SYNTHESIS OF 2,6-DIMETHYL-1,2,3,4-TETRAHYDRONAPHTHALENE-4-^{13}C AND 2,6-DIMETHYLNAPHTHALENE-4-^{13}C

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SUMMARY

The synthesis of specifically labeled β,4-dimethyl-benzenebutanoic acid-1-^{13}C, 3,4-Dihydro-3,7-dimethyl-1(2H)-naphthalenone-1-^{13}C, 2,6-dimethyl-1,2,3,4-tetrahydronaphthalene-4-^{13}C and 2,6-dimethylnaphthalene-4-^{13}C from Diethyl 2-(4-methylphenyl)-2-methylpropanediate is described.

Key Words: β,4-Dimethyl-benzenebutanoic acid-1-^{13}C, 3,4-dihydro-3,7-dimethyl-1(2H)-naphthalenone-1-^{13}C, 2,6-dimethyl-1,2,3,4-tetrahydronaphthalene-4-^{13}C and 2,6-dimethylnaphthalene-4-^{13}C.

INTRODUCTION

Hydroaromatic compounds are valuable as solvents and as hydrogen transfer agents in the thermally induced depolymerization of coal to coal liquids (1a-d). In model studies, Tetralin and related hydroaromatic hydrocarbons have proven useful in the study of the kinetics and mechanism of the depolymerization reactions (1a-d). Labeled compounds show promise in determining the fate of these solvents (1). To provide needed labeled compounds for use in coal depolymerization studies, we undertook the synthesis of the title compounds. Owing to cost of the label, we sought a synthesis which permitted introduction of ^{13}C at a late stage. Scheme I illustrates the route used for the synthesis of 2,6-dimethyl-1,2,3,4-tetrahydronaphthalene-4-^{13}C (6) and 2,6-dimethylnaphthalene-4-^{13}C (7). The ^{13}C-label is introduced through use of labeled carbon dioxide (2)

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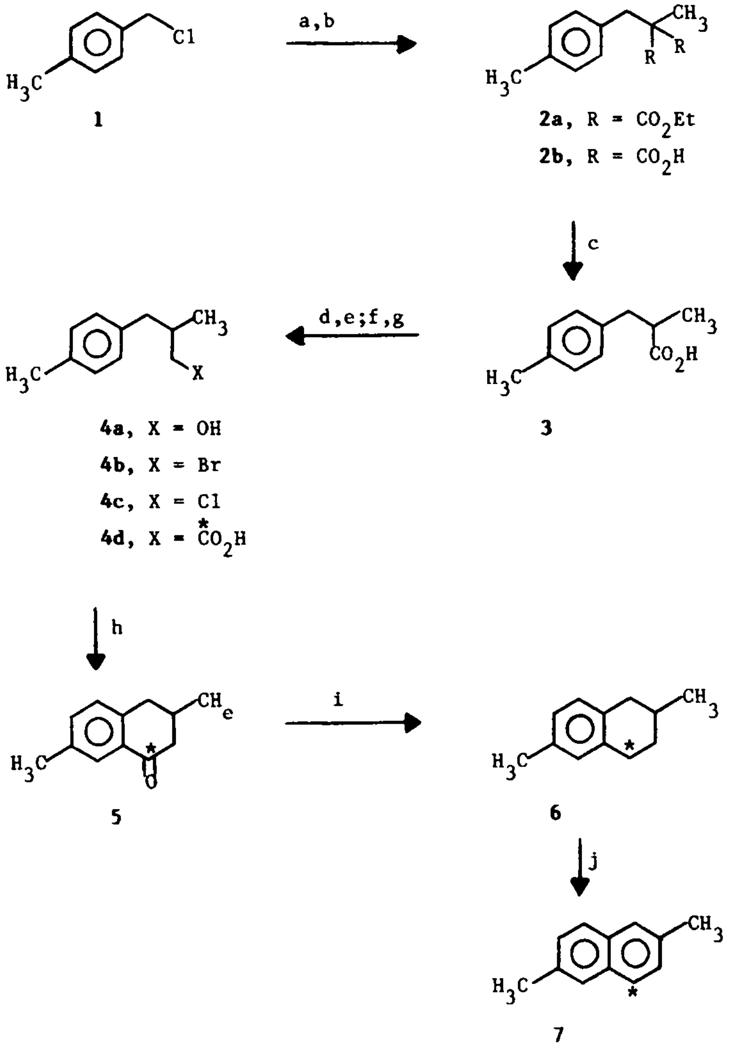
SCHEME I



