Hypervalent Iodine Oxidation of Ethynylcarbinols: A Short and Efficient Conversion of Dihydroxyacetonyl Groups from Keto Groups

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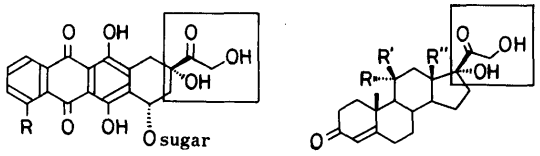
Oxidation of ethynylcarbinols (4a—g), prepared easily from ketones, with a hypervalent iodine reagent, phenyliodosyl bis(trifluoroacetate) (PIFA), in chloroform–acetonitrile–water gave the dihydroxyacetonyl compounds (6a—g) in high yields.

Keywords phenyliodosyl bis(trifluoroacetate); ethynylcarbinol; dihydroxyacetone; terminal alkyne; α-hydroxyketone

The dihydroxyacetone side chain is an important structural component in some biologically active compounds such as adriamycin and related antitumor agents (**1**)[1] and corticosteroid antiinflammatory drugs (**2**).[2] Therefore, a short and efficient conversion of keto groups into dihydroxyacetonyl groups would be a quite significant step in synthetic organic chemistry and medicinal chemistry.



1 2

R=OMe: adriamycin R,R′=O; R″=Me: cortisone
R=H; R′=OH; R″=Me: cortisol

Fig. 1

The conversion of the keto group into the dihydroxyacetone side chain has been investigated extensively in different ways.[3-9] Generally, dihydroxyacetones (**6**) are prepared *via* acetylcarbinols (**5**) by bromination followed by hydrolysis. The acetylcarbinol can be obtained by reaction of a ketone (**3**) with several acyl anion equivalents such as ethynyl lithium,[4,5] methoxyvinyl lithium,[6] lithium 1,3-dithiane,[7] *etc.* Dihydroxyacetone was also prepared by different routes using lead tetraacetate (LTA) oxidation of an enamide intermediate[8] or alkylation of a ketone with lithio dihydro-1,4-dioxin followed by epoxidation, sodium borohydride reduction and acidic hydrolysis[9] (Chart 1).

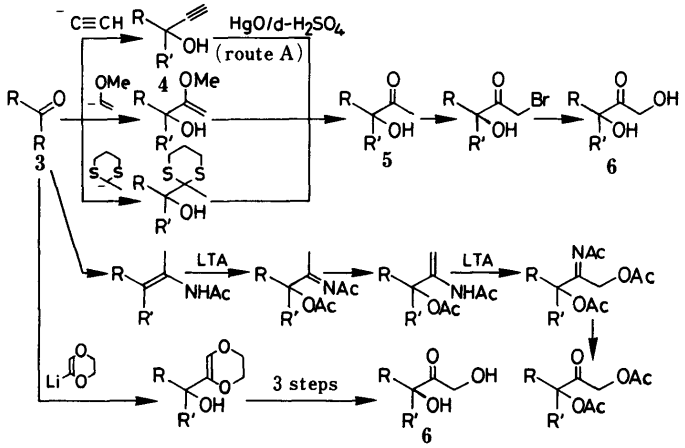
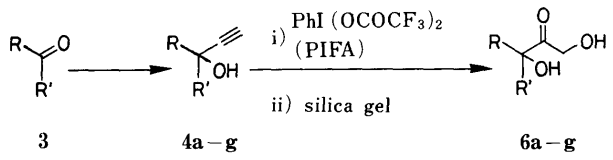


Chart 1

Dihydroxyacetones are most commonly prepared by route A in Chart 1. Although this method gives a satisfactory overall yield, an unfavorable oxidation of the ethynylcarbinol (**4**) using toxic mercuric (II) oxide and a total of 4 steps are involved. Recently, we have briefly reported that the use of a hypervalent iodine reagent, phenyliodosyl bis(trifluoroacetate) (PIFA) overcame these problems.[10] We now give a full account of this work and additional studies on the hypervalent iodine oxidation of acetylenic compound having a β-lactam ring in the molecule or a terminal trimethylsilyl group.

