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SYNTHESIS AND REACTIONS OF 1,6-DIBENZOYL-5H,10H-DIIMIDAZO-[1,5-*a*;1',5'-*d*]-PYRAZINE-5,10-DIONE

Yu. E. Ivanov, A. A. Yavolovsky, A. V. Mazepa, and S. P. Krasnoshchekaya

*5,10-Dioxo-5H,10H-diimidazo[1,5-a;1',5'-d]pyrazine-5,10-dicarboxylic acid dichloride in Friedel–Crafts reaction conditions formed with benzene the corresponding 1,6-dibenzoyl derivative **2**, which reacted with alcohols and amines to give the keto esters and keto amides of 4(5)-benzoylimidazol-5(4)-carboxylic acids. The reaction of compound **2** with hydrazine gave substituted imidazo[4,5-f]pyridazine, and with o-phenylenediamine gave a derivative of imidazo[4,5-f]-1,4-benzodiazocine – a new heterocyclic system.*

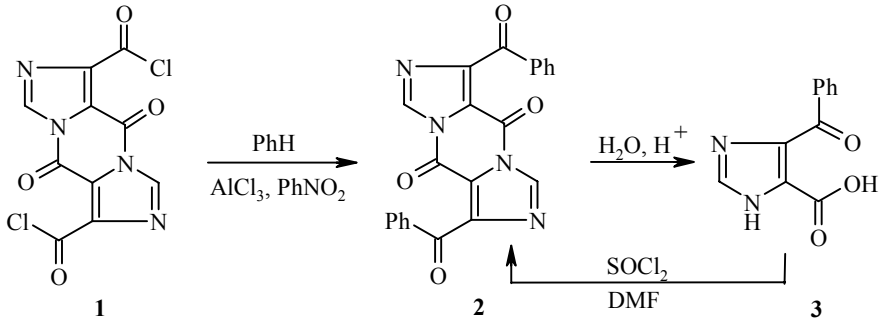
Keywords: imidazo[4,5-*f*]-1,4-benzodiazocine, imidazo[4,5-*d*]pyridazine, keto amides, keto esters, acylation.

5,10-Dioxo-5H-10H-diimidazo[1,5-*a*;1', 5'-*d*]pyrazinedicarbonyl-1,6-dichloride (**1**) has found a wide use in organic synthesis for the preparation of mono- and diesters, mono- and diamides, mixed esters and diamides of imidazole-4,5-dicarboxylic acids [1-4].

The possibility of using the acid dichloride **1** in the Friedel–Krafts acylation has not been studied previously.

Compound **1** interacted with benzene in $AlCl_3$–$PhNO_2$ to give diketone **2** and keto acid **3** after steam distillation of the organic solvent. In all likelihood compound **3** is formed by hydrolysis of diketone **2** under the isolation conditions.

Compound **3** is readily converted to compound **2** by boiling in $SOCl_2$–DMF.



A. V. Bogatsky Physico-Chemical Institute, National Academy of Sciences of Ukraine, Odessa 65080, Ukraine; e-mail: ivanov.u@raso.net. Translated from Khimiya Geterotsiklicheskikh Soedinenii, No.2, 281-286, February, 2003. Original article submitted December 20, 2000.

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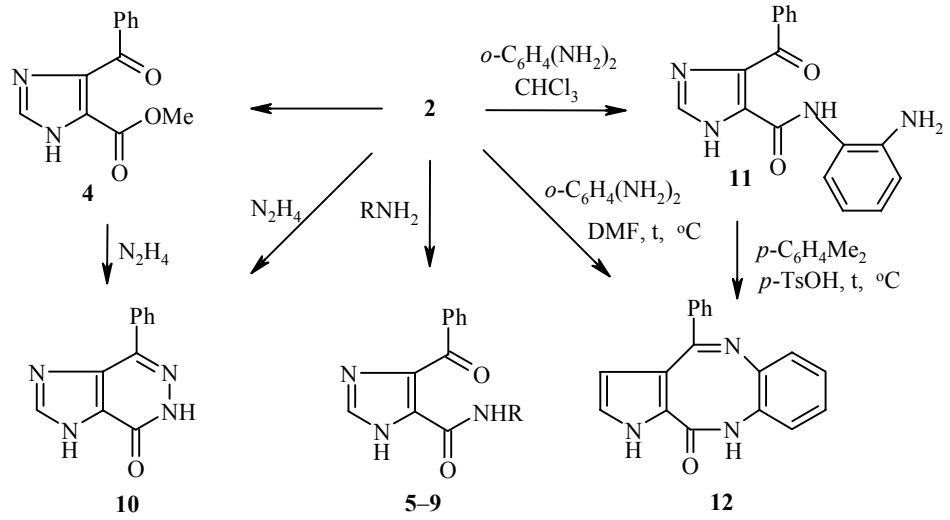
The increased susceptibility of compounds of type **2**, compared with trivial amides, to nucleophiles has been discussed previously [5, 6].

