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Substituted Butanolides and Butenolides: XVI.* Oxidative and Hydrolytic Transformations of Butanolide Fused to Dihydropyrazole Ring

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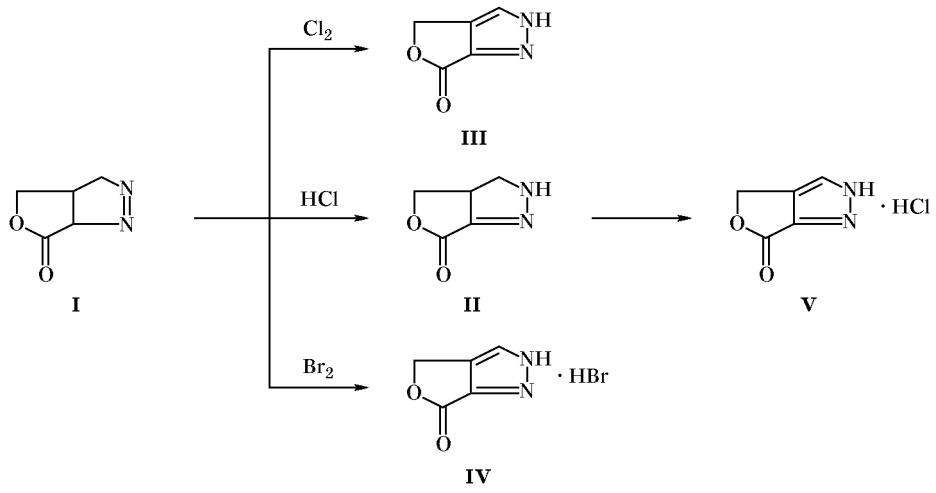
Abstract—Reactions of 3a,4,6,6a-tetrahydro-3*H*-furo[3,4-*c*]pyrazol-6-one with chlorine and bromine give the corresponding 2,6-dihydro-4*H*-furo[3,4-*c*]pyrazol-6-one hydrohalides. Hydrolysis of 3a,4,6,6a-tetrahydro-3*H*-furo[3,4-*c*]pyrazol-6-one is accompanied by oxidation of the dihydropyrazole ring to pyrazole and opening of the lactone ring.

We previously described the synthesis of 3a,4,6,6a-tetrahydro-3*H*-furo[3,4-*c*]pyrazol-6-one (**I**) and its isomerization to 2,3a,4,6-tetrahydro-3*H*-furo[3,4-*c*]-pyrazol-6-one (**II**) in the presence of acids and bases [2]. It was convenient to monitor the isomerization process by UV spectroscopy. Compound **I** shows in the electron spectrum an absorption maximum at λ 320 nm due to n,π^* transition in the azo group, which is typical of 4,5-dihydro-3*H*-pyrazoles. The absorption maximum of compound **II** is located at λ 276 nm, which is typical of compounds containing a CH=N bond conjugated with ester moiety.

We have effected oxidation of 3a,4,6,6a-tetrahydro-3*H*-furo[3,4-*c*]pyrazol-6-one (**I**) with chlorine in chloroform to obtain 2,6-dihydro-4*H*-furo[3,4-*c*]pyrazol-6-one (**III**). The reaction of **I** with bromine gave hydrobromide **IV** (Scheme 1). The transformation of dihydropyrazole ring into pyrazole was also observed when dry hydrogen chloride was passed through a boiling solution of compound **I** in alcohol. The product was isolated as hydrochloride **V**. The oxidation with chlorine and bromine is fast; nevertheless, in the reaction with hydrogen chloride we succeeded in detecting intermediate dihydropyrazole derivative **II**

Scheme 1.



I II III IV V

* For communication XV, see [1].

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Table 1. Yields, melting points, and elemental analyses of compounds **III**–**VI**

Comp. no.	Yield, %	mp, °C	Found, %				Formula	Calculated, %				R_f
			C	H	N	Hlg		C	H	N	Hlg	
III	78	190	47.92	3.40	22.38	–	$C_5H_4N_2O_2$	48.39	3.23	22.58	–	0.18
IV	83	185[a]	29.61	2.40	13.25	39.00	$C_5H_5BrN_2O_2$	29.27	2.44	13.66	39.02	–
V	71	142	37.59	3.18	17.32	21.86	$C_5H_5ClN_2O_2$	37.38	3.12	17.46	22.12	–
VI	48	225	42.58	4.51	19.42	–	$C_5H_6N_2O_3$	42.25	4.26	19.72	–	0.57

[a] With decomposition.