Reaction of Hypervalent Iodine Reagents with Alkynes Although the hypervalent iodine reagents have been shown to react with some alkynes to give various types of products, the reactivities are not fully understood: (i) the reaction of (perfluoroalkyl)phenyliodonium salt with terminal alkynes is complicated, since a mixture of substitution and addition products has been obtained,[11] (ii) diphenyl acetylene reacted with PIFA to afford the α-diketone, while phenyl acetylene was converted into ω-hydroxyacetophenone,[12] (iii) disubstituted alkynes were oxidized with iodosobenzene [PhI=O] in the presence of Ru catalysts to afford α-diketones, while under the same conditions terminal alkynes were cleaved to carboxylic acids,[13] (iv) PhI=O reacted with trimethylsilylalkynes in the presence of $BF_3 \cdot OEt_2$ to yield alkynyliodonium salts,[14] (v) [hydroxy(tosyloxy)iodo]benzene [PhI(OH)OTs] reacted with terminal alkynes to give alkynyliodonium tosylates,[15] and (vi) PhI(OH)OTs also reacted with disubstituted alkynes in methanol to afford esters *via* rearrangement.[16] We found a novel, general, and efficient conversion of ethynylcarbinols (**4**) into structually important dihydroxyacetones (**6**) by using PIFA. The typical experimental procedure is illustrated in the preparation of the dihydroxyacetone (**6a**). The ethynylcarbinol (**4a**, 1 mmol) was added dropwise to a solution of PIFA (2.2 mmol) in $CHCl_3$–CH_3CN–H_2O (4 ml, 80:10:1). The mixture was stirred at reflux for 10 h to give **6a** and its *O*-trifluoroacetate. The mixture was passed through a dry silica gel column with ethyl acetate to complete the hydrolysis of the trifluoroacetate. Similarly, other ethynylcarbinols (**4b—g**) readily reacted with a slight excess (1.1—2.2 eq) of PIFA to give the corresponding dihydroxyacetones (**6b—g**) in good yields. When the substrate was insoluble under these reaction conditions, 1,2-dichloroethane was used instead of chloroform to elevate the reaction temperature and to increase the solubility. Oxidation of the ethynylcarbinols (**4c, d, g**) having a phenolic hydroxyl group in the molecules should be carried out



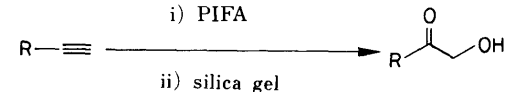
3 4a–g 6a–g

Chart 2

after protecting the phenolic hydroxyl group with an electron-withdrawing group such as an acetyl or tosyl group due to the higher reactivity of the phenolic hydroxyl group (runs 3, 4 and 7).

Recently trimethylsilylalkynes were shown to react with a hypervalent iodine reagent, PhI=O in the presence of $BF_3 \cdot OEt_2$ to give the alkynyliodonium salts.[14] Therefore, the reactivity of trimethylsilylalkyne (**4f**) with PIFA was examined. The reaction of **4f** with PIFA in $CHCl_3$–CH_3CN–H_2O (80:10:1) gave the same dihydroxyacetone (**6e**) as obtained from **4e** with PIFA, but the yield was slightly lower than that from **4e**.

Terminal alkynes (**7a**—**c**) were also readily converted into the corresponding α-hydroxyketones (**8a**—**c**) in high yields. Although Merkushev *et al.* reported[12] that *p*-diethynylbenzene reacted with PIFA in $CHCl_3$ containing water to give bis(α-hydroxyacetyl)benzene in good yield, oxidation of **7a** with PIFA in $CHCl_3$–CH_3CN–H_2O (80:10:1) gave a 4:1 mixture of **8a** and its *O*-trifluoroacetate without passage through the dry silica gel column. A characteristic feature of the present oxidation reaction was seen in the reaction of **7c** with PIFA. Oxidation of **7c** having a base- and acid-sensitive β-lactam ring in the molecule proceeded smoothly without any decomposition of the β-lactam ring (run 10). The reaction conditions and yields are summarized in Table I.



