Tetrahedron. Vol. 25, pp. 2487 to 2492. Pergamon Press 1969. Printed in Great Britain

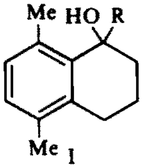
HYDROGEN ABSTRACTION FROM METHYL GROUPS ATTACHED TO AN AROMATIC RING

K. M. BAKER and B. R. DAVIS
Department of Chemistry, University of Auckland, New Zealand

(*Received in the UK* 17 *December* 1968; *Accepted for publication* 17 *January* 1969)

Abstract—The formation of cyclic ethers from methyl groups attached to an aromatic ring *via* decomposition of the hypobromite of a *tertiary* benzylic alcohol in an *ortho* position is described. The reaction occurs only for tertiary hydroxyl groups, and groups other than methyl are not functionalized.

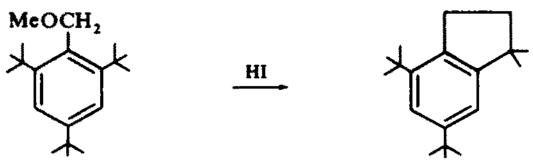
THE ABSTRACTION of hydrogen from non-activated carbon atoms in an aliphatic system is a well known reaction. A variety of routes are thus available for the functionalization of saturated carbon atoms.[1–4] We report experiments leading to formation of cyclic ethers from methyl groups attached to an aromatic ring using a benzylic hydroxy-group in an *ortho* position in a system of the type I (R = Me).



I

Several methods of using groups attached to an aromatic ring to functionalize other groups attached to the ring are known, e.g. photolysis of *ortho* methyl benzophenones:[5]

and the decomposition of *ortho-tertbutyl* benzyl alcohols or their methyl ethers with hydroiodic acid:[6]

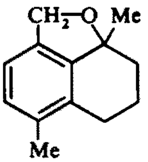


Initially attempts were made to carry out the hydrogen abstraction using either photolysis[7] or thermal activation[1] of the alkoxy lead salt formed by reaction of the alcohol with lead tetraacetate. However side reactions tended to predominate and a method developed by Sneen and Matheny[3,4] was utilized. In this reaction, the alcohol is reacted with bromine and yellow mercuric oxide to form the hypobromite, which is decomposed with silver oxide, to give a cyclic ether.

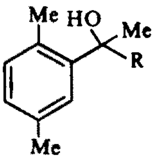
Sneen and Matheny have applied their reaction only to aliphatic systems and it was therefore decided to attempt this reaction on systems of the type I described above since the reaction was found to be ionic[4] rather than radical as is the case with the nitrite or lead tetraacetate reactions.[1, 2] Competing reactions might thus take a different course.

Treatment of 1,5,8-trimethyl-1,2,3,4-tetrahydronaphth-1-ol (I, R = Me) with bromine and yellow mercuric oxide in the dark for 5 min, followed by decomposition of the hypobromite with silver oxide gave, after ½ hr, the cyclic ether, 5,8a-dimethyl-6,7,8,8a-tetrahydro-2H-naphtha(1,8-bc)furan (II) in 86% yield. The working-up conditions for the reaction were critical. It was essential that after filtration of the metallic salts, the solution was evaporated to dryness without the application of heat, otherwise decomposition to polymeric products occurred. Evaporation of the solvent in the cold gave the product as a slurry with silver bromide, from which extraction with light petroleum or other suitable solvent gave a clean product.

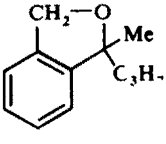
Similar treatment of the benzylic alcohol, 2-(2′,5′-xylenyl)pentan-2-ol (III, R = Pr^n) gave the cyclic ether, 1,6-dimethyl-1-propyl-1-3-dihydrobenzo(*c*)furan (IV) in 30% yield, as well as the alkenes, 2-(2′,5′-xylenyl)pent-1-ene (V) (20%) and 2-(2′,5′-xylenyl)-pent-2-ene (VI) (50%).