${}^{a}C_2H_5ONa$, $C_6H_5CH_3$, $CH_3CH(CO_2C_2H_5)_2$, Δ. ^{b}EtOH, NaOH, Δ; $H_3\overset{+}{O}$. ^{c} Δ. ${}^{d}(\underline{i}\text{-}C_4H_9)_2AlH$, $C_6H_5CH_3$. ${}^{e}(C_6H_5)_3P$, Br_2, Δ. ^{f}Mg, THF, C_6H_6 (1:9). ${}^{g}{}^{13}CO_2$. ^{h}PPA, Δ. ${}^{i}H_2$, Pd/C, HOAc, Δ. ^{j}Pd/C, Δ.

via an improved procedure for carbonation of Grignard reagents. An all-metal reactor assembly, capable of operating at 50-60 psig and thus insuring safe handling of the expensive ${}^{13}C$ label in relatively large quantities (0.2-0.4 mol), was developed. The details of the carbonation step and the operation of the apparatus have been described (3). Trial carbonation reactions with commercial Dry Ice (4) proved unsatisfactory, and were a contributing factor in the need to develop the all-metal reactor and the currently used carbonation procedure.

Other reaction steps involved in Scheme I are well known and widely documented. However, some steps deserve comment. Diester **2a** was unchanged by prolonged hydrolysis in refluxing $HCl/HOAc/H_2O$ (5). However, conversion of **2a** to **2b** was accomplished in high yield by alkaline hydrolysis (NaOH/ethanol) followed by acidification. Decarboxylation of **2b** to **3** is best carried out by heating the diacid **2b** at 175-220 °C.

Three routes were investigated for the conversion of alcohol **4a** to the corresponding halide **4b** or **4c**. The best route to the bromocompound **4b** (86% yield) utilized triphenylphosphine and bromine in CCl_4 at 40 °C (6). In contrast, treatment of **4a** with PBr_3 gave **4b** in 37% yield (7). The chlorocompound **4c** was obtained in 56% yield from **4a** by treating with thionyl chloride and pyridine (8).

Formation of the Grignard reagent from the bromocompound **4b** proceeded much faster than from the corresponding chloride **4c** and appeared to be quantitative. Reaction conditions for the formation of the Grignard reagents of both **4b** and **4c** are critical. Attempts to initiate formation of Grignard reagent by intermittent warming with a heat gun failed and constant heating at reflux with a heating mantle was required. Preformed methylmagnesium iodide was superior to iodine or dichloroethane for initiating the formation of Grignard reagent. Initiation without this treatment occurred slowly. Grignard reagent formation from **4b** and **4c** required 1.5-2.5 h at reflux regardless of the initiation method. Benzene/THF (9:1, V/V) (9) was found to be superior to THF or ethyl ether as solvent.

EXPERIMENTAL SECTION

Diethyl 2-(4-methylphenyl)-2-methylpropanediate (2a). In a 12-L fluted flask equipped with a turbine stirrer, addition funnel, heating mantle, Dean-Stark trap, thermometer, and nitrogen bubbler, was placed 1300 mL of anhydrous ethanol. Sodium (76 g, 3.3 g-atom) was added portionwise to the stirred solution during 30 min with reflux being maintained until all of the sodium had reacted. Ethanol (600 mL) was then removed by distillation, and 3 L of dry toluene added, followed by addition of diethyl methylmalonate (523 g, 3.0 mol) over 15 min. A toluene/ethanol azeotrope was removed until the head temperature reached 108 °C, with sufficient toluene being added to the reaction vessel to maintain a homogeneous system. 4-Methylbenzyl chloride (450 g, 3.2 mol) was added to the solution over 30 min. Subsequently, toluene was removed by distillation until the head temperature reached 110 °C. The mixture was then cooled, acidified with conc. HCl, and the organic layer was separated and washed twice with water, dried ($MgSO_4$), filtered, concentrated, and vacuum-distilled at 115-130 °C (0.1 mm) [lit. (10) 220 °C, 20 mm] to give 662-g (79% yield) of **2a**: IR (neat) 1730 cm^{-1} (C=O); ^1H-NMR ($DCCl_3$) δ 1.25 (t, J = 7 Hz, 6, $CH_2C\underline{H}_3$), 1.32 (s, 3, CCH_3), 2.30 (s, 3, $ArCH_3$), 3.18 (s, 2, $ArCH_2$), 4.18 (q, J = 6 Hz, 4, $C\underline{H}_2CH_3$), 7.02 (s, 4, ArH); ^{13}C-NMR ($DCCl_3$) ppm 14.0, 19.7, 20.9, 54.9, 61.1, 128.9, 130.2, 133.3, 136.3, 171.7; MS *m/z* (rel. abundance) M^+ 278 (23.44), 204 (54.50), 158 (28.75), 130 (21.23), 105 (100), 91 (11.06).