7a–c 8a–c

Chart 3

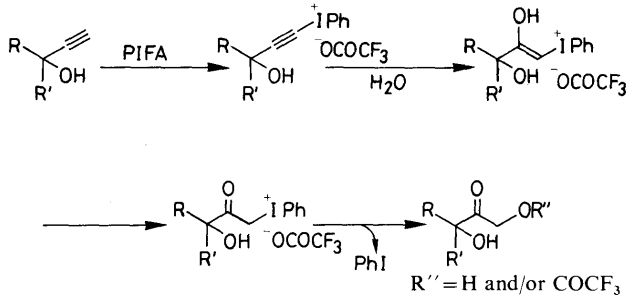
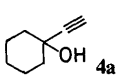
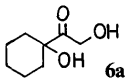
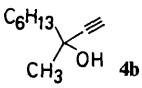
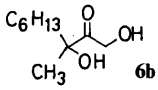
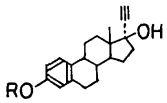
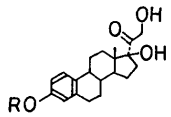
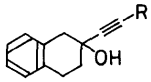
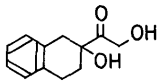
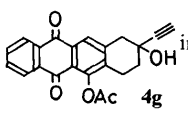
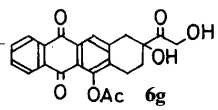
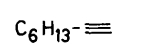
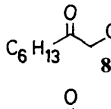
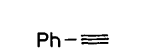
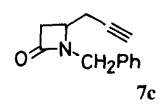
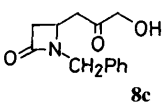


Chart 4

The reaction presumably proceeds with an initial formation of the alkynyliodonium salt and subsequent hydrolysis to dihydroxyacetones. The formation of the iodonium salt from terminal alkynes with some hypervalent iodine reagents is well documented by recent studies.[12,15,17]

TABLE I. Oxidation of Ethynylcarbinols with Phenyliodosyl Bis(trifluoroacetate)

Runs	Starting materials	Conditions[a]	Products	Yield (%)
1	 **4a**	80 °C, 10 h	 **6a**	77
2	 **4b**	80 °C, 10 h	 **6b**	77
3	 **4c**: R=Ac	80 °C, 19 h	 **6c**: R=Ac	53
4	**4d**: R=Ts	80 °C, 19 h	**6d**: R=Ts	60
5	 **4e**: R=H	80 °C, 12 h	 **6e**	76 from **4e**
6	**4f**: R=TMS	80 °C, 19 h		50 from **4f**
7	 **4g**	5 eq PIFA in $ClCH_2CH_2Cl$–CH_3CN–H_2O 100 °C, 4 h	 **6g**	85
8	 **7a**	80 °C, 5 h	 **8a**	78
9	 **7b**	80 °C, 6 h	 **8b**	82
10	 **7c**	in $ClCH_2CH_2Cl$–CH_3CN–H_2O 100 °C, 3 h	 **8c**	82

a) The reaction was carried out with 1.1—2.2 eq of PIFA in $CHCl_3$–CH_3CN–H_2O except for runs 7 and 10. TMS: trimethylsilyl.

Experimental

Melting points were determined on a Yanagimoto micro melting point apparatus and are uncorrected. The infrared (IR) spectra were obtained on a JASCO HPIR-102 spectrophotometer. ^{1}H-Nuclear magnetic resonance (^{1}H-NMR) spectra were recorded on Hitachi R-22 (90 MHz), JEOL FX-90Q (90 MHz), and JEOL JNW-GX500 (500 MHz) spectrometers using Me_4Si as an internal standard. Low- and high-resolution mass spectra were obtained with a JEOL JMS D-300 instrument, with a direct-inlet system at 70 eV. Column chromatography was carried out on Merck Silica gel 60.

Materials Ethynylcarbinols (**4b**, **4e**) were prepared from the parent ketones by trimethylsilylethynylation and subsequent desilylation as previously reported.[5,18] Compounds **4c**, **4d**, **4g**, and **7c** were prepared by acetylation, tosylation or benzylation of the known ethynylcarbinols or alkyne. PIFA, the ethynylcarbinol (**4a**), and the alkyne (**7a**) are commercially available.

3-Hydroxy-3-methyl-1-nonyne (4b) This was obtained from 2-octyne by treatment with trimethylsilylethynyl lithium in tetrahydrofuran (THF) at −78 °C for 1 h, followed by desilylation with 0.3 M KOH solution in EtOH at room temperature in 68% overall yield as a colorless oil, bp 88 °C/13 mmHg (lit.[19] 78 °C/5 mmHg). IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3600, 3500—3400, 3300. ^{1}H-NMR ($CDCl_3$) δ: 0.7—1.0 (m, 3H, CH_3CH_2–), 1.1—1.9 (m, 10H, $CH_2 \times 5$), 1.48 (s, 3H, CCH_3), 2.10 (br s, 1H, OH), 2.41 (s, 1H, C≡CH).

