The Preparation of o-, m-, *and* p-*Alkoxy- and -Phenoxy-methylbenzyl Chlorides.*

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[Reprint Order No. 5239.]

Several members of the above series of compounds, particularly in the *o*- and the *m*-series, were required for the investigation recorded in the following paper, and the comparative value of various synthetic routes has therefore been critically examined.

For the investigation described in the following paper several *o*-, *m*-, and *p*-alkoxy- and -phenoxy-methylbenzyl chlorides were required. The present paper affords a critical discussion of various syntheses of these compounds, more particularly in the *ortho*- and *meta*-series: their general properties are also described, except that their reaction with magnesium is reserved for the following paper.

o-Methoxymethylbenzyl chloride † (I) was prepared in a crude condition by Murahashi (*Sci. Papers Inst. Phys. Chem., Tokyo*, 1936, **30**, 180), who converted *o*-xylylene dibromide, $C_6H_4(CH_2Br)_2$, into *o*-xylylene dimethyl ether (II), which when treated with acetyl chloride and a trace of zinc chloride afforded the chloride (I), this selective demethylation being an application of that used earlier by Quelet (*Compt. rend.*, 1931, **192**, 1391) in the *para*-series. We find that the chloride (I) thus obtained and fractionally distilled, although of sufficiently high quality for use in certain syntheses, cannot be obtained pure, as it is always contaminated by unchanged ether (II) of almost identical b. p. This little known but potentially useful method of partial demethylation suffers generally from this difficulty

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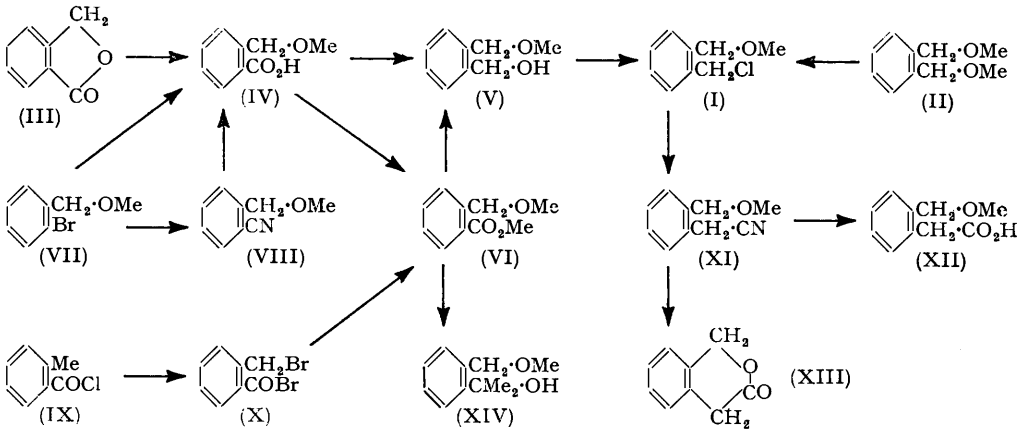
† This compound must be handled with great care. Not only is it strongly lachrymatory, but exposure to the vapour even at very high dilution at room temperature may cause visual derangement, headache, and gastric disturbance.

which could however probably be overcome by hydrolysing the chloride, *e.g.*, (I) to the alcohol (V), purifying the latter, and reconverting it into the chloride, or by the use of a higher alkyl homologue of the ether (II), the b. p. of which would differ from that of the chloride (as I). These possibilities were not, however, investigated in the present case in view of the following ready synthesis.

Phthalide (III) in alkaline solution, when treated with dimethyl sulphate, affords *o*-methoxymethylbenzoic acid (IV) which on reduction with lithium aluminium hydride gives *o*-methoxymethylbenzyl alcohol (V) : a higher yield of the alcohol is obtained if the acid is converted into the methyl ester (VI) before reduction. The alcohol (V) can then



be converted into the chloride (I) and the bromide (as I) by reaction with thionyl chloride and bromide respectively.

Alternative preparations of the acid (IV) and the ester (VI) have been examined. *o*-Bromobenzyl methyl ether (VII) (Holliman and Mann, *J.*, 1947, 1634) requires the " entrainment " method for adequate conversion into a Grignard reagent, and the latter on carboxylation gives the acid (IV) in only 13% yield. It is noteworthy that Mann and Millar (unpublished work) have found that this Grignard reagent also undergoes very little reaction with paraformaldehyde. This and related observations recorded below find a rational explanation on the assumption that the inertness is due to co-ordination of the oxygen to the magnesium atom, the reagent being stabilised by the five-membered ring so formed. The ether (VII), however, when heated with cuprous cyanide and pyridine at 215—225°, is converted into *o*-methoxymethylbenzonitrile (VIII) in 75% yield, and alkaline hydrolysis then furnishes the acid (IV) in 72% yield.

