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# REACTION OF DIMETHYL (*S*)-2-(*p*-TOLYL)CYCLOPROPANE-1,1-DICARBOXYLATE WITH ACETONITRILE

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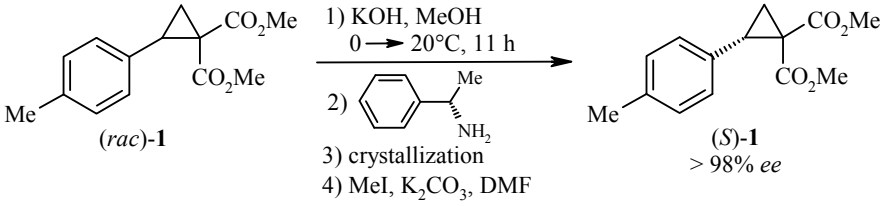
The Lewis acid-activated reactions of donor-acceptor cyclopropanes with nitriles are the basis of a convenient method for the synthesis of $\Delta^1$-pyrrolines and pyrroles [1-5]. The use of 1,2,3-substituted donor-acceptor cyclopropanes leads to the formation of $\Delta^1$-pyrrolines with high diastereoselectivity. Depending on the type of substrate and the reaction conditions, either reversal [5] or retention [1] of the configuration of the cyclopropane carbon atom bearing donor substituent and taking part in the interaction with the nitrile nitrogen atom is observed. In order to determine the stereoselectivity of nitrile reactions with 2-arylcyclopropane-1,1-dicarboxylates without a substituent at the C-3 atom [4], we have prepared the optically pure donor-acceptor cyclopropane (*S*)-**1** and studied its reaction with acetonitrile.

The synthesis of enantiomerically pure cyclopropane (*S*)-**1** includes the hydrolysis of the racemic diester (*rac*)-**1** to the 2-(*p*-tolyl)cyclopropane-1,1-dicarboxylic acid, its conversion to (*S*)-1-phenylethylamine salt as two diastereomers and recrystallization. We have modified the previously reported method [6] for the synthesis of enantiomerically pure 2-phenylcyclopropane-1,1-dicarboxylates. In particular, shorter hydrolysis time for the compound (*rac*)-**1** and two successive crystallizations of the salt allowed us to avoid lactonization and gave the diester (*S*)-**1** with *ee* > 98%.




In a study of the cyclopropane (*S*)-**1** reaction with acetonitrile using previously reported conditions (2 equiv. of $SnCl_4$, nitromethane, 55ºC) [4], we found that it occurs with a total loss of optical activity to give the pyrroline **2** as a racemic mixture. A similar result was obtained when the reaction was carried out in 1,2-dichloroethane (1 equiv. of $SnCl_4$, room temperature). Previously it was observed that under these conditions a

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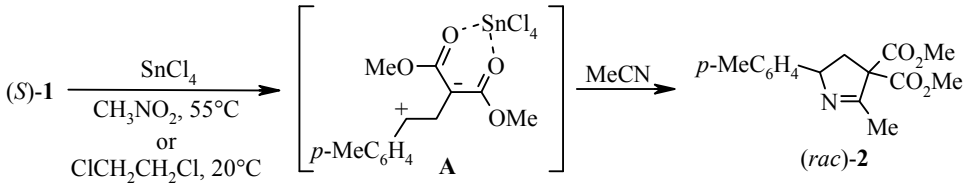


reaction of nitriles with analogs of compound **1** (with an acyl substituent at atom C-3) gave complete reversal of the configuration of the carbon atom bound to the aryl substituent [5].

We consider that the reason for the racemization is the occurrence of the reaction *via* the achiral zwitterionic intermediate **A**, which is formed as the result of heterolysis of the C(1)–C(2) bond of the cyclopropane *via* coordination of the $SnCl_4$ at the ester groups. This proposal agrees with the previously obtained data for the reactions of donor-acceptor cyclopropanes of type **1**, which are induced by $SnCl_4$ and other strongly activating Lewis acids in polar solvents [7, 8].

Subsequent study of the detailed mechanism of the formal [3+2] cycloaddition of donor-acceptor cyclopropanes to nitriles and the possibility of obtaining optically active $\Delta^1$-pyrrolines from type **1** cyclopropanes and Lewis acid complexes with chiral ligands will be the subject of our future investigations.