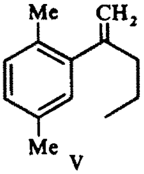


II

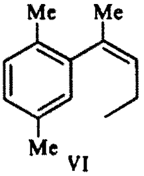


III

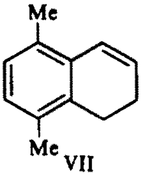




V

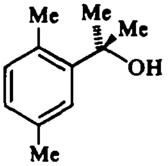


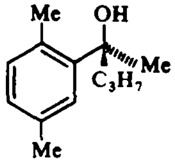
VI



VII

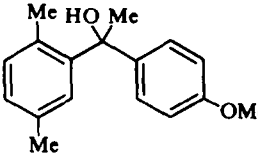
Attempts to carry out the cyclisation reaction on a number of similar systems were unsuccessful. Treatment of the secondary alcohol 5,8-dimethyl-1,2,3,4-tetrahydronaphth-1-ol (I, R = H) with bromine, mercuric oxide and silver oxide gave only 5,8-dimethyl-1, 2-dihydronaphthalene (VII) whose identity was confirmed by comparison of its spectral data with that of authentic material. Similar treatment of the tertiary alcohol 2-(2′,5′-xylenyl)propan-2-ol (III, R = Me) gave no reaction, in contrast to the pentan-2-ol, and starting material was recovered, possibly because the hydroxy-group is in an unfavourable position for a six-membered transition state to be formed, i.e. the preferred conformations of (III, R = Me) and (III, R = Pr^n) are as follows:

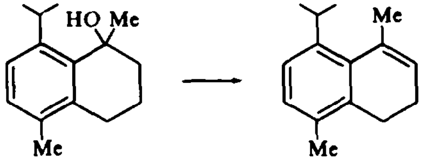


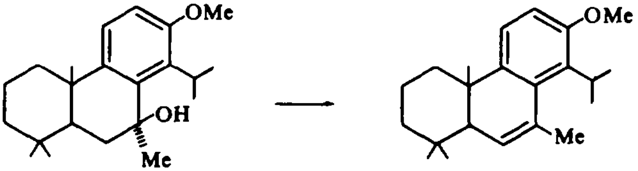


Treatment of the alcohol 1-(*p*-anisyl)-1-(2′,5′-xylenyl)ethanol (VIII) gave only the products of fragmentation, 2,5-dimethyl-acetophenone, and anisole.

The possibility of functionalizing isopropyl groups was also examined. Preparation and treatment of the compounds 1,5-dimethyl-8-*iso*propyl-1,2,3,4-tetrahydronaphth-1-ol (IX) and 7-hydroxy-7-methyl-totaryl methyl ether (XI) with bromine, mercuric oxide, and silver oxide gave only the products of dehydration X and XII.

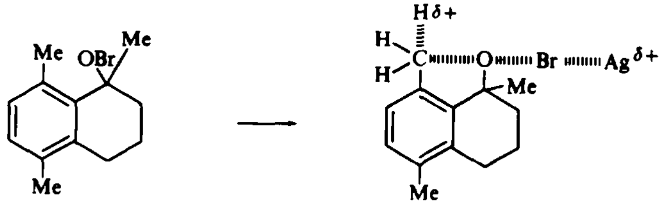

VIII


IX X


XI XII

The functionalizations of the methyl groups of I (R = Me) and III (R = Pr^n) are the first recorded examples of hydrogen abstraction from aromatic methyl groups.

The mechanism as formulated by Sneen and Matheny[3,4] would involve formation of an intermediate of the type:



This intermediate is similar to that proposed by Barclay and Macdonald[6] for the hydrogen abstraction from *tert*butyl groups attached to an aromatic ring. The formation of silver bromide is further evidence that the reaction proceeds through such an intermediate where the proposed function of the silver ion is to remove the bromine from the hypobromite as the anion and leave a positive charge on oxygen.

