2-Fluoronaphthalene–*tert*-Butyl Mercaptide Reaction (Run 6). This reaction was carried out in the same manner as run 5. *tert*-Butyl 2-naphthyl sulfide (IV, 48%, mp 58.5–59.5°) was the only aromatic product. Compound IV exhibited ir bands at 3060, 3040, 2980, 2960, 2940, 2920, 2900, 2860, 1585, 1470, 1455, 1360, 1350, 1340, 1270, 1240, 1220, 1170, 1150, 1130, 1075, 1020, 965, 950, 900, 865, 825, 745, 650, and 635 cm^{-1} and the following nmr peaks: δ 7.98 (m, 1), 7.25–7.80 (m, 6), and 1.30 (s, 9). *Anal.* Calcd for $C_{14}H_{16}S$: C, 77.73; H, 7.46; S, 14.82. Found: C, 77.68; H, 7.24; S, 14.58.

1-Bromo- and 2-Bromonaphthalene–*tert*-Butyl Mercaptide Reactions (Runs 7 and 8).—These reactions were carried out the same as runs 5 and 6. The conversions and yields are listed in Table I.

Registry No.—DMSO, 67-68-5.

Acknowledgment.—The authors wish to thank Professor R. T. Hawkins for his many helpful discussions.

The Specific Deuteration of the Camphor Skeleton. Reduction of Chlorosulfoxides[1]

G. C. JOSHI[2] AND E. W. WARNHOFF*

Department of Chemistry, University of Western Ontario, London, Canada

Received January 4, 1972

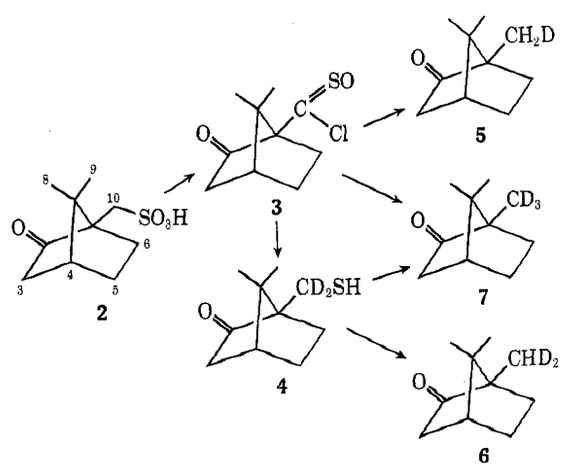
A convenient and inexpensive method has been developed for preparation of 9- and 10-deuterated camphors by the stepwise reduction of the corresponding chlorosulfoxide (oxythio acyl chloride) with deuterated amalgamated aluminum and/or Raney nickel. Simple procedures for stereoselective deuteration of camphor at C-3, C-4, C-5, and C-6 are also described.

For a proposed study of the stereochemistry of halogenation of camphor (**1**) and its enol derivatives, the analysis of product mixtures was to be done by nmr spectroscopy, a technique which had proved invaluable in a similar study with 3-keto steroid derivatives.[3] In particular, the chemical shifts of the C-8 methyl group and the C-3 and C-4 protons were to be used to assign halogen stereochemistry in the products. Therefore, it was essential to be certain which of the three methyl peaks belonged to C-8 in each of the compounds involved, and for this purpose deuterium labeling of methyl groups was the logical tool. Rather than deuterate the C-8 methyl group,[4] it appeared from the known chemistry of camphor to be easier and more generally useful to label the C-9 and C-10 methyl groups. Of the three reported procedures[6] for so doing, (a) reduction of the appropriate carboxylic acid to the primary alcohol and thence by way of hydride reduction of the tosylate to a methyl group,[6a,b] (b) zinc reduction of the C-9 primary bromide,[6c] and (c) hydride reduction of the appropriate primary sulfonyl chloride to a methyl group,[6d] two (a and c) require the use of the expensive lithium aluminum deuteride, while the third (b) gives a fragmentation side product.

Therefore, a convenient, inexpensive three- or four-step method has been developed for the incorporation of one, two, or three deuterium atoms into the C-9 and C-10 methyl groups of camphor.[1] The method involves the previously unreported stepwise reduction of the chlorosulfoxide group (oxythio acyl chloride or thioacyl chloride *S*-oxide) in the readily available camphor-10-chlorosulfoxide (**3**) and 3-*endo*-bromocamphor-9-chlorosulfoxide (**9**) with the cheapest source of deuterium, deuterium oxide. Since our halogenation study also required deuterium at C-4, it seemed worthwhile to develop practical procedures for stereoselective deuteration of C-6, C-5, and C-3 as well.

Very recently, Rodig and Sysko[7] have reported a nine-step synthesis of racemic camphor from norbornanone. Their synthesis has the advantage of allowing C labeling as well as H labeling of the methyl groups, but for H labeling it has the disadvantages, compared to the presently described synthesis, of being longer, of giving racemic camphor, and of not readily permitting the preparation of 9- or 10-mono- or dideuteriocamphor. Thus the two syntheses are complementary.

Our 10-methyl deuteration begins with conversion of the commercially available sulfonic acid **2** *via* the



sulfonyl chloride into the chlorosulfoxide **3** by the pyridine–toluenesulfonyl chloride procedure.[8] The chlorosulfoxide could now be reduced in stages by a suitable combination of two neutral reagents: (a) Raney nickel (Ra Ni) and (b) amalgamated aluminum (Al/Hg) with or without deuterium oxide. Raney nickel was found to reduce the chlorosulfoxide all the

(1) Presented in part at the 51st Canadian Chemical Conference, Vancouver, 1968, and taken from the Ph.D. Thesis of G. C. J., 1968.

