Synthesis of ^{14}C-Labeled 1,1-Dichloro-2,2-bis(*p*-ethylphenyl)ethane (Perthane) and Related Products

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^{14}C-Labeled 1,1-dichloro-2,2-bis(*p*-ethylphenyl)ethane (Perthane) (I), 1-chloro-2,2-bis(*p*-ethylphenyl)ethylene (II), bis(*p*-ethylphenyl)acetic acid (III), and 4,4′-diethylbenzophenone (IV) were synthesized and characterized by electron capture gas chromatographic, nuclear magnetic, mass, and infrared spectral data.

When possible, DDT may be replaced in many insect control programs by persistent but biodegradable insecticides. Perthane [Q-137; 1,1-dichloro-2,2-bis(*p*-ethylphenyl)ethane] is a possible candidate, for it is biodegradable and of lower toxicity to warm-blooded animals than other chlorinated hydrocarbon insecticides but still very toxic to many species of insects (Negherbon, 1959).

Perthane is related to DDT [1,1,1-trichloro-2,2-bis(*p*-chlorophenyl)ethane] and is an analog of 1,1-dichloro-2,2-bis(*p*-chlorophenyl)ethane (DDD or TDE). It was initially assumed that Perthane metabolism might resemble that of DDD, 1,1-bis(4-chlorophenyl)-2,2,2-trichloroethanol (Kelthane), and 2,2-bis(*p*-methoxyphenyl)-1,1,1-trichloroethane (Methoxychlor). Therefore, ^{14}*C*-Perthane (I), 1-chloro-2,2-bis(*p*-ethylphenyl)ethylene (II), di(*p*-ethylphenyl)acetic acid (III), and 4,4′-diethylbenzophenone (IV) were synthesized (Figure 1).

EXPERIMENTAL

Melting points were determined by use of a Fisher-Johns melting point apparatus. Electron capture gas chromatograms (ecgc) were obtained by using a Micro-Tek Model DSS-171 type DPT gas chromatograph with a tritium source electron capture detector and Model TR Sargent recorder. Analyses were made using 2% SE 52 on 60–80 mesh, DMCS-treated, acid-washed firebrick in an 8-ft × $^1/_4$-in. o.d. glass column. The nitrogen carrier gas was passed through a molecular sieve and maintained at a flow rate of 90 ml/min. Temperature of the injection port, column, and detector were maintained at 195, 195, and 200 °C, respectively. The specific activity data were obtained by liquid scintillation using a Nuclear Chicago ambient liquid scintillation spectrometer, Model 6822. The nuclear magnetic resonance (nmr) spectra were determined on a Varian HA-100 instrument using tetramethylsilane (TMS) as the internal standard. The infrared spectra were recorded by a double-beam Perkin-Elmer Model 337 grating infrared spectrophotometer. The mass spectra were obtained using a Hitachi Perkin-Elmer RMU-6E double-focusing mass spectrometer.

Synthesis of ^{14}*C*-Perthane (I). Modifications of a method suggested by Lyman (1969) for the laboratory preparation of Perthane were used involving the reaction of ethylbenzene with dichloroacetaldehyde diethyl acetal catalyzed by concentrated sulfuric acid (Figure 1).

Dichloroacetaldehyde diethyl acetal (2.1 ml, 0.013 mol) was added with swirling to ^{14}*C*-ethylbenzene (ethyl-1-^{14}*C*: Mallinckrodt/Nuclear, St. Louis, specific activity 0.96 mCi/m*M*; 0.128 ml, 0.001 mol) and unlabeled ethylbenzene (3 ml, 0.025 mol) in a 50-ml Erlenmeyer flask, then sulfuric acid (6.6 ml, 0.12 mol) was added dropwise during 20 min, while the temperature was maintained below 12 °C. The total reaction time was 65 min. The reaction mixture was diluted with distilled water and extracted with redistilled pentane. After evaporation of the pentane, the residue crystallized yielding 3.5 g, 88% of theoretical.

