however, that a kinetically controlled ethynylation[11] of that compound proceeds quite cleanly with formation of a single isomer resulting from α side attack.

Ethynylation of the 16α isomer also occurs predominantly from the α side although in this case the isomeric ethynyl alcohol is formed to a minor extent, too.

As these results were not in agreement with those reported by Atwater et al.[7] we reinvestigated their synthesis of 16α-methylspironolactone. The sequence of reactions in eq I was applied to both 3β-hydroxy-16β-methyl-5-androsten-17-one and its 16α isomer.[12]

In the 16β-methyl case we obtained a single lactone the physical and spectroscopic data of which were in agreement with the compound to which Atwater et al.[7] wrongly ascribed the 16α-methyl configuration.

The 16α-methyl compound was converted into a mixture of lactones which were separated by chromatography and identified as 16α-methyl compounds isomeric with respect to position C-17.

Experimental Section

3β-Hydroxy-16β-methyl-5-androsten-17-one:[5] mp 165–168 °C; $[\alpha]_D$ +4° ($CHCl_3$, *c* 0.5); ^1H NMR δ 0.84 (s, 3 H, H-18), 1.03 (s, 3 H, H-19), 1.22 (d, J = 7 Hz, 3 H, 16β-CH_3), 3.50 (m, 1 H, H-3), 5.38 (m, 1 H, H-6); IR (KBr) 3480 cm^{-1}, 1733; CD (dioxane) λ 301 nm ($\Delta\epsilon$ = +2.84), 307 (+3.31), 317 (+2.44).

3β-Hydroxy-16α-methyl-5-androsten-17-one. 3β-Hydroxy-5-androsten-17-one was protected as its 3-THP ether. Hydrazone formation, alkylation (using 2.2 equiv of *n*-butyllithium at 0 °C, 60 min), and hydrazone cleavage were performed following the literature scheme.[2,3] Hydrazone cleavage is accompanied by THP ether hydrolysis, if the reaction time is prolonged to 15 h: mp 145–148 °C; $[\alpha]_D$ −13° ($CHCl_3$, *c* 0.505); ^1H NMR ($CDCl_3$) δ 0.94 ppm (s, 3 H, H-18), 1.05 (s, 3 H, H-19), 1.10 (d, J = 7 Hz, 3 H, 16α-CH_3), 3.50 (m, 1 H, H-3), 5.39 (m, 1 H, H-6); IR (KBr) 3490 cm^{-1}, 1728; CD (dioxane) λ 304 nm ($\Delta\epsilon$ = +2.84).

Equilibration. 3β-Hydroxy(acetoxy)-16α-methyl-5-androsten-17-one as well as its 16β isomer were subjected to the equilibrating conditions of Bowers et al.,[8] the reaction times being prolonged to 24 h. Composition of the equilibrium mixture (by NMR): 78.5% of β-methyl, 21.5% of α-methyl.

Ethynylation. The ethynylations were performed according to the procedure of Phillips et al.[11]

17α-Ethynyl-16β-methyl-5-androstene-3β,17β-diol: mp 209–212 °C; $[\alpha]_D$ −97.6° ($CHCl_3$, *c* 0.505); ^1H NMR δ 0.84 (s, 3 H, H-18), 1.04 (s, 3 H, H-19), 1.10 (d, J = 7 Hz, 3 H, 16β-CH_3), 2.56 (s, 1 H, C≡CH), 3.50 (m, 1 H, H-3), 5.33 (m, 1 H, H-6); yield[13] 92%.

17α-Ethynyl-16α-methyl-5-androstene-3β,17β-diol: mp 221–223 °C; $[\alpha]_D$ −129.7° ($CHCl_3$, *c* 0.505); ^1H NMR δ 0.92 ppm (s, 3 H, H-18), 1.03 (s, 3 H, H-19), 1.16 (d, J = 7 Hz, 3 H, 16α-CH_3), 2.60 (s, 1 H, C≡CH), 3.51 (m, 1 H, H-3), 5.35 (m, 1 H, H-6); yield[13] 72%.

Lactones. The sequence of Radscheit et al.[12] (addition of 3-lithiopropionaldehyde dimethyl acetal, Oppenauer oxidation, acetal hydrolysis, Jones oxidation) was employed in the synthesis of the following lactones:

3-(3-Oxo-16β-methyl-17β-hydroxy-4-androsten-17α-yl)propionic acid lactone: mp 176–177 °C; $[\alpha]_D$ + 95.4° ($CHCl_3$, *c* 0.500); ^1H NMR ($CDCl_3$) δ 0.96 (s, 3 H, H-18), 1.06 (d, J = 7 Hz, 3 H, 16β-CH_3), 1.20 (s, 3 H, H-19), 5.74 (m, 1 H, H-4); IR (KBr) 1768 cm^{-1}, 1670, 1610; yield[13] 68%.

3-(3-Oxo-16α-methyl-17β-hydroxy-4-androsten-17α-yl)propionic acid lactone: mp 180–182 °C; $[\alpha]_D$ +49.5° ($CHCl_3$, *c* 0.505); ^1H NMR ($CDCl_3$) δ 1.00 ppm (d, J = 7 Hz, 3 H, 16α-CH_3), 1.04 (s, 3 H, H-18), 1.20 (s, 3 H, H-19), 5.73 (m, 1 H, H-4); IR (KBr) 1770, 1672, 1612 cm^{-1}; yield[13] 32%.

3-(3-Oxo-16α-methyl-17α-hydroxy-4-androsten-17β-yl)propionic acid lactone: mp 218–220 °C; $[\alpha]_D$ +51.4° ($CHCl_3$, *c* 0.505); ^1H NMR ($CDCl_3$) δ 0.86 (s, 3 H, H-18), 1.01 (d, J = 7 Hz, 3 H, 16α-CH_3), 1.19 (s, 3 H, H-19), 5.74 (m, 1 H, H-4); IR (KBr) 1760, 1675, 1612 cm^{-1}; yield[13] 34%.

Registry No.—3β-Hydroxy-16β-methyl-5-androsten-17-one, 67843-75-8; 3β-hydroxy-16α-methyl-5-androsten-17-one, 2891-00-1; 3β-acetoxy-16β-methyl-5-androsten-17-one, 2099-24-3; 3β-acetoxy-16α-methyl-5-androsten-17-one, 2099-25-4; 17α-ethynyl-16β-methyl-5-androstene-3β,17β-diol, 67800-69-5; 17α-ethynyl-16α-methyl-5-androstene-3β,17β-diol, 67800-70-8; 3-(3-oxo-16β-methyl-17β-hydroxy-4-androsten-17α-yl)propionic acid lactone, 67827-36-5; 3-(3-oxo-16α-methyl-17β-hydroxy-4-androsten-17α-yl)propionic acid lactone, 67800-71-9; 3-(3-oxo-16α-methyl-17α-hydroxy-4-androsten-17β-yl)propionic acid lactone, 67843-76-9.

References and Notes

(1) (a) G. Goto, K. Yoshioka, K. Hiraga, and T. Miki, *Chem. Pharm. Bull.*, **25**, 1295 (1977); (b) K. Yoshioka, G. Goto, H. Mabuchi, K. Hiraga, and T. Miki, *ibid.*, **23**, 3203 (1975).
(2) (a) E. J. Corey and D. Enders, *Tetrahedron Lett.*, 3 (1976); (b) *Chem. Ber.*, **111**, 1337 (1978).
(3) E. J. Corey and S. Knapp, *Tetrahedron Lett.*, 3667 (1976).
(4) Care must be taken that the THF employed in the cleavage reaction is absolutely free of peroxides. Otherwise formation of α-hydroxy ketones is observed: M. S. Kharasch and A. Fono, *J. Org. Chem.*, **23**, 324 (1958).
(5) R. Sciaky, *Gazz. Chim. Ital.*, **91**, 562 (1961).
(6) For detailed spectroscopic investigations on 16-alkyl steroids, see: B. Schönecker, D. Tresselt, J. Draffehn, and K. Ponsold, *J. Prakt. Chem.*, **319**, 419 (1977).
(7) N. W. Atwater, R. H. Bible, Jr., E. A. Brown, R. B. Burtner, J. S. Mihina, L. N. Nysted, and P. B. Sollman, *J. Org. Chem.*, **26**, 3077 (1961).
(8) A. Bowers, P. Holton, E. Necoechea, and F. Kincl, *J. Chem. Soc.*, 4057 (1961).
(9) P. De Ruggieri, C. Ferrari, and C. Gandolfi, *Gazz. Chim. Ital.*, **91**, 672 (1961).
(10) Alkylation of the corresponding D homosteroid leads, as expected, to a 17β-methyl-17*a*-keto derivative: G. Neef and U. Eder, unpublished results.
(11) (a) D. Phillips, P. Wickham, G. Potts, and A. Arnold, *J. Med. Chem.*, **11**, 924 (1968); (b) E. P. Oliveto in J. Fried and J. A. Edwards, "Organic Reactions in Steroid Chemistry", Vol. II, Van Nostrand-Reinhold, New York, N.Y., 1972, p 139.
(12) U.S. patent 3 847 906 (inventors: K. Radscheit, U. Stache, R. Brodersen), Farbwerke Hoechst AG; *Chem. Abstr.*, **81**, 13705 f (1974).
(13) Yields refer to 3β-hydroxy-16β-methyl-5-androsten-17-one or to its 16α isomer.
(14) Satisfactory analytical data were obtained for all compounds mentioned in the Experimental Section.

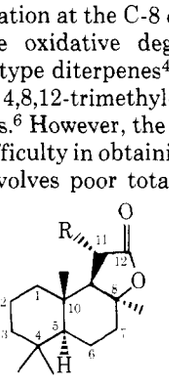
Synthesis of (±)-Norisoambreinolide and (±)-Isoambrox[1]

Sigeru Torii,* Kenji Uneyama, and Hisao Ichimura

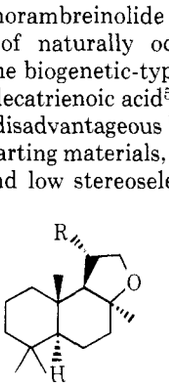
Department of Industrial Chemistry, School of Engineering, Okayama University, Okayama 700, Japan

Received June 27, 1978

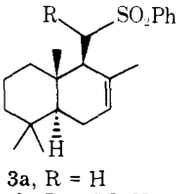
Norisoambreinolide (**1a**)[2] and isoambrox (**2a**),[3] amberlike odorous compounds, have been the object of numerous synthetic studies.[4-7] The major approaches to **1a** consist of (a) epimerization at the C-8 carbon of norambreinolide derived from the oxidative degradation of naturally occurring labdane-type diterpenes[4] and (b) the biogenetic-type cyclization of 4,8,12-trimethyl-3,7,11-tridecatrienoic acid[5] and its analogues.[6] However, the former is disadvantageous because of the difficulty in obtaining pure starting materials, and the latter involves poor total yields and low stereoselectivity.



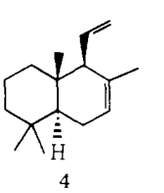
1a, R = H
b, R = SO_2Ph



2a, R = H
b, R = SO_2Ph



3a, R = H
b, R = CO_2H
c, R = CH_2OH



4

0022-3263/78/1943-4680$01.00/0

Meanwhile, effective syntheses of (±)-**2a** have not been reported yet.[7]

Recently, it was found that the stannic chloride catalyzed cyclization of farnesyl phenyl sulfone provided a drimane-type compound **3a** in 77% yield.[8] The sulfonyl group might facilitate alkylation at the α carbon of **3a** and would be removed smoothly after constructing the desired C_{16} skeleton. In this paper, we describe an efficient synthesis of (±)-**1a** and (±)-**2a** from the alicyclic sulfone **3a**.

Carboxylation of the carbanion of the sulfone **3a** was performed smoothly by treatment with 2 equiv of butyllithium in dry THF at −70 °C followed by carbon dioxide at room temperature, providing **3b** quantitatively. Similarly, hydroxymethylation of **3a** afforded **3c** in 86% yield. Cyclization of the α-sulfonylcarboxylic acid **3b** in sulfuric acid–acetic acid afforded the corresponding cis lactone **1b** in 93% yield as a sole product. The highly stereocontrolled preparation of **1b** seems to be superior to the cyclization of 4,8,12-trimethyl-3,7,11-tridecatrienoic acid[5] and 6-(2,6,6-trimethylcyclohexenyl)-4-methyl-3-hexenoic acid[6] into (±)-**1a**, whereby the epimeric isomers of **1a** at the C-8 and C-9 positions were obtained.

Cis fusion of the lactone ring of **1b** was established by comparing the coupling constant between H-9 and H-11 (J = 4 Hz) with that of *cis*-2,2,6-trimethyl-9-(phenylsulfonyl)-7-oxabicyclo[4.3.0]nonan-8-one (J = 6 Hz)[9] and also by the successful conversion of **1b** into (±)-**1a**. Reductive desulfonation of **1b** with lithium in liquid ammonia provided (±)-**1a** quantitatively. The synthetic (±)-**1a** was homogeneous on VPC, and its IR and ^{1}H NMR spectra were consistent with the reported data.[7c] Meanwhile, reductive desulfonation of **3b** with lithium in liquid ammonia lead to 13,14,15,16-tetranorlabd-7-en-12-oic acid,[10] and subsequent lactonization gave (±)-**1a** in quantitative yield.

The reported attempts for the preparation of ambrox and isoambrox reveal that dehydration of 8-hydroxy-13,14,15,16-tetranorlabdan-12-ol takes place by the action of sulfuric acid in acetic acid,[4a] naphthalenesulfonic acid,[9a] hydrogen chloride,[7b] and activated alumina,[3b] affording isomeric mixtures of **4** as a byproduct. To avoid the formation of the undesired olefin, tosylation of the primary hydroxy group followed by an amine-catalyzed intramolecular S_N2-type reaction has been employed for making the tetrahydrofuran ring.[7c,d] Fortunately, **3c** fits all of the requirements for the desired ring formation since the hydroxy group of **3c** is deactivated on account of the electron-withdrawing nature of the phenylsulfonyl group. In fact, cyclization of **3c** with boron trifluoride in refluxing benzene afforded **2b** in 97% yield.[11] Then, **2b** was desulfonated with lithium in liquid ammonia to give (±)-**2a** in 98% yield. The ^{1}H NMR and IR spectra of (±)-**2a** were in line with those of an authentic sample.[12]

In contrast with the favorable desulfonation of **2b**, the hydroxy sulfone **3c** suffered dehydroxylation on treatment with lithium in liquid ammonia, affording **4** exclusively.[13]

Experimental Section

IR spectra were determined with a Jasco IRA-1 infrared spectrometer. ^{1}H NMR spectra were obtained at 100 MHz with a JEOL FX 100 spectrometer, and chemical shifts are expressed in δ values (parts per million) relative to Me_4Si in $CDCl_3$.

11-(Phenylsulfonyl)-13,14,15,16-tetranorlabd-7-en-12-oic Acid (3b). An ether solution of BuLi (0.29 mmol) was added slowly to **3a** (50 mg, 0.14 mmol) dissolved in THF (1.5 mL) at −70 °C under N_2. After stirring for 10 min, dry CO_2 gas was introduced to the mixture at −70 °C for 1 h. The mixture was quenched with water and acidified with 5% HCl, and the organic substances were extracted with ether. The extracts were washed with brine, dried (Na_2SO_4), and concentrated in vacuo to give **3b** (57 mg, quantitative): mp 165.5–166.2 °C (hexane); IR (Nujol) 2400–3400 (CO_2H), 1727 (C=O), 1316, 1143 (SO_2) cm^{-1}; ^{1}H NMR δ 0.79 (s, 3, CH_3), 0.87 (s, 3, CH_3), 0.92 (br s, 3, CH_3), 1.01–1.78 (m, 7, CH_2, CH), 1.76–2.08 (m, 2, CH_2), 1.93 (s, 3, CH_3), 3.21 (br s, 1, CH), 4.17 (br s, 1, CO_2H), 4.27 (br s, 1, CH), 5.59 (br s, 1, CH=), 8.01–7.39 (m, 5, ArH). Anal. Calcd for $C_{22}H_{30}O_4S$: C, 67.67; H, 7.74. Found: C, 67.73; H, 7.92.

11-(Phenylsulfonyl)norisoambreinolide (1b). An ice-cooled mixture of AcOH (4 mL) and concentrated H_2SO_4 (3 mL) was added dropwise to an ethereal solution of **3b** (111 mg, 0.28 mmol, in 0.2 mL of ether) at 0 °C. The reaction mixture was stirred at 0–5 °C for 3 h and poured into ice water. The organic substances were extracted with ether–AcOEt (3:1). The usual workup and chromatography (SiO_2; benzene–AcOEt, 10:1) gave **1b** (103 mg, 93%) as colorless crystals: mp 197.2–198 °C; IR ($CHCl_3$) 1765 (C=O), 1588, 1309, 1150 (SO_2) cm^{-1}; ^{1}H NMR δ 0.85 (s, 3, CH_3), 0.88 (s, 3, CH_3), 0.92 (s, 3, CH_3), 0.94–2.04 (m, 11, CH_2, CH), 1.60 (s, 3, CH_3), 2.54 (d, J = 4 Hz, 1, CH), 3.87 (d, J = 4 Hz, 1, CH), 7.44–8.02 (m, 5, ArH). Anal. Calcd for $C_{22}H_{30}O_4S$: C, 67.67; H, 7.74. Found: C, 67.82; H, 7.76.

(±)-Norisoambreinolide (1a). Lithium wire (3 mm, 1.8 mmol) was added to **1b** (64 mg, 0.16 mmol) dissolved in THF (0.5 mL) and dry liquid ammonia (5 mL) at −78 °C, and the mixture was stirred for 2 min. After adding water (0.05 mL) and evaporating ammonia, the residue was worked up as usual to yield (±)-**1a** (40 mg, 98%) as colorless crystals, mp 77–77.5 °C (lit.[5] mp 78–79 °C).

13,14,15,16-Tetranorlabd-7-en-12-oic Acid. Desulfonation of **3b** was carried out in the same manner as used for **1b**, mp 141–141.8 °C. The IR and ^{1}H NMR spectra of the product were in line with those of the authentic data.[10]

11-(Phenylsulfonyl)-13,14,15,16-tetranorlabd-7-en-12-ol (3c). An ether solution of BuLi (0.29 mmol) was added dropwise to **3a** (50 mg, 0.14 mmol) dissolved in dry THF (1.5 mL) at −70 °C. After stirring at −70 °C for 5 min and then at room temperature for 15 min, dry CH_2O gas was introduced into the mixture, which was subsequently stirred for 1 h and quenched with saturated NH_4Cl. The usual workup and chromatography (SiO_2; benzene–AcOEt, 5:1) gave **3c** (46 mg, 86%) as a colorless oil: IR (neat) 3500 (OH), 1587, 1304, 1145 (SO_2) cm^{-1}; ^{1}H NMR δ 0.84 (s, 6, CH_3), 0.89 (s, 3, CH_3), 1.66 (br s, 3, CH_3), 0.81–1.63 (m, 6, CH_2), 1.76–2.08 (m, 2, CH_2), 2.20–2.62 (m, 1, CH), 2.48 (br s, 1, OH), 3.42–3.96 (m, 2, CH_2), 4.54 (dd, J_1 = 8 Hz, J_2 = 13 Hz, 1, CH), 5.60 (br s, 1, CH=), 7.40–8.06 (m, 5, ArH). Anal. Calcd for $C_{22}H_{32}O_3S$: C, 70.19; H, 8.57. Found: C, 70.09; H, 8.59.

8β,12-Epoxy-11-(phenylsulfonyl)-13,14,15,16-tetranorlabdane (2b). A benzene solution (8 mL) of **3c** (54 mg, 0.14 mmol) and boron trifluoride etherate (0.05 mL, ca. 0.4 mmol) was refluxed for 1 h and quenched with saturated $NaHCO_3$. The usual workup and chromatography (SiO_2; benzene–AcOEt, 10:1) provided **2b** (52 mg, 97%) as a slightly yellow oil: IR (neat) 1588, 1309, 1153 (SO_2) cm^{-1}; ^{1}H NMR δ 0.86 (s, 6, CH_3), 0.88 (s, 3, CH_3), 1.23 (s, 3, CH_3), 0.95–1.96 (m, 11, CH, CH_2), 2.04 (d, J = 2 Hz, 1, CH), 3.34–3.59 (m, 1, CH), 3.76 (dd, J_1 = 7 Hz, J_2 = 11 Hz, 1, CH), 4.24 (dd, J_1 = 4 Hz, J_2 = 11 Hz, 1, CH), 7.40–8.02 (m, 5, ArH). Anal. Calcd for $C_{22}H_{32}O_3S$: C, 70.19; H, 8.57. Found: C, 70.21; H, 8.76.

(±)-Isoambrox (2a). A lithium wire (1 mm, 0.6 mmol) was added to **2b** (44 mg, 0.12 mmol) dissolved in dry THF (0.5 mL) and liquid ammonia (4 mL) at −50 °C. The mixture was stirred for 15 min and quenched with saturated NH_4Cl. The usual workup and chromatography (SiO_2; n-hexane–ether, 10:1) gave (±)-**2a** (27 mg, 98%) as a colorless oil. The product was homogeneous on VPC (SE-30, 1 m–6φ) and spectral analyses.[12]

Registry No.—**1a**, 67844-42-2; **1b**, 67815-49-0; **2a**, 67844-43-3; **2b**, 67815-50-3; **3a**, 66901-39-1; **3b**, 67815-51-4; **3c**, 67815-52-5; (±)-13,14,15,16-tetranorlabd-7-en-12-oic acid, 67844-44-4.

References and Notes

(1) Alicyclic Terpenoids from Cyclocitryl Phenyl Sulfides. 9. Part 8: K. Uneyama, M. Kuyama, and S. Torii, *Bull. Chem. Soc. Jpn.*, **51**, 7 (1978).
(2) (a) H. Kaneko, *Agric. Biol. Chem.*, **35**, 1461 (1971); (b) J. N. Schumacher, *Tob. Sci.*, 116 (1974).
(3) (a) M. Stoll and M. Hinder, *Helv. Chim. Acta*, **33**, 1251 (1950); (b) M. Hinder and M. Stoll, *ibid.*, **33**, 1308 (1950).
(4) (a) M. Stoll and M. Hinder, *Helv. Chim. Acta*, **36**, 1996 (1953); (b) *ibid.*, **37**, 1859 (1954).
(5) G. Lucius, *Chem. Ber.*, **93**, 2663 (1960).
(6) (a) C. Collin-Asselineau and E. Lederer, *C. R. Hebd. Seances Acad. Sci., Ser. C*, **234**, 341 (1952); (b) G. Lucius, *Angew. Chem.*, **68**, 247 (1956); (c) E. J. Corey and R. R. Sauers, *J. Am. Chem. Soc.*, **79**, 3925 (1957); (d) *ibid.*, **81**, 1739 (1959).
(7) Transformations of labdane-type diterpenes into ambrox and isoambrox have been reported: (a) ref 3a and 3b; (b) M. Stoll, M. Hinder, and E. Palluy, *Helv. Chim. Acta*, **34**, 1664 (1951); (c) R. C. Cambie, K. N. Joblin, and A. F. Preston, *Aust. J. Chem.*, **24**, 583 (1971); (d) *ibid.*, **25**, 1767 (1972).
(8) S. Torii, K. Uneyama, I. Kawahara, and M. Kuyama, *Chem. Lett.*, 455 (1978).
(9) The molecular model reveals that H-9 and H-11 of **1b** are in the skew orientation, resulting in a small coupling constant (J = 4 Hz), while those of *trans*-**1b** are oriented in the staggered conformation. *trans*-2,2,6-Trimethyl-9-(phenylsulfonyl)-7-oxabicyclo[4.3.0]nonan-8-one shows the

corresponding coupling constant (J = 13 Hz): S. Torii, K. Uneyama, and M. Kuyama, *Tetrahedron Lett.*, 1513 (1976), and ref 1. The α isomer on C-11 may arise from epimerization at C-11 under the reaction conditions because of the steric repulsion between the phenylsulfonyl group and methyl at C-10.

(10) R. M. Carman and H. Deeth, *Aust. J. Chem.*, **24**, 1099 (1971). The authors are grateful to Professor R. M. Carman, Department of Chemistry, University of Queensland, Australia, for a kind gift of the IR and ^{1}H NMR spectra of 13,14,15,16-tetranorlabd-7-en-12-oic acid.

(11) The product **2b** was homogeneous on ^{1}H NMR, and the stereochemistry of the phenylsulfonyl group at C-11 was assigned on the basis of the coupling constant between H-8 and H-11 (J = 2 Hz).

(12) The authors are grateful to Dr. G. Ohloff, Firmenich SA Research Laboratory, Geneva, Switzerland, for a kind gift of the ^{1}H NMR chart of isoambrox.

(13) (a) M. Julia and J. M. Paris, *Tetrahedron Lett.*, 4833 (1973); (b) B. M. Trost and Y. Matsumura, *J. Org. Chem.*, **42**, 2036 (1977).

Communications

Sodium and Potassium Carbonates: Efficient Strong Bases in Solid–Liquid Two-Phase Systems[1]

Summary: Anhydrous potassium and sodium carbonates in the presence of catalysts–tetraalkylammonium salts or crown ethers were found to be efficient strong bases for generation and reactions of a variety of carbanions.

Sir: A recent paper by White,[2] in which the alkylation of diethyl malonate, ethyl cyanoacetate, and some other compounds in the presence of potassium carbonate in DMF was reported, prompts us to publish a preliminary communication describing some of our results concerning the application of alkali metal carbonates as efficient strong bases.

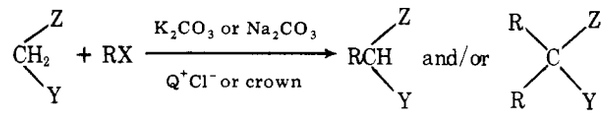
Among the variety of basic agents employed for the generation of carbanions, concentrated aqueous sodium hydroxide in the presence of catalysts such as tetraalkylammonium salts or crown ethers is of particular value.[3] Such reactions take place in a liquid–liquid two-phase system in which both phases, aqueous sodium hydroxide and organic reactants (neat or in nonpolar solvent) are mutually immiscible. This catalytic two-phase (CTP) system offers numerous advantages over other bases such as NaH, $NaNH_2$, and t-BuOK, inter alia elimination of hazardous and expensive reactants, anhydrous organic solvents, etc.