Table 2. UV and IR spectra of compounds **III**–**VI**

Comp. no.	UV spectrum (H_2O), λ_{max}, nm ($\log\varepsilon$)	IR spectrum, ν, cm^{-1}				
		C=O	N–H	C=N	CH_{arom}	–NH–
III	223 (4.07)	1710	3135, 3240	1625	3040, 945, 790	–
IV	223 (3.49)	1795	3440	1620	3035, 3005, 935, 840	2460, 2780
V	225 (3.38)	1800	3370	1630	3040, 3015, 940, 845	2450, 2720
VI	216 (3.21)	1710	3155	1660	3030, 960, 800	–

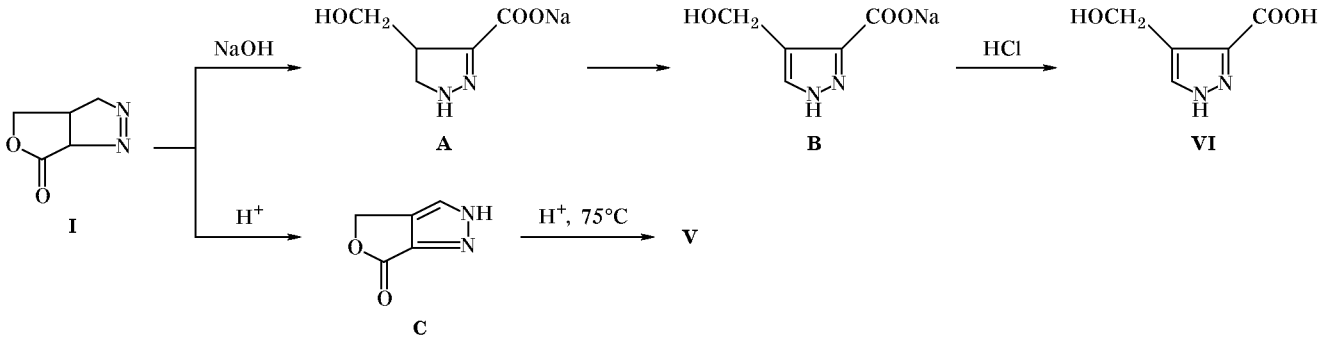
by spectrophotometry. Presumably, the oxidation with halogens includes the same transformation sequence. Oxidation of dihydropyrazoles has been extensively studied [3]. Most frequently, the main oxidation products are pyrazoles which are thermodynamically stable systems.

The assumed structures of compounds **III**–**V** are confirmed by the data of elemental analysis (Table 1) and UV and IR spectroscopy (Table 2). Their UV spectra contain an absorption maximum at λ 223 nm. According to [4], the *K* band of unsubstituted pyrazole is located at λ 211 nm. The red shift of the absorption maximum of compounds **III**–**V** results from conjugation with the lactone carbonyl group. The latter acts as auxochrome, leading to characteristic spectral changes. The absorption maxima in the UV spectra of salts **IV** and **V** also appear at λ 223 nm, presumably due to their complete hydrolysis in aqueous medium.

Compound **III** shows in the IR spectrum absorption bands belonging to the pyrazole ring: broadened bands in the region 3200–3400 cm^{-1} correspond to stretching vibrations of associated N–H bonds, a band at 3135 cm^{-1} arises from the dimer, and C–H bond gives rise to strong bands at 3040 cm^{-1} and 945–930 cm^{-1} (δ_{CH}). Stretching vibrations of the C=N bond appear at 1625–1630 cm^{-1}. The positions of the carbonyl absorption bands in the spectra of pyrazole **III** and its salts **IV** and **V** are considerably different. The C=O band of **III** suffers a strong low-frequency shift (1710 cm^{-1}) relative to the corresponding band of **I** (1780 cm^{-1}), which may be due to conjugation of the lactone carbonyl group with heteroaromatic pyrazole ring: The planar –C–C(O)–O–C– moiety in the butanolide ring [5] is coplanar to the pyrazole ring plane, giving rise to a relatively long conjugation chain. The pyrazole ring in salts **IV** and **V** has a positive charge; as a result, conjugation with the lactone carbonyl group weakens, and stretching vibration band of the latter is observed at 1795 and 1800 cm^{-1}, respectively. In addition, the IR spectra of salts **IV** and **V** contain a set of strong broadened bands in the region 2450–2780 cm^{-1}, which arise from vibrations of the $-\overset{+}{H}N-$ fragment [6].

