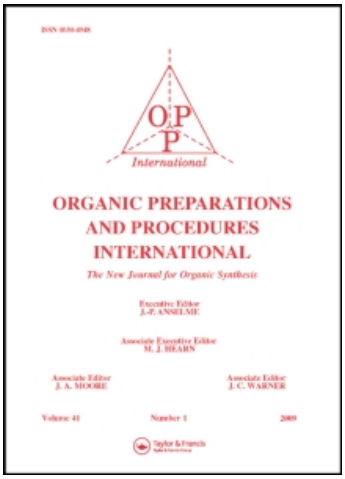

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SYNTHESIS OF DIMETHYL 1,2-DIHYDROPYRIDAZINE-1,2-DICARBOXYLATE

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SYNTHESIS OF DIMETHYL 1,2-DIHYDROPYRIDAZINE-1,2-DICARBOXYLATE

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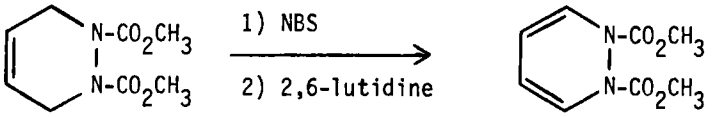
An increasing number of requests have prompted us to now report full experimental details on the synthesis of dimethyl 1,2-dihydropyridazine-1,2-dicarboxylate (II) [2,3]. Compound II was obtained from dimethyl 1,2,3,6-tetrahydropyridazine-1,2-dicarboxylate (I) [4] via allylic bromination followed by dehydrobromination.



I II

Satisfactory conversions were obtained in the bromination reaction by the use of a 15% excess of N-bromosuccinimide in a dilute CCl_4 (*ca.* 0.025M) solution of I. The resultant crude monobromide was transformed into II by dehydrobromination with 2,6-lutidine in refluxing toluene. Analytically pure II could best be obtained by preparative thin layer chromatography (silica gel GF). Although other chromatographic separations were effective (Florisil, 30% $AgNO_3$ on silica gel, alumina II), much higher losses were found due to the instability of II on the columns.

The diethyl- and di-t-butyl esters were similarly obtained. In order to obtain the bis-trichloroethyl ester, only the reaction of bis-trichloroethylazodicarboxylate with α-pyrone was found to be

effective[5].

EXPERIMENTAL

A mixture of N-bromosuccinimide (8.21 g; 46.1 mmole), dimethyl 1,2,3,6-tetrahydropyridazine-1,2-dicarboxylate (7.67 g; 38.4 mmole) and carbon tetrachloride (1700 ml) was refluxed until all of the NBS had been consumed (2 hrs). Solvent was removed from the cooled, filtered reaction mixture by rotary evaporation under reduced pressure. The crude product was quickly taken up in dry toluene (100 ml) and the solution was rapidly brought to reflux. At the first sign of reflux, 2,6-lutidine (5.3ml; 45.4 mmole; distilled from $LiAlH_4$ and stored over BaO) was injected all at once. After an additional five minutes reflux, the reaction mixture was quickly cooled, diluted with ether (100 ml) and washed with 3.7% HCl (2 x 70 ml), saturated NaCl (70 ml) and dried ($MgSO_4$). Removal of solvent under reduced pressure yielded an oil (6.45 g; 85% crude yield) which analyzed (nmr) to be a mixture of the desired dihydropyridazine contaminated with approximately 4% of the starting tetrahydropyridazine. Separation and purification was best effected (66% recovery) by preparative thin layer chromatography (silica gel GF; ether eluant; *ca.*400 mg of crude product per 20cm x 20cm x 1 mm plate). The proof of structure II follows from its spectral properties: nmr 6H (CO_2CH_3) singlet 3.81δ, 4H vinyl AA'XX' multiplet, ν_A = 5.71δ, ν_X = 6.73δ, $|J_{AX} + J_{AX'}|$ = 7.7 Hz; λ_{max} (EtOH) 296 (ε 2900) and its quantitative hydrogenation to dimethyl hexahydropyridazine-1,2-dicarboxylate[4] (2.05 moles H_2 uptake/mole II), identical to an authentic sample (tlc, ir).

Calc. for $C_8 H_{10} O_4 N_2$: C 48.48, H 5.09, N 14.14

Found: C 48.34, H 5.00, N 13.89.

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