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# A CONVENIENT SYNTHESIS OF 1,n-*BIS*-[4-CHLOROMETHYLPHENYL]ALKANES

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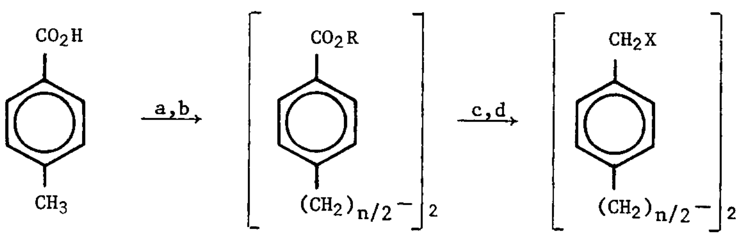
*Abstract: Both 1,12-bis-[4-chloromethylphenyl]dodecane and the tetradecane homolog are prepared from p-toluic acid and an α,ω-dibromoalkane in ~35% yield free from contamination by the non-parasubstituted isomers.*

Despite the usefulness of 1,n-*bis*-[4-chloromethylphenyl]alkanes (1d) as cross-linking agents in polymers[1] and as precursors to long-chain biradicals suitable for physical and synthetic studies, no general synthesis for this class of compounds is present in the literature. Our application, the attempted synthesis of catenanes and knotted paracyclophanes, requires intermediates of this structure with n = 12, 14, 18, or larger. Thus, we decided to explore various synthetic routes to these compounds. Unsatisfied by the yields and purity of products obtained by chloromethylation of the corresponding 1,n-diphenylalkanes,[2] and frustrated by attempts to use $Cu^{(I)}$ coupling,[3] we turned our attention to the Ivanov method[4] shown in the Scheme.

Scheme



1a,b 1c,d

(a) (i) 2 eq. LDA, (ii) $Br(CH_2)_{n-2}Br$; (1a) R = Li
(b) 1-BuOH,$H^+$; (1b) R = *n*-Bu
(c) LAH, work-up; (1c) X = OH
(d) $SOCl_2$; (1d) X = Cl

The key to this synthesis lies in the insolubility of the *bis*-benzoic acid salt (1a) which precipitates in almost quantitative yield (based on the α,ω-dibromoalkane). The insolubility of this diacid mitigates against forming the methyl or ethyl ester.[5] Only acidic 1-butanol was found to be effective in the esterification.

Specifically: A stirred solution of toluic acid (5.7 g, 0.042 mole) and diisopropylamine (8.5 g, 0.084 mole) in THF (200 ml) at 0° under $N_2$ is treated with *n*-BuLi (2.5 M in hexane) until a yellow color persists in the solution (1 equivalent or 16-20 ml). Following the procedure of Creger,[6] a stoichiometric quantity of *n*-BuLi (16.8 ml @ 2.5 M) is then added and stirred 2 hr at 0°.[7] Dropwise addition of $Br(CH_2)_{10}Br$ (6 g, 0.02 mole, vacuum distilled) in THF (50 ml) leads to the immediate formation of a yellow precipitate which is stirred at 0° for 2 hr and allowed to settle. The lithium salt thus obtained is collected by suction and used directly for esterification. A vigorously stirred suspension of the salt in 1-butanol is treated with 15 ml of $H_2SO_4$ conc. and the butanol distilled until the temperature rises to ~116° with addition of fresh butanol as needed. Most of the butanol is removed and both water (100 ml) and $CH_2Cl_2$ (100 ml) are added[8] and the organic layer is separated, washed with 5% $NaHCO_3$, $H_2O$ and dried. The butyl ester is obtained in 84-86% yield as a brown solid which can be purified to yield white crystals (m.p. 31.6-32.2°, n=12; 35.7-37.1°, n=14).[9] The crude residue is sufficiently pure for reduction by $LiAlH_4$ in ethyl ether.[10] Crystallization of the alcohol (1c) from ethyl ether and/or cyclohexane yields the diol (m.p. 104.5-105.5°, n=12; 105.8-107°, n=14) in 68-73% yield.[11] Chlorination via $SOCl_2$ (2 equivalents/mole of diol) in cyclohexane at r.t. affords the chloride in 60-70% yield based on the diol. Chromatography on Florisil® (FLORIDIN Co.) using benzene in petroleum ether (1:4) gives extremely pure dichloride (m.p. 86.2-86.5°, n=12; 88°, n=14)[12] although much material is lost (~50%) through adsorption on the solid support. The overall yield of (1d) is 33-35% based on the α,ω-dibromoalkane.

This method of preparing long-chain *bis*-benzyl derivatives is quite general. It works well even at 4 times the scale reported above.

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4. Ivanov, D.; Vassilev, G.; Panayotov, I. *Synthesis* 1975, 83-98.
5. Low yields (<50%/2 wks) of the diethyl ester can be obtained by standard procedures.
6. Creger, P.L. *J. Am. Chem. Soc.* 1970, 92, 1396-1397.
7. A significant amount of 1-[4-methylphenyl]-1-pentanone arising from direct reaction between *n*-BuLi and the Li salt of toluic acid forms but does not precipitate.
8. The crude butyl ester (1b) will crystallize with butanol encorporated if the water is not added.
9. 1,12-*bis*-[4-carbobutoxyphenyl]dodecane (1b); $^1H$ nmr ($CDCl_3$) δ: 7.94 and 7.22 (8H,AB), 4.30(4H,t), 2.64(4H,t), 1.64(8H,bm), 1.25(16H,s), 0.97(6H,t). Anal. Calc'd for $C_{34}H_{50}O_4$ C: 78.10; H: 9.64; O: 12.24%. Found C: 78.16; H: 9.73; O: 12.03%.
10. The crude butyl ester contains traces of 1,2-*bis*-[4-carbobutoxyphenyl]ethane.
11. 1,12-*bis*-[4-hydroxymethylphenyl]dodecane (1c); $^1H$ nmr ($CDCl_3$) δ: 7.26 and 7.17 (8H,AB), 4.64(4H,s), 2.59(4H,t), 1.62(6H,bm), 1.25(16H,s). Anal. Calc'd for $C_{26}H_{38}O_2$ C: 81.55; H: 10.01; O: 8.36%. Found C: 81.43; H: 10.11; O: 8.36%.
12. 1,12-*bis*-[4-chloromethylphenyl]dodecane (1d); $^1H$ nmr ($CDCl_3$) δ: 7.28 and 7.16 (8H,AB), 4.56(4H,s), 2.59(4H,t), 1.54(4H,bm), 1.25(16H,s). Anal. Calc'd for $C_{26}H_{36}Cl_2$ C: 74.38; H: 8.60; Cl: 16.90%. Found C: 74.54; H: 8.73; Cl: 16.72%.

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