To prepare the ester (VI), *o*-toluoyl chloride (IX) was converted by the action of bromine into ω-bromo-*o*-toluoyl bromide (X) (Davies and Perkin, *J.*, 1922, **121**, 2202), which with sodium methoxide gave the ester (VI) in 80% yield. These alternative routes are however inferior to that from phthalide.

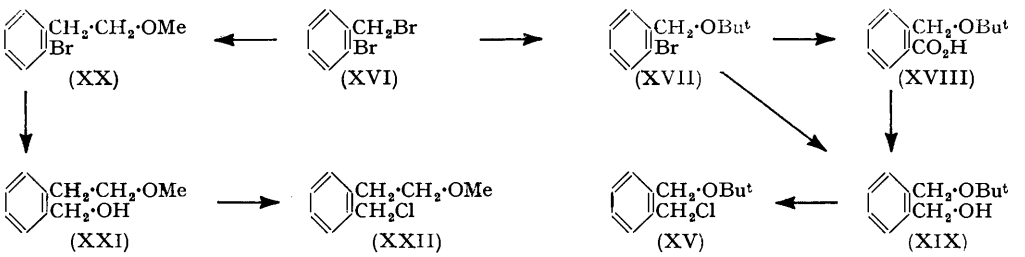
o-Methoxymethylbenzyl bromide (as I) is less stable than the chloride, and undergoes slight decomposition on distillation even at reduced pressure : for characterisation, the bromide and the chloride were heated with aqueous-ethanolic potassium cyanide to give the cyanide (XI), which on alkaline hydrolysis gave crystalline *o*-methoxymethylphenylacetic acid (XII) but on acidic hydrolysis readily gave 3 : 6-dihydro-4 : 5-benzo-2-pyrone (XIII).

The chloride (I) with sodium iodide in acetone readily gives the iodide, which could not be obtained pure by distillation, as this process caused considerable conversion into *o*-xylylene di-iodide.

2-*o*-Methoxymethylphenylpropan-2-ol (XIV), which was required for subsequent work, was prepared by the action of an excess of methylmagnesium iodide on the ester (VI) : it has considerable stability and can be distilled without decomposition.

To prepare *o*-phenoxymethylbenzyl chloride (as I), *o*-bromobenzyl bromide was

converted into *o*-bromobenzyl phenyl ether, the Grignard reagent from which on carboxylation gave *o*-phenoxymethylbenzoic acid (as IV) in 35% yield. This Grignard reagent, like that prepared from (VII), could also form an internal chelated complex, but the co-ordination of the oxygen of the phenoxyl group to the magnesium would probably be



weaker than that of the methoxyl group, and this would account for the higher yield of the phenoxy-acid (as IV). This acid was reduced as before to the alcohol (as V), and thence gave the required chloride.

For the investigation described in the following paper two types of homologues of the chloride (I) were required, in which the methyl group was replaced by (*a*) a *tert.*-butyl group (XV) and (*b*) a 2-methoxyethyl group (XXII).

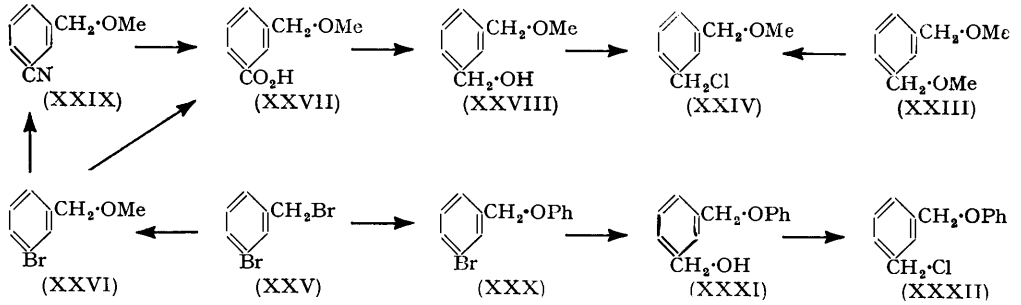
To prepare *o-tert.*-butoxymethylbenzyl chloride (XV), *o*-bromobenzyl bromide (XVI) was treated with sodium *tert.*-butoxide in the presence of benzene to give *o*-bromobenzyl *tert.*-butyl ether (XVII): in the absence of benzene, di-*o*-bromobenzyl ether was also formed. In the Grignard reagent from the bromo-ether (XVII) stabilisation by internal co-ordination was apparently largely prevented by the steric hindrance of the *tert.*-butyl group, for treatment with carbon dioxide gave *o-tert.*-butoxymethylbenzoic acid (XVIII) in 50% yield, and with formaldehyde gave *o-tert.*-butoxymethylbenzyl alcohol (XIX): the latter was also obtained by the lithium aluminium hydride reduction of the acid (XVIII). The action of thionyl chloride on the alcohol (XIX) then gave the required chloride (XV), an odourless non-lachrymatory liquid in marked contrast to (I).

