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PREPARATION OF FUNCTIONALIZED ISOCYANATES UTILIZING A NOVEL, REACTIVE PYRIDINIUM SALT

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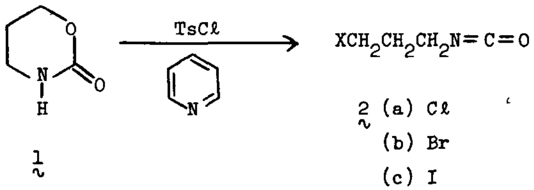
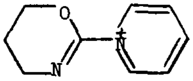
In the course of investigations involving tosylation of the urethane[1] 1 we have uncovered a useful route to terminally functionalized isocyanates[2] of general structure 2.



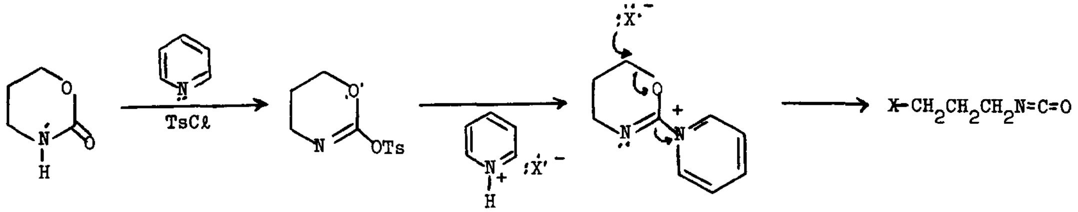
Heating a stirred methylene chloride solution of 1, p-toluenesulfonyl chloride (2 equiv.) and pyridine (3 equiv.) to 40° for 24 hr under nitrogen, resulted in a quantitative yield of 3-chloropropylisocyanate[3] 2(a). Alternatively, if the temperature of the methylene chloride solution was maintained between 20-25° for 36 hr the mixture was quantitatively converted to 15% of 2(a) and a solid 3, 85%, which crystallized from the solution after standing overnight at -18°C. Two recrystallizations of 3 from methylene chloride-ether (4:1) gave hygroscopic silvery-white crystals, $C_{16}H_{18}N_2O_4S$, m.p. 120° (dec.), $\delta_{ppm}^{CDC\ell_3}$ 2.05 (2H,m,J=6Hz), 2.31 (3H,s), 3.66 and 4.65 (each 2H,t,J=6Hz), 7.06 and 7.68 (each 2H,d,J=8Hz), 8.22, 8.74 and 9.44 (5H,m,AB_2X_2),$\nu^{CHC\ell_3}$ 1715 (s), 1625 (m) and 1600 cm^{-1} (w), $\lambda_{max}^{CH_3C\equiv N}$ 262 (ε~5400) and 229.5 nm(ε~5900), insoluble in benzene, ether and tetrahydrofuran. When **3** was mixed with pyridine-d_5 in deuterochloroform, the nmr signals of free pyridine appeared, indicating that **3** possesses an intact pyridine ring that is exchangeable at room temperature. Treatment of the tosylate **3** in methylene chloride with pyridinium bromide or iodide (2 equiv.) at 40°C for 24 hrs led to the corresponding, hitherto unknown, halopropylisocyanates **2**(b) and **2**(c) in greater than 90% yield. The halides could be isolated from the reaction mixture by adding p-toluene sulfonic acid and then extracting the product from the residue with ether Bromide **2**(b) had $\delta^{CDCl_3}_{ppm}$ 2.07 (2H,m,J=6Hz), 3.49 (2H,t,J=6Hz) and 3.54 (2H,t,J=6Hz), ν_{CHCl_3} 2260 cm^{-1} (vs), whereas iodide **2**(c) showed peaks at $\delta^{CDCl_3}_{ppm}$ 2.03 (2H,m,J=6Hz), 3.26 (2H,t,J=6Hz) and 3.47 (2H,t,J=6Hz) and a band at ν_{CHCl_3} 2260 cm^{-1} (vs).



3 OTs$^-$

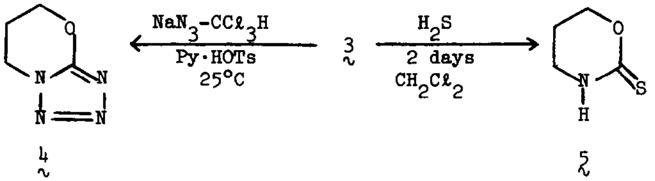
Based on the above physical and chemical properties and the similarity of its spectral properties to those of other pyridinium systems,[4] the solid is assigned the structure of a pyridinium salt, **3**.

Operationally, a path to haloisocyanates involving the following intermediates may be formulated.[2,5] The mechanistic role of protons in this system has not been elucidated, but the

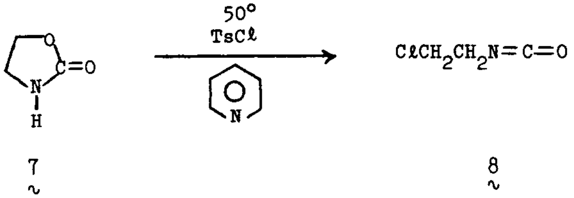


1 **3** OTs$^-$

formation of haloisocyanates from **3** appears to be accelerated by the addition of pyridinium tosylate In general, pyridinium salts promote the reaction of **3** with inorganic salts such as sodium azide. For example, although **3** is very slow to react with sodium azide for 24 hrs at room temperature (3 eq in chloroform), the addition of 1.2 eq. of pyridinium tosylate to the mixture rapidly and quantitatively converts 3 to the tetrazole 4 $C_4H_6N_4O$, m/e 126, m.p. (117-119, two recryst. from 4 1 ether-methylene chloride), ν^{CHCl_3} 1578 (s), 1500 (m), δ^{CDCl_3} 4.67 and 4.48 (each 2H,t,J-6Hz) and 2.38 ppm (2H,m,J=6Hz), λ^{CH_3CN} 225 nm (ε=105).



Competition from the reaction of 3 with water to give the starting urethane requires that the tosylate be handled in a dry atmosphere. The apparently analogous reaction of 3 (1.0 g in 20 mℓ of methylene chloride) with dry hydrogen sulfide gas for two days leads to 5,[7-9] which, if purified by chromatography on silica gel and recrystallized from methylene chloride-ether, has the following properties m.p. 128-130°C, lit m.p.[7] 129°, $\nu(CHCl_3)$ 1528 (s), 1568 (m) and 1155 (s) cm^{-1}, $\delta^{CDCl_3}_{ppm}$ 2 14 (2H,m,J-6Hz), 3.47 (2H,m,J_1=6Hz, J_2=3Hz), 4.48 (2H,t,J=6Hz) and 9.1 ppm (1H,broad), m/e 117 The product may result from a sequence involving nucleophilic attack by hydrogen sulfide on the imine carbon of 3.



The 5-member urethane[10] 7 is tosylated more slowly than 1. After 48 hr at 50° with tosyl chloride (2 mol. equiv) and pyridine (3 mol equiv.), a 46% conversion of 7 to β-chloroethyl isocyanate[11] 8 was achieved The comparative slowness of the tosylation coupled with nucleophilic attack by chloride to give product has prevented isolation of intermediate species in this system.

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