(2) Commonwealth Scholar, 1964–1968; Defence Research Laboratory (Materials), Kanpur, India.

(3) E. W. Warnhoff, *J. Org. Chem.*, **28**, 887 (1963).

(4) In principle, the C-10 methyl group of *d*-camphor could be labeled and then transformed into the C-8 methyl group of *l*-camphor by racemization and resolution,[5] but this procedure promised to be more tedious than the one adopted and would have given at most 50% yield per cycle.

(5) A. M. T. Finch and W. R. Vaughan, *J. Amer. Chem. Soc.*, **87**, 5520 (1965); *ibid.*, **91**, 1416 (1969).

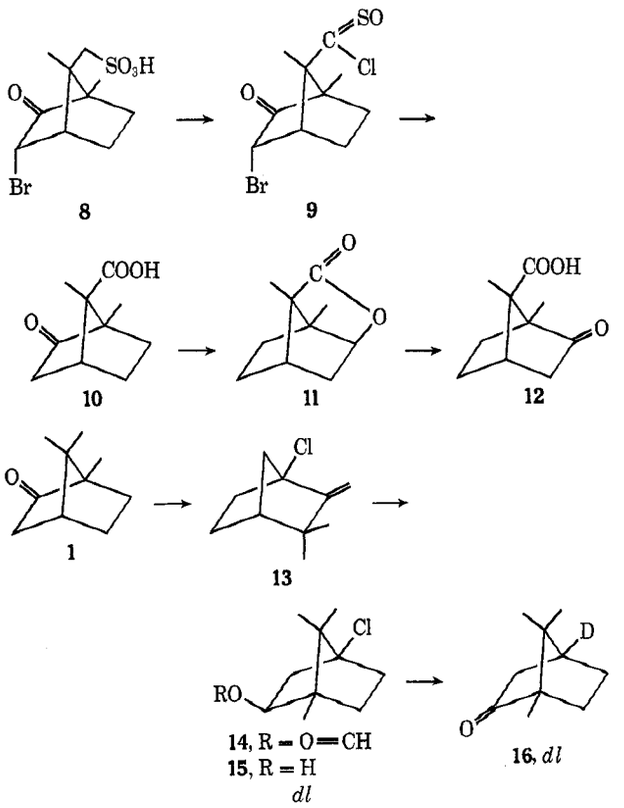
(6) (a) J. D. Connelly and R. McCrindle, *Chem. Ind. (London)*, 379 (1965); (b) W. L. Meyer and A. P. Lobo, *J. Amer. Chem. Soc.*, **88**, 3181 (1966); W. L. Meyer, A. P. Lobo, and R. N. McCarty, *J. Org. Chem.*, **32**, 1754 (1967); (c) K. M. Baker and B. R. Davis, *Tetrahedron*, **24**, 1655 (1968); (d) D. R. Dimmel and J. Wolinsky, *J. Org. Chem.*, **32**, 410 (1967).

(7) O. R. Rodig and R. J. Sysko, *J. Org. Chem.*, **36**, 2324 (1971).

(8) J. Strating, *Recl. Trav. Chim. Pays-Bas*, **83**, 94 (1964).

way to a methyl group, and camphor-*10,10,10-d*$_3$ (**7**) was prepared from **3** after the hydrogen on the Ra Ni had been exchanged for deuterium by equilibration with deuterium oxide. However, the amalgamated aluminum reagent[9] only reduces the chlorosulfoxide group to the thiol level.[10] Thus the action of Al/Hg and deuterium oxide on **3** gave camphor-10-thiol-*10,10-d*$_2$ (**4**) which was hydrogenolyzed by Ra Ni to camphor-*10,10-d*$_2$ (**6**).[11] The deuterated Ra Ni reduction of **4** (as done in the 9-chlorosulfoxide reductions) would be an alternative route to camphor-*10,10,10-d*$_3$ (**7**). On the other hand, camphor-*10-d*$_1$ (**5**) would result from the Al/Hg–water and Ra Ni–D_2O sequence.

The synthesis of the mono-, di- and tri-9-deuteriocamphors employs the same procedures except that the 3-*endo*-bromo-9-sulfonic acid **8** is the starting material because its preparation by sulfonation of 3-bromocamphor gives better and more reproducible yields than sulfonation of camphor. Moreover, optically active 3-bromocamphor affords optically active **8**, but sulfonation of camphor itself gives racemized camphor-9-sulfonic acid. The 3-bromo substituent is removed during the Al/Hg reduction of the 3-bromo-9-chlorosulfoxide **9**. In the use of this general deuteration

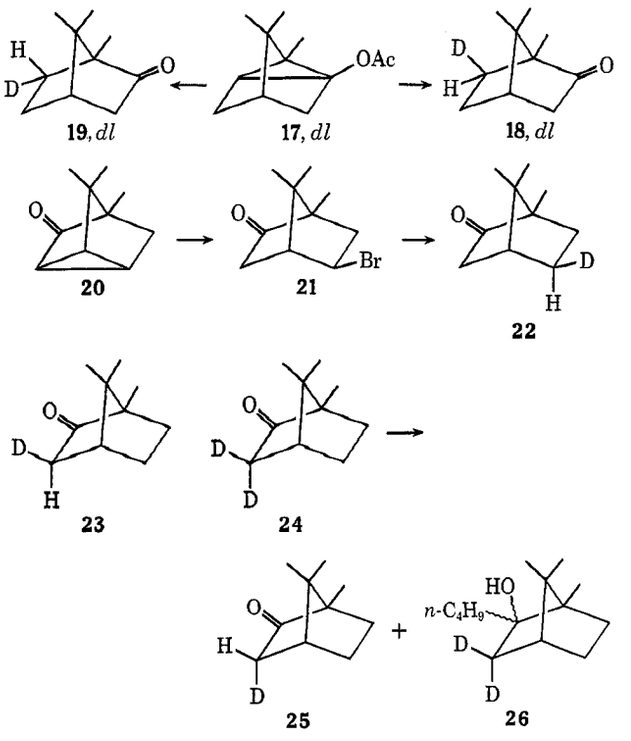


method there are two points requiring attention: the possible partial reduction of the carbonyl group if the Ra Ni is not sufficiently inactive and the introduction of deuterium at C-3 by enolization. Any difficulties from these side reactions can be overcome by oxidation and/or exchange.

