Experimental Section

Tetrahydrofuran was distilled from lithium aluminum hydride and stored under nitrogen. Acetylene (welding grade) was purified by passage through a −78° trap, then a sulfuric acid trap, and finally through soda lime. The acetylene was transferred to the reaction flask with a gas syringe.[7] *n*-Butyllithium in hexane (Alfa) was standardized by the method of Watson and Eastham.[8]

All ketones were obtained commercially and were used without further purification. All aldehydes were obtained commercially and were distilled under nitrogen prior to use.

All glassware was dried in an oven at 130° for several hours, then assembled hot and flushed with nitrogen while cooling. Liquids were transferred using syringe and double-ended needle techniques.[9,10] Solids were dissolved in tetrahydrofuran and transferred as the solution.

Melting points were determined with a Thomas-Hoover melting point apparatus and are uncorrected. Infrared spectra were taken on a Perkin-Elmer 700 spectrometer. ^{1}H and ^{13}C NMR spectra were recorded on a Varian T-60 and Varian CFT-20 spectrometer, respectively, using tetramethylsilane as an internal standard. High-resolution mass spectra were obtained on a CEC 21-110 instrument. A Hewlett-Packard 5750 gas chromatograph was used for VPC analysis using either a 6 ft × 0.25 in. 10% SE-30 or 10% XE-60 column with Chromosorb W as a stationary phase. Decane (Philips 99%) was used as an internal standard.

General Procedure for Monolithium Acetylide Preparation. 2-Ethynyl-*endo*-2-norbornanol. A dry 500-ml flask equipped with a magnetic stirring bar and septum-capped inlet was connected to a mercury bubbler and flushed with nitrogen. Tetrahydrofuran (200 ml) was placed in the flask and the flask was cooled in a Dry Ice–acetone bath. Acetylene (110 mmol) was added by means of a large gas syringe. *n*-Butyllithium (110 mmol, 49 ml of a 2.24 *M* solution in hexane) was measured into a graduated cylinder[10] by double-ended needle and then transferred dropwise into the reaction flask over a 15-min period. The solution was stirred for 10 min. Norcamphor (100 mmol, 11.1 g) was placed in a graduated cylinder and dissolved in 30 ml of tetrahydrofuran. The solution was added over a 5-min period to the monolithium acetylide. An additional 5 ml of tetrahydrofuran was used to wash the last of the norcamphor into the reaction flask. The solution was stirred for 20 min at −78° and then warmed to room temperature. Water (40 ml) was added followed by anhydrous potassium carbonate until the aqueous phase became pasty. The organic phase was decanted and the aqueous layer was washed with 2 × 30 ml of ether. The combined organic phase was dried (magnesium sulfate) and distilled through a short-path distillation head. There was obtained 12.5 g (92%), bp 84–86° (15 mm). The product solidified upon cooling on Dry Ice: mp 46–47° (lit.[11] mp 45–46°); ^{1}H NMR ($CDCl_3$) δ 2.47 (s, $C{\equiv}CH$), 2.43–1.2 (complex m, ring H and OH); proton-decoupled ^{13}C NMR δ C_1, 49.6; C_2, 73.1; C_3, 47.6; C_4, 36.8; C_5, 26.7; C_6, 21.0; C_7, 38.7; terminal acetylene, 90.1; internal acetylene, 71.1; exact mass (P − 1) 135.083 (calcd, 135.081).

VPC analyses were obtained from 5-mmol scale reactions. All products were isolated from these reactions by Kugelrohr distillation or preparative VPC. All products exhibited consistent ir, NMR, and mass spectra. Satisfactory exact mass measurements (±0.003 mass units) were obtained for all compounds.

Stability. In a dry 50-ml flask was prepared 5 mmol of monolithium acetylide in 10 ml of tetrahydrofuran. The solution was stirred for 6 hr in a Dry Ice–acetone bath. Then 5 mmol of hexanal was added. After 20 min the flask was warmed to room temperature and 2 ml of water was added. The solution was saturated with potassium carbonate and 5 mmol of decane was added. Analysis by VPC revealed 4.35 mmol (87%) of 1-octyn-3-ol.

In a similar manner, 5 mmol of monolithium acetylide was prepared and after 10 min it was warmed to 0° for 15 min, then cooled to −78°. A white precipitate had formed at 0°. Hexanal was added and the reaction was worked up as above. Analysis revealed 1.95 mmol (39%) of 1-octyn-3-ol.

Acknowledgment. The author wishes to thank Dr. Herbert C. Brown for his suggestions concerning this work and Gary W. Kramer and David P. Kelly for obtaining the ^{13}C spectra.

Registry No.—Monolithium acetylide, 1111-64-4; acetylene, 74-86-2; *n*-butyllithium, 109-72-8.