3-Acetoxy-17α-ethynyl-17β-hydroxyestra-1,3,5(10)-trien (4c) This was obtained from 17α-ethynylestradiol by acetylation with Ac_2O–pyridine as colorless crystals, mp 153—155 °C (MeOH). IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3600, 3500—3400, 3300, 1745, 1495. ^{1}H-NMR ($CDCl_3$) δ: 0.88 (s, 3H, CH_3), 1.0—3.0 (m, 16H), 2.26 (s, 3H, $OCOCH_3$), 2.58 (s, 1H, C≡CH), 6.7—6.9 and 7.2—7.4 (m, 3H, ArH). Exact mass Calcd for $C_{22}H_{26}O_3$: 338.1879. Found: 338.1864.

17α-Ethynyl-17β-hydroxy-3-tosyloxyestra-1,3,5(10)-trien (4d) This was obtained from 17α-ethynylestradiol by tosylation with TsCl–pyridine as colorless crystals, mp 112—114 °C (pet. ether). IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3600, 3500—3400, 3300, 1490, 1370, 1180. ^{1}H-NMR ($CDCl_3$) δ: 0.88 (s, 3H, CH_3), 1.0—3.0 (m, 16H), 2.45 (s, 3H, C$\underline{H}_3$-C_6H_4-), 2.57 (s, 1H, C≡C$\underline{H}$), 6.6—7.1 (m, 3H, ArH), 7.27 (d, 2H, J=8 Hz, ArH), 7.70 (d, 2H, J=8 Hz, ArH). Exact mass Calcd for $C_{27}H_{30}O_4S$: 450.1862. Found: 450.1842.

2-Trimethylsilylethynyl-1,2,3,4-tetrahydro-2-naphthol (4f) This was prepared from β-tetralone by the reported method[5] as colorless crystals, mp 126—127 °C (hexane) [lit.[5] 125.5—126 °C (Et_2O–hexane)].

2-Ethynyl-1,2,3,4-tetrahydro-2-naphthol (4e) Compound **4f** was desilylated by treatment with 0.3 M KOH solution in EtOH to give **4e** as colorless crystals, mp 74—75 °C (hexane). IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3600, 3500—3400, 3300, 1495. ^{1}H-NMR ($CDCl_3$) δ: 1.9—2.3 (m, 2H, CH_2), 2.42 (s, 1H, C≡C$\underline{H}$), 2.8—3.2 (m, 4H, CH_2×2), 7.18 (br s, 4H, ArH). Exact mass Calcd for $C_{12}H_{12}O$: 172.0888. Found: 172.0901.

6-Acetoxy-9-ethynyl-9-hydroxy-7,8,9,10-tetrahydronaphthacene-5,12-dione (4g) This was prepared from 6,9-dihydroxy-9-ethynyl-7,8,9,10-tetrahydronaphthacene-5,12-dione[18] by phase transfer-catalyzed acetylation[20] with AcCl–NaOH–tetrabutylammonium hydrogen sulfate in CH_2Cl_2 as light yellow crystals, mp 233.5—234.5 °C ($CHCl_3$). IR ν_{max}^{KCl} cm^{-1}: 3500—3400, 3300, 1725, 1670, 1665, 1585. ^{1}H-NMR ($CDCl_3$) δ: 2.0—2.3 (m, 2H, CH_2), 2.48 (s, 1H, C≡C$\underline{H}$), 2.54 (s, 3H, $OCOCH_3$), 2.85—3.1 (m, 3H, CH_2 and OH), 3.2—3.4 (m, 2H, CH_2), 7.7—7.9 (m, 2H, ArH), 8.01 (s, 1H, ArH), 8.1—8.3 (m, 2H, ArH). MS *m/z* (intensity): 360 (M^+, 0.6), 319 (22), 318 (99), 301 (25), 300 (base peak). Exact mass Calcd for $C_{22}H_{16}O_6$–CH_3COOH: 300.0787. Found: 300.0798.

