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NON-CONVENTIONAL SYNTHESES OF HETEROCYCLIC COMPOUNDS: A NEW SYNTHESIS OF 1,3,4-BENZOTRIAZEPINE DERIVATIVES[1]

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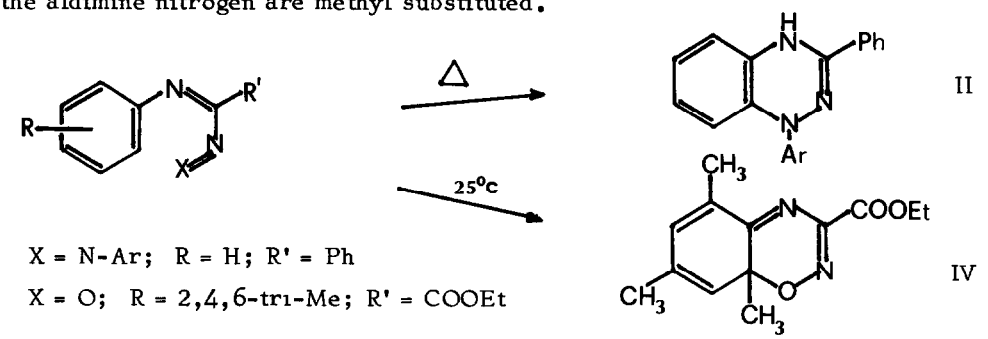
Abstract: 4,5-Dihydro-1,3,4-benzotriazepines were obtained in good yields by intramolecular thermal cyclization of arylazoanils with methyl or ethyl groups in the ortho positions of the aromatic ring on the imine nitrogen.

Some N-aryl-C-arylazoaldimines I are known to form dihydro-1,2,4-benzotriazines II upon treatment with acid or heat,[2] while compound III, with similar unsaturation, has been shown to give the 6-membered heterocycle IV, even though both ortho positions of the phenyl group on the aldimine nitrogen are methyl substituted.[3]

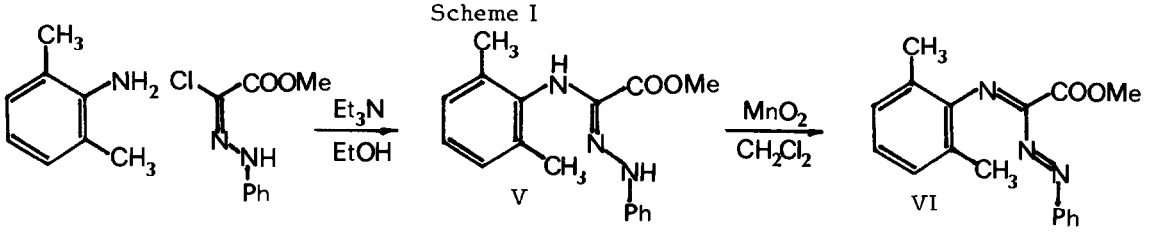


I X = N-Ar; R = H; R' = Ph

III X = O; R = 2,4,6-tri-Me; R' = COOEt

This note describes the preliminary results of a study of the behaviour upon treatment with heat of some compounds I with methyl or ethyl groups in the ortho positions of the aromatic ring on the imine nitrogen. The arylazo starting materials were prepared as in scheme I, which reports the first case we have considered.