The 3-*endo*-bromo-9-sulfonic acid **8** can also be used for deuteration of the 8-methyl group of camphor because the 3-*endo*-bromo-9-sulfonyl chloride or 9-chlorosulfoxide **9** can be oxidatively hydrolyzed and debrominated in high yield to isoketopinic acid (**10**) (see Experimental Section). The known transformation[13] of isoketopinic acid *via* the lactone **11** to keto acid **12** in effect converts the C-9 carboxyl into a C-8 carboxyl which would be reducible to an 8-deuteriomethyl camphor by appropriate modification of the earlier published method.[6a,b]

The 4 position of camphor was deuterated by sodium–ethanol-*O-d* reduction of 4-chloroisoborneol (**15**) followed by oxidation to camphor-*4-d*$_1$ (**16**), a procedure used by Nickon, *et al.*, to make norbornanone-*4-d*$_1$.[14] 4-Chloroisoborneol was available by known reactions from camphor (**1**) → 1-chlorocamphene (**13**) → 4-chloroisobornyl formate (**14**) → **15**.[15] A possible disadvantage of this sequence is that racemization by 6,2-hydride shift occurred during formic acid solvolysis of **13**, and the 4-chloroisoborneol is racemic. Racemization could presumably be avoided by the use of other solvolytic media.[15]

Monodeuteration at C-6 with a high degree of stereoselectivity was achieved by application of the findings of Nickon, *et al.*,[16] with 1-acetoxynortricyclene to the now readily available camphor 2,6-homoenol acetate (**17**).[17] Basic hydrolysis of **17** with potassium deuteroxide in methanol-*O-d* gave camphor-*6-exo-d*$_1$ (**18**),



(9) E. J. Corey and M. Chaykovsky, *J. Amer. Chem. Soc.*, **87**, 1345 (1965).

(10) Other reagents, such as tin (or zinc) and hydrochloric acid, and lithium aluminum hydride, which will also reduce sulfonyl chlorides to mercaptans, could probably be used on chlorosulfoxides, but the conditions would not be as mild or selective toward other functional groups.

(11) The nickel boride reagent[12] was also used for hydrogenolysis of this mercaptan but it offered no advantages over Raney nickel. In fact, there was more carbonyl reduction with nickel boride.

(12) W. E. Truce and F. M. Perry, *J. Org. Chem.*, **30**, 1316 (1965).

(13) E. J. Corey, M. Ohno, S. W. Chow, and R. A. Scherrer, *J. Amer. Chem. Soc.*, **81**, 6305 (1959).

(14) A. Nickon, J. L. Lambert, and J. E. Oliver, *ibid.*, **88**, 2787 (1966).

(15) J. Houben and F. Pfankuch, *Justus Liebigs Ann. Chem.*, **489**, 193 (1931).

(16) A. Nickon, J. L. Lambert, R. O. Williams, and N. H. Werstiuk, *J. Amer. Chem. Soc.*, **88**, 3354 (1966).

(17) G. C. Joshi, W. D. Chambers, and E. W. Warnhoff, *Tetrahedron Lett.*, 3613 (1967).

whereas acidic hydrolysis of **17** in trifluoroacetic acid–deuterium oxide produced camphor-*6-endo-d*$_1$ (**19**).

For deuteration at C-5, the starting material was 3,5-cyclocamphanone (**20**), whose cyclopropyl ketone system is opened by hydrobromic acid to 5-*exo*-bromocamphor (**21**).[18] The bromine atom of **21** was replaced by deuterium without reduction of the ketone by use of the Al/Hg–deuterium oxide reagent. The 5-deuterium atom was largely *exo* because the long-range coupling of the 5-exo hydrogen was missing from the 3-exo hydrogen pattern in the nmr spectrum of **22**.

For stereoselective 3-monodeuteration of camphor, advantage was taken of the well-studied preference for 3-exo protonation of the enolate anion.[19] The enolate was prepared conveniently and quantitatively by the action of commercial *n*-butyllithium on a solution of camphor in tetrahydrofuran,[17] and it was then protonated by addition to an excess of acetic acid-d_4–deuterium oxide under conditions hopefully approaching irreversibility. As far as could be judged by nmr spectra (see Experimental Section), the deuterium atom in the product **23** was entirely exo. For the preparation of the 3-*endo*-deuterium epimer **25** the same procedure was applied to camphor-*3,3-d*$_2$ (**24**), which was made by zinc–acetic acid-d_4 reduction of 3,3-dibromocamphor. The lithium enolate was protonated by addition to acetic acid–water. The deuterium atom in the camphor-*3-d*$_1$ was almost entirely endo according to the nmr coupling pattern of the CHOH proton in the derived isoborneol. The camphor-*3-endo-d*$_1$ was accompanied by about 25% of the tertiary alcohol **26** resulting from addition of *n*-butyllithium to the carbonyl group of camphor-*3,3-d*$_2$, whereas this product was absent from the reaction of *n*-butyllithium with camphor. The relative rates of 3-proton abstraction and carbonyl addition are so close that the decreased proton abstraction rate caused by deuterium substitution now allows carbonyl addition to become a product-forming process: the product composition is thus determined by the deuterium isotope effect.