2-(4-Methylphenyl)-2-methylpropanedioic acid (2b). A 355-g (1.27 mol) sample of **2a** was saponified in a refluxing mixture of ethanol (1500 mL) and 10% NaOH (2500 mL) during 4 h. The reaction mixture was distilled until ethanol was removed and then cooled and extracted with ether to remove any neutral impurities. The aqueous layer was acidified and extracted with ether. The extract was dried ($MgSO_4$), filtered, concentrated, and recrystallized (ether) to give 275-g (97% yield) of **2b**, mp 173-174 °C (dec) [lit. (11) 178-180 °C]: IR (KBr) 3000 (CO_2H), 1725 (C=O) cm^{-1}; ^1H-NMR (acetone-$\underline{d}_6$) δ 1.30 (s, 3, RCH_3), 2.27 (s, 3, $ArCH_3$), 3.18 (s, 2, $ArCH_2$), 7.09 (s, 4, Ar-H); ^{13}C-NMR ($DCCl_3$) ppm 20.0, 21.0, 41.3, 54.9, 129.5, 130.9, 131.3, 136.8, 173.6; MS *m/z* (rel. abundance) $M^+ - CO_2$ 178.05 (12), 117.04 (5.87), 106.03 (9.29), 105.04 (100), 91.05 (7.04), 77.06 (7.19). Anal. Calcd. for $C_{12}H_{14}O_4$: C, 64.85; H, 6.35. Found: C, 65.00; H, 6.35.

β,4-Dimethylbenzenepropionic acid (3). To a 500-mL flask equipped with thermometer, Vigreaux column, and gas bubble tube were added 127-g (0.57 mol) of **2b**. The temperature was increased and at 140 °C CO_2 evolved. Heating was continued until CO_2 evolution ceased at 220 °C. Distillation [Kugelrohr, 110 °C, 0.1 mm; lit. (12) 168-169 °C, 9 mm] gave 99-g (98% yield) of **3**, as white crystals, mp 39-41 °C: IR (KBr) 3278 (CO_2H), 1695 (C=O) cm^{-1}; ^1H-NMR ($DCCl_3$)

δ 1.11 (d, J = 3 Hz, 3, RCH$_3$), 2.26 (s, 3, ArCH$_3$), 2.46-3.06 (m, 3, ArCH$_2$, $\mathrm{C\underline{H}CH_3}$), 7.08 (s, 4, ArH); ^{13}C-NMR (DCCl$_3$) ppm 16.4, 21.0, 38.9, 41.4, 128.9, 129.1, 135.8, 136.0, 183.0; MS *m/z* (rel. abundance) M$^+$ 178.05 (9.92), 117.02 (9.20), 106.05 (10.36), 105.05 (100), 91.05 (10.56), 77.03 (8.73). Anal. Calcd. for $C_{11}H_{14}O_2$: C, 74.13; H, 7.92. Found: C, 74.31; H, 8.00.

β,4-Dimethylbenzenepropanol (4a). To a solution of 353-g (2.5 mol) of diisobutylaluminum hydride in 1 L of dry toluene was added a solution of 127-g (0.71 mol) of monoacid **3** in 300 mL of toluene over a 1-h period at 30 °C. After addition was complete, excess reducing agent was destroyed by the addition of 82 mL of ethyl acetate. The solution was carefully poured over 3 kg of ice, acidified with 1.5 L of conc. HCl, and extracted twice with toluene. The organic layers were combined, washed twice with water, dried (MgSO$_4$), filtered and concentrated. Distillation (Kugelrohr, 103 °C, 1 mm Hg) [lit. (12) 129 °C, 12 mm] afforded 98-g(84% yield) of **4a**: IR (neat) 3333 (OH), 1036 (C=O) cm^{-1}; ^{1}H-NMR (acetone-$\underline{d}_6$) δ 7.05 (s, 4, ArH), 3.45 (d, J = 6 Hz, 2, CH$_2$O), 2.85-2.21 (m, 2, ArCH$_2$), 2.3 (s, 3, ArCH$_3$), 1.9 (octet, J = 6 Hz, 1, CH). 0.88 (d, 3, J = 6 Hz, RCH$_3$); ^{13}C-NMR (DCCl$_3$) ppm 16.4, 20.9, 37.8, 39.2, 67.2, 128.9, 129.0, 135.0, 137.6; MS *m/z* (rel. abundance) M$^+$ 164.00 (20.81), 130.99 (25.36), 106.09 (30.09), 105.09 (100), 91.10 (18.81), 77.21 (12.24). Anal. Calcd. for $C_{11}H_{16}O$: C, 80.44; H, 9.83. Found: C, 80.16; H, 9.79.

