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ORGANOSILICON COMPOUNDS

XXXVIII*. THE PREPARATION AND OPTICAL RESOLUTION OF *p*-[ETHYLMETHYL(*p*-METHOXYPHENYL)SILYL]BENZOIC ACID

R. W. BOTT, C. EABORN AND P. W. JONES
Chemical Laboratory, University of Sussex, Brighton (Great Britain)
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INTRODUCTION

A few years ago, Eaborn and Pitt reported the optical resolution of the acid *p*-(EtMePhSi)$C_6H_4CO_2H$ by fractional crystallization of its (—)-quinine salt from ethanol[2], the first fully authenticated resolution of an organosilicon compound containing only one asymmetric silicon centre. We have now prepared, and resolved by a similar method, the closely related compound *p*-[EtMe(*p*-$MeOC_6H_4$)Si]$C_6H_4CO_2H$. We hoped, by selective stereo-specific cleavage by bromine (*cf.* ref. 3) of the Si–C_6H_4OMe-*p* bond in suitable derivatives of this acid, to make optically-active compounds having reactive groups attached to silicon, but this hope was not realized.

The preparations of several new asymmetric organosilicon compounds are described in the EXPERIMENTAL section.

DISCUSSION

The preparation of the acid *p*-(EtMePhSi)$C_6H_4CO_2H$ involved oxidation of the *p*-tolyl group of the compound *p*-(EtMePhSi)C_6H_4Me[1,2], but we thought it unlikely that a similar approach would succeed with a *p*-methoxyphenyl in place of a phenyl group because of the ease of oxidation of the methoxyl group. The required racemic acid, (I), m.p. 106–107°, was synthesized in good yield by the following route:

$$MeSi(OEt)_3 \xrightarrow{p\text{-}BrC_6H_4MgBr} Me(EtO)_2SiC_6H_4Br\text{-}p \xrightarrow{EtMgBr} EtMe(EtO)SiC_6H_4Br\text{-}p$$

$$EtMe(EtO)SiC_6H_4Br\text{-}p \xrightarrow{p\text{-}MeOC_6H_4Li} EtMe(p\text{-}MeOC_6H_4)SiC_6H_4Br\text{-}p$$

$$EtMe(p\text{-}MeOC_6H_4)SiC_6H_4Br\text{-}p \xrightarrow[(ii)\ CO_2,\ etc.]{(i)\ Mg/Et_2O} EtMe(p\text{-}MeOC_6H_4)SiC_6H_4CO_2H\text{-}p \quad (I)$$

The acid was resolved by fractional crystallization of its (—)-quinine salt from ethanol. Acidification of the less-soluble diastereomeric salt yielded the (±)-acid m.p. 106–107°, $[\alpha]_D^{25}$ ±1.2° (*c*, 3.7 in benzene). The rotation is only about half of that of the acid (±)-*p*-(EtMePhSi)$C_6H_4CO_2H$.

* For Part XXXVII, see ref. 1.

The (+)-acid was treated (*i*) with diazomethane to give the (—)-methyl ester (—)-EtMe(*p*-$MeOC_6H_4$)$SiC_6H_4CO_2Me$-*p* (II), $[\alpha]_D^{25}$ —0.16° (*c*, 40 in carbon tetrachloride), and (*ii*) with lithium aluminium hydride to give the (+)-benzyl alcohol, (+)-EtMe(*p*-$MeOC_6H_4$)$SiC_6H_4CH_2OH$-*p*, $[\alpha]_D^{25}$ +0.14° (*c*, 38 in benzene). This alcohol was converted into the methyl ether, (—)-EtMe(*p*-$MeOC_6H_4$)$SiC_6H_4CH_2OMe$-*p*, (III), having a negative rotation, $[\alpha]_D^{25}$ —0.25° (*c*, 40 in carbon tetrachloride).

Bromine cleavage of the (—)-methyl ester, (II), followed by isopropanolysis of the product gave the expected isopropoxy compound, EtMe(iso-PrO)$SiC_6H_4CO_2Me$-*p*, but optically-inactive. Bromine cleavage of (—)-benzyl methyl ether (III) and treatment of the product with lithium aluminium hydride gave only the racemic hydride, $EtMeHSiC_6H_4CH_2OMe$-*p*.