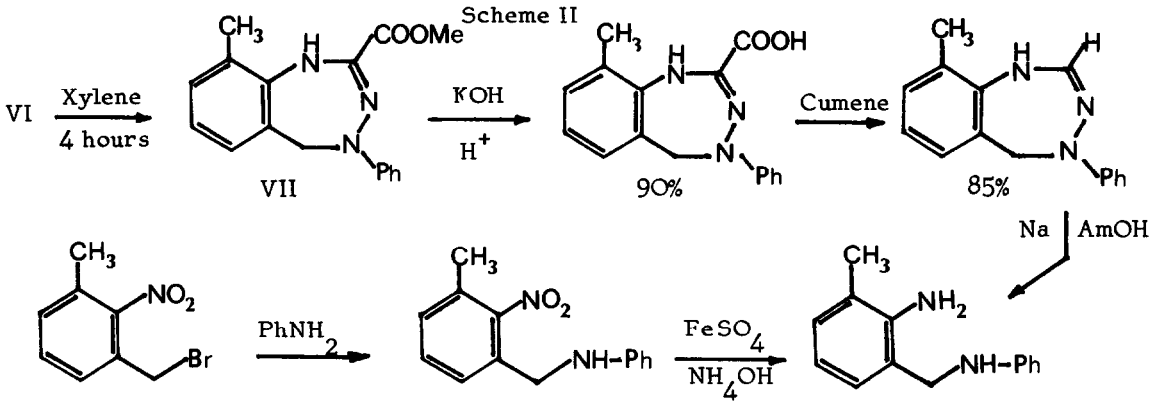
Scheme I



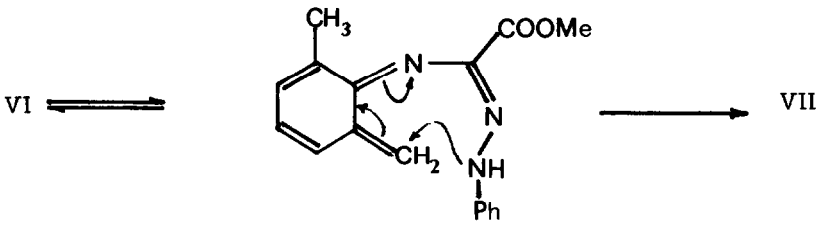
After 2 hours in refluxing EtOH, methyl chloro(phenylhydrazono)acetate (1 m), 2,6-xylidine (1 m) and Et_3N (1 m) gave a 75% yield of methyl [(2,6-dimethylphenyl)-amino] (phenylhydrazono)acetate (V), m.p. 85-86°C (EtOH). This compound was dissolved in CH_2Cl_2, treated with 2 parts by weight of active MnO_2 and stirred for 30 minutes at room temperature to give a 90% yield of methyl [(2,6-dimethylphenyl)-imino]phenylazoacetate VI, m.p. 72-73°C

(MeOH). In refluxing xylene, VI gradually turned from red to yellow, with the reaction complete after approximately 4 hours. Removal of the solvent and crystallization from n-hexane gave an 82% yield of a new yellow compound, m.p. 110°C, shown by analysis to be isomeric with VI. ^{1}H NMR($CDCl_3$, TMS, δ): 2.30 (3H,s,CH_3); 3.99 (3H,s,$COOCH_3$); 4.75 (2H,s, CH_2); from 6.70 to 7.70 (9H,m,aromatic and NH). On the basis of these data plus the reactions reported below in scheme II, the product was assigned the structure of 2-carbomethoxy-4,5-dihydro-4-phenyl-9-methyl-1H-1,3,4-benzotriazepine VII.

Scheme II



Thermal cyclization to form benzotriazepines was repeated with other arylazoaldimines, with quite good results. These experiments showed that cyclization is accelerated by the presence of both electron donating groups (methyl, ethyl) on the phenyl ring bonded to the imine nitrogen and electron withdrawing groups (like NO_2) on the phenyl ring bonded to the azo group. These observations are consistent with the mechanistic hypothesis reported below:



This mechanism involves an equilibrium which might be considered as an internal oxidation-reduction reaction.

Experiments are currently under way to determine the scope of this new reaction and to explain the surprising reactivity of aromatic methyl groups in these substrates.

REFERENCES AND NOTES

1) Presented at the VIIth Symposium on Chemistry of Heterocyclic Compounds, Bratislava, Czechoslovakia; August 31 - September 3, 1981.

2) H.M. Blatter and H. Lukaszewski, Tetrahedron Letters, 2701 (1968).

3) T.L. Gilchrist, M.E. Peek and C.W. Rees, Chem. Commun., 914 (1975).

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