1-(3-Bromo-2-Methylpropyl)-4-methylbenzene (4b). To a CCl$_4$ solution containing 149 g (0.91 mol) of alcohol **4a** was added 261 g (1.0 mol) of $P(C_6H_5)_3$ (13). Bromine (160 g, 0.01 mol) was added with the temperature kept at 40 °C. The reaction mixture was stirred overnight under N$_2$. The resulting precipitate was filtered, extracted with CCl$_4$ and this washed twice with H$_2$O. The CCl$_4$ extract was dried (MgSO$_4$), filtered, concentrated and fractionally distilled at 75 °C (0.13 mm) [lit. (12) 125 °C, 12 mm] to give an 86% yield (177 g, 0.78 mol) of bromide **4b**: IR (neat) 650, 792 (CBr) cm^{-1}; ^{1}H-NMR (DCCl$_3$) δ 1.01 (d, J = 6 Hz, 3, RCH$_3$), 1.8-2.2 (m, 1, CH), 2.31 (s, 3, ArCH$_3$), 2.55 (d, J = 6 Hz, 1, ArCH$_2$), 2.66 (d, J = 7 Hz, 1, ArCH$_2$), 3.29 (d, J = 2 Hz, 1, CH$_2$Br), 3.35 (d, J = 2 Hz, 1, CH$_2$Br), 7.07 (s, 4, Ar-H); ^{13}C-NMR (DCCl$_3$) ppm 18.7, 20.9, 37.1, 40.5, 129.0, 135.4, 136.5; MS *m/z* (rel. abundance) M$^+$+2 228 (6.74). M$^+$ 226 (6.74), 145 (55.2,

-HBr), 130 (100), 105 (94.61), 91 (84.80).

Attempts to use thionyl chloride in pyridine to prepare the chlorocompound **4c** or the bromocompound **4b** using PBr_3 were less satisfactory (56% and 37% yields respectively).

β,4-Dimethyl-benzenebutanoic acid-1-^{13}C (4d). Labeled carbon dioxide (2) ($^{13}CO_2$, 0.22 mol) was generated as described (3) by adding 200 mL of H_3PO_4 to an aqueous slurry of 48.5 g of $Ba^{13}CO_3$ (92% ^{13}C). Preparation of the Grignard reagent was accomplished in a previously described apparatus (3). In the 3-necked flask was placed 7.1 g (0.29 mol) of Mg turnings and 300 mL of 9:1 benzene:THF solution. This solution was brought to reflux as 60 g (0.26 mol) of bromide **4c** was added slowly through an addition funnel. After the reaction was initiated with methylmagnesium bromide, reflux was maintained for an additional 45 min; most of the Mg reacted.

The Grignard reagent was transferred to the stainless reaction vessel, cooled with liquid nitrogen and allowed to react overnight with $^{13}CO_2$. The unreacted $^{13}CO_2$ was collected by sweeping, with argon, into a barium hydroxide solution. The stainless steel vessel was opened, and its contents were poured over 500 g of ice, acidified with conc. HCl and extracted three times with ethyl ether. The combined ether layers were washed twice with saturated Na_2CO_3 (ca. 1 L), dried ($MgSO_4$),filtered, and concentrated to give 9.0 g of neutral product.