EXPERIMENTAL*

Ethylmethyl(p-chlorophenyl)fluorosilane

The Grignard reagent from *p*-bromochlorobenzene (129 g, 0.68 mole) and magnesium (16.4 g, 0.68 g-atom) in ether (500 ml) was added during 1 h to a stirred ice-cold solution of ethylmethyldichlorosilane, (87.8 g, 0.61 mole) in ether (200 ml). The mixture was refluxed for 3 h, then treated with an excess of aqueous 2 N hydrochloric acid. The ether layer was separated, washed and dried (Na_2SO_4), and the ether was distilled off. The residue was dissolved in ethanol (1500 ml), 40 wt-% aqueous hydrofluoric acid (100 ml) was added, and the mixture was kept at 60° for 8 h, during which time four additional 100 ml quantities of the hydrofluoric acid were added[1]. The solution was diluted with a large volume of water, and extraction with light petroleum (b.p. < 40°), followed by washing, drying (Na_2SO_4), and fractionation of the extract gave ethylmethyl(*p*-chlorophenyl)fluorosilane (37 g, 30 %), b.p. 91–93°/13 mm, n_D^{20} 1.4984. (Found: hydrolysable F, 9.2. $C_9H_{12}ClFSi$ calcd.: F, 9.37 %.)

Ethylmethyl(p-methoxyphenyl)chlorosilane

The Grignard reagent from *p*-bromoanisole (123.5 g, 0.66 mole) and magnesium (16.0 g, 0.66 g-atom) in ether (150 ml) was added dropwise to a cooled solution of ethylmethyldichlorosilane (78.5 g, 0.55 mole) in ether (100 ml). The mixture was refluxed for 2 h, then set aside overnight. The liquid was decanted from the salts, which were then washed several times with ether. The ether was taken off at atmosphere pressure, and the remaining volatile material distilled quickly at reduced pressure from the magnesium salts. Fractionation of the distillate gave ethylmethyl(*p*-methoxyphenyl)chlorosilane (20.1 g), b.p. 116°/5 mm, n_D^{20} 1.5173. (Found: hydrolysable Cl, 16.3. $C_{10}H_{15}ClOSi$ calcd.: Cl, 16.5 %.)

Methyl(p-bromophenyl)diethoxysilane

Methyltriethoxysilane (178 g, 1.0 mole) in ether (100 ml) was added rapidly to the mono-Grignard reagent from *p*-dibromobenzene (354 g, 1.5 mole) and magnesium (36.4 g, 1.5 g-atom) in ether (500 ml) and benzene (500 ml). The mixture was refluxed for 8 h, then treated with aqueous ammonium chloride. The ether layer was washed, dried (Na_2SO_4), and fractionated to give methyl(*p*-bromophenyl)diethoxysilane (121.5

* Unless otherwise indicated, all compounds for which analyses are given are new.

g, 42 %) b.p. 107°/3 mm, n_D^{25} 1.5016 (lit.[5] b.p. 87–88°/2–3 mm, n_D^{20} 1.4980). (Found: C, 45.8; H, 5.9. $C_{11}H_{17}BrO_2Si$ calcd.: C, 45.7; H, 5.9 %.)

Ethylmethyl(p-bromophenyl)ethoxysilane

(*a*). Methyl(*p*-bromophenyl)diethoxysilane (221 g, 0.77 mole) was added rapidly to the Grignard reagent from ethyl bromide (96.4 g, 0.88 mole), magnesium (21.5 g, 0.88 g-atom) and ether (500 ml), and the mixture was refluxed for 6 h and set aside at room temperature for 18 h. The ether was replaced by benzene, and the mixture was treated with aqueous ammonium chloride with cooling. The benzene layer was washed and dried (Na_2SO_4), the benzene was distilled off at atmospheric pressure, and the residue was fractionated at reduced pressure to give ethylmethyl(*p*-bromophenyl)-ethoxysilane (164 g, 78 %), b.p. 142°/18 mm, n_D^{20} 1.5168. (Found: C, 48.5; H, 6.4. $C_{11}H_{17}BrOSi$ calcd.: C, 48.35; H, 6.3 %.)

(*b*). *p*-Dibromobenzene (425 g, 1.80 mole) in ether (1 l) and benzene (500 ml) was added as quickly as possible to magnesium (43.8 g, 1.80 g-atom) in ether (200 ml), external cooling with alcohol/Drikold being used once reaction had started. The mixture was allowed to warm to room temperature and stirred for 1 h, during which time all the magnesium disappeared. Methyltriethoxysilane (267.4 g, 1.50 mole) in ether (100 ml) was added rapidly with ice-cooling, and the mixture was refluxed for 6 h. The Grignard reagent from ethyl bromide (196.2 g, 1.80 mole) magnesium (43.8 g, 1.80 g-atom) and ether (800 ml) was added rapidly with ice-cooling, and the mixture was then refluxed for 5 h. Treatment with aqueous ammonium chloride and working up as in (*a*) gave ethylmethyl(*p*-bromophenyl)ethoxysilane (269 g, 66 %), b.p. 120–122°/6 mm, n_D^{20} 1.5172.

