with 5% HCl, the precipitated solid was recrystallized from ethanol to give 0.84 g (85%) of **3**.

c. As in method *b* compound **5** converted to **3** after 3 h (yield 82%).

Ethyl N-[(5,5-diphenyl)-4-oxo-2-imidazolidinyl]glycinate (**4**)

A mixture of **3** (3.09 g, 0.01 mol), anhydrous ethanol (20 ml), and conc. H_2SO_4 (1.5 ml) was refluxed for 5 h and left overnight at room temp. After addition of water, the crude oily mass was recrystallized from ethanol with H_2O: m.p. 244-245 °C, yield 2.29 g (68%).– R_F (A) 0.89.– R_F (B) 0.41.– $C_{19}H_{19}N_3O_3$ (337.4) Calc. C 67.6 H 5.69 N 12.5 Found C 67.3 H 5.70 N 12.5.– IR: 3188 (NH) 1744, 1700 (C=O).– ^{1}H-NMR ([D$_6$]DMSO): 1.19 (t, 3H, J=7.1 Hz, CH_3), 4.11 (s, 2H, CH_2), 4.14 (q, 2H, J=7.1 Hz, CH_2), 7.34 (br.s., 10H, aromatic), 7.85 (br.s., 1H, N*H*CH_2), 9.29 (br.s., 1H, NH).– ^{13}C-NMR ([D$_6$]DMSO): 13.99 (CH_3), 43.68 (NCH_2), 60.82 (COO*C*H_2), 72.96 (Ph_2C), 127.14, 127.45, 128.39, 141.50 (aromatic), 170.07 (C=O), 170.84 (COO), 186.78 (C=N).– MS: 337(30, $M^{+\bullet}$), 308(16) 77(100).

1-Acetyl-5,5-diphenyl-2,3,5,6-tetrahydroimidazo[2,1-b]imidazoline-3,6-dione (**5**)

a. A suspension of **3** (3.09 g; 0.01 mol) in 30 ml of acetic anhydride was refluxed for 4 h. Next day water was added, the precipitate was filtered off and crystallized from ethanol, m.p. 200-202 °C, yield 3.09 g (93%).– R_F (A) 0.35.– R_F (C) 0.33.– R_F (D) 0.74.– $C_{19}H_{15}N_3O_3$ (333.3) Calc. C 68.5 H 4.53 N 12.6 Found C 68.5 H 4.57 N 12.5.– IR: 1756, 1736, 1722 (C=O), 1600 (C=N).– ^{1}H-NMR ($CDCl_3$): 2.72 (s, 3H, CH_3), 4.58 (s, 2H, CH_2), 7.37 (s, 10H, aromatic).– ^{13}C-NMR ($CDCl_3$): 24.42 (CH_3), 51.66 (CH_2), 77.16 (Ph_2C), 127.73, 128.86, 129.15, 135.65 (aromatic C), 161.60, 167.78 ($COCH_3$, C_3=O), 170.17 (C_6=O), 186.87 (C=N).– UV (MeOH), λ_{max} (log ε): 233 nm (4.22).– MS: 333 (100, $M^{+\bullet}$), 291 (79, $M - COCH_2)^{+\bullet}$.

b. A suspension of **3** (3.09 g; 0.01 mol), acetic anhydride (3 ml), and anhydrous pyridine was left at room temp. for a week. The precipitate was filtered off, washed with water, and recrystallized from ethanol, yield 1.70 g (51%).

c. A suspension of **3** (3.09 g; 0.01 mol) in 25 ml of acetic anhydride was left at room temp. for 2 days. After addition of water the precipitate was recrystallized from ethanol to give 1.83 g (55%) of **5**.

5,5-Diphenyl-2,3,5,6-tetrahydroimidazo[2,1-b]imidazoline-3,6-dione (**6**)

a. To a suspension of **3** (3.09 g; 0.01 mol) in dry CH_2Cl_2 (50 ml), DCC (2.06 g; 0.01 mol) in CH_2Cl_2 (30 ml) was added dropwise. The mixture was stirred for 24 h. The solid (dicyclohexyl urea) was filtered off. The filtrate was concentrated *in vacuo*. The residue was crystallized from EtOH. As the 1st fraction 1.73 g (55%) of **6** was collected (heavy, thick crystals), m.p. 269-270 °C.– R_F (D) 0.12.– IR: 3452 cm^{-1}, 3056 (NH), 1764, 1760 (C=O), 1742 (C=O), 1648 (C=N).– ^{1}H-NMR ([D$_6$]DMSO): 1.07 (t, 3H, CH_3 of EtOH), 3.45 (q, 2H, CH_3CH_2 of EtOH), 4.51 (s, 2H, COCH_2), 7.32–7.42 (m, 10H, aromatic), 10.30 (br. s., 1H, NH).– ^{13}C-NMR ([D$_6$]DMSO): 18.51 (CH_3 of EtOH), 51.48 (*C*H_2CO), 56.17 (CH_3CH_2 of EtOH), 74.97 (Ph_2C), 127.87, 128.58, 137.57 (aromatic C), 167.12, 172.78 (C_3=O) (C6=O), 187.23 (C=N).– UV (MeOH): λ_{max} (log ε): 228 nm (4.36).– MS: 291 (79, $M^{+\bullet}$), 262 (21), 165(100).– **6** dried in an exsiccator under reduced pressure and then at 100 °C.– $C_{17}H_{13}N_3O_2\bullet$ ½ C_2H_5OH (314.3) Calc. C 68.8 H 5.12 N 13.4 Found C 68.9 H 5.03 N 13.1.