Like other compounds of this class compound **2** is smoothly split by sodium methoxide or methanol in the presence of Et_3N, ammonia, or amines to give the corresponding keto esters **4** and keto amides **5-9** and **11**. The previously undescribed imidazo[4,5-*d*]pyridazine **10** was obtained by treatment of compound **2** with hydrazine hydrate in methanol. The independent synthesis of compound **10** was carried out by the reaction of keto ester **4** with hydrazine hydrate in boiling methanol.

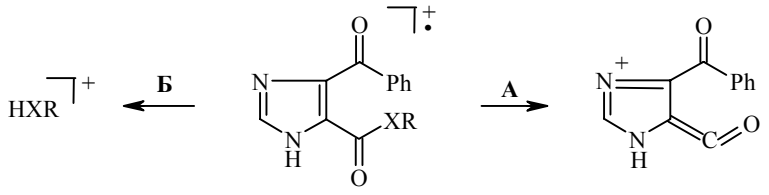


5 R = H, **6** R = Me, **7** R = Ph, **8** R = Bn, **9** R = 

Reaction of diketone **2** with *o*-phenylenediamine in chloroform gave keto amide **11**, which on heating in *p*-xylene in the presence of a catalytic amount of *p*-toluenesulfonic acid was converted into 11-phenyl-4,5-dihydro-1H-benzo[*b*]imidazo[4,5-*f*][1,4]diazocin-4-one **12**, which was also obtained by independent synthesis by boiling a mixture of compound **2** with *o*-phenylenediamine in anhydrous DMF. It should be noted that there is only one paper reporting the direct conversion of structure of type **2** into annelated cyclic systems [7].

As can be seen from Table 2, the mass spectra of compounds **4-12** contain intense molecular ion peaks. The primary fragmentation processes for compounds **4-6** begin with the loss of amide or ester groups, which leads to a series of even-electron fragment ions $[M-R]^+$, $[M-XR]^+$ (*m/z* 199), and $[M-COXR]^+$ (*m/z* = 171). Apart from the noted general directions of fragmentation, the mass spectrum of each compound has its own characteristics. Comparison of the mass spectra of ester **4** and amides **5** and **6** shows that the last two are more stable to the electron impact, which is characteristic of amides. Thus the molecular ion peak for compound **4** is 6.8% of the total ion current, whereas for compounds **5** and **6** this value is 16.2 and 15.4% respectively. In the mass spectrum of methylamide **6**, along with formation of the $[M-XR]^+$ ions, the elimination of the fragment $NH{=}CH_2$ was observed, leading to the formation of ions with *m/z* 200.

For compounds **8** and **9** two basic directions of fragmentation are observed:



X = NH, O

m/z 199

TABLE 1. Physicochemical Characteristics for Compounds **2-12**

Compound	Empirical dormula	Found, % / Calculated, %			mp, °C	IR spectrum, ν, cm^{-1}	Yield, % (method)
		C	H	N			
2	$C_{22}H_{12}N_4O_4$	66.67 / 66.80	3.05 / 3.12	14.14 / 14.19	>300	2950, 2870, 1720, 1615, 1570, 1450, 1380 (vaseline oil)	68 (A) 92 (B)
3	$C_{11}H_8N_2O_3$	61.11 / 60.70	3.73 / 3.59	12.96 / 13.3	205-206	3050, 2850, 1710, 1660, 1415, 1190, 1160, 1070, 920 (vaseline oil)	80
4	$C_{12}H_{10}N_2O_3$	62.61 / 62.70	4.38 / 4.31	12.17 / 12.07	200	2985, 2785, 1705, 1657, 1470, 1430, 1340, 1186, 1157, 1070, 900 (vaseline oil)	82
5	$C_{11}H_9N_3O_2$	61.39 / 61.27	4.22 / 4.16	19.52 / 19.60	>300	2985, 1665, 1625, 1600, 1565, 1465, 1450, 1410, 1360, 1335, 1300, 1125, 925 ($CHCl_3$)	87
6	$C_{12}H_{11}N_3O_2$	62.87 / 62.95	4.84 / 4.91	18.33 / 18.23	137-138	2990, 1660, 1630, 1605, 1565, 1470, 1455, 1415, 1360, 1340, 1300, 1130, 925 ($CHCl_3$)	78
7	$C_{17}H_{13}N_3O_2$	70.09 / 70.20	4.50 / 4.61	14.42 / 14.36	232	2990, 2980, 2910, 1660, 1625, 1590, 1560, 1480, 1345, 1325, 1300, 1110, 910 ($CHCl_3$)	72
8	$C_{18}H_{15}N_3O_2$	70.81 / 70.67	4.95 / 5.02	13.76 / 13.98	142-143	3050, 2980, 2910, 1640, 1565, 1480, 1360, 1350, 1310, 1300, 1140, 1110, 895 ($CHCl_3$)	74
9	$C_{16}H_{12}N_4O_2$	65.75 / 65.79	4.14 / 4.27	19.17 / 19.07	232-233	2950, 2880, 1780, 1640, 1440, 1365, 1270, 1125, 765 (vaseline oil)	43
10	$C_{11}H_8N_4O$	62.26 / 62.37	3.80 / 3.91	26.40 / 26.29	>300	3300, 3100, 2825, 2330, 1690, 1580, 1525, 1400, 1120, 1080, 800, 680 (vaseline oil)	94
11	$C_{17}H_{14}N_4O_2$	66.66 / 66.54	4.61 / 4.69	18.29 / 18.14	201-202	3010, 3000, 1650, 1600, 1560, 1480, 1350, 1320, 1300, 910 ($CHCl_3$)	62
12	$C_{17}H_{12}N_4O$	70.82 / 70.73	4.20 / 4.32	19.43 / 19.58	206-208	3050, 2985, 1625, 1590, 1560, 1490, 1465, 1400, 1300, 1275, 1165, 910, 900, ($CHCl_3$)	72 (A) 23 (B)

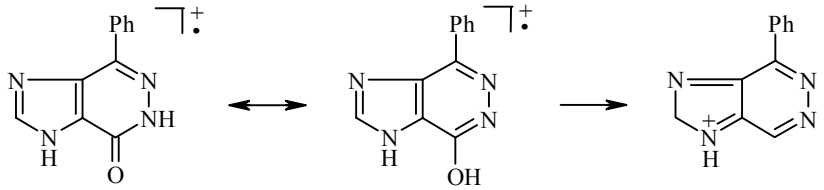
TABLE 1. Mass-spectral Characteristics of Compounds **4-12**

Compound	M^+	*m/z* (*I*, %)
4	230	230 (50), 216 (23), 199 (37), 171 (71), 153 (33), 144 (26), 121 (38), 105 (56), 77 (100)
5	215	215 (100), 199 (22),186 (38), 171 (47), 120 (30), 105 (31), 77 (54)
6	229	229 (100), 200 (93), 171 (30), 144 (30), 105 (33), 77 (48)
7	291	291 (50), 200 (29), 105 (6), 93 (100), 77 (10)
8	305	305 (35), 199 (24), 171 (7), 145 (19), 106 (100), 91 (22), 77 (29)
9	292	292 (7), 199 (15), 187 (100), 159 (6) 105 (17), 94 (38), 77 (22)
10	212	212 (100), 195 (6), 128 (13), 69 (8)
11	306	306 (32), 289 (31), 259 (100), 199 (12), 122 (20), 105 (76), 77 (65)
12	288	288 (53), 259 (100), 144 (10), 91 (7), 77 (13)

According to the scheme, both directions occur *via* breakage of the amide bond, but in direction **A** the charge is localized in the imidazole part of the molecule, giving rise to ions with *m/z* 199. Direction **B** is probably due to migration of the imidazole fragment hydrogen atom, as a result of which stable aromatic amide ions are formed, the peaks of which are maximal in the mass spectra of these compounds.

In the case of compound **7** directions **A** and **B** are accompanied by migration of hydrogen atom to the imidazole fragment, analogous to that observed with compound **6**, which leads to the formation of ions with *m/z* 200 and 106. The structure of the latter probably corresponds to that of the benzylimine ion, which explains its high stability.

Imidazo[4,5-*d*]pyridazine **10** is highly stable in the electron beam. The first decomposition process, which occurs to a negligible extent, is probably explained by lactam-lactim tautomerism and is assigned to formation of the $[M\text{-}OH]^+$ ions:



Fragmentation of compound **12** occurs *via* opening of the eight-membered ring and elimination of formyl radical.

Physicochemical characteristics of the compounds synthesised are given in Tables 1 and 2. The composition and purity of compounds **2-12** were confirmed by elemental analysis and TLC.

EXPERIMENTAL

Purity of substances was monitored by TLC on Silufol UV-254 strips. IR spectra were recorded on a Specord-80 instrument. Mass spectra were recorded with an MX 1321 apparatus with direct inlet of the sample into the ion source. Ionizing radiation was 70 eV, temperature of the ionizing chamber 220°C.

1,6-Dibenzoyl-5H,10H-diimidazo[1,5-*a*;1',5'-*d*]pyrazine-5,10-dione (2). A. Acid dichloride **1** (31.3 g, 0.1 mol) was added with stirring to solution of anhydrous aluminium chloride (37.4 g, 0.28 mol) in mixture of anhydrous benzene (150 ml) and nitrobenzene (150 ml), and the mixture was boiled while stirring for 3 h.

Nitrobenzene and benzene were steam distilled off. The residue was filtered off to give diketone **2** (26.9 g). Keto acid **3** (7.3 g) was isolated from the aqueous solution by evaporation.

B. Keto acid **3** (21.6 g, 0.1 mol) was boiled in mixture of anhydrous chloroform (150 ml) and thionyl chloride (60 ml) with a catalytic amount of DMF for 4 h. The residue was separated, washed with chloroform, and dried in a vacuum desiccator: yield of diketone **2** 18.2 g, (2%).

4(5)-Benzoylimidazole-5(4)-carboxylic Acid (3). Diketone **2** (19.8 g, 0.05 mol) was boiled in 10% sodium hydroxide solution (100 ml) until solution was complete. The solution was treated with activated charcoal, filtered, and acidified to pH 6. The precipitate was filtered off to give keto acid **3** (17.3 g, 80%).

4(5)-Benzoyl-5(4)methoxycarbonylimidazole (4). Diketone **2** (3.96 g, 0.01 mol) was boiled in anhydrous methanol (100 ml) in the presence of a catalytic amount of triethylamine for 40 min. The solution was evaporated in vacuum and the residue was recrystallized from DMF–water mixture to give compound **4** (3.77 g, 82%).

4(5)-Benzoyl-5(4)-aminocarbonylimidazole (5). Suspension of diketone **2** (3.96 g, 0.01 mol) in anhydrous methanol (100 ml) saturated with ammonia was kept at room temperature for 48 h. The solvent was distilled off and the residue was recrystallized from ethanol to give compound **5** (3.74 g, 87%).

4(5)-Benzoyl-5(4)-methylaminocarbonylimidazole (6) was made analogously to give keto amide **6** (3.57 g, 78%).

4(5)-Benzoyl-5(4)-phenylaminocarbonylimidazole (7). Diketone **2** (3.96 g, 0.01 mol) and aniline (1.86 g, 0.02 mol) were boiled for 40 min in anhydrous chloroform (100 ml) in the presence of a catalytic amount of triethylamine. The solution was evaporated to dryness on a rotary evaporator. The residue was recrystallized from ethanol to give keto amide **7** (4.2 g, 72%).

Compounds 8, 9, and 11 were obtained analogously in yields of 4.51 g (74%), 2.5 g (43%), and 3.8 g (62%) respectively.

7-Phenyl-4,5-dihydroimidazo[4,5-*d*]pyridazin-4-one (10). Hydrazine hydrate (2 ml, 80%) in methanol (10 ml) was added to boiling solution of keto ester **4** (2.3 g, 0.01 mol) in methanol (50 ml). The solution was boiled for 30 min. The precipitate which appeared on cooling was filtered off to give compound **10** (1.99 g, 94%).

11-Phenyl-4,5-dihydro-1H-benz[*b*]imidazo[4,5-*f*][1,4]diazocin-4-one (12). A. Solution of keto amide **11** (3.06 g, 0.01 mol) in *p*-xylene (100 ml) was boiled in the presence of a catalytic amount of *p*-toluenesulfonic acid for 36 h. Xylene was evaporated in vacuum. The residue was extracted with boiling hexane to give compound **12** (4.2 g, 72%).

B. Mixture of diketone **2** (3.96 g, 0.01 mol) and *o*-phenylenediamine (2.16 g, 0.02 mol) was boiled for 12 h in anhydrous DMF (50 ml). The solution was poured into water (200 ml), and the precipitate was filtered off. Purification was carried out by reprecipitation with hexane from acetone solution to give compound **12** (1.32 g, 23%).

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