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THE REACTION OF NITROSONIUM FLUOBORATE WITH OLEFINS IN NITRILE MEDIA A TWO-STEP SYNTHESIS OF IMIDAZOLES FROM OLEFINS

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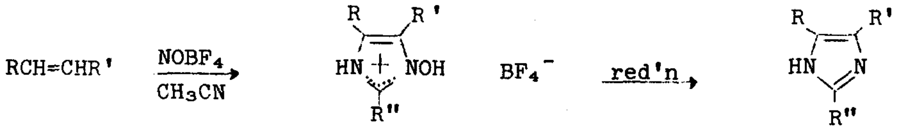
Olefins react with the electrophilic reagent, nitrosonium or nitrosyl fluoborate, $NOBF_4$, in nitrile media, to form heterocyclic compounds in one step. The products of reaction with primary or secondary olefins are conjugate acid salts of imidazole-N-oxides or N-hydroxyimidazolium ions I. Reduction of I with hydride reagents such as Red-Al furnishes the corresponding imidazoles II. A general, two-step synthesis of 2,4,5-substituted imidazoles from olefins with good selectivity is made available by this technique.

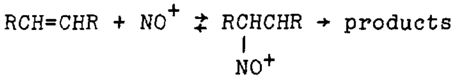


I

II

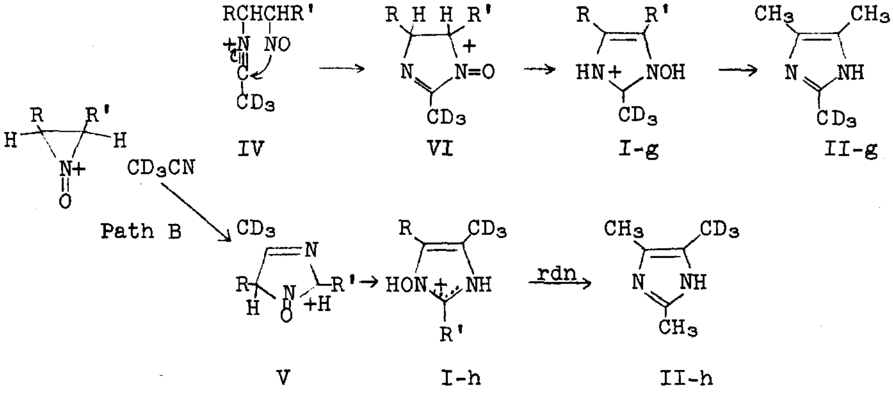
2-Methyl-N-hydroxyimidazolium salts are formed by reaction of acetonitrile solutions of nitrosyl fluoborate with the appropriate olefin at -15 to 0°. Thus, propylene gives Ia ($R=R''=CH_3$, $R'=H$), either cis or <u>trans</u>-butene-2 affords Ib ($R=R'=R''=CH_3$), styrene gives Ic ($R=C_6H_5$, $R'=H$, $R''=CH_3$), and cyclohexene affords Id ($R=R'=-(CH_2)_4-$,,$R''=CH_3$).[2] When benzonitrile is substituted for acetonitrile the corresponding N=hydroxyl-2-phenylimidazolium salt is obtained from propylene (Ie, $R=CH_3$, $R'=H$, $R''=C_6H_5$)[2]. Neutralization of the salts with aqueous base afford imidazole-N-oxide derivatives, which appear to be considerably associated, exhibiting high molecular weight values.[3]

These reactions most likely involve electrophilic attack of nitrosonium ion on olefin to form a nitrosated carbonium ion intermediate, which can react with the nucleophilic solvent to form products. In the absence of nitriles, using inert solvents, reaction of more than one equivalent of olefin with NO^+ occurs; products of nitrosative oligomerization are observed.[4]



$$RCH{=}CHR + NO^+ \rightleftarrows \underset{\displaystyle NO^+}{RCHCHR} \rightarrow \text{products}$$