To estimate the stability of dihydropyrazole ring fused to butanolide ring, compound **I** was subjected to hydrolysis in acid and alkaline medium (Scheme 2). The transformation of the dihydropyrazole ring was monitored by spectrophotometry, and accumulation of acids was monitored by acid–base titration. The hydrolysis of 3a,4,6,6a-tetrahydro-3*H*-furo[3,4-*c*]pyrazol-6-one (**I**) with hydrochloric acid at 25°C gives rise to equilibrium between the lactone and the corre-

Scheme 2.



sponding hydroxy acid; the equilibrium takes 14 days to establish, and the lactone conversion is 22%. At 70°C, no opening of the lactone ring occurs. According to the spectrophotometric data, the dihydropyrazole ring is completely converted into pyrazole in 1 h. Evaporation of the hydrolyzate gave hydrochloride **V** which was identical to a sample obtained in ethanol. Under milder conditions (25°C), the transformation of the dihydropyrazole ring in **I** occurs at a lower rate. The isomerization of 4,5-dihydro-3*H*-pyrazole into 4,5-dihydro-1*H*-pyrazole was complete in 24 h, and its oxidation to pyrazole required more than 14 days. Thus the transformation of the dihydropyrazole ring of compound **I** in aqueous medium at 25°C is accompanied by opening of the lactone ring. Evaporation of the reaction mixture obtained by acid hydrolysis of **I** at 25°C gave a mixture of products which we failed to separate. Presumably, it contained bicyclic compounds having a butanolide ring fused to 4,5-dihydro-1*H*-pyrazole or pyrazole ring and hydroxy acids having dihydropyrazole and pyrazole rings.

Alkaline hydrolysis of compound **I** is also accompanied by isomerization of 4,5-dihydro-3*H*-pyrazole ring into 4,5-dihydro-1*H*-pyrazole and subsequent transformation into pyrazole, as it occurred in the acid hydrolysis. By acidification of the alkaline hydrolyzate we succeeded in isolating 4-hydroxymethylpyrazole-3-carboxylic acid (**VI**). In this case, opening of the butanolide ring precedes the transformation of dihydropyrazole into pyrazole: Even after 10 min, the titration data indicated complete opening of the butanolide ring, whereas the transformation of the dihydropyrazole ring into pyrazole required 3 h under the same conditions.

The IR spectrum of acid **VI** (mineral oil) contains a strong absorption band at 1710 cm^{-1} belonging to stretching vibrations of the acid carbonyl group, and stretching vibrations of the acid OH group appeared as a set of bands in the region 2400–2700 cm^{-1}. It was difficult to identify absorption of the hydroxymethyl group because of overlap of OH and NH absorptions above 3000 cm^{-1}; however, a broad band at 3155 cm^{-1} is likely to belong to stretching vibrations of the associated NH group in the pyrazole ring, and a strong broad band at 3280 cm^{-1} may be attributed to vibrations of the alcoholic hydroxy group involved in hydrogen bond. The pyrazole ring in **VI** gives rise to characteristic absorption bands at 3030, 960, and 800 cm^{-1} (C–H), 1660 cm^{-1} (C=N), and 1580 cm^{-1} (δNH).

The presence of hydroxy and carboxy groups in molecule **VI** was confirmed by appropriate test reactions (decoloration of bromine and potassium permanganate in water and acid reaction of aqueous solution). The molecular weight of compound **VI** determined from the neutralization equivalent was 138 (calculated *M* 142).