The Na_2CO_3 extracts were acidified with conc. HCl, and extracted twice with ether. The extract was dried ($MgSO_4$), filtered, concentrated and distilled (Kugelrohr apparatus at 113 °C, 0.2mm) [lit. (14) 180-181 °C, 15 mm, for unlabeled acid] to give 39.3 g (0.22 mol) of **4d** in 92% yield: IR (KBr) 3000 (CO_2H), 1700 (C=O) cm^{-1}; ^{1}H-NMR ($DCCl_3$) δ 0.95 (d, J = 6 Hz, 3, RCH_3), 2.15-2.40 (m, 3, CH, $C\underline{H}_2CO_2H$), 2.29 (s, 3, $ArCH_3$), 2.49 (d, J = 3 Hz, 1, $ArCH_2$), 2.57 (d, J = 3 Hz, 1, $ArCH_2$), 7.05 (s, 4, ArH); ^{13}C-NMR ($DCCl_3$) ppm 19.5, 20.9, 32.1, 42.5, 129.1, 135.4, 136.9, 180 (^{13}C); MS m/z (rel. abundance) M^+ 193.02 (12.17), 131.96 (58.03), 116.96 (10.41), 104.99 (100), 77.02 (9.15).

3,4-Dihydro-3,7-dimethyl-1(2H)-naphthalenone-1-^{13}C (5). To 485 g of polyphosphoric acid was added 54 g (0.28 mol) of **4d**. The mixture was heated at 95-105 °C for 1 h, cooled, poured over ice and extracted with ether. The extract was dried ($MgSO_4$), filtered, concentrated, and vacuum-distilled at 80 °C (0.1 mm) [lit. (14) 140-150 °C, 15 mm, for unlabeled ketone] to give a 97% yield (47 g, 0.27 mol) of 5, as white crystals, mp 49-50 °C [lit. (14) 52-53 °C for unlabeled ketone]: IR (KBr) 1670 (C=O), 1645 cm^{-1}; ^1H-NMR ($DCCl_3$) δ 1.12 (d, J = 5 Hz, 3, RCH_3), 2.10-3.10 (m, 5, $ArCH_2$, CH, $CH_2C{=}O$), 2.35 (s, 3, $ArCH_3$), 7.05-7.40 (two doublets, J = 8 Hz ea., 3, ArH), 7.84 1(s, 1, ArH); ^{13}C-NMR ($DCCl_3$) ppm 20.9, 21.2, 36.6, 37.7, 48.2, 1127.1, 128.6, 128.8, 134.4, 198.6 (^{13}C); MS <u>m/z</u> (rel. abundance) M^+ 175.11 (71.78), 160.6 (52.96), 132.98 (100), 131.99 (16.14), 103.99 (79.61), 78.00 (18.92).

2,6-Dimethyl-1,2,3,4-tetrahydronaphthalene-<u>4</u>-^{13}<u>C</u> (6). A solution of 30.9 g (0.18 mol) of labeled ketone, **5**, in 500 mL of acetic acid containing 3 g of 5% Pd/C was hydrogenated at 70-95 °C at 35 psig to completion. The solution was filtered, concentrated, neutralized with Na_2CO_3, extracted with isohexane, dried ($MgSO_4$), and distilled (Kugelrohr at 57 °C, 0.1 mm) [lit. (15) 241.3 °C, 760 mm, for unlabeled hydrocarbon] to give 20.7 g (0.13 mol, 73%) of **6**: IR (neat) 1475, 1450 (C=C str), 800 (C=CH bend) cm^{-1}; ^1H-NMR ($DCCl_3$) δ 1.02 (d, J = 6 Hz, 3, RCH_3), 1.2-1.5 (m, 1, CH), 1.6-2.0 (m, 2, $ArCH_2\underline{CH_2}$), 2.25 (s, 3, $ArCH_3$), 2.65-2.80 (2 doublets, J = 4 Hz ea., 4, $Ar\underline{CH_2}CH$, $Ar\underline{CH_2}$), 6.88 (s, 3, ArH); ^{13}C-NMR ($DCCl_3$) ppm 20.9, 22.1, 29.3 (^{13}C), 29.5, 31.7, 37.8, 126.3, 128.9, 129.0, 133.6, 134.5, 136.2; MS <u>m/z</u> (rel. abundance) M^+ 161.05 (62.55), 146.04 (36.93), 118.95 (100), 117.94 (28.27), 115.94 (18.25), 105.98 (18.61).