The *o*-bromobenzyl bromide (XVI) was also converted by the method of Mann and Millar (*J.*, 1951, 2205) into 2-*o*-bromophenylethyl methyl ether (XX), the Grignard derivative of which, treated with formaldehyde, gave *o*-2-methoxyethylbenzyl alcohol (XXI) in 62% yield, and thence as usual the chloride (XXII). It seems significant also that carboxylation of this Grignard derivative gave *o*-2-methoxyethylbenzoic acid in 56% yield, for this Grignard reagent, if it underwent internal co-ordination, would form a six-membered and not a five-membered ring.

In the *para*-series, Quelet's reaction (*loc. cit.*), whereby *p*-xylylene dimethyl ether (as II) is treated with acetyl chloride containing zinc chloride, afforded a ready route to *p*-methoxymethylbenzyl chloride. Again, however, the chloride was contaminated with the unchanged dimethyl ether of almost identical b. p. Attempts to hydrolyse the chloride to the alcohol, in the hope that the latter could then be purified, proved unsatisfactory in this series. However the presence of the dimethyl ether did not affect our subsequent use of the chloride.

In the *meta*-series, two synthetic routes similar to those employed in the *ortho*-series proved of value. *m*-Xylylene dibromide was converted into the dimethyl ether (XXIII), which with acetyl chloride and zinc chloride gave *m*-methoxymethylbenzyl chloride (XXIV); this chloride, as in the two previous series, was not obtained pure but was nevertheless suitable for our subsequent purposes. To prepare the pure chloride (XXIV), however, *m*-bromobenzyl bromide (XXV) was converted into *m*-bromobenzyl methyl ether (XXVI), the Grignard reagent of which on carboxylation gave a 30% yield of *m*-methoxymethylbenzoic acid (XXVII) and thence the alcohol (XXVIII) and the chloride (XXIV). However, the alternative route *via* the nitrile (XXIX) again proved more efficient. It is significant that *m*-methoxymethylbenzyl chloride (XXIV) is an almost odourless liquid, apparently devoid of all the unpleasant physiological properties of the *o*-isomer (I).

The bromide (XXV) was similarly converted into *m*-bromobenzyl phenyl ether (XXX), the Grignard reagent of which with paraformaldehyde gave *m*-phenoxymethylbenzyl alcohol (XXXI), which in turn furnished the almost odourless chloride (XXXII). This



chloride was characterised by conversion into the nitrile and crystalline *m*-phenoxymethylphenylacetic acid.

Experimental

All compounds were colourless unless otherwise described. The yields recorded are those of products once distilled or recrystallised. The magnesium for Grignard reagents was activated as described by Holliman and Mann (*J.*, 1942, 739), but fine turnings were used to avoid the highly pyrophoric nature of the powdered metal. In addition, the " entrainment method " using ethyl bromide was employed when necessary to facilitate formation of the Grignard reagent.

o-*Methoxymethylbenzyl Chloride* (I).—The following preparation is based on Murahashi's directions (*loc. cit.*). Anhydrous zinc chloride (*ca.* 0·01 g.) was added to a mixture of the ether (II) (20 g.), acetyl chloride (6·6 g., 0·65 mol.), and carbon tetrachloride (16 c.c.). The stirred solution slowly became dark red as its temperature rose markedly. When cool, it was diluted with water and extracted with ether. Fractional distillation of the dried extract gave the lachrymatory chloride (I), b. p. 112—114°/13 mm. (14 g.). Analysis indicated that it contained *ca.* 55% of (I).

o-*Methoxymethylbenzoic Acid* (IV).—(*a*) Methyl sulphate (225 g., 6 mols.) was slowly added to a stirred chilled solution of phthalide (40 g.) in 20% aqueous sodium hydroxide (700 c.c.). After being stirred for 30 min., the mixture was heated on the water-bath to hydrolyse unchanged sulphate. The cold solution was acidified, and the precipitated acid (IV) collected and extracted with sodium carbonate solution; the extract, filtered from residual phthalide and then acidified, deposited the acid, m. p. 92—93°, sufficiently pure for further synthetic work.

