Tetrahedron. Vol. 27, pp. 1317 to 1322. Pergamon Press 1971. Printed in Great Britain

THE WOLFF, BECKMANN, HOFMANN, CURTIUS AND SCHMIDT REARRANGEMENTS IN THE SERIES OF 3-*o*-CARBORANE DERIVATIVES

1,2-DICARBA-CLOSO-DODECABORANES

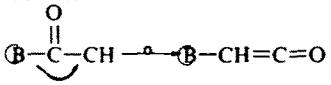
L. I. ZAKHARKIN, V. N. KALININ and V. V. GEDYMIN
Institute of Organo-Element Compounds, Academy of Sciences, Moscow, USSR

(*Received in the UK* 10 *October* 1970; *Accepted for publication* 28 *October* 1970)

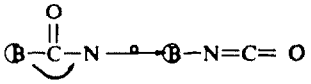
Abstract—Using 3-*o*-carborane derivatives as examples it has been shown that the Wolff, Beckmann, Hofmann, Curtius and Schmidt rearrangements proceed through B—C bond cleavage and migration of the electron rich 3-*o*-carboranyl group to an electron deficient center. The Bayer–Villiger reaction of (1-methyl-*o*-carborane-3-yl)phenylketone results in migration of the 1-methyl 3-*o*-carboranyl group.

THE Wolff, Beckmann, Hoffmann, Curtius and Schmidt rearrangements are well characterised molecular rearrangements. They represent the type of nucleophilic rearrangements which occur with C—C bond cleavage and displacement of an electron rich group to a center of electron deficiency.

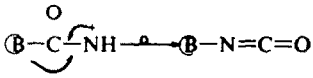
Employing 3-*o*-carborane derivatives as examples we found that the rearrangements may proceed with B—C bond cleavage, the *o*-carborane nucleus with the electron rich B atom being a migrating group. Schemes involving cleavage of B—C bond are shown below:



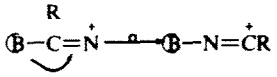
Wolff rearrangement



Hofmann, Curtius rearrangements

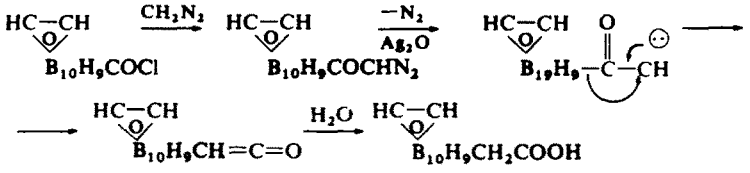


Schmidt rearrangement

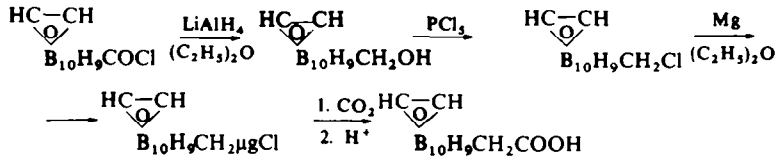


Beckman rearrangement

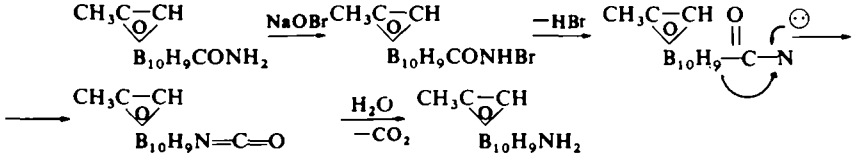
Treatment of 3-*o*-carboranecarboxylic acid chloride with excess diazomethane affords a diazoketone. This undergoes Wolff rearrangement (as in the case of regular diazoketones) upon heating in aqueous medium in the presence of silver oxide giving *o*-carborane-3-yl-acetic acid:



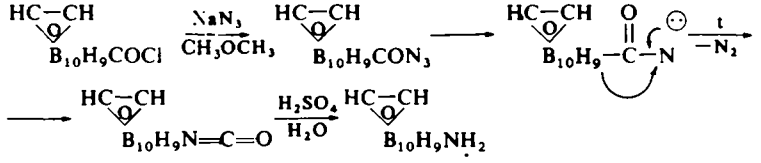
Undoubtedly this rearrangement is intermolecular with migration of *o*-carborane boron and its electron pair (primarily of the B—C bond). In the course of this rearrangement the electron pair does not shift to another *o*-carborane boron but a new B—C bond is formed at the B^- atom which was previously combined with the diazoketone carbon. *o*-Carborane -3-yl acetic acid obtained by the rearrangement was identical with an authentic sample prepared by an independent procedure:



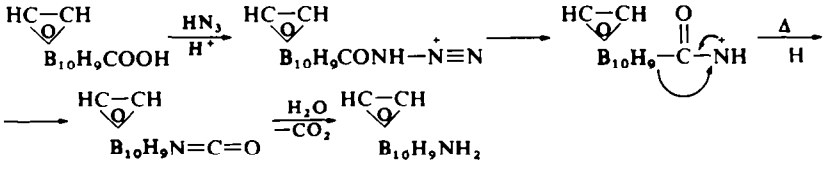
Hydrolysis of Grignard reagent[1] gives 3-methyl-*o*-carborane. Reaction of NaOBr with the amide of 1-methyl-3-*o*-carboranecarboxylic acid occurs through Hofmann rearrangement to give 1-methyl-3-amino-*o*-carborane:



Heating of 3-*o*-carboranecarboxylic acid azide (from the chloride and sodium azide) in sulfuric acid involves a Curtius rearrangement giving 3-amino-*o*-carborane:

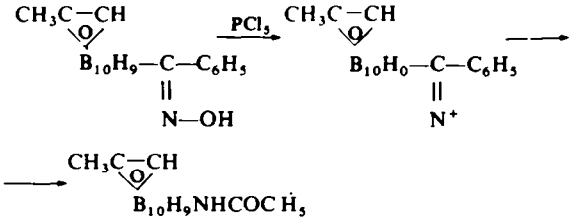


3-*o*-Carboranecarboxylic acid on reaction with HN_3 in sulfuric acid undergoes the Schmidt rearrangement to 3-amino-*o*-carborane.



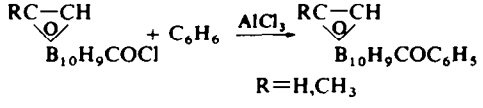
During Hofmann, Curtius and Schmidt rearrangements the bond between substituent and the *o*-carborane nucleus does not change its position upon migration of the 3-*o*-carboranyl group with its electron pair of the primary B—C bond. The resulting amine is identical to an authentic 3-amino-*o*-carborane, which on reaction with NOCl gives chloro-*o*-carborane identical with 3-chloro-*o*-carborane.

Heating of (1-methyl-*o*-carborane-3-yl)phenylketoxime with PCl_5 in benzene and subsequent hydrolysis gives only 1-methyl-3-N-benzoylamino-*o*-carborane via the Beckmann rearrangement:

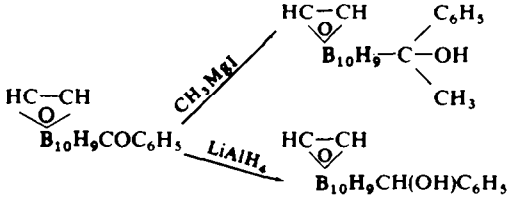


The phenyl group migration product (e.g. that of the phenyl amide of 3-*o*-carborane-carboxylic acid) was not found i.e. in Beckmann rearrangement the 3-*o*-carboranyl group migrates more readily than the phenyl group. Since the 3-*o*-carboranyl group is a stronger electron acceptor than the phenyl group, its more facile migration might be explained either by the lower strength of the B—C with respect to C—C bond or by a trans-orientation of 3-*o*-carboranyl group about hydroxyl in the oxime due to the more bulky carborane nucleus.