It appears that the CH$\cdots$O distance between the interacting groups is also significant in this type of reaction, as is the case for the methods such as the hypoiodite and lead tetraacetate reactions,[1] and nitrite photolysis.[2] Hence in the case of III (R = Pr^n), dehydration competes with hydrogen abstraction, whereas in I (R = Me), the hydroxyl has a fixed position and almost total reaction occurs to give the product of hydrogen abstraction.

All of the known cases of hydrogen abstraction using bromine and silver ions have been from tertiary hydroxyl groups and the hydrogen has been abstracted from a primary centre. Dehydration seems to predominate with secondary hydroxyl groups. In the cases IX and XI where the possible hydrogen abstraction is from an *iso*propyl group, the failure is probably due to a combination of the factors including an unfavourable orientation of the *iso*propyl group and the unlikelyhood of the formation of the hypobromite intermediate from the hindered tertiary hydroxy-group.

Attempts to utilize the photolysis or thermal decomposition of alkoxy lead salts of several benzylic alcohols to functionalize methyl groups attached to aromatic rings were unsuccessful in all cases and the main reactions in every case were fragmentations and polymerizations.

EXPERIMENTAL

Microanalyses were by Dr. A. D. Campbell and his associates, University of Otago, New Zealand. IR spectra were measured with a Perkin–Elmer 237 instrument. NMR spectra were measured with a Varian A-60 spectrometer using TMS as internal reference. Light petroleum was of b.p. 50–60° and alumina used for chromatography was P. Spence Type H material, deactivated with 5% of 10% acetic acid. M.ps on a Kofler block were uncorrected.

5,8a-*Dimethyl-6,7,8,8a-tetrahydro-2H-naphtha*(1,8-*bc*)*furan* (II)

Bromine (0·4 ml) was added in the dark to a stirred mixture of 1,5,8-trimethyl-1,2,3,4-tetrahydronaphth-1-ol[8] (1·0 g) and yellow mercuric oxide (8 g) in THF (100 ml). After 5 min, silver oxide (2·0 g) was added and the mixture was stirred for a further 20 min. The silver and mercuric salts were filtered off and washed thoroughly with ether. The combined filtrates were evaporated in the cold under reduced pressure. Light petroleum was added to the pasty white solid, and the solution chromatographed on alumina (70 ml). Elution with light petroleum gave the oily 5,8a-*dimethyl*-6,7,8,8a-*tetrahydro*-2H-*naphtha*(1,8-bc)*furan* (0·85 g, 86%). (Found: C, 83·2; H, 8·8. $C_{13}H_{16}O$ requires: C, 82·9; H, 8·6%); ν^{max} 1870, 1730, 1106, 1030, 1000, 990 cm^{-1}, δ (CCl_4) 1·30 (s, 3, C_{8a} methyl), 2·18 (s, 3, C_5 methyl), 4·63 and 5·07 (2 doublets, J = 12 c/s, 2, C_2 protons), 6·89 (s, 2, C_3 and C_4 aromatic protons).

2-(2',5'-*Xylenyl*)*pentan-2-ol* (III, $R = Pr^n$)

2,5-Dimethylacetophenone (6·0 g) in ether (100 ml) was added to an ethereal solution of *n*-propylmagnesium iodide (0·093 mole) and the mixture was heated under reflux for 3 hr. Working up gave an oil which was distilled to yield 2-(2',5'-*xylenyl*)*pentan-2-ol* (6·6 g, 82%), b.p. 162–164°/65 mm. (Found: C, 81·1; H, 10·4; O, 7·8. $C_{13}H_{20}O$ requires: C, 81·2; H, 10·5; O, 8·3%), ν_{max} 3590 and 3450 (OH), 1162 (C—OH) cm^{-1}.

1,6-*Dimethyl-1-propyl-1,3-dihydrobenzo*(*c*)*furan* (IV)

Bromine (0·45 ml) was added in the dark to a stirred mixture of 2-(2',5'-xylenyl)pentan-2-ol (0·50 g) and mercuric oxide (4·0 g) in THF (50 ml). After 7 min, silver oxide (1·5 g) was added and the mixture stirred for a further 30 min. Work up gave an oil which was separated into its three major components by preparative GLC.