(*b*) A solution of *o*-bromobenzyl methyl ether (VII) (60 g.) and ethyl bromide (32 g., 1 mol.) in ether (120 c.c.) was added to magnesium (15 g., 2·1 atoms) under ether (30 c.c.) so that gentle boiling ensued. The mixture was then boiled under reflux for 2 hr., cooled, and poured on an excess of solid carbon dioxide. After evaporation of the dioxide, the solution was treated with dilute hydrochloric acid, and extracted with more ether. The ether was then extracted with aqueous sodium carbonate, which on acidification deposited the acid (IV), m. p. 95—96° after recrystallisation from light petroleum (b. p. 80—100°) (Found: C, 65·3; H, 6·2. Calc. for $C_9H_{10}O_3$: C, 65·0; H, 6·0%) (6·5 g., 13%). Von Braun, Anton, and Weissbach (*Ber.*, 1930, **63**, 2861) give m. p. 93—94°.

Addition of copper sulphate to the sodium salt of (IV), each in aqueous solution, precipitated the *copper* salt, bluish-green crystals from ethanol–benzene (Found: C, 55·6; H, 4·9. $C_{18}H_{18}O_6Cu$ requires C, 55·0; H, 4·6%).

(*c*) A mixture of the ether (VII) (80 g.), cuprous cyanide (35·5 g.), and pyridine (55 c.c.) was heated at 215—225° for 15 hr., cooled, and poured into aqueous ammonia (*d* 0·88; 250 c.c.) diluted with water (250 c.c.). The mixture was then extracted with benzene and ether, and the united extracts were washed in turn with aqueous ammonia, dilute hydrochloric acid, and water. Distillation after drying gave *o*-methoxymethylbenzonitrile (VIII), b. p. 118—121°/15 mm. (44 g., 75%). Von Braun and Zobel (*Ber.*, 1923, **56**, 690) give b. p. 114°/14 mm.

Hydrolysis. (*a*) A mixture of the nitrile (VIII) (11 g.), ethanol (30 c.c.), and 10% aqueous sodium hydroxide (150 c.c.) was boiled under reflux for 2 hr., cooled, acidified, and extracted

with ether. The extract furnished the acid (IV), m. p. 95—96° alone and mixed, after recrystallisation (9·0 g., 72%).

A mixture of the nitrile (VIII) (3 g.), concentrated sulphuric acid (10 c.c.), and water (6 c.c.) was boiled under reflux for 30 min., cooled, and diluted with water. The precipitated crystalline phthalide (III) had m. p. 72·5—73° alone and mixed, after recrystallisation from light petroleum (b. p. 60—80°).

Methyl o-*Methoxymethylbenzoate* (VI).—(*a*) This ester, b. p. 126°/15 mm., was readily obtained by the interaction of the silver salt of the acid and methyl iodide. (*b*) ω-Bromo-*o*-toluoyl bromide (X) (65 g.) was gradually added to a chilled solution obtained by the interaction of sodium (12 g.) and methanol (350 c.c.). The mixture was then boiled under reflux for 1 hr., concentrated, cooled, poured into water, and extracted with ether. Distillation gave the almost odourless ester (VI) (28 g., 80%), b. p. 124—125°/15 mm., the value quoted by Staudinger and Mächling (*Ber.*, 1916, **49**, 1976).

o-*Methoxymethylbenzyl Alcohol* (V).—(*a*) A solution of the acid (IV) (33 g.) in ether (300 c.c.) was added to a stirred suspension of lithium aluminium hydride (12 g.) in ether (360 c.c.) so that steady boiling ensued. The mixture was then stirred for 30 min., cooled, mixed with ice-water, and finally shaken with dilute sulphuric acid. The dried ethereal layer on distillation gave the oily *alcohol* (V) (20 g., 66%), b. p. 132°/13 mm., 154—156°/35 mm. (Found: C, 71·2; H, 7·9. $C_9H_{12}O_2$ requires C, 71·0; H, 7·8%).

(*b*) The alcohol (12·1 g., 80%) was similarly obtained by the reduction of the ester (VI) (17 g.) with the hydride (3 g.) in ether (80 c.c. and 140 c.c. respectively).

o-*Methoxymethylbenzyl Chloride* (I).—A solution of thionyl chloride (16·2 g.) in chloroform (36 c.c.) was added during 1 hr. to a chilled stirred solution of the alcohol (V) (20·8 g.) and pyridine (10·8 g.) in chloroform (85 c.c.), and the mixture was then boiled under reflux for 2 hr. The cold solution was added to much water and extracted with ether; the extract was washed repeatedly with water and then with a 1% aqueous solution of sodium hydroxide. Fractional distillation gave the mobile *chloride* (I) (19·3 g., 82%), b. p. 114—116°/13 mm., 144°/42 mm. (Found: C, 63·7; H, 6·3. $C_9H_{11}OCl$ requires C, 63·4; H, 6·4%).

o-Methoxymethylbenzyl bromide (as I), b. p. 126—127°/16 mm., was similarly prepared in 63% yield by using freshly distilled thionyl bromide (Mayes and Partington, *J.*, 1926, 2594), as an intensely lachrymatory, colourless liquid, the vapour of which caused marked irritation of the skin. Since however it underwent partial decomposition when distilled even under reduced pressure, it was characterised by treatment with potassium cyanide in hot aqueous ethanol, whereby the nitrile (XI), b. p. 155—156°/17 mm., was obtained in 70% yield (Found: C, 74·3; H, 6·6; N, 8·6. Calc. for $C_{10}H_{11}ON$: C, 74·5; H, 6·8; N, 8·7%).