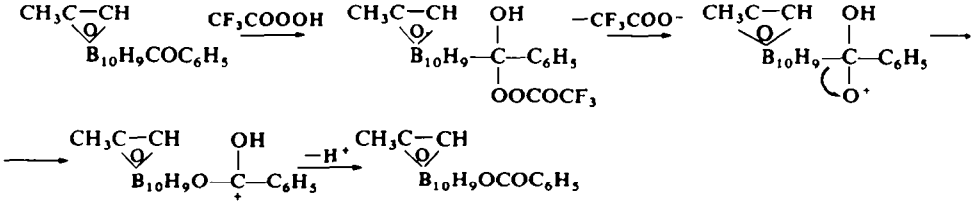
(1-Methyl-*o*-carborane-3-yl)phenylketone was prepared by the Friedel-Crafts syntheis from 3-*o*-carboranecarboxylic acid chloride and benzene:



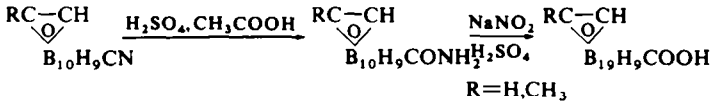
Unlike 1-*o*-carborane ketones[1] 3-*o*-carborane ketones react readily with hydroxylamine and 2,4-dinitrophenylhydrazine to give oximes and hydrazones respectively. By reduction with LAH they smoothly convert to secondary alcohols and with Me MgI they give tertiary alcohols.



We also found that (1-methyl-*o*-carborane-3-yl)phenylketone undergoes a Bayer–Villiger reaction with pertrifluoroacetic acid to give 3-benzoxy-*o*-carborane, the 3-*o*-carboranyl fragment being the migrating group.

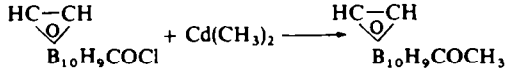


The required 3-*o*-carboranecarboxylic acids were obtained by a two step synthesis from the readily available 3-cyano-*o*-carborans.[2] Owing to a steric hindrance in the carborane nucleus the cyano-group can not immediately hydrolyse to COOH. Hydrolysis by sulfuric acid affords the amide which with sodium nitrite gives the acid:



3-*o*-Carboranecarboxylic acids exhibit the properties of ordinary organic acids. Thus with diazomethane in ether they give methyl esters. With PCl_5 they form chlorides which are similar to organic acid chlorides.

For example, reaction of 3-*o*-carboranecarboxylic acid chloride and dimethylcadmium leads to (*o*-carborane-3-yl)methylketone



The p*Ka*'s of 3-*o*-carboranecarboxylic and 1-methyl-3-*o*-carboranecarboxylic acids determined in 50% ethanol are 5·38 and 5·47 respectively. Comparison of these values with p*Ka*'s of benzoic (5·70)[3] and 1-*o*-carboranecarboxylic acids (2·60)[4] determined in 50% ethanol shows that the 3-*o*-carboranyl group is a stronger electron acceptor than the phenyl but it is essentially weaker than the 1-*o*-carboranyl group. This is in conformity with earlier studies by the authors.[7]

The p*Ka* of *o*-carborane-3-yl-acetic acid in 80% methylcellosolve is 6·57, thus from a relation[5] it follows that the inductive constant of the 3-*o*-carboranyl group is 0·12.

EXPERIMENTAL

3-o-*Carboranecarboxylic acid amide.* 3-Cyano-*o*-carborane (1·7 g) in AcOH (50 ml) and H_2SO_4 (50 ml) was stirred at 105–110° for 2·5 hr. The mixture was poured on ice and extracted with ether. The extracts were washed with $NaHCO_3$ aq and dried ($MgSO_4$) to give 1·73 g of 3-*o*-carboranecarboxylic acid amide (91%), m.p. 147·5–148° after crystallization from heptane. (Found: C, 19·01; H, 7·07; B, 57·31; N, 7·58. $C_3H_{13}B_{10}NO$ requires: C, 19·22; H, 6·99; B, 57·82; N, 7·47%).