(a) 2-(2',5'-*Xylenyl*)*pent-1-ene* (20%), ν^{max} 3100, 3035, 1688 (C=C), 902 (C=CH_2) cm^{-1}, δ(CCl_4) 0·90 (t, J = 7 c/s, 3, C_5 methyl protons), 2·20 and 2·27 (2s, 6, $C_{2'}$ and $C_{5'}$ methyls), 4·77 and 5·07 (2 broad singlets, 2, C_1 methylene), 6·80 (m, 3, aromatics), (Found: C, 89·3; H, 10·5. $C_{13}H_{18}$ requires: C, 89·6; H, 10·4%).

(b) 2-(2',5'-*Xylenyl*)*pent-2-ene* (50%), (Found: C, 89·7; H, 10·1). ν_{max} 3030, 3035, 1610, 885, 865 cm^{-1}, δ (CCl_4) 1·05 (t, J = 7 c/s, 3, C_5 methyl), 1·87 (s, 3, C_1 methyl), 2·17 and 2·25 (2s, $C_{2'}$ and $C_{5'}$ methyls), 5·22 (t, J = 8 c/s, 1, C_3 vinyl), 6·82 (m, 3, aromatics).

(c) 1,6-*Dimethyl-1-propyl-1,3-dihydrobenzo*(*c*)*furan* (30%), (Found: C, 81·7; H, 9·3. $C_{13}H_{18}O$ requires: C, 82·0; H, 9·5%). ν_{max} 1610, 1040 cm^{-1}, δ (CCl_4) 1·37 (s, 3, C_1 methyl), 2·28 (s, 3, C_6 methyl), 4·88 and 5·22 (2d, J = 10 c/s, 2, C_3 methylene), 6·90 (m, 3, aromatics).

Attempted intramolecular hydrogen abstraction on 5,8-*Dimethyl*-1,2,3,4-*tetrahydronaphth*-1-*ol* (*I*, *R* = *H*)

Treatment of I (R = H)[8] in the same manner as I (R = Me) with bromine, mercuric oxide and silver oxide, gave as the only product, 5,8-dimethyl-1,2-dihydronaphthalene (VII), identified by comparison with a sample prepared below.

5,8-*Dimethyl*-1,2-*dihydronaphthalene* (VII)

5,8-Dimethyl-1,2,3,4-tetrahydronaphth-1-ol (1·0 g) and fused $KHSO_4$ were heated together at 100° for 1 hr to give an oil which after chromatography on alumina gave 5,8-*dimethyl*-1,2-*dihydronaphthalene* (VII) (0·72 g, 80%). (Found: C, 90·8; H, 9·1. $C_{12}H_{14}$ requires: C, 91·1; H, 8·9%). ν_{max} 3038, 1863, 1735, 1634, 806, 783, 685 cm^{-1}, $\delta(CCl_4)$ 2·18 and 2·23 (2s, 6, C_5 and C_8 methyls), 6·00 (d, J = 10 c/s, each arm split into a triplet, J = 4 c/s, 1, C_3 vinyl), 6·65 (d, J = 10 c/s, 1, C_4 vinyl), 6·80 (s, 2, C_6 and C_7 aromatics).

2-(2′,5′-*Xylene*)*propan*-2-*ol* (III, R = Me)

2,5-Dimethylacetophenone (10·0 g) in ether (100 ml) was added to a solution of MeMgI in ether (0·17 mole) and the mixture was heated under reflux for 90 min. Work-up gave 2-(2′,5′-*xylenyl*)*propan*-2-*ol* (9·6 g, 86%), b.p. 134–135°/45 mm. (Found: C, 80·5; H, 9·7; O, 10·2. $C_{11}H_{16}O$ requires: C, 80·4; H, 9·8; O, 9·7%). ν^{max} 3590 and 3430 (OH), 1252 (C—OH) cm^{-1}, δ ($CDCl_3$) 1·55 (s, 6, C_1 and C_3 methyls), 2·27 and 2·48 (2s, 6, aromatic methyls), 6·97 (s, 2, $C_{3'}$ and $C_{4'}$ aromatics), 7·27 (s, 1, $C_{6'}$ aromatic).

