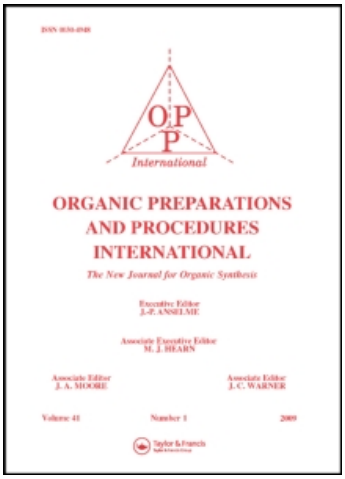

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STEROIDAL ALLYLIC OXIDATION WITH CHROMIUM TRIOXIDE IN THE PRESENCE OF PYRAZOLE

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7. Commercial DMSO (max. 0.03 water) was used with same results.
8. Ultrasound irradiation was carried out by immersion of the reaction flask in a Branson Ultrasound Laboratory Cleaner (150w, 50-60 Hz); the temperature rose to 25-30° during the irradiation.
9. NMR analysis ($CDCl_3$, TMS) of the crude base showed a δ 9.4 signal corresponding to the H at carbon 1 of unreacted isoquinoline, which remained in concentrations of ~ 5% after the process; it disappeared after one crystallization.
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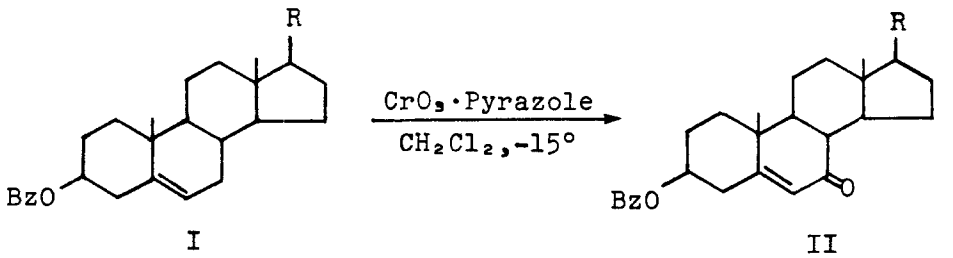
Synthetically useful changes in the properties and reactivity of chromium(VI) reagents have been brought about by the formation of amine complexes. Complexation of chromium trioxide with pyridine[1-3] or 3,5-dimethylpyrazole (DMP)[3,4] has been successfully used for the introduction of



I II

ketone functionality into steroidal olefins by allylic oxidation. The limited number of amines reported to form synthetically useful complexes with chromium(VI) reagents prompted us to investigate the use of other amines for this purpose. We have found that pyrazole when complexed with chromium trioxide, augments the allylic oxidation of cholesteryl benzoate(I) to 7-oxocholesteryl benzoate(II).

The allylic oxidation of cholesteryl benzoate chosen as a model had previously been studied[3] and our results were compared with the data from these studies which used the acetate derivative.[2,5] Treatment of cholesteryl benzoate with 15 equiv. of CrO_3·pyrazole complex for 6 hrs afforded a 76% yield of enone II; these results are comparable to those obtained previously by alternate methods. This is the first report of the use of pyrazole to augment an allylic chromium(VI) oxidation.

EXPERIMENTAL SECTION

Procedures for the recording of melting points (mp), infrared (IR) spectra, low resolution mass spectra (MS), proton nuclear magnetic resonance (^1H NMR), and ultraviolet (UV) spectra have been reported previously.[6] Similarly, details concerning the use of gas-liquid (GLC), thin-layer (TLC), and column chromatography have been described.[6] Cholesteryl benzoate was prepared in 89% yield by treatment of purified commercial cholesterol (98% pure by GLC analysis[7]) with benzoyl chloride in pyridine (mp 148.5-150°, lit.[8] mp. 147°). A sample of authentic 7-ketocholesteryl benzoate was prepared by the procedure of Salmond, Barta, and Havens.[3] Chromium trioxide and pyrazole were obtained from the Aldrich Chemical Co. TLC solvent systems included: toluene, 10% ether-hexane, and 10% ethyl acetate-hexane.

7-Oxocholesteryl Benzoate(II).- Pyrazole (1.04 g; 15.3 mmol) was dissolved in 20 ml of CH_2Cl_2 containing 50 mg of molecular sieves (type 3A). The solution was cooled to -20° and chromium trioxide (1.53 g, 15.3 mmol) was added. After stirring at -20° for 30 min., cholesteryl benzoate I (500 mg, 1.02 mmol) was added; the mixture was stirred for 12 hrs while the temperature was maintained at -10° to -15° (inside a commercial freezer). The mixture was then poured into a saturated NaCl solution containing 5% HCl and the mixture was thoroughly extracted with $CHCl_3$. The resulting extracts

were dried over $MgSO_4$, filtered and evaporated to dryness under reduced pressure to give a residue, which was subjected to column chromatography using a solvent gradient of ether in toluene. The purified product was recrystallized from acetone-water to yield 7-ketocholesteryl benzoate (II) (0.39 g; 76%), mp. 158-159.5°, lit.[8] 159°.

IR(KBr): 1735, 1685, 1670, 1245, 1039, cm^{-1}; ^1H NMR: δ 0.69 (s, 3H, C-18-CH_3), 1.25 (s, 3H, C-19-CH_3), 4.93 (m, 1H, C-3-H), 5.73 (m, 1H, C-6-H), 7.73 (m, 5H, benzoate); MS, m/e (relative intensity): 504 (M, 5%), 382 (M-benzoic acid, 8%), 367 (M-CH_3-benzoic acid, 29%), 121 (benzoyloxy, 6%), 105 (benzoyl, 100%); TLC analysis showed identical mobility with an authentic compound in three different solvent systems.

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