1-Methyl-3-*o*-carboranecarboxylic acid amide was obtained analogously, m.p. 140–141·5° after crystallization from heptane. (Found: C, 24·72; H, 7·30; B, 53·74; N, 6·75. $C_4H_{15}B_{10}NO$ requires: C, 23·88; H, 7·51; B, 53·70; N, 6·96%).

o-*Carboranecarboxylic acid.* $NaNO_2$ (1 g) was added with stirring at 0° to 3-*o*-carboranecarboxylic acid amide (1·9 g) in AcOH (50 ml) and H_2SO_4 (50 ml). The mixture was heated at 90° for 1·5 hr, poured on ice, extracted with ether, and the ethereal extracts washed with dilute NaOH aq. The alkaline layer was acidified, and the ppt extracted with ether and the soln dried ($CaCl_2$) to give 1·7 g of 3-*o*-carboranecarboxylic acid (89%), m.p. 144–145·5°* after crystallization from heptane; IR: 1690 cm^{-1} (C=O). (Found: C, 19·57; H, 6·28; B, 57·60. $C_3H_{12}B_{10}O_2$ requires: C, 19·12; H, 6·42; B, 57·50%).

1-Methyl-*o*-carboranecarboxylic acid was obtained analogously, m.p. 176·5–177°. (Found: C, 23·40; H, 6·96; B, 53·28. $C_4H_{12}B_{10}O_2$ requires: C, 23·75; H, 6·96; B, 53·40%).

The 3-*o*-carboranecarboxylic acids were prepared in similar yields without intermediate separation of the amides. From diazomethane and 3-*o*-carboranecarboxylic acid its methyl ester was obtained, m.p. 92–93·5° after crystallization from hexane; IR: 1700 cm^{-1} (C=O). (Found: C, 24·05; H, 6·88; B, 53·07. $C_4H_{14}B_{10}O_2$ requires: C, 23·78; H, 6·97; B, 53·62%).

* This acid accidentally has been reported to have an incorrect m.p.[4]

Analogously the methyl ester of 1-methyl-3-*o*-carboranecarboxylic acid was obtained, m.p. 78·5–79° after crystallization from hexane; IR: 1700 cm^{-1} (C=O). (Found: C, 28·28; H, 7·40; B, 49·42. $C_5H_{16}B_{10}O_2$ requires: C, 27·75; H, 7·44; B, 49·90%).

3-*o*-Carboranecarboxylic acid (1·9 g) and PCl_5 (2·1 g) were refluxed in benzene (50 ml) for 2 hr, the solvent evaporated, the residue extracted with cold hexane and distilled, b.p. 138–139°/2 mm, to give 1·59 g of 3-*o*-carboranecarboxylic acid chloride (79%), m.p. 89–91° after crystallization from hexane.

Analogously 1-methyl-3-*o*-carboranecarboxylic acid chloride was obtained, m.p. 129–131° after crystallization from hexane.

(o-*Carborane-3-yl)diazomethylketone.* 3-*o*-Carboranecarboxylic acid chloride (2 g) in ether (100 ml) was added at 0° to 1 M ethereal diazomethane soln (100 ml) and the mixture allowed to stand for 4 hr. The soln was filtrated to give 0·74 g of (*o*-carborane-3-yl)diazomethylketone (35%), m.p. 89–91° (dec) after crystallization from hexane; IR: 1700 (C=O), 2120 (N=N) cm^{-1}. (Found: C, 23·04; H, 5·95; B, 51·19; N, 13·15. $C_4H_{12}B_{10}N_2O$ requires: C, 22·26; H, 5·70; B, 51·39; N, 13·23%).

Wolff rearrangement of (o-*carborane-3-yl)diazomethylketone.* Ag_2O prepared from $AgNO_3$ (1 g) was added with stirring to $Na_2S_2O_3$ (2 g) and Na_2CO_3 (3 g) in water (25 ml) and then (*o*-carborane-3-yl) diazomethylketone (0·75 g) in dioxan (25 ml) was added at 70°. The mixture was refluxed for 2 hr. The hot soln was filtered, poured into water (50 ml) and extracted with ether. The ethereal layer was washed with dilute NaOH aq, the alkaline layer acidified, the ppt extracted with ether, and dried ($CaCl_2$) to give 0·22 g of *o*-carborane-3yl-acetic acid (33%), m.p. 160–161°, after crystallization from heptane, identical with an authentic sample prepared by an independent method.