4-*Methoxy*-2′,5′-*dimethylbenzophenone*

Anhydrous $AlCl_3$ (24 g) was added to a solution of *p*-xylene (10 g) and *p*-methoxybenzoylchloride (16·6 g) in CS_2 and the mixture stirred at 20° for 90 min. Work-up gave 4-*methoxy*-2′,5′-*dimethylbenzophenone* as needles m.p. 92–93° from light petroleum–benzene (14·5 g, 64%). (Found: C, 80·0; H, 6·7. $C_{16}H_{16}O_2$ requires C, 80·0; H, 6·7%), ν_{max} 1660 (C═O), 1603 and 1580 (aromatic C═C), 1274 (C—OMe), 862, 851, 820 cm^{-1}, δ (CCl_4) 2·20 and 2·30 (2s, 6, $C_{2'}$ and $C_{5'}$ aromatic methyls), 3·80 (s, 3, methoxyl), 6·82 (d, J = 9 c/s, 2, C_3 and C_5 aromatics), 7·08 (s, 2, $C_{3'}$ and $C_{4'}$ aromatic protons), 7·28 (s, 1, $C_{6'}$ aromatic), 7·72 (d, J = 9 c/s, 2, C_2 and C_6 aromatics).

1-(p-*Anisyl*)-1-(2′,5′-*xylenyl*)*ethanol* (VIII)

4-Methoxy-2′,5′-dimethylbenzophenone (1·50 g) in ether (75 ml) was added to an ethereal solution of MeMeI (0·072 mole) and the mixture was heated under reflux for 3 hr. Work-up gave 1-(p-*anisyl*)-1-(2′,5′-*xylenyl*)*ethanol* (1·42 g 88%) as needles, m.p. 92–93°, from n-hexane, (Found: C, 79·9; H, 8·1. $C_{17}H_{20}O_2$ requires: C, 79·7; H, 7·9%). ν_{max} 3590 and 3440 (OH), 1618 and 1588 (aromatic C═C), 1248 (C—OMe), 1170 (C—OH), 836, 812 cm^{-1}.

Attempted intramolecular hydrogen abstraction reaction on 1-(p-*anisyl*)-1-(2′,5′-*xylene*)*ethanol*

Treatment of VIII in the same manner as I (R = Me), with bromine, mercuric oxide and silver oxide gave an oil identified as a 1:1 mixture of 2,5-dimethylacetophenone and anisole by comparison of GLC retention times, and by IR and NMR spectra.

1,5-*Dimethyl*-8-*isopropyl*-1,2,3,4-*tetrahydronaphtha*-1-*ol* (IX)

5-Methyl-8-isopropyl-1,2,3,4-tetrahydronaphthalen-1-one[9] (10·0 g) in ether (100 ml) was added to an ethereal solution of MeMgI (0·15 mole) and the mixture was heated under reflux for 1 hr. Work-up and chromatography gave 1,5-*dimethyl*-8-*isopropyl*-1,2,3,4-*tetrahydronaphtha*-1-*ol* (7·2 g, 67%) as a low melting solid. (Found: C, 82·1; H, 10·7. $C_{15}H_{22}O$ requires: C, 82·5; H, 10·2%), ν_{max} 3580 and 3430 (OH), 1612 and 1575 (aromatic C═C), 1110 (C—OH), 880 cm^{-1}.