1-Benzyl-4-(2-propynyl)-2-azetidinone (7c) This was prepared from 4-(2-propynyl)-2-azetidinone[21] by phase transfer-catalyzed benzylation[22] with benzyl bromide–KOH–tetrabutylammonium bromide in THF as colorless crystals, mp 52—53 °C (hexane). IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3300, 1745, 1600. ^{1}H-NMR ($CDCl_3$) δ: 2.03 (t, 1H, J=2 Hz, C≡C$\underline{H}$), 2.42 (dd, 2H, J=2, 5 Hz, -CH_2-C≡C), 2.77 (dd, 1H, J=2, 14 Hz, C_3-H), 3.07 (dd, 1H, J=2, 14 Hz, C_3-H), 3.5—3.7 (m, 1H, C_4-H), 4.16 (d, 1H, J=15 Hz, Ph$C\underline{H}_2$×1/2), 4.64 (d, 1H, J=15 Hz, Ph$C\underline{H}_2$×1/2), 7.26 (s, 5H, ArH). Exact mass Calcd for $C_{13}H_{13}NO$: 199.0994. Found: 199.0979.

General Procedure for the Oxidation of Ethynylcarbinols (4a—g) and Terminal Alkynes (7a—c) An ethynylcarbinol or terminal alkyne (1 mol) was added dropwise to a solution of PIFA (1.1—2.2 mmol) in $CHCl_3$ or $ClCH_2CH_2Cl$–CH_3CN–H_2O (4 ml, 80:10:1). The mixture was stirred at reflux for 10 h, then cooled to room temperature, and partitioned between water and CH_2Cl_2. The aqueous layer was extracted with CH_2Cl_2. The combined extract was washed with saturated NaCl solution, dried over $MgSO_4$, and concentrated under reduced pressure to give a mixture of the dihydroxyacetone or α-hydroxyketone and its *O*-trifluoroacetate. The mixture was passed through a dry silica gel column with ethyl acetate to hydrolyze the trifluoroacetate. The eluate was concentrated and purified by column chromatography on silica gel with benzene–ethyl acetate (5:1) to give pure **6a**—**f** or **8a**—**c**.

1-Hydroxycyclohexyl Hydroxymethyl Ketone (6a) This (121 mg) was obtained from **4a** (124 mg, 1 mmol) and PIFA (946 mg, 2.2 mmol). Recrystallization from hexane gave pure **6a** as colorless crystals, mp 90 °C. IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3550—3400, 1710. ^{1}H-NMR ($CDCl_3$) δ: 1.6—1.8 (m, 10H, CH_2×5), 2.76 (br s, 2H, OH×2, disappeared on addition of D_2O), 4.49 (s, 2H, $COC\underline{H}_2OH$). *Anal.* Calcd for $C_8H_{14}O_3$: C, 60.74; H, 8.92. Found: C, 60.52; H, 9.16.

1,3-Dihydroxy-3-methyl-2-nonanone (6b) This (72 mg) was obtained from **4b** (77 mg, 0.5 mmol) and PIFA (473 mg, 1.1 mmol). Distillation under reduced pressure gave pure **6b** as a colorless oil, bp 105—115 °C/5 mmHg (bath temperature). IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3550—3400, 1710. ^{1}H-NMR ($CDCl_3$) δ: 0.7—1.0 (m, 3H, C$\underline{H}_3CH_2$-), 0.9—1.8 (m, 10H, CH_2×5), 1.33 (s, 3H, CCH_3), 2.93 (br s, 2H, OH×2, disappeared on addition of D_2O), 4.43 (s, 2H, $COC\underline{H}_2OH$). *Anal.* Calcd for $C_{10}H_{20}O_3$: C, 63.83; H, 10.64. Found: C, 63.95; H, 10.71.

3-Acetoxy-17β-hydroxy-17α-(α-hydroxyacetyl)estra-1,3,5(10)-trien (6c) This (13.7 mg) was obtained from **4c** (23.7 mg, 0.07 mmol) and PIFA (66.2 mg, 0.154 mmol). Recrystallization from ligroin gave pure **6c** as colorless crystals, mp 111—112 °C. IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3550—3400, 1750, 1710. ^{1}H-NMR ($CDCl_3$) δ: 0.9—3.2 (m, 17H), 0.95 (s, 3H, CH_3), 2.28 (s, 3H, $OCOCH_3$), 4.54 (br s, 2H, $COC\underline{H}_2OH$), 6.7—7.3 (m, 3H, ArH). Exact mass Calcd for $C_{22}H_{28}O_5$: 372.1935. Found: 372.1965.