References and Notes

(1) L. F. Fieser and M. Fieser, "Reagents for Organic Synthesis", Vol. 1, Wiley, New York, N.Y., 1967, pp 573–574.
(2) M. Corbellini and L. Turner, *Chim. Ind.* (*Milan*), **42**, 251 (1960); *Chem. Abstr.*, **54**, 19250 (1960).
(3) O. F. Beumel and R. F. Harris, *J. Org. Chem.*, **28**, 2775 (1963).
(4) Badische Anilin- and Soda-Fabrik Akt.-Ges., British Patent 771,708 (April 3, 1957); *Chem. Abstr.*, **51**, 18510 (1957).
(5) K. Suga, S. Watanabe, and T. Suzuki, *Can. J. Chem.*, **46**, 3041 (1968).
(6) O. F. Beumel and R. F. Harris, *J. Org. Chem.*, **29**, 1872 (1964).
(7) G. W. Kramer, *J. Chem. Educ.*, **50**, 227 (1973).
(8) S. C. Watson and J. F. Eastham, *J. Organomet. Chem.*, **9**, 165 (1967).
(9) D. F. Shriver, "The Manipulation of Air-Sensitive Compounds", McGraw-Hill, New York, N.Y., 1969.
(10) H. C. Brown, G. W. Kramer, A. B. Levy, and M. M. Midland, "Organic Syntheses via Boranes", Wiley, New York, N.Y., 1975, Chapter 9.
(11) B. Görlich and G. Hildebrandt, *Chem. Ber.*, **91**, 2388 (1958).

A Facile Synthesis of 1-(Carbethoxyethoxymethyl)camphene

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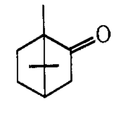
Received January 28, 1975

The potential of camphene derivatives possessing a functionalized C-1 side chain as synthetic precursors of natural products and related compounds has been realized in the recent syntheses of isolongifolene[1] and zizaane-type sesquiterpenoids.[2,3] The methods available for their preparation[1–7] were, however, limited to multistep transformations of camphor (1) and often gave the desired products in unsatisfactory yields. In connection with our studies on the regioselectivity of boron trifluoride catalyzed ring enlargement of unsymmetrically substituted cycloalkanones,[8] we have discovered an efficient conversion of *dl*-camphor (1) to the title compound (2) which should prove synthetically useful, particularly in constructing naturally occurring compounds of the zizaane family.[9]



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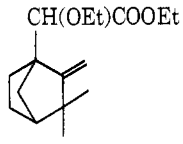

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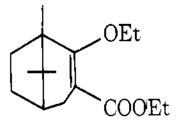

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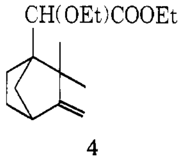
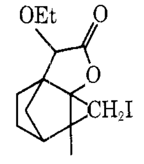


4

Prolonged treatment of *dl*-camphor (1) with an excess of boron trifluoride etherate and ethyl diazoacetate in ether afforded, in addition to a minor amount of 3-carbethoxy-2-ethoxy-1,8,8-trimethylbicyclo[3.2.1]oct-2-ene (3),[8] a mixture of 1-(carbethoxyethoxymethyl)camphene (2) and its positional isomer 4 (2:1) in 63% yield.[10] Subsequent treatment of the mixture with zinc dust and glacial acetic acid at reflux for 24 hr resulted in an essentially quantitative and clean rearrangement of 4 to 2. The structure of 2 was readily assigned on the basis of its spectral data (see Experimental Section) and was further confirmed by its conversion to crystalline iodo lactone 5. The sharp spectral peaks and thin layer chromatographic behavior of 2 and 5 coupled with the sharp melting point of 5 are suggestive of single stereoisomers of both 2 and 5. The data presently available, however, do not permit unambiguous definition of their stereochemistry.



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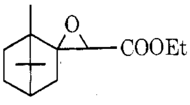

6

The formation of **2** and **4** from *dl*-camphor (**1**) might be rationalized by invoking Wagner–Meerwein rearrangements[11] of an intermediate of glycidic ester[12] **6**.

Experimental Section[13]

1- (2) and 4-(Carbethoxyethoxymethyl)camphene (4). To a chilled solution (0°) of 3.04 g (0.02 mol) of *dl*-camphor (**1**) and 4.26 g (0.03 mol) of boron trifluoride etherate in 25 ml of ether under a nitrogen atmosphere was added dropwise, over a period of 15 min, a solution of 3.42 g (0.03 mol) of ethyl diazoacetate in 5 ml of ether. The resulting solution was stirred in the dark at room temperature for 120 hr; at the end of each 24-hr period, a further 1.42 g (0.01 mol) of boron trifluoride etherate and 1.14 g (0.01 mol) of ethyl diazoacetate were added. The reaction mixture was cautiously made basic at 0° with saturated aqueous sodium bicarbonate and extracted with chloroform. The organic solution was washed with 1 *N* aqueous hydrochloric acid and water, dried ($MgSO_4$), filtered, and concentrated. Column chromatography of the oily product on silica gel with benzene elution gave 1.275 g (24% yield) of **3**[8] (slower moving) and 3.36 g (63% yield) of a mixture of **2** and **4**. The ir and mass spectra of the mixture were similar to those of pure **2** (see below). Its NMR spectrum (CCl_4) displayed two partly superimposed sets of signals integrated in a ratio of 2:1. The bands of the major set were found to coincide with those of **2** (see below) and the minor set contained the following diagnostic signals of **4**:[14] δ_{TMS} 4.64 (s, 1 H, vinylic), 4.46 (s, 1 H, vinylic), 4.12 (q, 2 H, J = 7.2 Hz, $COOCH_2CH_3$), 4.05 (s, 1 H, OCH), 3.54 [q of d, 1 H, J = 8.5, J' = 7 Hz, $OCH(H)CH_3$], 3.35 [q of d, 1 H, J = 8.5, J' = 7 Hz, $OCH(H)CH_3$], 2.55 (br s, 1 H, allylic), 1.25 (t, 3 H, J = 7.2 Hz, $COOCH_2CH_3$), 1.16 (t, 3 H, J = 7 Hz, OCH_2CH_3), 1.05 (s, 3 H, methyl), and 0.99 (s, 3 H, methyl).

Isomerization of 4 to 2. A stirred mixture of 0.5 g (0.0019 mol) of the above mixture of **2** and **4** and 2.5 g (0.038 g-atom) of zinc dust in 20 ml of glacial acetic acid was heated at gentle reflux under an atmosphere of nitrogen for 24 hr. After cooling to room temperature, the reaction mixture was filtered and the filtrate was concentrated. Bulb-to-bulb distillation of the residue at 75° (oven temperature) (1.5 mm) gave 0.482 g (96% yield) of **2**: ir (film) 1740 (C═O) and 1650 cm^{-1} (C═C); NMR (CCl_4) δ_{TMS} 4.79 (s, 1 H, vinylic), 4.55 (s, 1 H, vinylic), 4.12 (t, 2 H, J = 7.2 Hz, $COOCH_2CH_3$), 4.01 (s, 1 H, OCH), 3.54 [q of d, 1 H, J = 8.5, J' = 7 Hz, $OCH(H)CH_3$], 3.35 [q of d, 1 H, J = 8.5, J' = 7 Hz, $OCH(H)CH_3$], 1.25 (t, 3 H, J = 7.2 Hz, $COOCH_2CH_3$), 1.20 (t, 3 H, J = 7 Hz, OCH_2CH_3), 1.05 (s, 3 H, methyl), and 0.99 (s, 3 H, methyl); mass spectrum m/e 266.1888 (M^+, calcd for $C_{16}H_{26}O_3$, 266.1882) and 193 (base peak).

Anal. Calcd for $C_{16}H_{26}O_3$: C, 72.14; H, 9.84. Found: C, 72.18, 72.42; H, 10.06, 9.88.

Under other applied conditions (boiling acetic acid; *p*-toluenesulfonic acid in benzene at room temperature or at reflux), the isomerization was found to proceed less effectively.

2-Ethoxy-5-(iodomethyl)-6,6-dimethyl-4-oxatricyclo[5.2.1.0^{1,5}]decan-3-one (5). A solution of 0.42 g (0.0016 mol) of **2** and 10 ml of 4 *N* aqueous sodium hydroxide in 10 ml of methanol was refluxed with stirring under a nitrogen atmosphere for 16 hr. After cooling to room temperature, the reaction mixture was diluted with 20 ml of water and washed twice with ether. The aqueous solution was then acidified with 1 *N* aqueous hydrochloric acid and extracted with chloroform. Work-up of the chloroform solution in the usual manner afforded 0.36 g of acidic product which, without purification, was dissolved in 20 ml of 0.5 *N* aqueous sodium bicarbonate. To this solution, 1.59 g (0.0096 mol) of potassium iodide and 0.81 g (0.0064 mol) of iodine were added.[15] After stirring at room temperature in the dark for 20 hr, the mixture was poured into a slurry of 40 ml of 1 *N* aqueous sodium hydroxide and ice. Extraction with methylene chloride followed by the usual work-up of the organic solution gave 0.471 g (82% yield based on **2**) of **5**: mp 137–138° (ether); ir ($CHCl_3$) 1775 cm^{-1} (C═O); NMR ($CDCl_3$) δ_{TMS} 4.57 (s, 1 H, OCH), 4.11 [q of d, 1 H, J = 9, J' = 7 Hz, $OCH(H)CH_3$], 3.66 [q of d, 1 H, J = 9, J' = 7 Hz, $OCH(H)CH_3$], 3.51 [d, 1 H, J = 11 Hz, CH(H)I], 3.30 [d, 1 H, J = 11 Hz, CH(H)I], 1.22 (t, 3 H, J = 7 Hz, OCH_2CH_3), 1.19 (s, 3 H, methyl), and 1.10 (s, 3 H, methyl); mass spectrum m/e 364.0527 (M^+, calcd for $C_{14}H_{21}O_3I^{127}$, 364.0536) and 193 (base peak).

Acknowledgments. This work was generously supported by the National Research Council of Canada and the University of Alberta.

Registry No.—**1**, 21368-68-3; **2**, 55319-46-5; **4**, 55319-47-6; **5**, 55319-48-7; ethyl diazoacetate, 623-73-4.

References and Notes

(1) R. R. Sobti and S. Dev, *Tetrahedron*, **26**, 649 (1970).

(2) F. Kido, H. Uda, and A. Yoshikoshi, *Chem. Commun.*, 1335 (1969).

(3) D. F. MacSweeney and R. Ramage, *Tetrahedron*, **27**, 1481 (1971).

(4) S. S. Nametkin, A. S. Kichkina, and D. N. Kursanov, *J. Russ. Phys.-Chem. Soc.*, **61**, 1065 (1929).

(5) J. Houben and E. Pfankuch, *Justus Liebigs Ann. Chem.*, **483**, 271 (1930).

(6) C. D. Hurd and R. E. Christ, *J. Am. Chem. Soc.*, **59**, 118 (1937).

(7) I. N. Nazarov and M. S. Burmistrova, *J. Gen. Chem. USSR*, **20**, 2173 (1950).

(8) H. J. Liu and S. P. Majumdar, *Synth. Commun.*, **5**, 125 (1975).

(9) For leading references, see T. K. Devon and A. I. Scott, "Handbook of Naturally Occurring Compounds", Vol. II, Academic Press, New York, N.Y., 1972, p 152.

(10) Separation of **2** and **4** was attempted without much success by means of column and gas chromatography and by distillation. The structural assignment of **4** follows from its rearrangement to **2** (vide infra) and from the spectral data of the mixture (see Experimental Section).

(11) J. A. Berson in "Molecular Rearrangements", P. de Mayo, Ed., Interscience, New York, N.Y., 1963, Chapter 3.

(12) The reported isolation of ethyl β,β-dimethylglycidate in large quantity from the boron trifluoride catalyzed reaction of acetone and ethyl diazoacetate [W. T. Tai and E. W. Warnhoff, *Can. J. Chem.*, **42**, 1333 (1964)] serves as a precedent.

(13) The following spectrometers were used: ir, Perkin-Elmer Model 457; NMR, Varian HA-100; mass spectra, AEI MS-9. The melting point was determined on a Kofler hot stage apparatus and is uncorrected. Elemental analyses were performed by the microanalytical laboratory of this department.

(14) Three signlets at δ 4.64, 4.46, and 2.55 were most significant in assigning its structure; the corresponding hydrogen atoms of camphene appeared in the NMR spectrum taken under the same conditions at δ 4.68 (s), 4.47 (s), and 2.65 (br s).

(15) E. E. van Tamelan and M. Shamma, *J. Am. Chem. Soc.*, **76**, 2315 (1954).

Activated Metals. IX. A New Reformatsky Reagent Involving Activated Indium for the Preparation of β-Hydroxy Esters[1]

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Received February 18, 1975

Until recently, synthesis using the direct reaction of indium metal was at best limited. Use was restricted to the preparation of triaryl- and trialkylindium compounds from the reaction of indium metal and diorganomercury compounds[3–5] and the preparation of alkylindium halides[6] from alkyl halides. We have recently reported a new procedure for the preparation of activated metals[1,7] and we have shown that by using this procedure highly reactive indium metal powders are generated.[8,9] In this paper, we would like to report that this highly reactive indium metal reacts readily with α-halo esters to give a Reformatsky-type reagent which will add to ketones and aldehydes to give β-hydroxy esters. The Reformatsky reaction using zinc metal has been used in the preparation of β-hydroxy esters for many years. Recent improvements have made this reaction a fairly reliable reaction.[7,10,11]

The activated indium powder was prepared by reducing anhydrous $InCl_3$ (Alfa ultrapure) with freshly cut potassium metal in dry, freshly distilled xylene. The mixture is