Ethylmethyl(p-bromophenyl)fluorosilane

Ethylmethyl(*p*-bromophenyl)ethoxysilane was prepared in solution as described in (*b*) above, but 2 N hydrochloric acid was used subsequently in place of aqueous ammonium chloride. The organic layer was left for 1 h in contact with the acid, then separated, washed, and dried (Na_2SO_4). Removal of solvent left a high boiling residue, which was dissolved in ethanol (2 l) and treated with 40 % aqueous hydrofluoric acid (600 ml in total) at 60° during 6 h[4]. Working-up as for the *p*-chlorophenyl analogue, above, gave ethylmethyl(*p*-bromophenyl)fluorosilane (67 g, 18 %), b.p. 232°, n_D^{20} 1.5161. (Found: hydrolysable F, 7.6. $C_9H_{12}BrFSi$ calcd.: F, 7.7 %.)

Ethylmethyl(p-chlorophenyl)(p-methoxyphenyl)silane

To ethylmethyl(*p*-chlorophenyl)fluorosilane (36.5 g, 0.18 mole) in ether (100 ml) was added the organolithium reagent from *p*-bromoanisole (50.5 g, 0.27 mole), lithium (3.8 g, 0.54 g-atom) and ether (100 ml). The mixture was refluxed for 2 h, then treated with dilute acid and worked-up in the usual way to give, on fractionation, ethylmethyl(*p*-chlorophenyl)(*p*-methoxyphenyl)silane, (28 g), b.p. 156–157°/1–2 mm, n_D^{20} 1.5719. (Found: C, 66.1; H, 6.5. $C_{16}H_{19}ClOSi$ calcd.: C, 66.1; H, 6.6 %.)

Ethylmethyl(p-bromophenyl)(p-methoxyphenyl)silane

(*a*). n-Butyllithium (0.12 mole) in ether (200 ml) was added dropwise under nitrogen with ice-cooling and stirring to *p*-dibromobenzene (24.3 g, 0.10 mole) in ether (100 ml). The mixture was refluxed for 0.5 h, then cooled and added dropwise

under nitrogen to a stirred solution of ethylmethyl(*p*-bromophenyl)chlorosilane (20.1 g, 0.094 mole) in ether (50 ml). The mixture was refluxed for 2 h, and the ether was replaced by benzene (200 ml). Filtration, followed by fractionation of the filtrate gave ethylmethyl(*p*-bromophenyl)(*p*-methoxyphenyl)silane (16.3 g, 52 %), b.p. 168°/3 mm, n_D^{20} 1.5860. (Found: C, 57.5; H, 5.85. $C_{16}H_{19}BrOSi$ calcd.: C, 57.3; H, 5.7 %.)

(*b*). The organolithium reagent from *p*-bromoanisole (280.5 g, 1.50 mole), lithium (20.8 g, 3.0 g-atom) and ether (750 ml) was added to a stirred, cooled solution of ethylmethyl(*p*-bromophenyl)ethoxysilane (269 g, 0.98 mole) in ether (50 ml). The mixture was stirred for 1 h, kept at room temperature for 70 h, then added to crushed ice. Dilute hydrochloric acid was added until two clear layers separated, and the ethereal layer was washed, dried (Na_2SO_4), and fractionated to give ethylmethyl(*p*-bromophenyl)(*p*-methoxyphenyl)silane (227 g, 69 %), b.p. 192°/4 mm, n_D^{20} 1.5864.

p-[Ethylmethyl(p-methoxyphenyl)silyl]benzoic acid

(*a*). Ethylmethyl(*p*-bromophenyl)(*p*-methoxyphenyl)silane (189 g, 0.56 mole) was added dropwise under nitrogen to magnesium (15.0 g, 0.62 g-atom) in ether (300 ml), and the mixture was refluxed for 2 h then cooled, diluted with more ether (200 ml) and added to a slurry of ether and solid carbon dioxide. The mixture was allowed to come to room temperature, water was added, and the mixture was made just acid by cautious addition of dilute sulphuric acid. The ethereal layer was washed several times with water, then extracted with 1 N aqueous sodium hydroxide (2 × 1 l). Ether (1 l) was added to the aqueous extract, which was then, with occasional shaking, made just acid with 2 N sulphuric acid. The ethereal layer was washed and dried (Na_2SO_4) and the solvent was removed to leave a solid which on recrystallization from light petroleum (b.p. 60–80°) gave racemic *p*-[ethylmethyl(*p*-methoxyphenyl)silyl]benzoic acid (115.5 g, 68 %), m.p. 106–107°. Recrystallization from aqueous ethanol gave material of m.p. 106.5–107.0°. (Found: C, 67.9; H, 6.7. $C_{17}H_{20}O_3Si$ calcd.: C, 68.0; H, 6.7 %.)