Ecgc indicated that the ^{14}*C*-Perthane contained 74% *p,p′* isomer, 12% *o,p′* isomer, and 14% other impurities. Retention times of the *o,p′* and *p,p′* isomers were 10 min and 11 min 35 sec, respectively.

Two recrystallizations from hot ethanol gave 0.71 g of the *p,p′* isomer, 95% pure, with a melting point of 57–58 °C. Bleiberg (1961) gives 56–57 °C for pure Perthane.

Liquid scintillation analysis indicated the specific activity of the ^{14}*C*-Perthane to be 0.081 mCi/m*M*, while that of the purified *p,p′* isomer was 0.086 mCi/m*M*.

The nmr spectrum of the purified *p,p′* isomer of **I** consisted of τ 2.86 (m, 8 H, 2 × C_6H_4; J = 8 Hz), 3.72 (d, 1 H, $\mathrm{CHC}\mathit{H}\mathrm{Cl_2}$; J = 8 Hz), 5.55 (d, 1 H, $\mathrm{C}\mathit{H}\mathrm{CHCl_2}$; J = 8 Hz), 7.4 (q, 4 H, 2 × $\mathrm{C}\mathit{H}_2\mathrm{CH_3}$; J = 8 Hz), 8.8 (t, 6 H, 2 × $\mathrm{CH_2C}\mathit{H}_3$).

The mass spectrum was interpreted as *m/e* 306 (m + $^{35}Cl_2$), 223 (m − $CHCl_2$), 201 (m − $CH_3CH_2C_6H_4$), 105 (m + $CH_3CH_2C_6H_4$), 83 (m + $CHCl_2$), 29 (m + CH_3CH_2), 15 (m + CH_3).

The ir spectra of ^{14}*C*-Perthane and the purified ^{14}*C*-Perthane showed characteristic absorption at 690–750, 1090–1250, 1400–1550, and 2800–3100 cm^{-1}.

Synthesis of 1-Chloro-2,2-bis(*p*-ethylphenyl)ethylene (II). Unlabeled *p,p′* isomer of Perthane (25 g, 0.081 mol) was added to 150 ml of 5% KOH in 95% ethanol, and refluxed 3 hr (Figure 1). The reaction mixture was then diluted with 100 ml of distilled water and extracted with hexane. The hexane extract was filtered through anhydrous sodium sulfate and evaporated, leaving a clear, colorless oil yielding 21 g, 97% of theoretical.

The ecgc analysis indicated 96% purity with a retention time of 7 min and 40 sec.

The nmr spectrum consisted of τ 2.875 (m, 8 H, 2 × C_6H_4), 3.54 (s, 1 H, $\mathrm{C{=}C}\mathit{H}\mathrm{Cl}$), 7.36 (q, 4 H, 2 × $\mathrm{C}\mathit{H}_2\mathrm{CH_3}$; J = 8 Hz), 8.174 (t, 6 H; 2 × $\mathrm{CH_2C}\mathit{H}_3$).

The mass spectrum was interpreted as *m/e* 270 (m + ^{35}Cl), 165 (m − $CH_3CH_2C_6H_4$), 105 (m + $CH_3CH_2C_6H_4$), 29 (m + CH_3CH_2).

The ir showed characteristic absorption at 650–760, 1580–1625, and 2800–3100 cm^{-1}.

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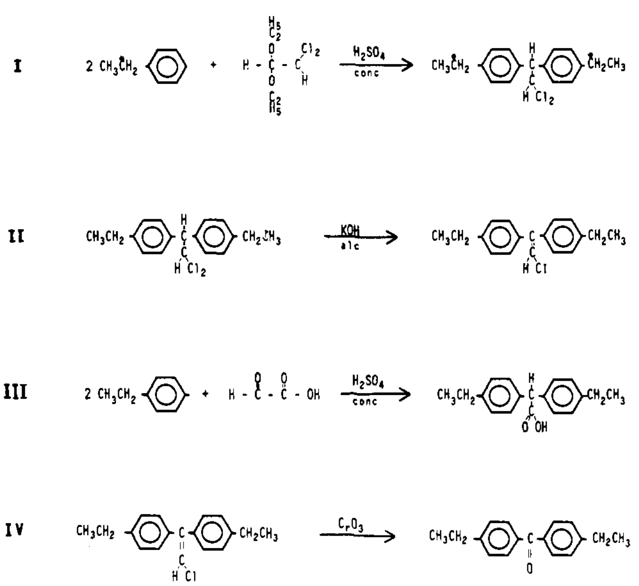