A bridged nitrosonium-olefin complex ion III might be involved in the initial step of the nitrosation reaction. Were this to be the case, either carbon-nitrogen bond opening, as in path A, leading to intermediate IV or carbon-carbon bond cleavage leading to V could be envisaged on reaction with nitrile. These possibilities are readily distinguished by using d_3-acetonitrile as a reactant with the hypothetical complex from NO^+ and butene-2. Were the reaction to involve path A, the final product after reduction would be II-g, path B would afford II-h, easily differentiated by NMR spectroscopy. The results indicate the product to be II-g, with only one methyl singlet at δ 2.13ppm ($CDCl_3$); path B is incorrect. However, there is no evidence for or against postulating a bridged ion intermediate (III).



R=R'=CH_3

The first step in path A, the formation of intermediate IV, is essentially an extension of the Ritter reaction.[5] Modifications of this reaction often give α-substituted amides[6]; however several routes to heterocycles involving modified Ritter reactions have been reported.[7] Alkylation of nitroso compounds to nitrones by triethyloxonium ion is known[8], and an analogous reaction very likely occurs intramolecularly in the Ritter-derived intermediate IV. Cyclization to the heterocyclic ion VI followed by tautomerization to the N-hydroxyimidazolium ion I-g ensues.

The two-step preparation of imidazoles II has been applied successfully employing various olefins with acetonitrile. Thus propylene gives 2,4(5)-dimethylimidazole ($R=R''=CH_3$, $R=H$)[9] (80%). Both <u>cis</u> and <u>trans</u>-butene-2 give the same product, 2,4,5-trimethylimidazole ($R=R'=R''=CH_3$)[10] (80%). Styrene affords 2-methyl-4(5)-phenylimidazole ($R=C_6H_5$, $R'=H$, $R''=CH_3$)[10] (50%) and cyclohexene gives 2-methyltetrahydrobenzimidazole ($R,R = (CH_2)_4$-,-$R''CH_3$)[11] (50%). 2-Phenyl-4(5)-methylimidazole[10] could be prepared by reduction of the product from propylene and $NOBF_4$ in benzonitrile in less than 5% yield. Attempts to prepare 2-phenyl-4,5-dimethylimidazole by reducing the product from butene-2 and $NOBF_4$ in benzonitrile were unsuccessful.

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<u>References</u>

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2. 1a. oil, nmr (D_2O): δ2.15 (d, 3, $C\underline{H}_3C=CH$, J=1Hz), δ2.45 (S, 3, $C\underline{H}_3C{\langle}^{N}_{N}$), δ4.9 (S, 2, NH and OH) and δ7.05 ppm (q, 1, CH, J=1Hz).

   1b. solid, mp 76-84° (CH_2Cl_3-ether): nmr ($CDCl_3$): δ2.2 (S, 6, $CH_3C=CCH_3$), δ2.55 (S, 3, $CH_3C{\langle}^{N}_{N}$), δ9.0 (broad, 1, NH and OH) and δ11.0 ppm (broad, 1, NH or OH). The nmr spectrum of the product obtained with CD_3CN is identical to the above but lacks the singlet at δ=2.55 ppm.

Ic. Semisolid, nmr (1:1 CD_3OD: D_2O): δ2.92 (S, 3, CH_3), δ7.2 (m, 5, C H) and δ7.57 ppm (S, 1, C=CH).

Id. oil; nmr ($CDCl_3$): δ1.85 (m, 4, $CH_2(C\underline{H}_2)_2CH_2$), δ2.6 (S, 3, CH_3), δ2.6 (m, 4, $C\underline{H}_2(CH_2)_2C\underline{H}_2$), δ7.3 and δ11.4 ppm (broad signals, 2, OH and NH).

Ie. oil; nmr ($CDCl_3$): δ2.2 (S, 3, CH_3), δ7.0 (S, 1, CH), δ7.5 (m, 5, C H) and δ13.5 ppm (broad, 2, NH and OH).

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