3-*Oxymethyl*-o-*carborane.* 3-*o*-Carboranecarboxylic acid chloride in ether was added at 20° to an ethereal soln of LAH (0·5 g). The mixture was heated for 1 hr and decomposed with water. The ethereal soln was dried ($MgSO_4$) to give 1·1 g of 3-oxymethyl-*o*-carborane (63%), m.p. 149–151° after crystallization from heptane; IR: 3200–3600 cm^{-1} (OH). (Found: C, 21·15; H, 7·89; B, 62·47. $C_3H_{14}B_{10}O$ requires: C, 20·62; H, 8·08; B, 62·17%).

Analogously 1-methyl-3-oxymethyl-*o*-carborane was prepared m.p. 214–215·5°, after crystallization from heptane. (Found: C, 24·90; H, 8·32. $C_4H_{16}B_{10}O$ requires: C, 25·51; H. 8·55%).

3-Chloromethyl-o-*carborane.* 3-Oxymethyl-*o*-carborane (1·7 g) and PCl_5 (2·1 g) in benzene (50 ml) were refluxed for 3 hr. The benzene was evaporated and the residue passed through alumina (hexane:chloroform 1:1) to give 1·34 g of 3-chloromethyl-*o*-carborane (65%), m.p. 42–43° after crystallization from pentane. (Found: C, 19·42; H, 6·79; Cl, 18·35. $C_3H_{13}B_{10}Cl$ requires: C, 18·71; H, 6·77; Cl, 18·44%).

Analogously 1-methyl-3-chloromethyl-*o*-carborane was obtained m.p. 96–98° after crystallization from pentane. (Found: Cl, 17·41. $C_4H_{15}B_{10}Cl$ requires: Cl, 17·16%).

o-*Carborane-3-yl-acetic acid.* An ethereal soln of 3-chloromethyl-*o*-carborane (1·9 g) was added with stirring to Mg (0·3 g) in ether (10 ml). The mixture was refluxed for 1 hr, then dry CO_2 was bubbled through for 6 hr to give 0·67 g of *o*-carborane-3-yl-acetic acid (33%), m.p. 161·5–162·5° after crystallization from heptane; NMR, 1·81 (CH), 2·57 (C—H of carborane), 10·2 ppm (OH) (HMDS as standard). (Found: C, 24·30; H, 7·13; B, 53·10. $C_4H_{14}B_{10}O_2$ requires: C, 23·79; H, 6·96; B, 53·70%).

3-*methyl*-o-*carborane.* (78%) was prepared by a hydrolysis of the Grignard reagent obtained in the previous run, m.p. 101–102° after crystallization from hexane. (Found: C, 22·57; H, 8·68; B, 67·82. $C_3H_{14}B_{10}$ requires: C, 22·74; H, 8·89; B, 68·40%).

Hofmann rearrangement of 1-*methyl*-3-o-*carboranecarboxylic acid amide.* 1-Methyl-3-*o*-carboranecarboxylic acid amide (2 g) in MeOH (40 ml) was added to NaOBr (from Br_2 (3·2 g) and NaOH (0·5 g)) in water (20 ml). The mixture was heated at 50° for 0·5 hr. Most of the alcohol was evaporated and the residue extracted with ether to give 1-methyl-3-amino-*o*-carborane identified by GLC and IR spectra. This was converted to 1-methyl-3-chloro-*o*-carborane described.[6]

3-o-*Carboranecarboxylic acid azide.* NaN_3 (1·3 g) in H_2O (5 ml) was added with stirring to 3-*o*-carboranecarboxylic acid chloride (2·1 g) in acetone (30 ml) at 20°. The mixture was heated to 40°, poured into water (0·25 l), extracted with ether and dried ($CaCl_2$) to give 1 g of 3-*o*-carboranecarboxylic acid azide (49%). m.p. 121–123° after crystallization from heptane. (Found: C, 16·52; H, 5·30. $C_3H_{11}B_{10}N_3$ requires: C, 16·91; H, 5·19%).