Experimental Section

For general details see ref 20. Deuterium oxide was >98% isotopically pure. Acetic acid-d_4 (Merck) contained 99.5 atom % excess D. The conditions for deuteration were not optimized and further improvement is to be expected. Unless otherwise specified, petroleum ether refers to the fraction of bp 30–60°.

***d*-Camphor-10-chlorosulfoxide (3).**—*d*-Camphor-10-sulfonic acid (**2**) (50 g, 0.21 mol, Aldrich Chemical Co.) was added with swirling to a mixture of 50 g of $CaCO_3$ and 100 ml of freshly distilled $SOCl_2$. The reaction mixture was refluxed for 4 hr. Excess $SOCl_2$ was removed by distillation with a petroleum ether (bp 60–80°) chaser. The product was separated from inorganic salts by solution in ether and filtration. The residue from evaporation of the filtrate was recrystallized from petroleum ether to give 45 g (83%) of white flakes of the sulfonyl chloride: mp 66–66.5° (lit.[21] mp 67–68°); nmr δ 0.93 (s, CH_3), 1.13 (s, CH_3), 3.73 and 4.29 ppm (AB of CH_2SO_2Cl, J = 15 Hz).

d-Camphor-10-sulfonyl chloride (50 g, 0.20 mol) dissolved in 30 ml of hot dioxane was added dropwise during 45 min to a hot (90°) stirred mixture of 38 g (0.20 mol) of *p*-toluenesulfonyl chloride (TsCl) and 40 ml of pyridine.[8] Heating and stirring were continued for 1 hr. The cooled reaction mixture was vigorously stirred with 600 ml of refluxing ether. Filtration to remove pyridine hydrochloride and evaporation of the ethereal solution left a residue which was recrystallized from petroleum ether (bp 80–100°). Two crops of light pinkish yellow crystals totaling 39 g (85%) of the chlorosulfoxide **3**, mp 84.5–85° (lit.[22] mp 85°), were obtained, nmr δ 1.13 (s, 2 CH_3).

Hydrogenolysis of *d*-Camphor-10-chlorosulfoxide (3).—A solution of 200 mg (0.92 mmol) of **3** in 10 ml of absolute ethanol was refluxed with 1 g of W-4 Raney nickel[23] for 3 hr. Filtration, evaporation, dilution with water, and extraction with ether gave 85 mg (64%) of *d*-camphor (**1**): $[\alpha]_D$ +39.6° (*c* 2.36, EtOH) (lit.[24] $[\alpha]_D$ +41–43°); nmr δ 0.84 (s, CH_3), 0.92 (s, CH_3), and 0.96 (s, CH_3).

***d*-Camphor-*10,10,10-d*$_3$ (7).**—The hydrogen on W-6 Raney Ni[25] was replaced by D by heating the Ni with D_2O and a trace of DCl for several hours after decantation of EtOH and rinsing with D_2O. A solution of 382 mg (1.63 mmol) of the 10-chlorosulfoxide **3** in 5 ml of EtOD containing 2 ml of D_2O was refluxed for 4 hr with 2 g of the deuterated Raney Ni. Filtration and evaporation left 225 mg (90%) of crude deuterated camphor which contained small amounts of two more polar (tlc) impurities. In the nmr spectrum the methyl peak at δ 0.91 was very weak in relation to the two methyl peaks at δ 0.84 and 0.96, indicating that the product was mainly camphor-*10,10,10-d*$_3$.

***d*-Camphor-10-thiol-*10,10-d*$_2$ (4).**—Aluminum metal (15 g, granular, <20 mesh, Fisher Co.) was amalgamated with a solution of 1 g of $HgCl_2$ dissolved in 100 ml of dry THF. The amalgamated metal was washed repeatedly by decantation with small portions of THF (200 ml total). Then 200 ml of dried THF (distilled from $LiAlH_4$)[26] and 10 g (43 mmol) of the 10-chlorosulfoxide **3** were added with stirring to the Al metal while the reaction mixture was protected from moisture by a $CaCl_2$ tube. A solution of 10 ml of D_2O in 50 ml of the dried THF was added dropwise with stirring during 30 min. The reaction mixture was heated to reflux and stirred for 10 hr with the addition of 100 mg of $HgCl_2$ and 5 ml of D_2O after the first 4 hr. The hot solution was filtered and the filtrate was concentrated to leave 7.7 g (96%) of crude *d*-camphor-10-thiol-*10,10-d*$_2$ (**4**). Recrystallization from petroleum ether gave colorless crystals: mp 65.5–66°; $[\alpha]_D$ +4.0° (*c* 1.37, EtOH) [lit.[27] mp 66°; $[\alpha]_D$ +6° (*c* 10, acetone) for non-*d* compound]; nmr δ 0.92 (s, CH_3) and 1.03 ppm (s, CH_3). As Lowry says,[27] the compound has "a characteristic and not unpleasant odour, faintly recalling with camphor the odour of burnt india-rubber."

***d*-Camphor-*10,10-d*$_2$ (6).**—A solution of 3.71 g (20 mmol) of *d*-camphor-10-thiol-*10,10-d*$_2$ (**4**) in 100 ml of absolute ethanol was refluxed and stirred with 40 g of W-4 Raney Ni[23] for 10 hr. The catalyst was removed by filtration and washed with fresh ethanol. The filtrate was concentrated to ~10 ml, diluted with water, and extracted with petroleum ether. The dried extracts were evaporated to leave 2.25 g (73%) of colorless camphor-*10,10-d*$_2$ (**6**). The crude product was sublimed at atmospheric pressure to give crystals: mp 177–177.5° (sealed capillary); nmr δ 0.84 (s, CH_3), 0.91 (s, CHD_2), and 0.95 ppm (s, CH_3). Analysis by mass spectroscopy gave 4% d_3, 81% d_2, 12.5% d_1, and 2.5% d_0.

