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A FACILE AND EFFICIENT SYNTHESIS OF PYRROLE-3-CARBOXYLIC ACID FROM PYRROLE

Carlos Cativiela^a; Jose I. Garcia^a

^a Instituto de Ciencia de los Materiales de Aragon Department of Organic Chemistry University of Zaragoza, Zaragoza, SPAIN

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pure RDX, mp. 202° (dec.), lit.⁷ 204° (dec.), by comparison with an authentic sample.

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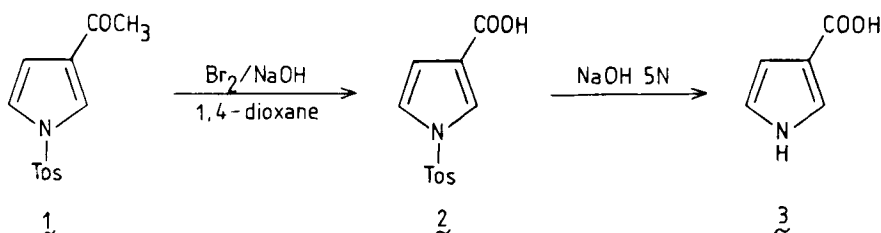
Submitted by Carlos Cativiela* and Jose I. Garcia
(03/03/86)

Instituto de Ciencia de los Materiales de Aragon
Department of Organic Chemistry
University of Zaragoza, 50009 Zaragoza, SPAIN

Only a few procedures have been described for the synthesis of pyrrole-3-carboxylic acid (3),¹ and these procedures give very low overall yields and require special conditions and reagents. Pyrrole-3-carboxylic acids and derivatives are frequently obtained by ring syntheses which lead in most cases to polysubstituted pyrroles.² Recently, a method for the

regioselective synthesis of 3-acylpyrroles has been reported;³⁻⁵ however, since the introduction of the formyl (by means of dimethylformamide or dichloromethyl butyl ether) and of the cyano units (by means of chlorosulphonyl isocyanate or cyanogen bromide) is unsuccessful by this method, it cannot be used directly for the synthesis of compound 3 or analogues.

Our interest in the synthesis of 3-substituted pyrroles led us to devise a new route to compound 3, based on the above-mentioned method by the haloform reaction on 1-tosyl-3-acetylpyrrole (1); it has two major



advantages over the previously mentioned syntheses,¹ in that it utilizes simple starting reagents such as pyrrole, toluenesulfonyl chloride and acetic anhydride, and secondly affords considerably higher overall yield (60-65%).

EXPERIMENTAL SECTION

1-Tosylpyrrolecarboxylic Acid (2).— To a solution of 2.63 g (0.01 mol) of 1-tosyl-3-acetylpyrrole (1)⁵ in 100 ml of dioxane diluted with 40 ml of water and cooled in an ice bath (0°), was added in steady stream a cold solution of sodium hypobromite (freshly prepared from a solution of 5.25 g (0.13 mol) of sodium hydroxide in 45 ml of water and 5.26 g (0.033 mol) of bromine, diluted with 30 ml of dioxane); the temperature of the mixture was kept below 10° throughout the reaction. The mixture was stirred for an additional 2 hrs at room temperature, and then the excess sodium hypobromite was destroyed by the addition of a solution of sodium sulfite.

The solution was acidified with conc. hydrochloric acid and the precipitate collected and recrystallized from ethanol-water to yield 2.25 g (85%) of 1-tosylpyrrole-3-carboxylic acid, mp. 197-198°.

IR(nujol): 1690 cm^{-1} ; ^1H NMR(DMSO- d_6): δ 2.40 (3H, s), 6.63 (1H, m), 7.40 (4H, dd), 7.83 (1H, m).

Pyrrole-3-carboxylic Acid (3).— A solution of 1.325 g (0.005 mol) of compound 2 in 25 ml of 5N NaOH was stirred for 2 hrs at room temperature. The solution was then acidified and the precipitate collected and recrystallized from ethanol-water to yield 0.51 g (92%) of pyrrole-3-carboxylic acid, mp. 150-151°, lit.¹ mp. 148°, 150-150.5°.

IR(nujol): 3230, 1650 cm^{-1} ; ^1H NMR (DMSO- d_6): δ 6.40 (1H, m), 6.78 (1H, m), 7.35 (1H, m), 11.54 (1H, broad s); ^{13}C NMR (DMSO- d_6): δ 109.1, 115.9, 119.1, 123.5, 165.8

Anal. Calcd. for $\text{C}_5\text{H}_5\text{NO}_2$: C, 54.06; H, 4.54; N, 12.61

Found: C, 53.96; H, 4.50; N, 12.73

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