17β-Hydroxy-17α-(α-hydroxyacetyl)-3-tosyloxyestra-1,3,5(10)-trien (6d) This (16.3 mg) was obtained from **4d** (25.2 mg, 0.056 mmol) and PIFA (53.0 mg, 0.123 mmol). Recrystallization from ligroin gave pure **6d** as colorless crystals, mp 75—76 °C. IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3550—3400, 1710. ^{1}H-NMR ($CDCl_3$) δ: 0.9—3.2 (m, 17H), 0.93 (s, 3H, CH_3), 2.41 (s, 3H, C$\underline{H}_3C_6H_4$-), 4.47 (br s, 2H, $COC\underline{H}_2OH$), 6.5—7.1 (m, 3H, ArH), 7.23 (d, 2H, J=8 Hz, ArH), 7.65 (d, 2H, J=8 Hz, ArH). Exact mass Calcd for $C_{27}H_{32}O_6S$: 484.1917. Found: 484.1911.

2-Hydroxy-1,2,3,4-tetrahydro-2-naphthyl Hydroxymethyl Ketone (6e) (i) This (39.2 mg) was obtained from **4e** (43.0 mg, 0.25 mmol) and PIFA (236.6 mg, 0.55 mmol). Recrystallization from benzene–hexane gave pure **6e** as colorless crystals, mp 103—104 °C (lit.[23] 105—106 °C). IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3550—3400, 1725. ^{1}H-NMR ($CDCl_3$) δ: 1.8—2.2 (m, 2H, CH_2), 2.5—3.4 (m, 4H, CH_2×2), 4.63 (s, 2H, $COC\underline{H}_2OH$), 6.9—7.3 (m, 4H, ArH).

(ii) This (20.0 mg) was obtained from **4f** (48.8 mg, 0.2 mmol) and PIFA (189.2 mg, 0.44 mmol).

6-Acetoxy-9-hydroxy-9-(α-hydroxyacetyl)-7,8,9,10-tetrahydronaphthacene-5,12-dione (6g) This (15.7 mg) was obtained from **4g** (17.0 mg, 0.047 mmol) and PIFA (101.5 mg, 0.236 mmol). Recrystallization from iso-PrOH gave pure **6g** as light yellow crystals, mp 198—199 °C. IR ν_{max}^{KCl} cm^{-1}: 3500—3400, 1760, 1720, 1670. ^{1}H-NMR ($CDCl_3$) δ: 2.0—2.1 (m, 2H, CH_2), 2.55 (s, 3H, $OCOCH_3$), 2.8—3.1 (m, 3H, CH_2 and OH), 3.4—3.5 (m, 2H, CH_2), 3.6—3.7 (m, 1H, OH), 4.68 (s, 2H, $COC\underline{H}_2OH$), 7.75—7.9 (m, 2H, ArH), 8.02 (s, 1H, ArH), 8.2—8.3 (m, 2H, ArH). Exact mass Calcd for $C_{22}H_{18}O_7$: 394.1053. Found: 394.1081.

1-Hydroxy-2-octanone (8a) This (112 mg) was obtained from **7a** (110 mg, 1 mmol) and PIFA (473 mg, 1.1 mmol). Distillation under reduced pressure gave pure **8a** as a colorless oil, bp 71—74 °C/6 mmHg (lit.[24] 70—76 °C/7 mmHg). IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3550—3400, 1715. ^{1}H-NMR ($CDCl_3$) δ: 0.90 (t, 3H, J=6 Hz, C$\underline{H}_3CH_2$-), 1.1—1.8 (m, 8H, CH_2×4), 2.40 (t, 2H, J=6 Hz, $CH_2C\underline{H}_2CO$), 3.10 (br s, 1H, OH, disappeared on addition of D_2O), 4.23 (s, 2H, $COC\underline{H}_2OH$). Without passage through a dry silica gel column, a 4:1 mixture of **8a** and its *O*-trifluoroacetate was obtained. IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3550—3400, 1790, 1715. ^{1}H-NMR ($CDCl_3$) δ: 0.90 (t, 3H, J=6 Hz, C$\underline{H}_3CH_2$-), 1.1—1.8 (m, 8H, CH_2×4), 2.41 (t, 3H, J=6 Hz, $CH_2C\underline{H}_2CO$), 3.67 (br s, 4/5H, OH), 4.24 (s, 8/5H, $COC\underline{H}_2OH$×4/5), 4.90 (s, 2/5H, $COC\underline{H}_2OCOCF_3$×1/5).