EXPERIMENTAL

The IR spectra were recorded on a UR-20 instrument. The UV spectra were measured on a Specord UV-Vis spectrophotometer in ethanol and water. TLC analysis was performed on Silufol plates using 20:1 dioxane–water as eluent; spots were visualized by treatment with iodine vapor, Bromophenol Blue, and potassium permanganate.

2,6-Dihydro-4*H*-furo[3,4-*c*]pyrazol-6-one (III). Dry chlorine, 0.49 l (0.022 mol), was passed over a period of 30 min through a solution of 1.26 g (0.01 mol) of compound **I** in chloroform. The solvent was immediately distilled off on a water bath, and the residue (0.97 g) was recrystallized from benzene.

2,6-Dihydro-4*H*-furo[3,4-*c*]pyrazol-6-one hydrobromide (IV). A solution of 1.60 g (0.01 mol) of bromine in chloroform was added dropwise with stirring to a solution of 1.26 g (0.01 mol) of compound **I** in 100 ml of chloroform. The precipitate was filtered off and washed with cold chloroform. Yield 1.7 g.

2,6-Dihydro-4*H*-furo[3,4-*c*]pyrazol-6-one hydrochloride (V). Concentrated hydrochloric acid, 1 ml, was added to a solution of 1.26 g (0.01 mol) of compound **I** in 50 ml of ethanol, and the mixture was refluxed for 10 min on a water bath. The solution was evaporated under reduced pressure, the residue was ground with an equal volume of diethyl ether, and the precipitate was filtered off. Yield 1.14 g, mp 142°C.

4-Hydroxymethylpyrazole-3-carboxylic acid (VI). A solution of 1.26 g (0.01 mol) of compound **I** in 20 ml of 20% aqueous NaOH (0.1 mol) was heated for 3 h at the boiling point. The mixture was cooled, acidified with dilute (1:1) hydrochloric acid to pH 1, and saturated with sodium chloride. After 24 h, the precipitate was filtered off and recrystallized from aqueous ethanol. Yield 0.68 g.

REFERENCES

1. Strizhov, N.K., Poskonin, V.V., Badovskaya, L.A., and Kupina, E.P., *Russ. J. Org. Chem.*, 2002, vol. 38, no. 2, pp. 251–255.
2. Pavlenko, Z.I., Badovskaya, L.A., and Kul'nevich, V.G., *Khim. Geterotsikl. Soedin.*, 1977, no. 12, pp. 1610–1612.
3. Jacobs, T., *Heterocyclic Compounds*, Elderfield, R.C., Ed., New York: Wiley, 1957, vol. 5. Translated under the title *Geterotsiklicheskie soedineniya*, Moscow: Inostrannaya Literatura, 1961, vol. 5, pp. 42–134; Kost, A.N. and Grandberg, I.I., *Advances in Heterocyclic Chemistry*, Katritzky, A.R., Ed., New York: Academic, 1966, vol. 6, pp. 347–430; Auwers, K. and Konio, F., *Justus Liebigs Ann. Chem.*, 1932, vol. 496, pp. 27–51; Vinogradova, N.B. and Khromov-Borisov, N.V., *Khim. Geterotsikl. Soedin.*, 1968, no. 4, pp. 685–694; Bapat, J.B., Black, D.S.S., and Clack, R.W., *Aust. J. Chem.*, 1972, vol. 25, no. 6, pp. 1321–1323; Molchanov, A.P., Stepakov, A.V., and Kostikov, R.R., *Russ. J. Org. Chem.*, 2001, vol. 37, no. 1, pp. 128–135.
4. *Physical Methods in Heterocyclic Chemistry*, Katritzky, A.R., Ed., New York: Academic, 1963. Translated under the title *Fizicheskie metody v khimii geterotsiklicheskikh soedinenii*, Moscow: Khimiya, 1966, pp. 319–397.
5. Hussain, S.A.M., Tayyeb, O.W.D., Smith, G., and Stoddart, J.E., *J. Chem. Soc., Perkin Trans. 1*, 1975, no. 15, pp. 1480–1492.
6. Vinokurov, V.G., Troitskaya, V.S., Solokhina, N.D., and Grandberg, I.I., *Zh. Obshch. Khim.*, 1963, vol. 33, pp. 506–511.