(*b*). An attempt to make the acid from ethylmethyl(*p*-chlorophenyl)(*p*-methoxyphenyl)silane by lithiation in ether followed by carbonation gave only impure product in low yield.

Optical resolution of (±)-p-[ethylmethyl(p-methoxyphenyl)silyl]benzoic acid

A solution of the (±)-acid [120.5 g, 0.40 mole, in ethanol (250 ml)] was added to a solution of (—)-quinine (135 g, 0.42 mole) in ethanol (750 ml). The resulting salt was allowed to crystallize, washed with ethanol, then recrystallized 6 times from ethanol to constant m.p. 194–197° (decomp.), $[\alpha]_D^{25}$ —121.8° (*c*, 1.1 in chloroform). This diastereomeric salt (25 g) was placed in a separatory funnel with ether (400 ml) and water (300 ml) and 0.1 N hydrochloric acid was added with vigorous shaking until all the solid dissolved. The ethereal layer was washed and dried (Na_2SO_4) and the solvent was removed to leave a solid (12.3 g), which was recrystallized from aqueous ethanol to give (+)-*p*-[ethylmethyl(*p*-methoxyphenyl)silyl]benzoic acid, m.p. 106–107°, $[\alpha]_D^{25}$ +1.2° (*c*, 3.7 in benzene).

(±)- and (—)-{Methyl p-[ethylmethyl(p-methoxyphenyl)silyl]benzoate}

(*a*). The (±)-acid (18.4 g, 0.6 mole) was added in portions to an excess of diazomethane in ether (150 ml). Dilute hydrochloric acid was then added to ensure

complete removal of residual diazomethane, and the ethereal layer was washed with dilute aqueous sodium hydroxide and with water, and dried (Na_2SO_4). Removal of the solvent and fractionation gave (±)-{methyl *p*-[ethylmethyl(*p*-methoxyphenyl)silyl]-benzoate} (16.2 g, 84 %) b.p. 168°/0.05 mm, n_D^{25} 1.5632. (Found: C, 68.6; H, 6.95. $C_{18}H_{22}O_3Si$ calcd.: C, 68.8; H, 7.06 %.)

(*b*). Similar treatment of the (+)-acid (44 g) gave the (—)-ester (92 %), b.p. 183/0.1 mm, n_D^{25} 1.5632, $[\alpha]_D^{25}$ —0.16° (*c*, 40 in carbon tetrachloride).

(±)- and (+)-p-[Ethylmethyl(p-methoxyphenyl)silyl]benzyl alcohol

(*a*). The (±)-acid (36.8 g, 0.12 mole) in ether (200 mole) was refluxed with lithium aluminium hydride (7.0 g, 0.18 mole) in ether (400 ml) for 3 h. The usual working up, culminating in fractionation, gave (±)-*p*-[ethylmethyl(*p*-methoxyphenyl)silyl]benzyl alcohol (30 g, 85 %), b.p. 183°/0.02 mm, n_D^{25} 1.5737.

(*b*). From the (+)-acid was similarly obtained the (+)-alcohol, b.p. 167°/0.015 mm, n_D^{25} 1.5735, $[\alpha]_D^{25}$ +0.14 (*c*, 38 in benzene). (Found: C, 71.5; H, 7.8. $C_{17}H_{22}O_2Si$ calcd.: C, 71.3; H, 7.7 %.)

