REACTION OF ENAMINE ESTERS WITH DIAZONIUM SALTS[1].

A Facile One-Pot Synthesis of Imidazo[1,2a]azacycloalkanes.

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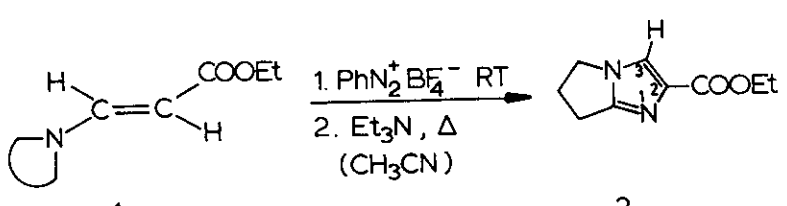
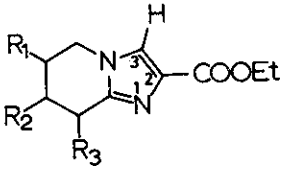
Reaction of β-aminoacrylic esters with benzenediazonium fluoroborate, followed by treatment with triethyl amine leads to the formation of imidazole derivatives.

As a part of our study on the synthetic potential of functionalized enamines[1], we have examined the reaction of enamine esters (β-aminoacrylic esters) with diazonium salts. In this communication we report a new two-step facile synthesis of imidazo-[1,2a]azacycloalkanes. A particular advantage of the approach, above the ones described in the literature[3a-d], is that the sequence of reactions can be carried out in the same reaction-vessel by successive addition of the reagents. Furthermore, the starting materials required are readily accessible.

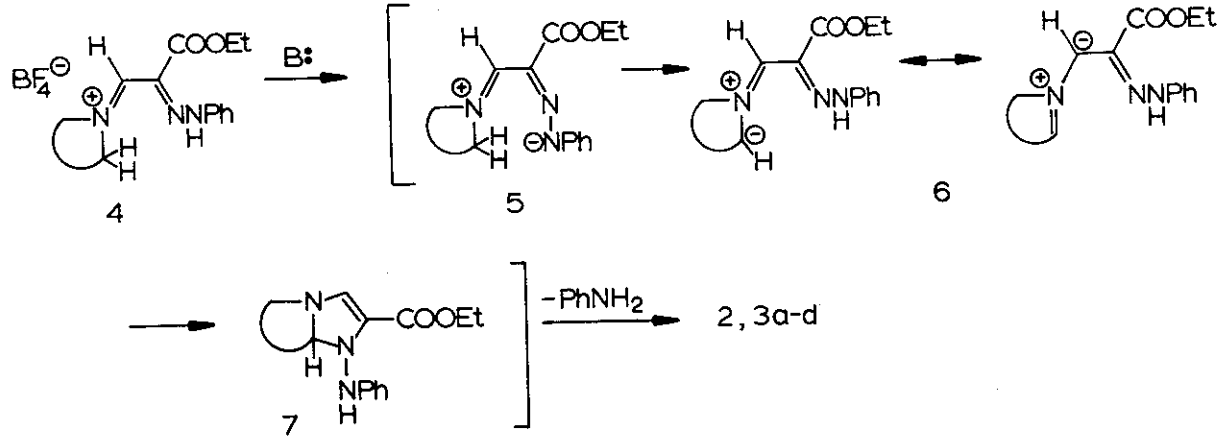
β-Aminoacrylic esters of type 1 can be conveniently prepared by the addition of the corresponding cyclic secondary amines to ethyl propiolate. When the esters were allowed to react with benzenediazonium fluoroborate and the reaction mixture treated with a tertiary amine, the imidazoazacycloalkanes 2, 3a-d,