Hydrolysis of the Nitrile (XI).—(*a*) The nitrile (2·2 g.), when heated with ethanol (5 c.c.) and 10% aqueous sodium hydroxide (35 c.c.), followed by acidification, gave the acid (XII), m. p. 52—53° after crystallisation from light petroleum (b. p. 60—80°) (Found: C, 66·6; H, 6·5. Calc. for $C_{10}H_{12}O_3$: C, 66·7; H, 6·6%). Murahashi (*loc. cit.*) gives b. p. 151—153°/17 mm. and m. p. 52—54° for (XI) and (XII) respectively.

(*b*) The mixture obtained by the addition of the nitrile (10 g.) to concentrated sulphuric acid (100 c.c.) previously diluted with water (400 c.c.) was boiled under reflux with stirring for 6 hr. and then further diluted with water and cooled, whereupon 3 : 6-dihydro-4 : 5-benzo-2-pyrone (XIII) crystallised (8 g., 87%); it had m. p. 81—82° after recrystallisation from water (Found: C, 72·8; H, 5·2. Calc. for $C_9H_8O_2$: C, 73·0; H, 5·4%). The use of more concentrated sulphuric acid gave an alkali-soluble resin as the sole product.

In an attempt to prepare the iodide (as I), the chloride (5 g.) was added to a solution of sodium iodide (4·5 g.) in acetone (30 c.c.). The red solution was set aside overnight, and when filtered and distilled gave the crude iodide as a yellow lachrymatory oil, b. p. 89—93°/0·3 mm. (5·4 g.), which readily became red. Redistillation caused partial decomposition, and gave a residue of *o*-xylylene di-iodide, m. p. 108—109° (alone and mixed) after crystallisation from ethanol (Found: C, 27·4; H, 2·9. Calc. for $C_8H_8I_2$: C, 27·0; H, 2·2%).

2-o-*Methoxymethylphenylpropan*-2-*ol* (XIV).—A solution of methyl *o*-methoxymethylbenzoate (VI) (8·2 g.) in ether was added slowly to the cooled stirred Grignard reagent prepared from methyl iodide (12·7 g.) and magnesium (2·2 g.) in ether (35 c.c.). The product was set aside overnight, cooled, and hydrolysed with dilute sulphuric acid. The oil obtained by the evaporation of the ether layer was added to a solution of potassium hydroxide (2·4 g.) in methanol (20 c.c.), which was boiled for 15 min., poured into water, and extracted with ether. Distillation of the extract gave the *alcohol* (XIV) (5·7 g., 70%), b. p. 74—76°/0·1 mm., 92—94°/0·4 mm. (Found: C, 73·1; H, 8·5. $C_{11}H_{16}O_2$ requires C, 73·3; H, 8·9%).

o-*Bromobenzyl Phenyl Ether* (*as* VII).—Phenol (19 g.) and then molten *o*-bromobenzyl bromide (50 g.) were added with stirring to the solution from sodium (4·7 g.) and ethanol (50 c.c.), which was then boiled under reflux, concentrated, diluted with water, and extracted with ether. Distillation of the dried extract gave the ether (42 g., 83%), b. p. 187—188°/16 mm., m. p. 40° (Found: C, 58·95; H, 4·5. Calc. for $C_{13}H_{11}OBr$: C, 59·3; H, 4·2%). Huston, Neeley, Fayerweather, D'Arcy, Maxfield, Ballard, and Lewis (*J. Amer. Chem. Soc.*, 1933, **55**, 2146) give m. p. 34—36°.

o-*Phenoxymethylbenzoic Acid* (*as* IV).—A Grignard reagent was prepared by adding a solution of the above ether (30 g.) and ethyl bromide (6 g.) in ether (60 c.c.) to activated magnesium (4·5 g.) under ether (10 c.c.). It was boiled under reflux for 2 hr., cooled, and carboxylated as usual. It yielded the above acid, m. p. 123—124° after crystallisation from light petroleum (b. p. 100—120°), in 7·7 g. (35%) yield. Oppé (*Ber.*, 1913, **46**, 1091) gives m. p. 126°.

