

PHENOL COMPOUNDS FROM ISOXAZOLES, CONSIDERED AS MASKED β -POLYKETONES

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The synthesis of methylenediisoxazole systems differently substituted in positions 3 and 3' (I) in the heterocyclic rings has been recently studied¹ in order to investigate the behaviour of imino derivatives, obtained by hydrogenation, depending on the operating conditions adopted.

As a matter of fact, compound (II), being a derivative of a tetra β -polyketone, may give different cyclic products in addition to the corresponding linear polyketone².

The results obtained in the presence of HCl are reported here. Early attempts done both directly with aqueous HCl at room temperature or through prior preparation, in an anhydrous medium, of hydrochlorides of (II), have given the corresponding resorcinols (V) in good yields.

The analytical data of compounds (V) are summarized in Table I.

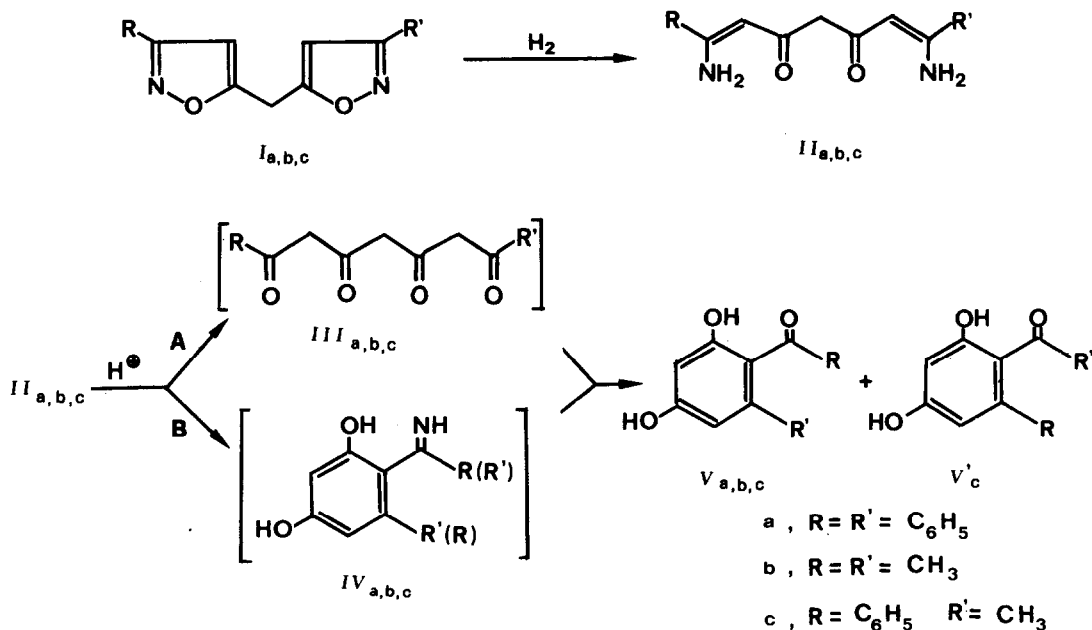


Table 1

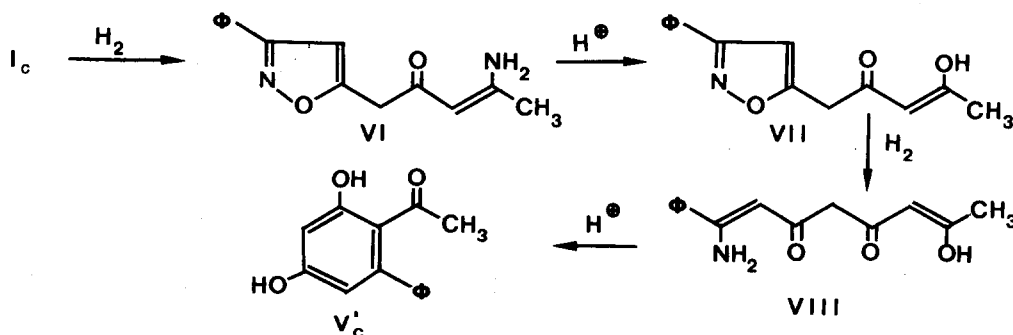
	m. p. °C	MS m/e	NMR (CDCl ₃) δ ppm Jab = 2 Hz				Yield
			R	R'	Ha	Hb	
V _a	148	290 (M ⁺); 289; 213; 105	6.9-7.4 (10 H) m		6.50 d	6.43 d	55%
V _b ³	158	166 (M ⁺); 151; 93	2.54 (3 H) s	2.60 (3 H) s	6.03 d	6.02 d	80%
V _c ³	140	228 (M ⁺); 227; 210; 151; 105	1.87 (3 H) s	7.3-7.7 (5 H) m	6.34 d	6.22 d	60%
V' _c	139	228 (M ⁺); 227; 213; 167; 139; 43	7.3-7.5 (5 H) m	1.77 (3 H) s	6.38 d	6.30 d	

In the case of II_c, the ratio between the obtained resorcinols V_c/V'_c is 8:2.

Resorcinols V may be a priori formed through: a) hydrolysis of (II) and subsequent cyclization (via tetraketone III); b) cyclization of (II) and subsequent hydrolysis.

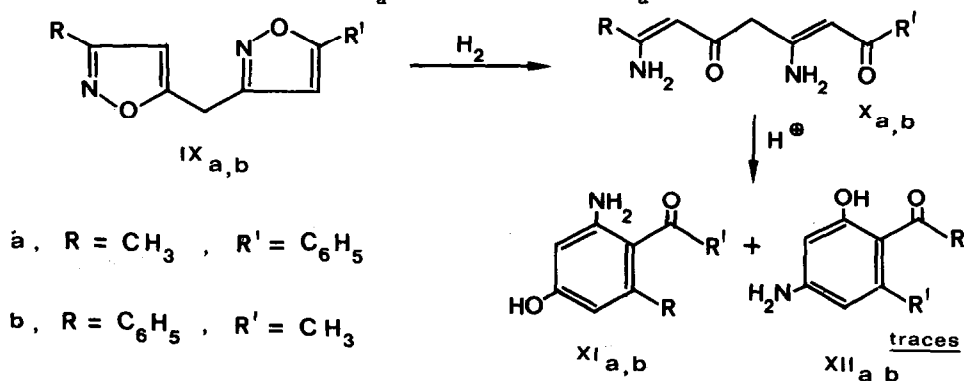
In order to obtain more detailed information on the reaction course, we thought it convenient to prepare from (I_c) a monoimino triketone that by cyclization might give resorcinols (V_c) and (V'_c) in ratio either equaling or differing from those obtained from (II_c). If cyclization of the system involves direct removal of NH₃, in the case of an imino ketone with structure (VIII), one should observe a sharp increase in the formation of (V'_c), which is unfavoured in the case of (II_c); at the same time, formation of polyketonic systems as intermediates should be excluded.

By subjecting I_c (R = C₆H₅, R' = CH₃) to controlled hydrogenation, a selective opening of the ring with a methyl group in position 3 takes place; in this way the imino isoxazolketone (VI) has been obtained, which by acid treatment, gives diketone (VII) in quantitative yields.⁴



After repeated hydrogenation, (VII) gives the imino triketone (VIII). By precipitation and water dissolution of (VIII) hydrochloride, resorcinol (V'_c) is exclusively obtained. Formation of (V'_c) clearly indicates that the reaction follows route B, where cyclization is the first reaction step and ring closing involves the carbon linked to nitrogen.

Since, under the reaction conditions adopted, cyclization is the determining step, conveniently joined isoxazoles might give aromatic compounds with different functions. In this way, isoxazole (IX_a), hydrogenated in the presence of Ni-Raney, gives (X_a); its water-dissolved hydrochloride gives the expected aminophenol (XI_a), with traces of (XII_a).



The ratio (XI_a)/(XII_a), determined by GLC, resulted as being 96 : 4.

The evidence therefore indicates that systems like (X_a) can undergo cyclization eliminating NH_3 instead of H_2O . Similarly, the isomeric compound (X_b), upon identical conditions afforded the aminophenols (XI_b) close to traces of (XII_b).⁵ Spectroscopical data of the aminophenols obtained are reported in Table 2.

Table 2

	m. p. °C	MS m/e	NMR (CD_3COCD_3) δ ppm				Yield
			R	R'	H _a	H _b	
XIIa	118	227 (M^+); 226; 212; 166; 43	1.62 (3H) s	7.5-7.6 (5 H) m	5.98 d	5.88 d	90%
XIa	162	227 (M^+); 226; 209; 150; 105	1.84 (3 H) s	7.4-7.8 (5 H) m	6.20 d	6.07 d	
XIb	192	227 (M^+); 226; 212; 71; 43	7.3-7.4 (5 H) m	1.61 (3 H) s	6.27 d	6.13 d	n. d.
XIIb	125	227 (M^+); 226; 150; 105; 94	7.4-7.7 (5 H) m	1.81 (3 H) s	6.16 d	6.09 d	

The obtainment of aromatic compounds from isoxazole systems under the investigated conditions, offers the advantage - over the corresponding β -polyketones⁸- of enabling the orientation of cyclizations independently of the nature of the substituents, being cyclizations determined by the preferential removal of NH_3 in respect of H_2O .

Cyclizations are being investigated by varying the reaction medium in order to obtain further informations on the cyclization mechanism.

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References and Footnotes

- (¹) S. Auricchio, A. Ricca, *Gazz. Chim. Ital.* **103**, 37, (1973).
- (²) G. Casnati, A. Ricca, *Tetrahedron Letters*, 327-330 (1967).
- (³) K. Hoesch, *Chem. Ber.*, **48**, 1122 (1915).
- (⁴) Compound VII : MS m/e: 243 (M^+); 201; 159; 144; 130; 104. NMR δ ppm CDCl_3 : 2.07 (3H, s, CH_3); 3.82 (2H, s, $-\text{CH}_2-$); 5.60 (1 H, s, $-\text{CH}-$); 6.53 (1 H, s, H isoxazole ring); 7.3-7.9 (5 H, m, aromatic hydrogens). M. P. : 125 °C.
- (⁵) Compounds (XIb) and (XIIb) give two peaks by GLC. We could not have the exact ratio between (XIb) and (XIIb), by GLC, owing to the partial overlapping of the two peaks; clearly (XIb) is by far the most abundant.
- (⁶) For different approaches to the cyclization reactions see :
T. Money, *Chem. Rev.*, **70**, 553, (1970).