3-*endo*-Bromo-*d*-camphor-9-chlorosulfoxide (9).—The sodium salt of 3-bromo-*d*-camphor-9-sulfonic acid (**8**) was prepared by sulfonation of 3-*endo*-bromo-*d*-camphor with 10% fuming sulfuric acid according to the procedure of Kipping and Pope.[28] The crude sodium salt (29.3 g, contaminated with Na_2CO_3) was triturated with 25 g of PCl_5 in a mortar. The slurry was leached with 200 ml of chloroform. The chloroform solution was washed (H_2O), dried, and evaporated to leave a residue which was recrystallized from petroleum ether. There was obtained 11.5 g (~55%) of ill-defined crystals. Recrystallization from CH_2Cl_2 gave better crystals of the endo bromo sulfonyl chloride: mp 138–139° (lit.[28] mp 137°); nmr δ 1.04 (s, CH_3), 1.33 (s,

(18) J. Bredt and W. Holz, *J. Prakt. Chem.*, **95**, 133 (1917).

(19) A. F. Thomas and B. Willhalm, *Tetrahedron Lett.*, 1309 (1965); A. F. Thomas, R. A. Schneider, and J. Meinwald, *J. Amer. Chem. Soc.*, **89**, 68 (1967); T. T. Tidwell, *ibid.*, **92**, 1448 (1970).

(20) E. W. Warnhoff and D. R. Marshall, *J. Org. Chem.*, **32**, 2000 (1967).

(21) (a) A. Reychler, *Bull. Soc. Chim. Fr.*, **19**, 120 (1898); (b) P. D. Bartlett and L. H. Knox, *Org. Syn.*, **45**, 12 (1965).

(22) E. Wedekind, D. Schenk, and R. Stüsser, *Chem. Ber.*, **56**, 633 (1923).

(23) H. Adkins and A. A. Pavlic, *J. Amer. Chem. Soc.*, **69**, 3039 (1947); **68**, 1471 (1946).

(24) C. F. Poe and E. M. Plein, *J. Phys. Chem.*, **38**, 883 (1934).

(25) H. R. Billica and H. Adkins, "Organic Syntheses," Collect. Vol. III, Wiley, New York, N. Y., 1955, p 176.

(26) If the THF was not distilled from $LiAlH_4$, no reduction took place, and starting material was recovered.

(27) T. M. Lowry and G. C. Donington, *J. Chem. Soc.*, **83**, 479 (1903).

(28) F. S. Kipping and W. J. Pope, *ibid.*, **63**, 548 (1893).

CH_3), 3.05 (1 H, m, C_4 H), 3.83 and 4.12 (AB of CH_2SO_2Cl), and 2.78 ppm (b d, $J \cong 5$ Hz, CHBr).

Crude 3-bromo-*d*-camphor-9-sulfonyl chloride (66 g, 0.20 mol, a mixture of endo and exo bromo isomers) was treated with 38 g (0.20 mol) of TsCl and 40 ml of pyridine according to the procedure described for the preparation of *d*-camphor-10-chlorosulfoxide. Crystallization from petroleum ether gave 44 g (71%) of a gray, powdery mass which was a mixture of 3-*exo*-bromo and 3-*endo*-bromo stereoisomers, nmr δ 4.23 (s, 3-endo H of CHBr) and 4.85 ppm (d, $J \cong 5$ Hz, 3-exo H of CHBr). Recrystallization from acetone gave buff-colored powdery **9**: mp 156.5–157°; $[\alpha]_D$ +23.7° (*c* 3.18, benzene) [lit.[29] mp 159°; $[\alpha]_D$ +31° (*c* 5.5, benzene)]; nmr δ 1.33 (s, CH_3), 1.37 (s, CH_3), 3.08 (m, C_4 H), and 4.70 ppm (d, $J \cong 5$ Hz, 3 exo H of CHBr).

Isoketopinic Acid (10) by Oxidative Hydrolysis of 9.—To a stirred (magnetic bar) solution of 20 g of crude 3-bromocamphor-9-chlorosulfoxide in 100 ml of acetone and 100 ml of water was added 40 g of $Na_2CO_3 \cdot 10H_2O$ followed by 40 g of $KMnO_4$ over a period of 1.5 hr. After another hour the mixture was filtered, acidified with concentrated HCl, and extracted with ether. The crude 3-bromoisoketopinic acid (12.6 g) obtained was a mixture of 3-*exo*- and 3-*endo*-bromo stereoisomers, nmr δ 1.25 (s, 2 CH_3), 4.16 (s, 3 endo H of CHBr, minor), 4.80 (d, $J \cong 5$ Hz, 3-exo H of CHBr, major), and 9.38 ppm (s, COOH). The bromine was removed by Zn dust (7 g) reduction of 12.2 g of the bromo acid in a refluxing mixture of 30 ml of dioxane and 10 ml of HOAc. Filtration, dilution with water, and extraction with ether gave 7.6 g (91%) of crude isoketopinic acid (**10**). Recrystallization from petroleum ether gave 4.6 g of white crystals: mp 248–249.5°; $[\alpha]_D$ +54° (*c* 4.95, EtOH) (lit.[22] mp 250°; $[\alpha]_D$ +28° in benzene); nmr δ 1.15 (s, 2 CH_3) and 10.36 ppm (s, COOH).