Phenyl Hydroxymethyl Ketone (8b) This (112 mg) was obtained from **7b** (102 mg, 1 mmol) and PIFA (473 mg, 1.1 mmol). Recrystallization from hexane gave pure **8b** as colorless crystals, mp 82.5—83.5 °C (lit.[25] 82—84 °C). IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3550—3400, 1690. ^{1}H-NMR ($CDCl_3$) δ: 3.33 (br s, 1H, OH, disappeared on addition of D_2O), 4.84 (s, 2H, $COC\underline{H}_2OH$), 7.2—8.0 (m, 5H, ArH).

1-Benzyl-4-(3-hydroxy-2-oxopropyl)-2-azetidinone (8c) This (95 mg) was obtained from **7c** (100 mg, 0.5 mmol) and PIFA (473 mg, 1.1 mmol) as a colorless oil. IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3600—3400, 1745, 1730. ^{1}H-NMR ($CDCl_3$) δ: 2.58 (d, 2H, J=6 Hz, C$\underline{H}_2COCH_2OH$), 2.63 (dd, 1H, J=2, 14 Hz, C_3-H), 3.19 (dd, 1H, J=5, 14 Hz, C_3-H), 2.8—3.1 (br s, 1H, OH), 3.72 (d, 1H, J=19 Hz, Ph$C\underline{H}_2$×1/2), 4.04 (d, 1H, J=19 Hz, Ph$C\underline{H}_2$×1/2), 3.9—4.2 (m, 1H, C_4-H), 4.32 (s, 2H, $COC\underline{H}_2OH$), 7.1—7.4 (m, 5H, ArH). Exact mass Calcd for $C_{13}H_{15}NO_3$: 233.1053. Found: 233.1070.

References and Notes

1) "Anthracycline Antibiotics," ed. by H. S. El Khadam, Academic Press, New York, 1982; Y. Tamura and Y. Kita, *Yuki Gosei Kagaku Kyokai Shi*, **46**, 205 (1988).
2) J. Redpath and F. J. Zeelen, *Chem. Soc. Rev.*, **12**, 75 (1983); V. VanRheenen and K. P. Shephard, *J. Org. Chem.*, **44**, 1582 (1979); A. R. Daniewski and W. Wojciechowska, *ibid.*, **47**, 2993 (1982); D. van Leusen and A. M. van Leusen, *Tetrahedron Lett.*, **25**, 2581 (1984); M. Numazawa and M. Nagaoka, *J. Org. Chem.*, **50**, 81 (1985) and references cited therein.
3) D. H. R. Barton, W. B. Motherwell, and S. Z. Zard, *J. Chem. Soc., Chem. Commun.*, **1981**, 774; *idem, ibid.*, **1982**, 551; L. Nědělec, V. Torelli, and M. Hardy, *ibid.*, **1981**, 775.
4) For example of mercury-catalyzed hydration of ethynylcarbinols, see: H. E. Stavely, *J. Am. Chem. Soc.*, **63**, 3127 (1941); K. Krohn, and K. Tolkiehn, *Chem. Ber.*, **112**, 3453 (1979); H. Umezawa, Y. Takahashi, M. Kinoshita, H. Naganawa, K. Tatsuta, and T. Takeuchi, *J. Antibiot.*, **33**, 1581 (1980); P. C. B.-Page and S. V. Ley, *J. Chem. Soc., Perkin Trans. 1*, **1984**, 1847. The conventional mercury-catalyzed hydration of alkynes, see: M. W. Goldberg, R. Aeschbacher, and E. Hardegger, *Helv. Chim. Acta*, **26**, 680 (1943); W. L. Budde and R. E. Dessy, *J. Am. