Tetrahedron Letters No. 49, pp 4959 - 4960, 1972. Pergamon Press. Printed in Great Britain.

MONONUCLEAR HETEROCYCLIC REARRANGEMENTS - V.

1,2,4-OXADIAZOLES ⟶ IMIDAZOLES

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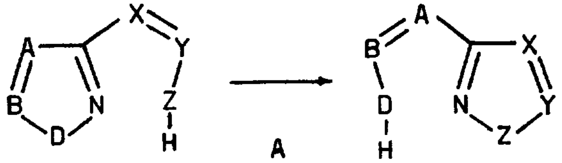
(Received in UK 26 October 1972; accepted for publication 1 November 1972)

According to schema (A), proposed by Katritzky and coworkers[1] to generalize mononuclear heterocyclic rearrangements, a large range of transformations is available for different ABD and XYZ combinations. Nevertheless, all the examples in the literature[1,2,3] are related to systems where D is always an oxygen atom and Z is always either an oxygen or a nitrogen atom.

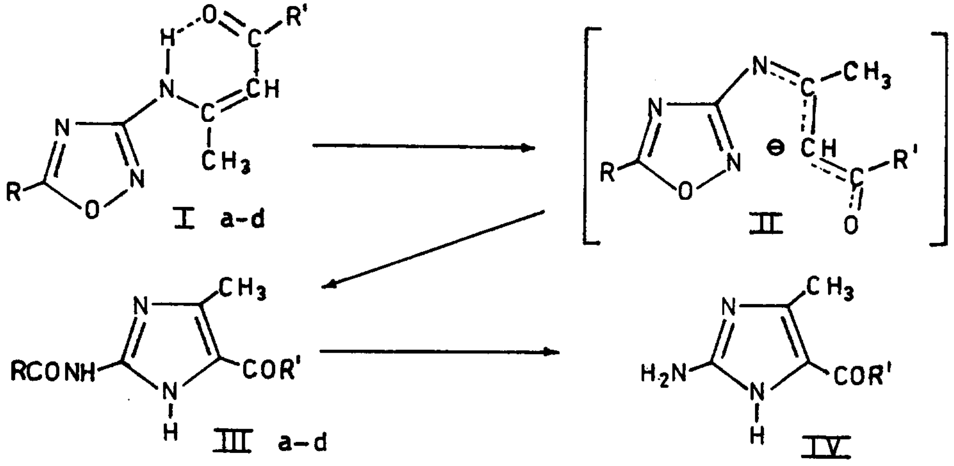


Thus, in connection with previous research in the field[3], we have now investigated, within this type of reactions, the reaction behaviour of 1,2,4--oxadiazole enaminoketones Ia-d[4]. In fact, the NCC sequence[5] (with terminal C potentially nucleophile) for these compounds, which are obtained by condensation between 3-amino-5-phenyl(methyl)-1,2,4-oxadiazoles and acetylacetone or benzoylacetone[6], may show a reactivity analogous to that observed for sequences XYO and XYN, the only ones investigated so far.

Isomerization tests, carried out by heating (3 hrs. at 110°C) Ia-d with equimolar amounts of sodium ethoxide in N,N-dimethylformamide[7], have allowed to ascertain the validity of this hypothesis. In fact, imidazole derivatives IIIa-d[4] have been obtained with yield 60-80%. Their structures have been confirmed by acid hydrolysis which yielded benzoic or acetic acid and 2-aminoimidazoles IVa-b[8].

The particular interest in the transformation of 1,2,4-oxadiazole enaminoketones Ia-d into imidazole derivatives IIIa-d depends on the fact that the latter represents the first example of mononuclear heterocyclic rearrangement (see schema A) where the new heterocycle closure occurs through the formation of C-N bond. The observed reaction is undoubtedly a simple and elegant way to synthesize certain imidazole derivatives.

Work in progress aims at elucidating the intrinsic mechanism of this rearrangement and at checking a possible generalization of the transformation realized, i.e. with Z = C, by changing the combination of both the starting heterocycle (ABD) and the side chain (XYC).



In I and III

a: $R=C_6H_5$; $R'=CH_3$; b: $R=CH_3$; $R'=CH_3$

c: $R=C_6H_5$; $R'=C_6H_5$; d: $R=CH_3$; $R'=C_6H_5$

In IV

a: $R'=CH_3$

b: $R'=C_6H_5$

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2. Ref. 1 and references therein; K. Korbonits, Ger.Offen., 2.038.919 (1969); C.A., 74, 112039d (1971).
3. M. Ruccia and D. Spinelli, Gazz.Chim.Ital., 89, 1654 (1959); M. Ruccia and N. Vivona, Ann.Chim.(Italy), 57, 680 (1967); M. Ruccia and N. Vivona, Chem.Comm., 866 (1970); M. Ruccia, N. Vivona, and G. Cusmano, J.Heterocyclic Chem., 8, 137 (1971).
4. All the new compounds i.e., Ia (m.p. 112°C, ethanol), Ib (50°, petroleum ether), Ic (154°, ethanol), Id (125°, ethanol), IIIa (221°, ethanol/water 1:1), IIIb (233°, ethanol), IIIc (173°, ethanol/water 1:1), IIId (170°, benzene) gave satisfactory analitical and nmr data.
5. Such a sequence in the side chain has been assumed by A.R. Katritzky (ref. 1).
6. Equimolar amounts are heated (8-10 hrs.) in anhydrous toluene, removing azeotropically the reaction water and using p-toluensulphonic acid as catalyzer.
7. Under different experimental conditions, a side reaction occurs when Ia-b are involved. Such reaction is now under study.
8. V. Grinsteins and A. Veneris, Latvijas PSR Zinatnu Akad.Vestis, Kim.Ser., N°. 3, 463 (1962); C.A. 59, 12784a (1963).