***d*-Camphor-*9,9*-d_2.**—A solution of 13.4 g (42 mmol) of 3-bromo-*d*-camphor-9-chlorosulfoxide (**9**) in 200 ml of THF[26] was reduced with 15 g of Al/Hg and a total of 15 ml of D_2O in the same way as described for the preparation of *d*-camphor-10-thiol-*10,10*-d_2. There was obtained 8.0 g (99%) of oily liquid camphor-9-thiol-*3,9,9*-d_3 (**27**): $[\alpha]_D$ +103° (*c* 5.12, EtOH) (lit.[30] mp 94°; $[\alpha]_D$ +108°, for non-D compound); nmr δ 0.94 ppm (s, 2 CH_3).

Desulfurization of 5.0 g (26 mmol) of the thiol **27** with 50 g of W-4 Raney Ni[23] in refluxing ethanol for 12 hr according to the procedure used on camphor-10-thiol-*10,10*-d_2 gave 3.2 g of oil which still contained considerable starting material. A second treatment with 40 g of Raney Ni for 8 hr yielded 2.5 g of solid. Percolation through Woelm neutral alumina (grade III) in petroleum ether and sublimation gave 1.19 g (28%) of camphor-*9,9*-d_2: $[\alpha]_D$ +43.8° (*c* 3.35, EtOH) (lit.[24] $[\alpha]_D$ +41–43° for non-D compound); nmr δ 0.85 (s, CH_3), 0.91 (s, CH_3), and 0.96 (s, CHD_2). Deuterium analysis by mass spectroscopy gave 9% d_3, 63% d_2, 15% d_1 and 13% d_0. Most of the D atom at C-3 was exchanged during the Raney Ni treatment.

***d*-Camphor-*3,9,9,9*-d_4.**—A solution of 425 mg (2.30 mmol) of camphor-9-thiol-*3,9,9*-d_3 in 10 ml of THF was added to ~2 g of deuterated (see preparation of **7**) W-5 Ra Ni[25] in 10 ml of D_2O. The suspension was stirred overnight at room temperature and then refluxed for 3 hr. Filtration, drying, and concentration gave 152 mg (43%) of crude deuterated camphor. Sublimation and thick layer chromatography (petroleum ether–ethyl acetate, 80:20) gave pure camphor-*3,9,9,9*-d_4. Analysis by mass spectroscopy gave 72% d_4, 24% d_3, 3% d_2, and 1% d_1.

***d*-Camphor-*9*-d_1.**—A stirred solution of 903 mg (2.90 mmol) of **9** in 13.5 ml of THF[26] was reduced with 1.35 g of Al/Hg (see preparation of **4**) and 0.9 ml of H_2O at reflux for 5.5 hr. The reaction mixture was filtered, dried, and evaporated to leave 480 mg (90%) of crude camphor-9-thiol. Thick layer chromatography on silica gel (petroleum ether–ethyl acetate, 80:20) gave 262 mg of pure thiol as a clear viscous oil. A solution of 120 mg of the pure camphor-9-thiol in 4 ml of THF was stirred with a suspension of ~0.6 g of deuterated (see preparation of **7**) W-5 Ra/Ni in 3 ml of D_2O for 20 hr under protection (drying tube) from atmospheric moisture. Filtration, drying, and evaporation of solvent gave camphor-*9*-d_1. Analysis by mass spectroscopy gave 1% d_2, 86% d_1, and 13% d_0.

4-Chloroisoborneol (15).—To a stirred solution of 15.2 g (0.10 mol) of *d*-camphor in 25 ml of CH_2Cl_2 chilled in an ice bath was added in small portions 12.8 g of PCl_3 and 22.2 g of PCl_5. After 2 hr the reaction mixture was allowed to come to room temperature for 10 hr. The reaction mixture was poured onto ice and extracted with petroleum ether. The extract was washed with water and evaporated to leave 20.8 g of clear, colorless liquid which was refluxed for 12 hr with 20 g of KOAc in 100 ml of EtOH–H_2O (75:25). The solution was then poured into water and extracted with petroleum ether. Evaporation of the washed and dried solution left 16.5 g (97%) of pale yellow 1-chlorocamphene (**13**), which was essentially pure according to its nmr spectrum, δ 1.10 (s, 6 H, *gem*-diMe), 3.91 (s, =CH), and 5.10 (s, =CH). A solution of the crude **13** (16.2 g, 0.095 mol) in 50 ml of formic acid was refluxed for 14 hr, poured onto ice, and extracted with petroleum ether. Evaporation of the washed and dried organic extract left 16.7 g (81%) of 4-chloroisobornyl formate (**14**), nmr δ 0.88 (s, CH_3), 0.93 (s, CH_3), 1.01 (s, CH_3), 4.80 (dd, X part of ABX, $J_{AX} + J_{BX} = 11$ Hz, CHOC=O), and 8.00 ppm (1 H, s, HCOO), which was saponified at room temperature for 10 hr with 5.6 g of KOH, 70 ml of MeOH, and 30 ml of H_2O. The hydrolysate was poured onto ice and extracted with five 60-ml portions of ether. Evaporation of the washed and dried extracts left a brownish solid which was recrystallized from petroleum ether (bp 80–100°). There was obtained 10.2 g (54% overall from camphor) of light yellow crystals of racemic 4-chloroisoborneol: mp 202–203° with sublimation;[31] $[\alpha]_D$ +0.18° ± 0.5 (*c* 4.90, EtOH); nmr 0.84 (s, CH_3), 0.97 (s, CH_3), 1.04 (s, CH_3), 1.80 (s, OH), and 3.67 ppm (dd, X part of ABX, $J_{AX} + J_{BX} = 12$ Hz, CHOH). Racemization most likely occurred during the reaction of 1-chlorocamphene with formic acid.