(±)- and (—)-p-[Ethylmethyl(p-methoxyphenyl)silyl]benzyl methyl ether

(*a*). (±)-*p*-[Ethylmethyl(*p*-methoxyphenyl)silyl]benzyl alcohol (47 g, 0.17 mole) in toluene (100 ml) was added to a vigorously stirred refluxing mixture of sodium (4.8 g, 0.21 g-atom) and toluene (200 ml). The mixture was stirred and refluxed for 1.5 h, heating was stopped, dimethyl sulphate (22.0 g, 0.18 mole) was added, and after the vigorous reaction had died away, refluxing was continued for 1.5 h. The mixture was cooled, and methanol (100 ml) was added to destroy residual sodium, followed by concentrated aqueous ammonia (250 ml) to destroy residual dimethyl sulphate. Addition of an excess of water, followed by ether extraction, and washing, drying (Na_2SO_4) and fractionation of the extract gave (±)-*p*-[ethylmethyl(*p*-methoxyphenyl)silyl]benzyl methyl ether (26.4 g, 52 %), b.p. 172°/0.07 mm, n_D^{25} 1.5563. (Found: C, 71.7; H, 8.0. $C_{18}H_{24}O_2Si$ calcd.: C, 71.9; H, 8.05 %.) The infrared spectrum showed that no residual hydroxyl groups were present.

(*b*). The (+)-alcohol (58 g, 0.20 mole) was refluxed with sodium (7.2 g, 0.30 g-atom) in xylene (100 ml) for 6 h with stirring, and the mixture was set aside overnight. Methyl iodide (50 g, 0.35 mole) was added, and the mixture was set aside at room temperature for 5 days, then worked up as above (but without addition of aqueous ammonia), to give the (—)-ether, b.p. 152–156°/0.04 mm, n_D^{25} 1.5565, $[\alpha]_D^{25}$ —0.19° (*c*, 40 in benzene), —0.25 (*c*, 40 in carbon tetrachloride).

Bromine cleavage of the methyl ester

(*a*). To (±)-{methyl *p*-[ethylmethyl(*p*-methoxyphenyl)silyl]benzoate} (12.6 g, 0.04 mole) in carbon tetrachloride (15 ml) was added bromine (5.6 g, 0.035 mole) in carbon tetrachloride (25 ml), with exclusion of light. After 30 min light petroleum (b.p. 60–80°) (50 ml) was added and the mixture was added rapidly to a solution of cyclohexylamine (7 ml) and isopropyl alcohol (14 ml) in light petroleum. The mixture was shaken vigorously, water (200 ml) was added and the mixture was again shaken. The organic layer was washed and dried (Na_2SO_4), and the solvent was removed under reduced pressure. The residual oil was taken up in light petroleum (300 ml) and the solution was filtered, washed several times with water, dried, and fractionated to give

(±)-[methyl *p*-(ethylmethylisopropoxysilyl)benzoate], (5.0 g), b.p. 152°/8–9 mm, n_D^{25} 1.4919. (Found: C, 63.2; H, 8.2: $C_{14}H_{22}O_3Si$ calcd.: C, 63.1; H, 8.3 %.)

(*b*). The methyl *p*-(ethylmethylisopropoxysilyl)benzoate obtained similarly from the (—)-benzoate had b.p. 152°/8 mm, $[\alpha]_D^{25}$ 0.00 ± 0.005° (*c*, 18 in carbon tetrachloride). The residue from the fractionation had a substantial optical activity, the source of which could not be identified.

Bromine cleavage of the methyl ether

To the (—)-methyl ether (10.2 g, 0.034 mole) in n-pentane (100 ml), bromine (4.9 g, 0.031 mole) in n-pentane (50 ml) was added dropwise during 7 h. A slurry of lithium aluminium hydride (1.5 g) in ether (100 ml) was added and the mixture was refluxed for 3 h. The pentane was replaced by cyclohexane, and acetone was added carefully to destroy residual lithium aluminium hydride. The cyclohexane solution was washed with hydrochloric acid and water, dried (Na_2SO_4), and concentrated to 20 ml to give a solution of positive rotation corresponding to $[\alpha]_D^{25}$ +0.12 ± 0.02°. Fractionation gave *p*-bromoanisole and inactive *p*-(ethylmethylsilyl)benzyl methyl ether (1.5 g), b.p. 124–128°/20 mm, n_D^{25} 1.4975. (Found: C, 67.9; H, 9.3. $C_{11}H_{18}OSi$ calcd.: C, 68.0; H, 9.3 %.) The optical activity remained in the high-boiling residues in the still-pot.

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SUMMARY

The acid *p*-[EtMe(*p*-$MeOC_6H_4$)Si]$C_6H_4CO_2H$ (RCO_2H) has been prepared, and resolved by fractional crystallization of its (—)-quinine salt to give the (+)-acid, $[\alpha]_D^{25}$ +1.2° (*c*, 3.7 in benzene). The (+)-acid, has been converted into the corresponding RCO_2Me, RCH_2OH, and RCH_2OMe compounds. Attempts to replace the *p*-methoxyphenyl group of the ester and ether by other groups have given only inactive products.

The preparations of several asymmetric organosilicon compounds are described.

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