o-*Phenoxymethylbenzyl Alcohol* (*as* V).—The above acid, when reduced with lithium aluminium hydride, gave the alcohol, b. p. 222—224°/21 mm., m. p. 49—50°, in 78% yield. Von Braun and Zobel (*Ber.*, 1923, **56**, 2142) give b. p. 216°/15 mm., m. p. 50°.

o-*Phenoxymethylbenzyl Chloride* (*as* I).—A solution of thionyl chloride (2·35 g.) in chloroform (7 c.c.) was added to an ice-cold solution of the above alcohol (4·2 g.) and pyridine (1·55 g.) in chloroform (15 c.c.). The normal treatment then gave the *chloride* (2·7 g., 60%) as an oil, b. p. 206—209°/23 mm., m. p. 38—39·5° after crystallisation from light petroleum (b. p. 40—60°) (Found: C, 72·4; H, 5·8. $C_{14}H_{13}OCl$ requires C, 72·3; H, 5·6%).

o-*Bromobenzyl* tert.-*Butyl Ether* (XVII).—Sodium wire (6 g.) was brought into reaction with a mixture of *tert.*-butanol (16·5 g.) and benzene (100 c.c.) by boiling the stirred mixture under reflux for 15 hr. A solution of *o*-bromobenzyl bromide (XVI) (55 g.) in benzene (100 c.c.) was then added and the boiling continued for 48 hr. Filtration followed by distillation gave the ether (XVII), b. p. 127—128°/16 mm., but analysis showed it was always contaminated with unchanged bromide (XVI), which has b. p. 127—128°/16 mm. When, to avoid this difficulty, an excess of sodium *tert.*-butoxide in the absence of benzene was used, *di-o-bromobenzyl ether*, m. p. 66—67° after recrystallisation from ethanol, was formed as a by-product (Found: C, 47·0; H, 3·3. $C_{14}H_{12}OBr_2$ requires C, 47·2; H, 3·3%).

o-tert.-*Butoxymethylbenzoic Acid* (XVIII).—The Grignard reagent, prepared by the action of a mixture of the ether (XVII) (20 g.) and ethyl bromide on magnesium, when carboxylated as usual gave o-tert.-*butoxymethylbenzoic acid* (10·6 g., 50%), m. p. 86—87° after crystallisation from light petroleum (b. p. 60—80°) (Found: C, 69·4; H, 7·9. $C_{12}H_{16}O_3$ requires C, 69·2; H, 7·7%).

o-tert.-*Butoxymethylbenzyl Alcohol* (XIX).—(*a*) The Grignard reagent prepared from the ether (XVII) but on twice the above scale was treated with paraformaldehyde, and the product, when worked up as usual, gave the alcohol (XIX), b. p. 94—97°/0·2 mm. (10·5 g., 40%), with a fore-run of benzyl *tert.*-butyl ether, b. p. 92—94°/15 mm.

(*b*) The acid (XVIII), when reduced as usual with lithium aluminium hydride, gave the alcohol (XIX), b. p. 160—162°/21 mm., in 58% yield.

The alcohol even when very carefully distilled underwent some decomposition and thus could not be obtained pure (Found: C, 72·6; H, 7·8. Calc. for $C_{12}H_{18}O_2$: C, 74·2; H, 9·2%); incautious heating may cause almost total decomposition with copious evolution of fumes.

o-tert.-*Butoxymethylbenzyl Chloride* (XV).—This *chloride*, prepared in the usual way by the action of thionyl chloride (5 g.) in chloroform (12 c.c.) on the alcohol (XIX) (8·3 g.) and pyridine (3·3 g.) in chloroform (30 c.c.), when cautiously distilled once was obtained as a mobile liquid (5·9 g., 67%), b. p. 69—73°/0·2 mm. (Found: C, 66·8; H, 7·5. $C_{12}H_{17}OCl$ requires C, 67·7; H, 8·0%).

o-2-*Methoxyethylbenzyl Alcohol* (XXI).—The Grignard reagent, prepared by the action of the methyl ether (XX) (13·5 g.) and ethyl bromide (3·4 g.) in ether (50 c.c.) on magnesium (3·6 g.) in the usual way, was treated with paraformaldehyde (2·8 g.) and then boiled under reflux for 16 hr., cooled, and hydrolysed with dilute sulphuric acid. Distillation gave a fore-run of methyl phenethyl ether, b. p. 88—95°/21 mm., followed by the odourless *alcohol* (6·5 g., 62%) (XXI), b. p. 162—166°/23 mm. on refractionation (Found: C, 72·2; H, 8·7. $C_{10}H_{14}O_2$ requires C, 72·3; H, 8·4%).