(±)-Camphor-*4*-d_1 (16).—The procedure of Nickon, *et al.*,[14] for the preparation of norbornanone-4-d_1 was adapted. To a refluxing solution of 8.0 g (0.042 mol) of 4-chloroisoborneol **15** in 45 g of EtOD (>99% OD) was added 12 g (0.52 g-atom) of sodium in small pieces during 1 hr. Reflux was continued for 3 hr with the addition of 2 ml of D_2O at the end of the period. Dilution of the cooled reaction mixture with 50 ml of water and extraction with five 20-ml portions of ether yielded 6.17 g (84%) of crude isoborneol-*4*-d_1, which was oxidized without purification.

The crude isoborneol-4-d_1 in 27 ml of acetone was stirred in an ice bath and oxidized with a solution of 3.2 g of CrO_3 dissolved in 15 ml of H_2O and 2.8 ml of concentrated H_2SO_4. After 4 hr, SO_2 was introduced until the solution became green. The layers were separated, and the lower green aqueous layer was extracted with three 25-ml portions of petroleum ether. The combined upper layer and extracts were washed, dried, and evaporated to leave 6.01 g (98%) of ***dl*-camphor-*4*-d_1 (16)** which was further purified by sublimation, mp 177–179° (lit.[24] mp 178.5°), $[\alpha]_D$ 0° (*c* 3.70, EtOH).

The nmr spectrum of 3-*endo*-bromocamphor prepared from **16** had a 1 H singlet at δ 4.65 instead of the doublet ($J \cong 5$ Hz) of the non-D compound because the C_4-H-exo C_3-H coupling was missing. The nmr spectrum of a sample of camphorquinone-*4*-d_1 prepared by SeO_2 oxidation of **16** lacked the doublet ($J \cong 4$ Hz) appearing at δ 2.63 in the protio analog.

***d*-Camphor-*5*-*exo*-d_1 (22).**—A refluxing solution of 895 mg (3.87 mmol) of 5-*exo*-bromo-*d*-camphor (**21**) (prepared by the action of HBr on 3,5-cyclocamphanone[18]) in 20 ml of dried THF was treated for 1 hr with 1 g of Al/Hg (made as described for the preparation of **4**) and 1 ml of D_2O. Filtration, evaporation, and sublimation yielded 436 mg (73%) of *d*-camphor-*5*-*exo*-d_1, nmr δ 0.85 (s, CH_3), 0.91 (s, CH_3), and 0.95 ppm (s, CH_3). A signal present as a sharp peak at δ 1.41 in the spectrum of camphor had collapsed to a broad band in the spectrum of camphor-*5*-d_1. Analysis by mass spectroscopy gave 4% d_2, 85% d_1, and 11% d_0.

That most of the D was in the 5-exo position was evident from the nmr spectrum of the compound. The well-separated four-line pattern of half of the 3-exo H absorption in camphor at δ 2.53 was now a two-line pattern (superimposed on residual absorption from the original four-line pattern) because the exo-C_5-H–exo-C_3-H coupling was missing.

(±)-Camphor-*6*-*endo*-d_1 (19).—A solution of 6 ml of $(CF_3CO)_2O$, 2 ml of D_2O, and 1.92 g (~60% camphor homoenol acetate **17**) of the crude product of oxidation of tricyclene with $Pb(OAc)_4$[17] was sealed in a glass tube and heated at 120° for 6 hr. The contents of the tube were poured into water and extracted with petroleum ether. The extracts were washed with aqueous

(29) H. Burgess and T. M. Lowry, *J. Chem. Soc.*, **127**, 282 (1925).

(30) T. Tukamoto, *J. Pharm. Soc. Jap.*, **59**, 37 (1939).

(31) The racemate was synthesized by J. Houben and E. Pfankuch, *Justus Liebigs Ann. Chem.*, **501**, 219 (1933), by mixing equal quantities of *d* and *l*, but its physical properties were not reported.

$NaHCO_3$, dried, and chromatographed on 30 g of Woelm neutral alumina (grade III). Ether–petroleum ether (5:95) eluted 462 mg (~50%) of deuterated camphor. Deuterium was removed from C-3 by heating the product with acetic and hydrochloric acid in a sealed tube at 150°, and the camphor-*6-endo-d*$_1$ was finally sublimed, nmr δ 0.85 (s, CH_3), 0.91 (s, CH_3), and 0.95 ppm (s, CH_3). Analysis by mass spectroscopy gave 1% d_2, 74% d_1, and 24% d_0.

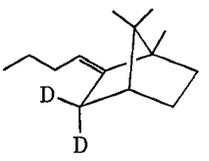
(±)-**Camphor-*6-exo-d*$_1$** (**18**).—To the solution obtained by dissolving 0.8 g of K metal in 10 ml of MeOD was added 1.94 g (~60% camphor homoenol acetate **17**) of the crude product of oxidation of tricyclene with $Pb(OAc)_4$[17] dissolved in 5 ml of MeOD and 2 ml of D_2O. After ~12 hr at room temperature the mixture was poured into water and extracted with petroleum ether. Chromatography of the crude product (1.4 g) on 40 g of Woelm neutral alumina (grade III) gave 901 mg (~97%) of deuterated camphor. Deuterium was removed from C-3 by reflux with methanolic KOH, and the camphor-*6-exo-d*$_1$ was finally sublimed at atmospheric pressure, nmr δ 0.85 (s, CH_3), 0.91 (s, CH_3), and 0.95 ppm (s, CH_3).

The stereochemistry of the D atom in each camphor-*6-d*$_1$ was proved by bromination to 3-*endo*-bromocamphor and $LiAlH_4$ reduction of the product to 3-*endo*-bromoborneol-*6-d*$_1$. In the nmr spectrum of the product from *6-exo-d*$_1$ camphor (from the basic reaction) the C-2 exo-H lacked the long range coupling to the 6-exo hydrogen which coupling was present in the product from *6-endo-d*$_1$ camphor from the acidic reaction.

d-**Camphor-*3-exo-d*$_1$** (**23**).—A solution of 7.6 g (50 mmol) of *d*-camphor in 200 ml of THF (distilled from $LiAlH_4$) under a N_2 atmosphere was treated with 40 ml (64 mmol) of 1.6 *M* *n*-butyllithium solution (Foote Mineral Co.) at room temperature for 30 min. The solution of camphor enolate was then added dropwise (stopcock in bottom of reaction flask) with stirring to a solution of 4 ml (65 mmol) of CD_3COOD and 2 ml of D_2O. After 1 hr the colorless THF solution was decanted from a white paste on the walls of the flask. The THF solution was diluted with petroleum ether, dried, filtered, and evaporated to leave 6.95 g (91%) of crude product. A 4.00-g portion was sublimed at atmospheric pressure to give 3.56 g of pure colorless crystals of *d*-camphor-3-*exo*-d_1. Analysis by mass spectroscopy gave 96.6% d_1 and 3.4% d_0. From the coupling pattern of the CHOH proton in the nmr spectrum of the derived ($LiAlH_4$) isoborneol the D is almost entirely exo.

d-**Camphor-*3,3-d*$_2$** (**24**).—A solution of 25.0 g (81 mmol) of 3,3-dibromo-*d*-camphor in 50 ml of dioxane (distilled from $LiAlH_4$) and 15 ml of CD_3COOD was stirred and heated (steam bath) with 15 g of Zn powder (B. D. H. Analar). Dilution with 200 ml of petroleum ether and 2 ml of D_2O followed by washing (H_2O), drying, and evaporation gave 11.3 g (91%) of crude product which was sublimed to yield 11.0 g of colorless feathery camphor-*3,3-d*$_2$, mp 177–178° (sealed capillary). Analysis by mass spectroscopy gave 83.5% d_2 and 16.5% d_1.

d-**Camphor-*3-endo-d*$_1$** (**25**).—This compound was prepared from 7.58 g (49 mmol) of camphor-*3,3-d*$_2$ by the procedure described above for the preparation of camphor-*3-exo-d*$_1$ except that the enolate was added to a solution of 10 ml of HOAc in 25 ml of water. There was obtained 7.05 g of crude product which consisted of ~70% camphor, ~25% of a slightly more polar (tlc) product, and ~5% of three still more polar compounds. The major contaminant was apparently the product **26** of addition of *n*-butyllithium to the carbonyl group of **24**. Chromatography of 1.6 g of the crude product on silica gel resulted in dehydration of this tertiary alcohol and elution of 382 mg of (probably) **28** together with camphor. Further elution gave 800



28

mg of camphor-*3-endo-d*$_1$ which was sublimed to give colorless crystals. Analysis by mass spectroscopy gave 94% d_1 and 6% d_0. From the coupling pattern of the CHOH proton in the nmr spectrum of the derived ($LiAlH_4$) isoborneol the D is almost entirely endo.

Registry No.—**4**, 34733-67-0; **6**, 34733-68-1; **9**, 34733-69-2; **10**, 10334-07-3; **15**, 34733-71-6; **16**, 34733-72-7; **24**, 34733-73-8; *d*-camphor-*9,9-d*$_2$, 34739-97-4.

Acknowledgment.—The financial assistance of the National Research Council of Canada is gratefully acknowledged.

Anodic Oxidations. VIII. The Anodic Oxidation of *N,N*-Dimethylmethanesulfonamide in Alcohols and in Acetic Acid

SIDNEY D. ROSS,* MANUEL FINKELSTEIN, AND ERIC J. RUDD

Sprague Research and Development Center, Sprague Electric Company, North Adams, Massachusetts 01247

Received January 27, 1972

The anodic oxidation of *N,N*-dimethylmethanesulfonamide has been studied in alcohols and in acetic acid, using quaternary ammonium fluoborates and nitrates as the supporting electrolytes. The structures of the products, *N*-alkoxymethyl-*N*-methylmethanesulfonamides and *N*-acetoxymethyl-*N*-methylmethanesulfonamide, were established by synthesis.

Compounds containing the grouping XCH_2Y, where Y is halogen, OH, OR, or O(C=O)R and X is S, O, or N, are effective electrophilic reagents, frequently used to introduce a new carbon–carbon bond in aromatic compounds or in aliphatic compounds containing reactive methylene or methine groups. Some typical reagents, with, *e.g.*, Y a halogen atom, are the chloromethylamines, the chloromethyl sulfides, the chloromethyl ethers, the chloromethyl amides, and the chloromethyl imides. When the electrophilic reagent is one in which the X above is the nitrogen of an amide group or an imide group, the reaction is an amidoalkylation reaction, and these reactions have been reviewed by Hellman[1] and by Zaugg and Martin.[2]

Many mechanisms are possible for these reactions, but the most common is the acid-catalyzed $A_{AL}1$ mechanism[3] in which the rate-determining step is the formation of the ion I. The most active reagents are

$$-XCH_2^+ \longleftrightarrow \underset{I}{-\overset{+}{X}=CH_2}$$

(1) H. Hellman in "Newer Methods of Preparative Organic Chemistry," Vol. II, W. Foerst, Ed., Academic Press, New York, N. Y., 1963.

(2) H. E. Zaugg and W. B. Martin, *Org. React.*, **14**, 52 (1965).

(3) S. D. Ross, M. Finkelstein, and R. C. Petersen, *J. Org. Chem.*, **31**, 133 (1966).