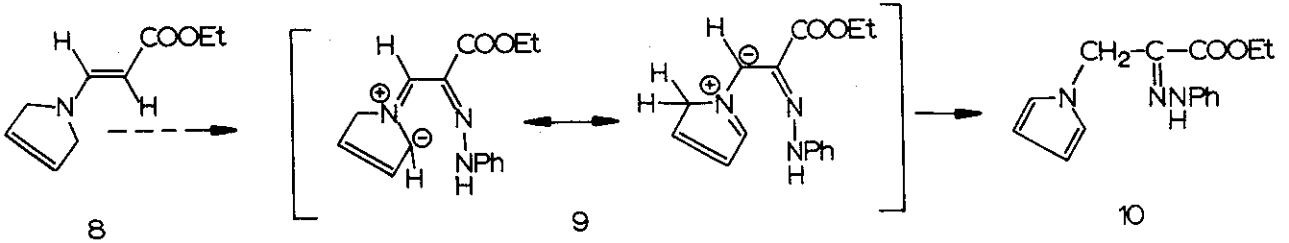




3a $R_1=R_2=R_3=H$
3b $R_1=CH_3$, $R_2=R_3=H$
3c $R_2=CH_3$, $R_1=R_3=H$
3d $R_3=CH_3$, $R_1=R_2=H$

Mechanism





could be isolated in fair to good yields (40-70%). The structure of the products was attested by their elemental analysis and spectral data. Pertinent spectral data are presented in the Table. Typical procedure employed was as follows. Benzenediazonium fluoroborate (1 eq.) was added with stirring, to a solution of the β-aminoacrylic ester (1) in dry CH_3CN at room temperature. After the addition, the mixture was stirred further till the enamine ester had been consumed (tlc, 30 min.). Thereafter, a solution of triethylamine (1 eq.), in CH_3CN, was added and the reaction mixture heated to reflux for 2 hours. The solvent was removed under reduced pressure and the residue chromatographed on a silicagel column with ethyl acetate/isopropanol (10:1) as eluent. Except in the case of 3d all the imidazole derivatives were isolated as crystalline products (Table).

Table. Imidazo[1,2a]azacycloalkanes.

Compound	m.p.	Yield	δC_3-H	$\nu_{COOEt}(cm^{-1})$
2	88-89°	40%	7.57 s	1705
3a	59-63°	63%,	7.41 s	1710
3b	66-67°	32%[a]	7.45 s	1710
3c	98-101°	70%	7.49 s	1710
3d	oil	21%[a]	7.44 s	1710

[a]. 3b and 3d are isolated from the isomeric mixture obtained (53%) from the same reaction.

The mechanism of formation of the imidazoazacycloalkanes may be visualized as follows. Addition of the diazonium salt to 1 would result in the formation of the iminium salts of the cor-

responding phenylhydrazones (4). In fact, in all cases, the latter salts have been isolated, in excellent yields (> 90%), after completion of the first step of the reaction. Treatment with base is visualized to result in the resonance-stabilized zwitter-ion intermediate 5 which is formed by the loss of the most acidic proton in 4. An intramolecular proton transfer in 5 gives rise to an ylid 6, which is poised for a symmetry-allowed disrotatory 1,5-dipolar cyclization to the imidazoline system 7. The latter reaction represents a case of 1,5-dipolar cyclization to a 5-membered heterocycle, of which a number of examples have been reported[4a-d]. Loss of aniline from 7 would result in completion of the reaction with concomitant aromatization. Support for the proposed mechanism also comes from the reaction of enamine ester 8. When 8 was subjected to the aforementioned sequence of reactions, the only product isolated was the pyrrole derivative 10. [m.p. 84-86°; 57%; νKBr 1675; δ $CDCl_3$ 1.27 t and 4.22 q (CH_3CH_2), 4.82 s (N-CH_2), 6.3 and 6.74 2 × t, J=2 Hz (pyrrole protons)]. The formation of 10 can be best rationalized in terms of a prototropic rearrangement in ylid 9 (corresponding to 6) for which process both, neutralization of the system and aromatization, would constitute the obvious driving forces. The scope of this facile heterocyclic synthesis is under active investigation.

Acknowledgement. We wish to thank Prof. Reinhoudt, Twente University of Technology, Enschede, for the communication of unpublished results.

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1 This paper may be regarded as Part XXV of the series Functionalized Enamines. For Part XXIV see H. Bieräugel, J.M. Akkerman, J.C. Lapierre Armande and U.K. Pandit, Rec.Trav.Chim., 1976, 95, 266.

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Received, 22th March, 1978