b. A mixture of **5** (3.33 g, 0.01 mol), 50 ml of ethanol and 7 ml of conc. NH_3 was left overnight at room temp. The mixture was concentrated *in vacuo* to 1/3 volume. **6** was filtered off and recrystallized from ethanol, m.p. 269-270 °C, yield 2.17 g (69%).

1-(Acetamidoacetyl)-5,5-diphenylimidazolidine-2,4-dione (7)

a. A mixture of **5** (3.33 g, 0.01 mol) in 60 ml of 2% HCl was refluxed for 4 h. The precipitate was filtered off and recrystallized from ethanol giving 2.21 g (63%) of **7** as a white powder: m.p. 290-291 °C.– R_F (A) 0.29.– $C_{19}H_{17}N_3O_4$ (351.3) Calc. C 65.0 H 4.87 N 12.0 Found C 64.7 H 4.73 N 11.7.– IR: 3360 cm^{-1} (NH), 1788, 1736 (C=O), 1640 (C=N).– ^{1}H-NMR ([D$_6$]DMSO): 1.82 (s, 3H, CH_3), 4.54 (d, 2H, J=5.5 Hz, CH_2), 7.37 (s, 10H aromatic), 8.12 (t, 1H, J=5.6 Hz, NH), 12.40 (br.s., 1H, 3-NH).– ^{13}C-NMR ([D$_6$]DMSO): 22.20 (CH_3), 44.48 (CH_2), 75.08 (Ph_2C), 128.36, 128.7, 135.69 (aromatic C), 154.15 (CH_3CO), 168.36 (CH_2CO), 170.19 (C_4=O), 173.46 (C_2=O).– MS: 351 (52, $M^{+\bullet}$), 80 (100).

b. To a suspension of **9** (3.93 g, 0.01 mol) in ethanol (50 ml), conc. aqueous ammonia (0.5 ml) was added. The reaction mixture was left at room temp. for 24 h. The solid dissolved. Next day the solvent was evaporated *in vacuo* to ½ volume. The precipitate was filtered off and recrystallized from ethanol. Yield 2.49 g (71%).

c. Acidic hydrolysis of **7**

A suspension of **7** (0.351 g, 1 mmol) in 20 ml of ethanol and 10 ml of 2% HCl was refluxed. After *ca* 50 h **7** had disappeared (TLC). The precipitate was recrystallized from ethanol and identified as **10**, yield 0.159 g (63%).

Hydrochloride of 1-(aminoacetyl)-5,5-diphenylimidazolidine-2,4-dione (8)

A suspension of **6** (3.14 g, 0.01 mol) in 2% aqueous HCl (25 ml) was refluxed until the solid had dissolved (*ca* 45 min). The hot mixture was filtered, then left to cool. The solid was filtered off and recrystallized from:

a. water: m.p. 257–259 °C, yield 2.66 g (75%).– R_F (A) 0.21.– $C_{17}H_{15}N_3O_3 \bullet HCl \bullet \frac{1}{2} H_2O$ (354.8) Calc. C 57.6 H 4.82 N 11.8 Found C 57.5 H 4.92 N 11.6.– ^{1}H-NMR ([D$_7$]DMF): 3.57 (br.s., H_2O), 4.68 (s, 2H, CH_2), 7.43–7.55 (m, 10H, aromatic), 9.25 (br.s., 3H, $^+NH_3$; D_2O exchange).– ^{13}C-NMR ([D$_7$]DMF): 44.94 (CH_2), 76.18 (Ph_2C), 128.72, 129.24, 129.50, 136.14, (aromatic C), 162.94 (CH_2CO), 166.45 (C_4=O), 173.71 (C_2=O).– MS: 309 (26, $M^{+\bullet}$), 60 (100).

b. acetic acid: m.p. 252–254 °C, yield 2.59 g (64%).– $C_{17}H_{15}N_3O_3 \bullet HCl \bullet CH_3COOH$ (405.8) Calc. C 56.2 H 4.98 N 10.4 Found C 56.2 H 5.18 N 10.2.– IR: 3432, 3068 ($^+NH_3$), 1790, 1750 (C=O, C_4=O), 1716 (C_2=O).– ^{1}H-NMR ([D$_6$]DMSO): 1.91 (s, 3H, CH_3 of AcOH), 4.42 (s, 2H, CH_2), 7.47 (s, 10H, aromatic), 8.33 (br.s., 3H, $^+NH_3$, D_2O exchange), 11.80 (br.s., 1H, NH, D_2O exchange).