Curtius rearrangement of 3-o-*carboranecarboxylic acid azide.* The azide (1 g) in H_2SO_4 (20 ml) was heated at 80–90° until the evolution of N_2 subsided. The mixture was poured on ice and made alkalein. The ethereal extracts were dried ($MgSO_4$) to give 0·33 g of 3-amino-*o*-carborane (41%), m.p. 218–219°, which showed no depression upon mixing with an authentic sample. The amine purity was also confirmed with GLC and IR spectra.

Schmidt rearrangement of 3-*o*-*carboranecarboxylic acid.* A 0·047 M benzene soln of HN_3 (30 ml) was added dropwise with stirring to 3-*o*-carboranecarboxylic acid (1·9 g) in H_2SO_4 (30 ml) at 40–50°. The mixture was poured on ice, made alkalein, extracted with ether and dried ($MgSO_4$) to give 0·84 g of 3-amino-*o*-carborane (53%), identified by m.p., GLC, and IR spectrum.

(*o*-*Carborane*-3-*yl*)*phenylketone.* 3-*o*-Carboranecarboxylic acid chloride (2·1 g) and $AlCl_3$ (3 g) in benzene (50 ml) were refluxed for 3 hr, decomposed with dilute HCl and the benzene soln dried ($CaCl_2$). The residue was passed through an alumina column (hexane:chloroform 1:1) to give 1·7 g (*o*-carborane-3-yl)phenylketone (68%), m.p. 110–111° after crystallization from heptane; IR: 1630 cm^{-1} (C=O). (Found: C, 43·05; H, 6·43; B, 43·45. $C_9H_{16}B_{10}O$ requires: C, 43·45; H, 6·48; B, 43·51%).

Analogously (1-methyl-*o*-carborane-3-yl)phenylketone was obtained, m.p. 77–78° after crystallization from hexane. (Found: C, 46·50; H, 7·11. $C_{10}H_{18}B_{10}O$ requires: C, 45·71; H, 6·90%).

The 2,4-dinitrophenylhydrazone of (1-methyl-*o*-carborane-3-yl)-phenylketone had m.p. 220–222° after crystallization from AcOH. (Found: N, 12·54. $C_{16}H_{22}B_{10}N_4O_4$ requires: N, 12·68%).

(1-*Methyl*-o-*carborane*-3-*yl*)*phenylketoxime.* $NH_2OH \cdot HCl$ (0·75 g) was added to (1-methyl-*o*-carborane-3-yl)phenylketone (2·6 g) in EtOH (30 ml) and pyridine (30 ml) was added, and the mixture heated at 90° for 2 hr. Solvent evaporation gave 1·8 g of (1-methyl-*o*-carborane-3-yl)phenylketoxime (65%), m.p. 170·5–172°. (Found: N, 5·20. $C_{10}H_{19}B_{10}NO$ requires: N, 5·06%).

Beckmann rearrangement of (1-*methyl*-o-*carborane*-3-*yl*)*phenylketoxime.* PCl_5 (1 g) was added to (1-methyl-*o*-carborane-3-yl)phenylketoxime (1 g) in benzene (20 ml). The mixture was stirred at 20° for 2 hr, decomposed with NaOH aq and the benzene layer dried ($MgSO_4$). The residue was passed through an alumina column (hexane:chloroform 1:1) to give 0·3 g 1-methyl-3-N-benzoylamino-*o*-carborane (30%) m.p. 168–170° after crystallization from heptane; lit. data:[6] m.p. 170–171°. The product was shown by GLC and IR spectrum to be identical with an authentic sample.

(*o*-*Carborane*-3-*yl*)*phenylcarbinol.* (*o*-Carborane-3-yl)phenylketone (2·5 g) in ether (10 ml) was added at 20° to a stirred soln of LAH (0·5 g) in ether (20 ml). The mixture was heated for 1 hr to give 1·65 g (*o*-carborane-3-yl)phenylcarbinol (66%), m.p. 80·5–81·5° after crystallization from hexane. (Found: C, 43·45; H, 7·40; B, 42·82. $C_9H_{18}B_{10}O$ requires: C, 43·22; H, 7·23; B, 43·30%).

(*o*-*Carborane*-3-*yl*)(*phenyl*)*methylcarbinol.* An ethereal soln of MeMgI (1 M, 15 ml) was added to (3-*o*-carborane-3yl)phenylketone (2·5 g) in ether (20 ml), and the mixture heated for 0·5 hr, to give 1·6 g of *o*-carborane-3-yl-(phenyl)methylcarbinol (61%), m.p. 98–98·5° after crystallization from hexane. (Found: C, 45·75; H, 7·76; B, 40·29. $C_{10}H_{20}B_{10}O$ requires: C, 45·50; H, 7·63; B, 40·95%).

Bayer–Villiger reaction of (1-*methyl*-o-*carborane*-3-*yl*)*phenylketone.* A soln of CF_3COOOH [from trifluoroacetic acid anhydride (2·1 ml) and 90% H_2O_2 (0·3 ml)] in CH_2Cl_2 (10 ml) was slowly added with stirring to (1-methyl-*o*-carborane-3-yl)phenylketone (2·6 g) in CH_2Cl_2 (20 ml) and the mixture heated for 24 hr. The organic phase was washed with water, $NaHCO_3$ aq, and dried ($CaCl_2$) to give 2·1 g of 3-benzoxy-*o*-carborane (75%), m.p. 88–89° after crystallization from heptane. The product was shown to be identical by GLC and IR spectrum with an authentic 3-benzoxy-*o*-carborane (m.p. 89–90°).

(*o*-*Carborane*-3-*yl*)*methylketone.* 3-*o*-Carboranecarboxylic acid chloride (4·15 g, 0·02 mole) in benzene (20 ml) was added at 20° to 1 M benzene soln of Me_2Cd (25 ml), and heated with stirring for 2 hr, decomposed with dilute HCl and dried ($CaCl_2$) to give 0·4 g (*o*-carborane-3-yl)methylketone (11%), m.p. 129·5–130·5° after crystallization from heptane; IR: 1700 cm^{-1} (C=O). (Found: C, 26·08; H, 7·52; B, 57·89. $C_4H_{14}B_{10}O$ requires: C, 25·74; H, 7·57; B, 58·01%).

The pH measurements of the solns of 3-*o*-carboranecarboxylic-, 1-methyl-*o*-carboranecarboxylic and *o*-carborane-3-yl-acetic acids were performed on an LPU-01 pH meter using glass electrode. Titration was conducted at 25°. Acid sample ($5 \cdot 10^{-3}$ mole) was dissolved in EtOH [50% (vol.), 50 ml] or methylcellosolve [80% (vol)] and titrated with 0·1 N NaOH in EtOH (50%) or cellosolve. The p*Ka*'s were calculated in accord with the procedure described.

REFERENCES

[1] L. I. Zakharkin and A. I. L'vov, *Zh. Obshch. Khim.* **37**, 1217 (1967)

[2] L. I. Zakharkin, V. N. Kalinin, V. V. Gedymin and G. S. Dzarasova, *J. Orggnometall. Chem.* in press

[3] O. Exner and J. Jones, *Collection* **27**, 2296 (1962)

[4] L. I. Zakharkin and V. N. Kalinin, *Izv. Akad. Nauk SSSR, Ser. Khim.* 1968, 1423

[5] M. Charton, *J. Org. Chem.* **29**, 1222 (1964)

[6] L. I. Zakharkin, V. N. Kalinin and V. V. Gedymin, *J. Organometall. Chem.* **16**, 371–379 (1969)

[7] L. I. Zakharkin, V. N. Kalinin and I. P. Shepilov, *Dokl. Akad. Nauk SSSR* **174**, 606 (1967)