IR spectra were recorded on a UR-20 instrument using vaseline oil. $^1H$ and $^{13}C$ NMR spectra were recorded on a Bruker Avance 600 spectrometer (600 and 150 MHz respectively) using $CDCl_3$, and chemical shifts were determined relative to the solvent signal at δ 7.26 ppm for $^1H$ and 77.13 ppm for $^{13}C$. The enantiomeric purity was determined chromatographically using an AmyCoat chiral support column (150×4.6 mm) and heptane–2-PrOH (95:5) as eluent.

**Dimethyl (*S*)-2-(4-tolyl)cyclopropane-1,1-dicarboxylate ((*S*)-1))** was prepared by two successive crystallizations of the diastereomeric salts of (*S*)-1-phenylethylamine with (*rac*)-2-(*p*-tolyl)cyclopropane-1,1-dicarboxylic acid and subsequent alkylation of the optically pure diacid using the method reported previously for 2-phenylcyclopropane-1,1-dicarboxylate [6]. *ee* > 98º. $[\alpha]_D^{20}$ -135º (c 2.0, $CH_2Cl_2$) ($[\alpha]_D^{20}$ -141º (c 0.9, $C_6H_6$) [9]). The spectroscopic data agreed with the literature [10].

**Dimethyl 2-Methyl-5-(4-tolyl)-4,5-dihydropyrrole-3,3-dicarboxylate (2)**. A. $SnCl_4$ (300 mg, 0.13 ml, 1.15 mmol) in $MeNO_2$ (2 ml) was added to a solution of the cyclopropane (*S*)-**1** (150 mg, 0.6 mmol) and MeCN (123 mg, 0.16 ml, 3 mmol) in $MeNO_2$ (15 ml). The reaction mixture was stirred under an argon atmosphere for 3 h at 55ºC, poured into aqueous $NaHCO_3$ solution (50 ml) and extracted with $CH_2Cl_2$ (3×40 ml). The combined organic extracts were washed with a solution of Trilon B (3×20 ml), water (3×20 ml) and dried over anhydrous $Na_2SO_4$. The solvent was evaporated, and compound **2** was isolated by column chromatography on silica using petroleum ether–EtOAc (4: 1) as eluent.

B. $SnCl_4$ (166 mg, 0.07 ml, 0.6 mmol) in $ClCH_2CH_2Cl$ (2 ml) was added to a solution of the cyclopropane (*S*)-**1** (150 mg, 0.6 mmol) and MeCN (123 mg, 0.16 ml, 3 mmol). The reaction mixture was stirred under argon for 12 h at 20ºC and then treated as in method A.

Yield 149 mg (86%, method A), 134 mg (77%, method B). Colorless oil. $R_f$ 0.55 (petroleum ether–EtOAc, 2:1). IR spectrum, ν, $cm^{-1}$: 3020, 2970, 1740 (C=O), 1665 (C=N), 1520, 1440, 1380, 1290, 1095, 1030, 830. $^1H$ NMR spectrum, δ, ppm (*J*, Hz): 2.29 (3H, d, $^5J$ = 2.2, 2-$CH_3$); 2.33 (3H, s, C$\underline{H}_3C_6H_4$); 2.36 (1H, dd, $^2J$ = 13.4, $^3J$ = 8.3) and 3.14 (1H, dd, $^2J$ = 13.4, $^3J$ = 7.2, 4-$CH_2$); 3.78 (3H, s, $OCH_3$); 3.82 (3H, s, $OCH_3$); 5.12 (1H, ddq, $^3J$ = 8.3, $^3J$ = 7.2, $^5J$ = 2.2, 5-CH); 7.14-7.17 (4H, m, H Ar). $^{13}C$ NMR spectrum, δ, ppm: 18.1 ($CH_3$); 21.0 ($CH_3$); 42.6 (4-$CH_2$); 53.0 ($OCH_3$); 53.1 ($OCH_3$); 72.2 (C-3); 73.4 (5-CH); 126.4 (2CH Ar); 129.2 (2CH Ar); 136.8 (C Ar); 139.3 (C Ar); 168.2; 168.3; 169.2. Found, %: C 66.45; H 6.71; N 5.00. $C_{16}H_{19}NO_4$. Calculated, %: C 66.42; H 6.62; N 4.84.

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