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IMIDAZOLE CARBOXYLATES BY A CLAISEN-TYPE REARRANGEMENT OF AMIDOXIME-PROPIOLATE ADDUCTS[1]

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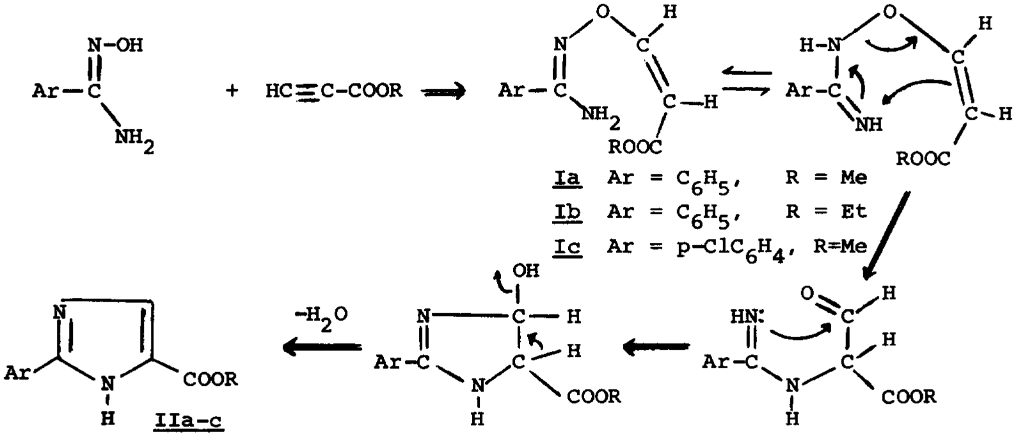
Recent publications on Claisen-type rearrangements in nitrogen heterocyclics[2,3,4] prompt us to report our discovery of a new imidazole carboxylate synthesis which apparently involves the intermediacy of a similar 1,3 sigmatropic shift. Several aromatic amidoximes have been condensed at the alkyne linkage of propiolate esters in 50 to 60% yields by refluxing the components in MeOH for 3 hrs. Since acylation and alkylation studies have shown that the oxygen function of amidoximes is generally the most nucleophilic locus,[5] and since O-methyl amidoximes did not react with the acetylene ester, we concluded that the adducts represented a transoid addition of OH to C≡C (vicinal coupling $\underline{J}$ = 6 Hz in $\underline{\mathrm{I}}$ $\underline{a}$,$\underline{b}$,$\underline{c}$). Ketoxime addition to dimethyl acetylenedicarboxylate is apparently non-stereospecific.[6]

The adducts — $\underline{\mathrm{Ia}}$ (mp 121 — 123°), $\underline{\mathrm{Ib}}$ (mp 78 — 79°), and $\underline{\mathrm{Ic}}$ (mp 179 — 180°)[7] — were pyrolyzed by refluxing in phenyl ether for 30 minutes, and the products precipitated by addition of cold hexane. Recrystallization from MeOH yielded 72% $\underline{\mathrm{IIa}}$ (mp 219 — 221°), 70% $\underline{\mathrm{IIb}}$ (mp 188 — 189°)[8], and 61% $\underline{\mathrm{IIc}}$ (mp 244 — 246°). Elemental and mass spectral analysis confirmed that the products corresponded to the loss of a molecule of water from the starting adducts. Saponification of $\underline{\mathrm{IIa}}$ produced 2-phenyl-4-imidazolecarboxylic acid which was identical with an authentic sample prepared by Fargher and Pyman's method.[9]

An attractive mechanism for this transformation involves a pyrolytic "no mechanism"



Ia Ar = C_6H_5, R = Me

Ib Ar = C_6H_5, R = Et

Ic Ar = p-ClC_6H_4, R=Me

IIa-c

rearrangement of the tautomer of the amidoxime adduct through the intermediate amidine, which eluded isolation under the reaction conditions, to the final heterocyclic. Although Sheradsky has proposed a similar rearrangement to account for the formation of pyrroles from ketoxime-dimethyl acetylenedicarboxylate adducts[6], our example not only represents a unique case of a Claisen-type shift with three hetero atoms in the rearranging cycle but also provides a far more direct synthesis of such imidazole carboxylates than that formerly available.[9]

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8. Lit. mp for ethyl 2-phenyl-4-imidazolecarboxylate, 187 — 188°, see ref. 9.
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