Despite many advantages, the CTP system has some limitations, one of them being the hydrolytic activity of concentrated aqueous alkali. Although due to the mutual immiscibility of the phases, hydrolysis of starting materials and/or products interferes much less than one would expect; carboethoxy and carbomethoxy groups are hydrolyzed in this system to a considerable extent. As a consequence alkylation of diethyl malonate, methyl cyanoacetate, and similar compounds cannot be performed efficiently in the CTP system.

We have found that many reactions proceeding via carbanions can be efficiently carried out using anhydrous sodium or potassium carbonates as bases. In these cases the reactions proceed in liquid–solid two-phase systems. Organic reactants neat (if liquids) or in aprotic solvents form the organic phase in which solid sodium or potassium carbonate is suspended. In this system reactions are catalyzed by tetraalkylammonium salts or crown ethers. The catalysts are unable to transfer carbonate anions (CO_3^{2-}) into the organic phase,[4] thus solid–liquid phase-transfer phenomena are probably not involved here. It is more plausible that the first step, namely proton abstraction, takes place on the surface of the solid carbonate. The anions formed then migrate into the organic phase as ion pairs with tetraalkylammonium cations or crown ether complexed alkali metal cations. Since anhydrous alkali carbonates form fine powders with well-developed surfaces and also show no tendency to form lumps, the speed of stirring is not of crucial importance. When K_2CO_3 or Na_2CO_3 are used as bases the reactions should be carried out at higher temperatures than if aqueous NaOH is used in the CTP system. This normally does not cause any difficulties, since the carbonates are rather mild bases.

Up to now the following reactions have been found to proceed efficiently in the presence of alkali carbonates.

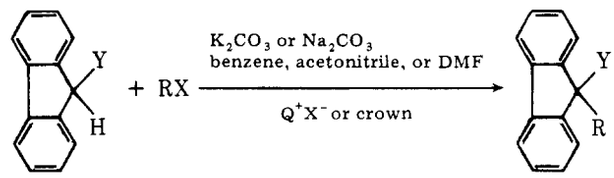
1. Alkylation of diethyl malonate, methyl cyanoacetate, and ethyl acetoacetate.



Z = COOEt, Y = COOEt, COMe
Z = COOMe, Y = CN

These reactions are conducted between 50 and 100 °C depending on the alkylating agent used. In the case of diethyl malonate the process is highly selective in the sense of mono- vs. dialkylation. Methyl cyanoacetate is much more prone to undergo dialkylation. Nevertheless in both cases, mono- and dialkylated products can be prepared in high yields.

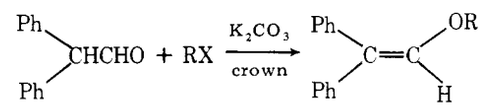
2. Alkylation and nitroarylation of 9-substituted fluorene derivatives.



Y = –COOEt, –CN, or –NC; RX = alkyl halide, *p*-chloronitrobenzene, etc.

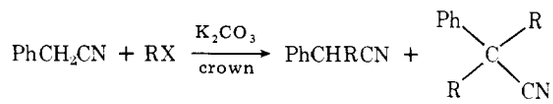
Since the starting compounds are solids, small amounts of solvents are necessary.

3. Alkylation and nitroarylation of diphenylacetaldehyde.



Exclusively O-alkylated derivatives are formed in high yields.

4. Alkylation of phenylacetonitrile.



Although phenylacetonitrile is a quite weak carbon acid it can still be deprotonated and subsequently alkylated using the potassium carbonate system at elevated temperatures. Since phenylacetonitrile is efficiently alkylated under CTP conditions,[5] this method is advantageous only for alkylation with compounds sensitive toward alkaline hydrolysis (e.g., ethyl chloroacetate).

0022-3263/78/1943-4682$01.00/0