2,6-Dimethylnaphthalene-<u>4</u>-^{13}<u>C</u> (7). Labeled hydrocarbon **6** (1.79 g, 0.01 mol) was heated at 180-200 °C with 0.2 g of 10% Pd/C until H_2 evolution ceased. The mixture was then brought to reflux for an additional 15 min, cooled, dissolved in ether, filtered through Dicalite, concentrated, and chromatographed on silica gel with cyclohexane as a solvent. Concentration gave 1.5 g (0.01 mol 86%) of 7 as white flakes: mp 111 °C [lit. (16) 110-111 °C for unlabeled hydrocarbon]: IR (KBr) 1600 (C=C str), 820, 890 (ArH bend) cm^{-1}; ^1H-NMR ($DCCl_3$) δ 2.46 (s, 6, $ArCH_3$), 7.18-7.68 (m, 6, ArH); ^{13}C-NMR ($DCCl_3$) ppm 21.5, 126.6, 127.0 (^{13}C), 128.1, 132.0, 134.4; MS <u>m/z</u> (rel. abundance) M^+ 157.0 (100), 156.0 (43.1), 154.0 (10.7), 141.0 (50.2), 129.0 (13.6), 115.9 (10.9).

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REFERENCES AND NOTES

1. (a) Cronauer, D. C., Jewell, D. M., Shah, Y. T. and Modi, R. J. - Ind. Eng. Chem. Fund. 18:153 (1979).

(b) Cronauer, D. C., Jewell, D. M., Shah, Y. T., Modi, R. J. and Seshadri, K. S. - Ind. Eng. Chem. Fund. 18:368 (1979).

(c) Cronauer, D. C., McNeil, R. I., Young, D. C. and Ruberto, R. G. - Fuel 61:610 (1982).

(d) Cronauer, D. C., McNeil, R. I., Danner, D. A., Wieland, J. H. and Abichandani, J. S. - Am. Chem. Soc. Preprints Div. Fuel Chem. 28(5):40 (1983).

(e) Pickering, R. E., Wysocki, M. A. and Eisenbraun, E. J. - J. Label. C. R. 22:837 (1985).

(f) Pickering, R. E., Bymaster, D. L. and Eisenbraun, E. J. - "Synthesis of 1,2,3,4-Tetrahydronaphthalene-1-^{13}C, Naphthalene-1-^{13}C, and 1-Naphthalenol-1-^{13}C." Accepted for publication by J. Label. C. R.

2. The $^{13}CO_2$ as 90% $BaCO_3$ (92% $^{13}CO_2$) was obtained from Mound Laboratories, Miamisburg, Ohio 45342.

3. Vickery, E. H., Browne, C. E., Bymaster, D. L., Dobbs, T. K., Ansell, L. L. and Eisenbraun, E. J. - Chem. Ind.:954 (1977).

4. Kharasch, M. S. and Reinmuth, O. - Grignard Reaction of Nonmetallic Substances, Prentice-Hall:New York, 1954, pp. 909-960.

5. Johnson, W. S., Bannister, B., and Pappo, R. - J. Am. Chem. Soc. 78:6331 (1956).

6. (a) Wiley, G. A., Hershkowitz, R. L., Rein, B. M. and Chung, B. C. - J. Am. Chem. Soc. 86:964 (1964).

(b) Fieser, L. F. and Fieser, M. - Reagents for Organic Synthesis, 1, Wiley: New York, 1967, p. 1247.

7. Coulson, E. J., Gerrard, W. and Hudson, H. R. - J. Chem. Soc.:2364 (1965).

8. Brown, G. W. and Patia, S., Ed., - The Chemistry of the Hydroxyl Group, pt. 1, Interscience:New York, 1971, pp 593-622.

9. (a) Leigh, T. - Chem. Ind.:426 (1965).

   (b) See ref. 6(b):p. 418.

10. Trivedi, J. P. and Trivedi, J. J. - J. Indian Chem. Soc. 35:687 (1958).

11. Bachman, W. E., Cook, J. W., Hewett, C. L. and Iball, J. - J. Chem. Soc.:54 (1936).

12. Ruzicka, L. and Ehmann, L. - Helv. Chim. Acta 15:140 (1932).

13. Horner, L., Oediger, H. and Hoffmann, H. - Liebigs Ann. Chem. 626:26 (1959).

14. Mayer, F. and Stamm, G. - Ber. 56B: 1424 (1923).

15. Eru, I. I., Sukhorukov, V. P. and Shcherbakova, T. G. - Koks. Khim.: 45 (1968) [Chem. Abstr. 70:45743; (1969)].

16. Huisgen, R. and Sorge, G. - Liebigs Ann. Chem. 566:162 (1950).