Reissert Compound Formation with Five-membered Ring Heterocycles using Trimethylsilyl Cyanide

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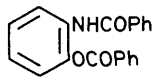
Treatment of benzothiazole with trimethylsilyl cyanide and an acid chloride in CH_2Cl_2 gives the *N*-acyl-2-cyano-2,3-dihydrobenzothiazole in good yield; benzoxazole similarly is converted into a five-membered ring Reissert compound, providing the first examples in these series.

Formation of Reissert compounds from a wide range of aromatic six-membered ring nitrogen heterocycles by use of an acid chloride and a source of cyanide has been utilized as a key step for the modification of the heterocyclic ring in a variety of different ways.[1] Attempts to extend the method to five-membered ring analogues have failed because under the normal two-phase conditions of Reissert compound formation ring opening occurs. For example, we have observed that benzoxazole with benzoyl chloride and potassium cyanide in CH_2Cl_2–H_2O gives (**1**) in high yield; analogous products result from benzothiazole and benzimidazole.

We now report the formation in good yield of Reissert compounds from five-membered ring heterocycles, utilizing trimethylsilyl cyanide[2] as the source of cyanide in a single phase system. For example, treatment of benzothiazole (1 mol) with *p*-toluoyl chloride (1 mol) and trimethylsilyl cyanide (1.1 mol) in the presence of a catalytic amount of aluminium chloride in anhydrous CH_2Cl_2 for 72 h at room temperature gives Reissert compound (**2**, R = 4-MeC_6H_4), 86%, as pale yellow needles from ethyl acetate, m.p. 158—160 °C, ν_{max} (KBr) 1662 cm^{-1}, δ_H 7.4—7.2 (8H), 6.3 (1H, s, C-2-H), and 2.4 (3H).† Use of other aroyl chlorides gave (**2**, R = Ph), 44%, m.p. 140—141 °C; and (**2**, R = 4-ClC_6H_4), 85%, m.p.

† All new compounds gave satisfactory microanalytical data.



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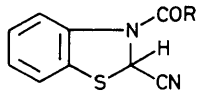

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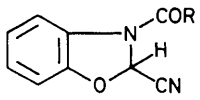

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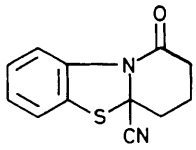

(4)

115—118 °C; 4-chlorobutanoyl chloride gave (**2**, R = $Cl[CH_2]_3$) 84%, m.p. 104—105 °C, and ethyl chloroformate provided (**2**, R = EtO), 72%, m.p. 89—90 °C.

Similarly benzoxazole has been converted in good yields into Reissert compounds (**3**). Use of benzoyl chloride provided (**3**, R = Ph), 50%, m.p. 104.5—105.5 °C, ν_{max}(KBr) 1670 cm^{-1}, δ_H 7.6—6.8 (9H) and 6.7 (1H, s, C-2-H). Also obtained were (**3**, R = 2-$ClCH_2C_6H_4$), 43%, m.p. 106—108 °C; (**3**, R = $Cl[CH_2]_3$), 47%, m.p. 86—87.5 °C; and (**3**, R = EtO), 52%, m.p. 74—75 °C.

Carbanion generation at C-2 in both series can be achieved by treatment of the Reissert compound with sodium hydride in *N,N*-dimethylformamide, an immediate red colouration being given with evolution of hydrogen. The process can be used to effect further heterocyclic modification. For example, intramolecular cyclisation results when the anion of the benzothiazole Reissert compound (**2**, R = $Cl[CH_2]_3$) is stirred under nitrogen for 2 h at 0—5 °C, providing the novel tricyclic derivative (**4**), m.p. 92—93 °C, 83%, ν_{max}(KBr) 1678 cm^{-1}, δ_H 8.15—7.15 (4H) and 2.9—2.1 (6H). Also, treatment of the anion of *N*-benzoyl-2-cyano-2,3-dihydrobenzoxazole (**3**, R = Ph) with MeI gives alkylation at C-2, which when followed by base hydrolysis provides 2-methylbenzoxazole, b.p. 178 °C, δ_H 7.85—7.25 (4H), 2.6 (3H).‡

The five-membered ring Reissert compounds provide a new and potentially versatile means of extending the chemistry of these ring systems.

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‡ I.r. spectrum identical with that of an authentic sample.