Acidic hydrolysis of **8**

A suspension of **8** (0.354 g, 1 mmol) in 10 ml of 2% HCl was refluxed for 2h. The solid filtered off and recrystallized from ethanol (m.p. 298-300 °C) was identified as **10**. Yield 0.234 g (93%).

1-(N,N-bis-acetylaminoacetyl)-5,5-diphenylimidazolidine-2,4-dione (9)

a. A mixture of **7** (3.51 g, 0.01 mol) in 40 ml of acetic anhydride was refluxed for 4 h. The mixture was poured into water. When the acetic anhydride had decomposed, the water layer was separated and the oily residue was dissolved in $CHCl_3$. The chloroform extract was washed with water, then dried with Na_2SO_4. After evaporation the residue was recrystallized from ethanol giving 2.43 g (62%) of white solid, m.p. 212–214 °C. R_F (D) 0.59.– $C_{21}H_{19}N_3O_5$ (393.3) Calc. C 64.1 H 4.86 N 10.7 Found C 63.9 H 4.81 N 10.7.– IR: 3156 cm^{-1} (NH), 1786, 1744, 1716, 1680 (C=O).– ^{1}H-NMR ([D$_7$]DMF): 2.22 (s, 6H, CH_3), 5.26 (s, 2H, CH_2), 7.41–7.51 (m, 10H aromatic), 12.53 (br.s., 1H, NH).– ^{13}C-NMR ([D$_7$]DMF): 25.90 (CH_3), 50.39 (CH_2), 76.36 (Ph_2C), 128.72, 129.24, 136.27 (aromatic C), 154.81 (CH_3CO), 167.97 (CH_2CO), 173.33 (C_4=O), 173.83 (C_2=O).– MS: 393 (0.3, $M^{+\bullet}$), 351 (20, $M - OCH_2)^+$, 333 (10), 43 (100, $COCH_3)^+$.

b. Upon acetylation of **8** with acetic anhydride, **9** was obtained as described for *a*, 55% yield.

Crystallographic Measurements

KM-4 diffractometer with CuK_α radiation (λ = 1.54178 Å). The ω-2θ scan technique was applied for $2\theta < 164°$. Two reflections were used as standards and remeasured during data collection; no crystal decomposition was observed. With **7**, of 2053 reflections measured ($0 < h < 12$, $0 < k < 14$, $0 < l < 17$), 1630 were classified as observed i.o. $F > 4\sigma(F)$; with **8** the corresponding values were 4321 ($0 < h < 21$, $0 < k < 11$, $16 < l < 16$), and 3026 i.o. $F > 4\sigma(F)$. The cell dimensions were obtained and refined by the least-squares method on the basis of the diffractometric measurement for 25 reflections. The structures were solved by direct methods with SHELXTL PC [14] programs with R(E) used as a figure of merit (0.216 for 26 non-H atoms in **7** and 0.340 for 28 non-H atoms in **8**). These were refined on F's by the full-matrix least-squares method (SHELX-76) first isotropically. The position of all H atoms were found from $\Delta\varphi$ maps at the end of the anisotropic refinement; they were refined with fixed isotropic factors (1.5 of the respective factor for the parent atom). During the refinement 7 and 12.2 reflections/parameter were used for **7** and **8**, respectively. The R factors at the end of the refinement were: for **7**: R = 0.0535 and R_w = 0.0646 with $w = 1/[\sigma^2(F) + 0.000435F^2]$ and the extinction correction factor g = 0.00574, s = 2.81; and for **8**: R = 0.064, R_w = 0.0772, $w = 1/[\sigma^2(F) + 0.003912F^2]$, and g = 0.021, s = 1.61. The maximum changes $[(\Delta/\sigma)_{max}]$ in the parameter were 0.005 and 0.002 for **7** and **8**, respectively.

Crystal data for **7**: $C_{19}H_{17}N_3O_4$, mol. mass 351.36, orthorhombic, $P2_12_12_1$ space group; a = 9.940(2), b = 12.560(3), c = 14.110(3) Å; V = 1761.6(7) $Å^3$; d_x = 1.325 $g \cdot cm^{-3}$; Z = 4; F(000) = 736; T = 293 K; $\mu(CuK_\alpha)$ = 7.45 cm^{-1}. Final R = 0.0535 for 1630 reflections with $F > 4\sigma(F)$ (1835 unique data).

Crystal data for **8**: $C_{17}H_{16}N_3O_3^+ \bullet Cl^- \bullet CH_3COOH$, mol. mass 405.84, monoclinic, $P2_1/c$ space group; a = 17.349(3), b = 9.234(2), c = 13.403(3) Å; β = 110.33(3)°; V = 2013.5(8) $Å^3$; d_x = 1.339 $g \cdot cm^{-3}$; Z = 4; F(000) = 848; T = 293 K; $\mu(CuK_\alpha)$ = 1.99 mm^{-1}. Final R = 0.064 for 3026 reflections with $F > 4\sigma(F)$ (3672 unique data).

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