Figure 1. Synthesis of ^{14}C-labeled 1,1-dichloro-2,2-bis(*p*-ethylphenyl)ethane (Perthane) (I), 1-chloro-2,2-bis(*p*-ethylphenyl)ethylene (II), di(*p*-ethylphenyl) acetic acid (III), and 4,4′-diethylbenzophenone (IV)

Synthesis of Bis(*p*-ethylphenyl)acetic Acid (III). Modification of a method used by White and Sweeney (1945) for the synthesis of bis(*p*-chlorophenyl)acetic acid was used to synthesize **III.**

Glyoxylic acid monohydrate (3.0 g, 0.033 mol) was added to ethylbenzene (75 ml, 0.61 mol), cooled to 10°C, then sulfuric acid (15 ml, 0.28 mol) was added dropwise, followed by the addition of fuming sulfuric acid (1.5 ml, 0.028 mol). The reaction was continued for an additional hour (Figure 1). The mixture was then poured over 100 g of crushed ice, diluted with five volumes of distilled water, and extracted with redistilled diethyl ether. The ether extracts were then washed with 5% KOH and cooled to 10°C, acidified using concentrated HCl which precipitated **III**, yielding 7.0 g, 80% of theoretical.

To increase the sensitivity of ecgc the methyl ester of **III** was prepared by reacting **III** (10.0 mg in 2.0 ml of benzene) with excess diazomethane in diethyl ether, completing the reaction in 2 hr. The excess diazomethane and ether were evaporated, and the methylated **III** was analyzed by ecgc.

The retention times for the *o,p′* and *p,p′* isomers of **III** were 10 min 30 sec and 13 min 15 sec, while the retention times for the methylated **III** isomers were 9 min 25 sec and 10 min 15 sec.

The mass spectrum of **III** was interpreted as m/e 268 (m + $^{16}O_2$), 223 (m − COOH), 45 (m + COOH), 29 (m + CH_2CH_3), 15 (m + CH_3).

The ir spectrum showed characteristic absorption at 1725 and 2500–3500 cm^{-1}.

Synthesis of 4,4′-Diethylbenzophenone (IV). The synthesis of **IV** was accomplished by using Cristol and Haller's (1948) method for the synthesis of 4,4′-dichlorobenzophenone.

Chromium trioxide (9.0 g, 0.090 mol) was added in small amounts over a 2-hr period to a refluxing solution of **II** (10 g, 0.037 mol) in glacial acetic acid (170 ml). This mixture was refluxed for an additional 1.5 hr, cooled to room temperature, extracted with hexane, and evaporated, leaving a yellow oil 6.6 g, 75% of theoretical.

The retention time by ecgc analysis was 10 min 5 sec.

The nmr spectrum consisted of τ 2.56 (m, 8 H, 2 × C_6H_4; J = 8 Hz), 7.25 (q, 4 H, 2 × $C\mathit{H}_2CH_3$; J = 8 Hz), 8.75 (t, 6 H, 2 × $CH_2C\mathit{H}_3$; J = 8 Hz).

The mass spectrum was interpreted as m/e 238 (m + ^{16}O), 133 (m − $CH_3CH_2C_6H_4$), 105 (m + $CH_3CH_2C_6H_4$), 29 (m + CH_3CH_2), 28 (m + C=O), 15 (m + CH_3).

The infrared spectrum showed very characteristic absorption at 1550–1750 and 2800–3100 cm^{-1}.

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