Attempted intramolecular hydrogen abstraction reaction on 1,5-*dimethyl*-8-*isopropyl*-1,2,3,4-*tetrahydronaphth*-1-*ol* (IX)

Treatment of IX with bromine, mercuric oxide, and silver oxide in the same manner as described for I (R = Me) gave only 4,8-dimethyl-5-isopropyl-1,2-dihydronaphthalene (X), ν_{max} 1630 (C═C), 1609 (aromatic C═C, 871 cm^{-1}.

7-*Hydroxy*-7-*methyltotaryl methyl ether* (XI)

7-Oxototaryl methyl ether[10] (2·0 g) in ether (50 ml) followed by benzene (100 ml) was added to an ethereal solution of MeMgI (0·036 mole). The mixture was heated under reflux for 4 hr and work up gave 7β-

hydroxy-7-methyltotaryl methyl ether (1·85 g, 86%) as needles from hexane, m.p. 153–154°. (Found: C, 80·1; H, 10·2; O, 9·6. $C_{22}H_{34}O_2$ requires: C, 80·0; H, 10·4; O, 9·7%), ν_{max} 3595 and 3440 (OH), 1590 and 1575 (aromatic C═C), 1391 and 1380 (*gem* methyls), 1270 (C—OMe), 913, 813 cm^{-1}, δ ($CDCl_3$) 0·90 and 0·97 (2s, 6, C_4 *gem* methyls), 1·22 (s, 3, ang. Me), 1·30 (d, J = 7 c/s, 6, isopropyl Me's), 1·65 (s, 3, C_7 α-methyl), 2·65 (d, J = 10 c/s, 1, c_6-β proton), 3·75 (s, 3, OMe), 4·22 (m, 1· isopropyl methine), 6·75 and 7·08 (2d, J = 9 c/s. C_{12} and C_{11} aromatics).

Attempted intramolecular hydrogen abstraction reaction on 7β-*hydroxy-7-methyltotaryl methyl ether* (XI)

Treatment of XI with bromine, mercuric oxide and silver oxide in the manner described for I (R = Me) gave as the only product 7-*methyl-6,7-dehydrototaryl methyl ether* (XII), as needles from methanol, m.p. 126–127°, (Found: C, 84·7; H, 10·3; O, 5·3. $C_{22}H_{32}O$ requires: C, 84·6; H, 10·3; O, 5·1%), ν_{max} 1573 (C═C), 1392 and 1373 *gem* methyls, 1260 (C—OMe) cm^{-1}, δ (CCl_4) 0·93, 0·98 and 1·02 (3s, 9, C_4 *gem* methyls and C_{17} methyl), 1·07 and 1·34 (2d, J = 7 c/s, 6, isopropyl methyls), 2·22 (s, 3, C_7 methyl), 3·78 (s, 3, OMe), 5·85 (m, 1, C_6 vinyl), 6·62 and 6·90 (2d, J = 8 c/s, C_{12} and C_{11} aromatics).

Acknowledgements—We thank the New Zealand Universities Grants Committee for continued support. K.M.B. was the holder of a N.Z.U.G.C. Post-graduate Scholarship.

REFERENCES

[1] K. Heusler and J. Kalvoda, *Angew. Chem. Int. Ed.* 3, 525 (1964).
[2] M. Akhtar, *Adv. Photochem.* 2, 263 (1964).
[3] R. Sneen and N. P. Matheny, *J. Am. Chem. Soc.* **86**, 3905 (1964).
[4] R. Sneen and N. P. Matheny, *Ibid.* **86**, 5503 (1964).
[5] T. Matsuura and Y. Kitaura, *Tetrahedron Letters* 3309 (1967).
[6] L. R. C. Barclay and M. C. Macdonald, *Ibid.* 881 (1968).
[7] J. Kalvoda and K. Heusler, *Chem. & Ind.* 1431 (1963).
[8] E. de B. Barnett and F. G. Sanders, *J. Chem. Soc.* 434 (1933).
[9] L. Ruzicka and M. Mingazzini, *Helv. Chim. Acta* **5**, 710 (1922).
[10] R. C. Cambie and L. N. Mander, *Tetrahedron* **18**, 465 (1962).