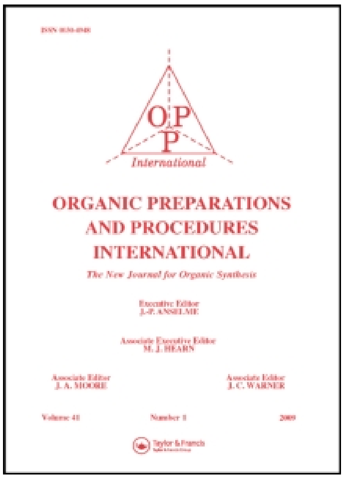

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OPPI BRIEFS

THE SYNTHESIS OF SOME BENZO[b]THIOPHENE SUBSTITUTED ARYLACETIC ACID ESTERS

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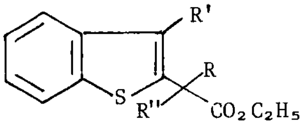
During a study of the chemistry of thiophene analogues of glycolic acid[1] some disubstituted acetic acid esters were synthesized in order to measure the chemical shift values of the methine hydrogen atoms. The synthesis of compounds I-III needed for another study, is described here.



I $R = C_6H_5$, $R' = R'' = H$
II $R = 4\text{-}C_6H_5C_6H_4$, $R' = R'' = H$
III $R = R' = C_6H_5$, $R'' = H$
IV $R = C_6H_5$, $R' = H$, $R'' = OH$
V $R = 4\text{-}C_6H_5C_6H_4$, $R' = H$, $R'' = OH$
VI $R = R' = C_6H_5$, $R'' = OH$

2-Benzo[b]thienyllithium[2] was reacted with ethyl phenylglyoxylate[3] and ethyl 4-biphenylylglyoxylate[4] respectively to afford the corresponding hydroxyesters IV and V, a small amount of 1-(2-benzo[b]thienyl)-2-phenylethanedione was also obtained along with IV. Reduction of the hydroxyesters with $SnCl_2$-HCl[5] afforded the compounds I and II in the yields reported. In a similar manner, 3-phenylbenzo[b]thionyllithium[6] was used to prepare III.

EXPERIMENTAL

Melting points are not corrected. Elemental analyses were performed by Galbraith Laboratories, Inc., Knoxville, Tennessee.

Ethyl 2-Benzo[b]thienylmandelate (IV).- A cooled (-40°) ether solution of 2-benzo[b]thienyllithium[2] (0.05 mol) was added dropwise to a cooled (-40°) solution of ethyl phenylglyoxylate[3] (13.35 g, 0.075 mol) in 100 mL of ether and the resulting green solution was allowed to warm to 16° over a period of 2 hrs. Hydrolysis (saturated NH_4Cl), followed by extraction with ether gave an orange oil that partially solidified when cooled under hexane. Washing the solid with cold hexane yielded 9.57 g. of a pale yellow solid, mp. 75-83°. The solid, in benzene, was chromatographed over silica gel and was eluted with 1:1 benzene-hexane containing 1.5% (v) glacial acetic acid. The yellow impurity was eluted first and was found to be 1-(2-benzo[b]thienyl)-2-phenylethanedione (0.45 g, 3.4% yield, mp. 140-142°). Recrystallization from hexane yielded an analytically pure sample as pale yellow platelets, mp. 141-142°.

Anal. for $C_{16}H_{10}O_2S$: Calcd: C, 72.16; H, 3.78; S, 12.04.
Found: C, 72.18; H, 3.65; S, 11.89.

IR (KBr): 3080 (w), 1680 (s), 1660 cm^{-1} (s).

NMR ($CDCl_3$): δ 7.4-8.2 (m).

The hydroxy ester product was eluted from the column immediately following the diketone as a white crystalline solid (8.12 g, 57%, mp. 84-86°). Recrystallization from hexane afforded an analytically pure sample of ethyl 2-benzo[b]thienylmandelate, mp. 85-86°.

Anal. for $C_{18}H_{16}O_3S$: Calcd: C, 69.20; H, 5.16; S, 10.27.
Found: C, 69.40; H, 5.33; S, 10.06.

