Tetrahedron. Vol. 29, p. 2393. Pergamon Press 1973. Printed in Great Britain

CHLOROSULFONYLISOCYANATE AS A CHLORINATING AGENT

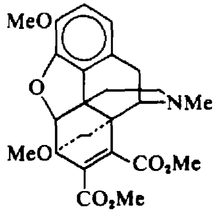
R. GIGER, R. RUBINSTEIN and D. GINSBURG*
Department of Chemistry, Israel Institute of Technology, Haifa.

(*Received in UK* 3 *January* 1973; *Accepted for publication* 2 *April* 1973)

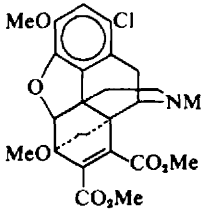
Abstract—CSI rather than adding to the double bond in **1**, chlorinates the aromatic ring.

We were interested in adding chlorosulfonylisocyanate to the (hindered) tetrasubstituted double bond of **1**[1] if this could be accomplished. In fact the reagent served as a very suitable one for chlorinating position 1 in the aromatic ring.

Proof of structure was afforded in part by observing the disappearance of H-1 in the product **2** as compared to its presence in a two proton singlet assigned to H-1 and H-2 in the starting material **1**. Still better, we employed the reaction known for codeine hydrochloride in which oxidative treatment of the salt with hydrogen peroxide in formic acid produces the 1-chlorocodeine.[2] Thus, when this reaction was applied to the hydrochloride of **1**, **2** was again obtained.



1



2

EXPERIMENTAL

Chlorination of **1**. To a solution of **1**[1] (0·46 g) in CH_2Cl_2 (5 ml) was added chlorosulfonylisocyanate (1 ml) and the soln was heated under reflux for 5 hr. After cooling, ice water (20 ml) was added dropwise and the whole was extracted with CH_2Cl_2 (4 × 10 ml) and dried (Na_2SO_4). The solvent was removed and the glassy residue was triturated with diisopropyl ether. The yellow solid was removed (658 mg). It was dissolved in MeOH and treated with excess diazomethane to methylate a small amount of demethylated material. After standing overnight the solvent was removed and the residue was triturated with MeOH. It afforded after drying colorless **2** (395 mg; 81%), m.p. 219–221°. The analytical sample had m.p. 224–225° (CH_2Cl_2–MeOH). (Found: C, 60·71; H, 5·62; N, 2·81; Cl, 7·72; M.W. 489. $C_{25}H_{28}O_4N$ Cl requires: C, 61·15; H, 5·74; N, 2·83; Cl, 7·22%; M.W. 490·93); IR(KBr): 1720 cm^{-1} (ester CO); UV(MeOH): nm(ϵ) 221 (end, 23400); 288 (3300); NMR ($CDCl_3$): τ 3·19 (s, H-2); 5·33 (br s, H-5); 6·11, 6·19, 6·25 (3s, $6CO_2C\underline{H}_3 + 3\,C_3$–$OC\underline{H}_3$), 6·44 (d, $J_{9\alpha,10\alpha} = 6$ Hz, H-9α); 6·47 (s, 3 C_6–$OC\underline{H}_3$); 6·95 (d, $J_{10\beta,10\alpha} = -19$ Hz); 7·40–9·35 (m, H-10α, 8H at positions 15, 16, 17, 18); 7·73 (s, $3NC\underline{H}_3$); M.S. (m/e >20%): 491(37), 490(30), 489(100), 474(44), 458(33), 430(31), 371(24), 248(32).

Hydrochloride of **1** was obtained by adding conc HCl to **1** in THF, m.p. 193–213°.

Alternative preparation of **2**. To a soln of the hydrochloride (491 mg) in formic acid (33%; 1·7 ml) was added H_2O_2 (30%; 1·33 ml) and the soln was warmed rapidly until strong bubbling began. Heating was discontinued and the soln was allowed to stand until it cooled down to room temp. 3N NaOH aq was added dropwise with stirring to pH 7. The precipitated solid was removed and dried in a high vacuum (222 mg; 45%), m.p. 213–215°. Twice crystallized material had m.p. 224–225° and was identical in all respects with **2** described above.

REFERENCES

[1] H. Rapoport and P. Sheldrick, *J. Am. Chem. Soc.* **85**, 1636 (1963)
[2] E. Speyer and H. Rosenfeld, *Ber. Dtsch. Chem. Ges* **58**, 1110 (1925)