The above Grignard reagent, when cautiously treated with solid carbon dioxide, gave o-2-*methoxyethylbenzoic acid* (56%), b. p. 131—133°/0·3 mm., m. p. 39—41° after recrystallisation from light petroleum (b. p. 40—60°) (Found: C, 66·7; H, 6·5. $C_{10}H_{12}O_3$ requires C, 66·7; H, 6·6%).

o-2-*Methoxyethylbenzyl Chloride* (XXII).—This *chloride*, prepared by the action of thionyl chloride (3·8 g.) in chloroform (10 c.c.) on a mixture of the alcohol (XXI) (5·6 g.) and pyridine

(2·6 g.) in chloroform (25 c.c.), formed an almost odourless mobile liquid (4·4 g., 75%), b. p. 134—136°/17 mm. (Found : C, 65·7; H, 7·4. $C_{10}H_{13}OCl$ requires C, 65·2; H, 7·2%).

p-*Methoxymethylbenzyl Chloride*.—This was prepared from *p*-xylylene dimethyl ether precisely as described for (I), and obtained after fractional distillation as a liquid, b. p. 132—134°/20 mm. Analysis showed that it contained 76% of the chloride.

m-*Xylylene Dimethyl Ether* (XXIII).—*m*-Xylylene dibromide was prepared by Atkinson and Thorpe's method (*J.*, 1907, **91**, 1196). The dibromide (32 g.), when added to a solution obtained from sodium (6·4 g.) and methanol (220 c.c.), gave the *ether* (17·2 g., 86%), an odourless liquid b. p. 128—129°/23 mm. (Found : C, 72·5; H, 8·7. $C_{10}H_{14}O_2$ requires C, 72·3; H, 8·4%).

m-*Bromobenzyl Bromide* (XXV).—*m*-Bromotoluene (41 g.) was maintained at 135—140° whilst bromine (33 g., 11 c.c.) was slowly added without stirring through a tube leading to the bottom of the liquid (cf. Holliman and Mann, *J.*, 1942, 739 : Lyon, Mann, and Cookson, *J.*, 1947, 668). Distillation gave the bromide (XXV) (37 g., 74%), b. p. 132—134°/17 mm., which solidified and had m. p. 36—38°. Jackson (*Ber.*, 1876, **9**, 932) gives m. p. 41°.

m-*Bromobenzyl Methyl Ether* (XXVI).—The bromide (XXV) (37 g.) was added to a solution obtained from sodium (3·8 g.) and methanol (120 c.c.), which was then boiled under reflux for 1 hr. When worked up as usual, the *ether* (XXVI) was obtained as a liquid (24·7 g., 82%), b. p. 117—118°/21 mm., having a very pleasant odour (Found : C, 47·7; H, 4·8. C_8H_9OBr requires C, 47·7; H, 4·5%).

m-*Methoxymethylbenzonitrile* (XXIX).—A mixture of the ether (XXVI) (67 g.), cuprous cyanide (30 g.), and dry pyridine (50 c.c.) was heated at 215—225° for 16 hr. Working up as described for (VIII) gave the *nitrile* (37·5 g., 76%), a highly refractive liquid, b. p. 123—126°/11 mm., having a faint benzonitrile-like odour (Found : C, 73·2; H, 6·0; N, 9·6. C_9H_9ON requires C, 73·4; H, 6·1; N, 9·5%).

m-*Methoxymethylbenzoic Acid* (XXVII).—(*a*) The Grignard reagent, prepared by the action of the ether (XXVI) (22 g.) and ethyl bromide (6 g.) in ether (60 c.c.) on magnesium (4·2 g.) under ether (5 c.c.), gave on carboxylation the *acid* (XXVII) (5·1 g., 30%) as a colourless liquid, b. p. 120—126°/0·1 mm., which solidified, and when recrystallised from light petroleum (b. p. 60—80°) had m. p. 63—64° (Found : C, 65·0; H, 6·2. $C_9H_{10}O_3$ requires C, 65·0; H, 6·0%).

(*b*) A mixture of the nitrile (XXIX) (17·5 g.), ethanol (45 c.c.), and 10% aqueous sodium hydroxide (220 c.c.) was boiled under reflux for 2 hr. The acid (XXVII), isolated as usual and recrystallised as before, had m. p. 64—66°, alone and mixed; the yield was 16·4 g. (85%).

m-*Methoxymethylbenzyl Alcohol* (XXVIII).—A solution of the acid (XXVII) (5 g.) in ether (50 c.c.) was reduced with lithium aluminium hydride (1·5 g.) in ether (60 c.c.). The product when worked up gave the alcohol (XXVIII), b. p. 156°/20 mm. (Found : C, 69·7; H, 7·8. Calc. for $C_9H_{12}O_2$: C, 71·0; H, 7·8%) (2·35 g., 51%). Since low carbon values were obtained even after repeated refractionation, the alcohol was converted into the 1-*naphthylurethane*, m. p. 89—90° after recrystallisation from light petroleum (b. p. 80—100°) (Found : N, 4·5. $C_{20}H_{19}O_3N$ requires N, 4·4%).