IR (KBr): 3480 (OH), 1730 cm^{-1} (C=O).

NMR ($CDCl_3$): δ 7.2-7.8 (m, 10 H), 4.67 (s, 1 H, OH), 4.32 (q, 2 H, CH_2), 1.23 (t, 3 H, CH_3).

Ethyl 2-Benzo[b]thienylphenylacetate (I).- A solution of hydroxy ester IV (0.05 g, 1.6 mmol) in 30 mL of glacial acetic acid, 0.5 mL of water and 0.9 g of stannous chloride dihydrate (4.0 mmol) was cooled to 10° and a stream of HCl gas was bubbled into the reaction for 30 min while maintaining the temperature between 10-15°. The reaction mixture turned cloudy white when poured onto ice. Extraction with ether yielded 0.51 g of yellow oil which solidified to a white solid (0.47 g, mp. 60-65°) when cooled. Recrystallization from hexane afforded white crystalline ethyl 2-benzo[b]thienylphenylacetate (I) (0.32 g, 68%, mp. 65-67°).

Anal. for $C_{18}H_{16}O_2S$: Calcd: C, 72.95; H, 5.44; S, 10.80.

Found: C, 72.78; H, 5.58; S, 10.69.

IR (KBr): 1732 (C=O), 697, 744 cm^{-1}.

NMR ($CDCl_3$): δ 7.73-7.13 (m, 10 H), 5.19 (s, 1 H, methine), 4.20 (q, 2 H, CH_2), 1.23 (t, 3 H, CH_3).

Ethyl 4-Biphenylyl(2-benzo[b]thienyl)acetate (II).- A solution of 2-benzo[b]-thienyllithium[2] (0.02 mol) was added dropwise to a solution of ethyl 4-biphenylylglyoxylate[4] (4.83 g, 0.019 mol) in 50 mL of anhydrous ether at a temperature of -5°.

After 1 hour of stirring at 9° the solution was hydrolyzed (NH_4Cl) and extracted with ether to yield upon workup, 6.86 g of orange oil shown by IR to be crude hydroxy ester V. The oil was not purified but was reduced to the corresponding ester II as IV above. From 2.84 g of unpurified hydroxy ester V there was obtained a tan oily solid (1.88 g, mp. 90-93°) which was purified by chromatography over silica gel. The resulting pure ester (1.3 g, 55%, mp. 114-115°) was recrystallized from cyclohexane to afford white fluffy analytically pure sample of ethyl (4-biphenylyl)-2-benzo[b]thienylacetate (II), mp. 117-118°.

Anal. for $C_{24}H_{20}O_2S$: Calcd: C, 77.39; H, 5.41; S, 8.61.

Found: C, 77.59; H, 5.57; S, 8.45.

IR (KBr): 1737, 758, 750, 695 cm^{-1}.

NMR ($CDCl_3$): δ 7.63-7.26 (M, 14 H), 5.22 (s, 1 H, methine), 4.23 (q, 2 H, CH_2), 1.27 (t, 3 H, CH_3).

Ethyl 2-(3-Phenylbenzo[b]thienyl)phenylacetate (III). - Lithiation of 3-phenylbenzo[b]thiophene[6] (5.25 g, 0.025 mole) at -5°, followed by reaction with ethyl phenylglyoxylate[3] (4.45 g, 0.020 mole) gave, following the procedure for IV above, the hydroxyester VI (8.7 g) which was not purified but was reduced as above to give III. From 2.3 g of the hydroxy ester there was obtained 1.90 g of III, mp. 82-84°. Recrystallization from hexane gave III as white prisms, mp. 84-88°.

Anal. for $C_{24}H_{20}O_2S$: Calcd: C, 77.39; H, 5.41; S, 8.61.

Found: C, 77.29; H, 5.57; S, 8.68.

IR (KBr): 1730, 735, 690 cm^{-1}.

NMR ($CDCl_3$): δ 7.9-7.2 (M, 14 H, arom.), δ 5.32 (s, 1 H, methine), δ 4.18 (q, 2 H, CH_2), δ 1.2 (t, 3 H, CH_3).

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