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THE REACTION OF A 1,2-DISUBSTITUTED IMIDAZOLE-4,5-DICARBOXALDEHYDE WITH THIO-, SULFINYL-, AND SULFONYLDIACETIC ACID METHYL ESTER.

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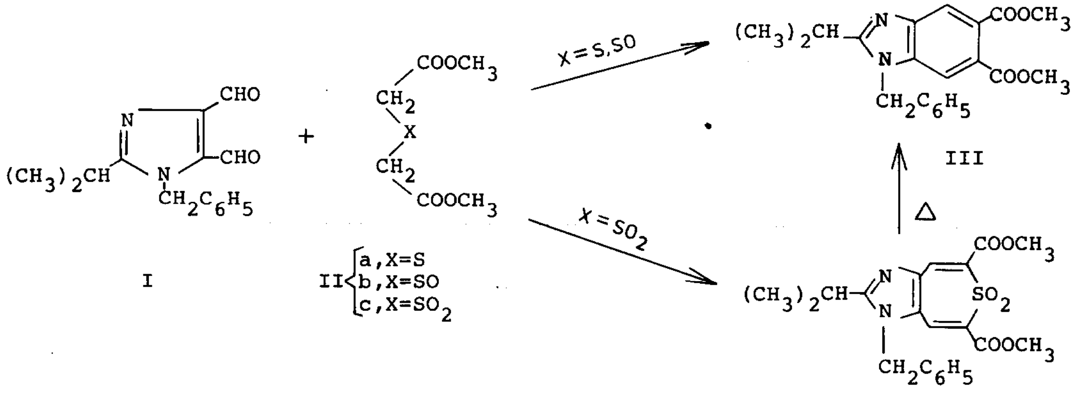
Base catalyzed condensations of o-phthalaldehyde with sulfides of type RCH_2SCH_2R (R=aroyl, alkoxycarbonyl) are well documented.[1] Such transformations, leading initially to 2,4-disubstituted 3-benzothiepins, are at times accompanied by sulfur extrusion, thereby producing 2,3-disubstituted naphthalenes. In a recent report from these laboratories the preparation of certain 1,2-disubstituted imidazole-4,5-dicarboxaldehydes is described.[2] Having these compounds on hand prompted us into examining the behavior of one of them, namely I, with thio-, sulfinyl-, and sulfonyldiacetic acid methyl esters (IIa-c) respectively, thereby hoping to gain facile entry into imidazothiepins and 5,6-disubstituted benzimidazoles.

Compound I, mp 74-75° is readily prepared by refluxing 1-benzyl-2-isopropylimidazole[3] for 96 hr in buffered (AcOH-AcONa) formol, followed by oxidation of the resulting 1-benzyl-2-isopropyl-imidazole-4,5-dimethanol (mp 170-171°) with $Pb(OAc)_4$ in pyridine. Condensations of I with IIa-c were best carried out at room temperature. Treatment of I with IIa in CH_3OH containing 2 equiv of CH_3ONa gave as only isolable product a sulfur-free material $C_{21}H_{22}N_2O_4$ (10-15%) whose spectral data were consistent with structure III: ν_{max}^{KBr} cm^{-1} 1740, 1720 (2 C=O). $\delta^{CDCl_3-(CD_3)_2CO}$ 7.55, 7.28 S (2H, Ar-$\underline{H}$), 7.04-6.57 m (5H, $C_6\underline{H}_5$), 5.32 S (2H, $C\underline{H}_2C_6H_5$), 3.66, 3.60 S (6H, 2 $C\underline{H}_3O$), 3.10 m (1H, $(CH_3)_2C\underline{H}$) 1.31, 1.20 d (6H, $(C\underline{H}_3)_2CH$) . Variation in reaction conditions (DMF-CH_3ONa; DMF-Et_3N) or prolonged reaction-times were of no avail in bringing about yield increments. In contrast, reaction of I with diphenacyl sulfide and dipinacolyl sulfide did give, under comparable reaction conditions, 80% of the 5,6-dibenzoylbenzimidazole, mp 189-190° and 79% of the 5,6-dipivaloylbenzimidazole, mp 156-157°.[4]

Attention was hereafter focussed on the reaction of sulfinyl diester (IIb) with I. Addition of CH_3ONa to a methanolic solution of the reagents led to a moderately exothermic reaction.

isolation after 3 hr at room temperature gave once again compound III, this time, however, in 75% yield. To the best of our knowledge carbonyl-condensations on IIb are novel and we are currently investigating the applications of IIb as a synthetic tool.

Sulfone IIc has been reported to undergo Knoevenagel reactions.[5] On the other hand, IIc has been shown to be inert towards o-phtalaldehyde.[6] In our case, heterocyclic dialdehyde I did react smoothly with IIc; the reaction, carried out in CH_3OH containing 2 equiv of Et_3N led, after 18 hr at room temperature, to the deposition of a product $C_{21}H_{22}N_2O_6S$, mp 160-161°,(60%). Spectral data, ν_{max}^{KBr} cm^{-1} 1720, 1710 (2 C=O), 1350, 1140, (SO_2). δ^{CDCl_3} 8.33, 7.88 S (2H, C=C$\underline{H}$) 7.33-6.75 m (5H, $C_6\underline{H}_5$), 5.37 S (2H, $C\underline{H}_2C_6H_5$), 3.86, 3.78 S (6H, 2 $C\underline{H}_3O$), 3.12 m (1H, $(CH_3)_2C\underline{H}$), 1.37, 1.23 d (6H, $(C\underline{H}_3)_2CH$) leave no doubt as to its being IV. It proved to be remarkably stable, being unaffected by 2.5 hr in refluxing DMF. The compound decomposed slowly in refluxing sulfolan; SO_2 was evolved and after 1.5 hr at least 35% of III was isolated.



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