In view of the high yield of the acid (XXVII) from the nitrile (XXIX), in contrast to the low yield from the Grignard reagent (cf. *a* above), the action of formaldehyde on this reagent to give the alcohol (XXVIII) was not investigated.

m-*Methoxymethylbenzyl Chloride* (XXIV).—(*a*) Addition of thionyl chloride (1·85 g.) in chloroform (5 c.c.) to a solution of the alcohol (XXVIII) (2·35 g.) and pyridine (1·15 g.) in chloroform (12 c.c.), followed by the usual working up, gave the *chloride* (1·9 g., 74%), b. p. 122—124°/13 mm. (Found : C, 63·2; H, 6·3. $C_9H_{11}OCl$ requires C, 63·4; H, 6·4%).

(*b*) The crude chloride (XXIV) was also prepared as described for (I), zinc chloride (*ca.* 0·01 g.) being added to a solution of *m*-xylylene dimethyl ether (XXIII) (8·5 g.) and acetyl chloride (3·5 g.) in carbon tetrachloride (6 c.c.), which became very hot. Distillation of the extract gave a sample of the chloride (6·7 g.), b. p. 126—127°/17 mm., the analysis of which indicated the presence of *ca.* 16% of unchanged ether (Found : C, 64·9; H, 7·4%).

m-*Bromobenzyl Phenyl Ether* (XXX).—This ether, prepared from the bromide (XXV) precisely as the *o*-isomer, was isolated as a liquid, b. p. 198—201°/20 mm., which readily solidified and then had m. p. 36—38° (Found : C, 59·6; H, 4·5. Calc. for $C_{13}H_{11}OBr$: C, 59·2; H, 4·2%). Huston *et al.* (*loc. cit.*) give m. p. 36—37°.

m-*Phenoxymethylbenzyl Alcohol* (XXXI).—The Grignard reagent prepared by the action of the ether (XXX) (32 g.) and ethyl bromide (6·7 g.) in ether (70 c.c.) on magnesium (4·8 g.) under ether (5 c.c.) was treated with paraformaldehyde (5·8 g.), and the mixture was boiled under reflux for 12 hr. Working up as usual gave the *alcohol* (XXXI) as an oil, b. p. 220—228°/18 mm., which solidified on cooling (14·1 g., 54%). Recrystallisation from light petroleum (b. p. 60—

80°) gave leaflets, m. p. 57—58° (Found: C, 78·6; H, 6·7. $C_{14}H_{14}O_2$ requires C, 78·5; H, 6·5%). A considerable earlier fraction, b. p. 158—180°/19 mm., was presumably crude benzyl phenyl ether.

m-*Phenoxymethylbenzoic Acid.*—The Grignard reagent, prepared as above, on carboxylation gave this *acid*, m. p. 116—117° after recrystallisation from light petroleum (b. p. 80—100°) (Found: C, 73·3; H, 5·6. $C_{14}H_{12}O_3$ requires C, 73·6; H, 5·3%), in 40% yield.

m-*Phenoxymethylbenzyl Chloride* (XXXII).—This chloride, prepared by the action of thionyl chloride (7·6 g.) in chloroform on a solution of the alcohol (XXXI) (13·9 g.) and pyridine (5·1 g.) in chloroform (45 c.c.), was isolated as an oil (12·7 g., 86%), b. p. 160—161°/0·3 mm., 211—214°/21 mm., which however underwent slight decomposition on fractionation and could not be obtained pure (Found: C, 71·3; H, 5·6. Calc. for $C_{14}H_{13}OCl$: C, 72·3; H, 5·6%). It was converted into the *nitrile*, b. p. 160—162°/0·2 mm., which readily solidified and when recrystallised from light petroleum (b. p. 60—80°) had m. p. 47—48° (Found: C, 80·7; H, 5·5; N, 6·0. $C_{15}H_{13}ON$ requires C, 80·7; H, 5·8; N, 6·2%). Hydrolysis with aqueous-ethanolic sodium hydroxide furnished m-*phenoxymethylphenylacetic acid*, leaflets (from ethanol), m. p. 113—114° (Found: C, 74·3; H, 5·8. $C_{15}H_{14}O_3$ requires C, 74·3; H, 5·7%), in 80% yield.

A Rouse Ball Research Studentship, awarded by Trinity College, is gratefully acknowledged (F. H. C. S.).

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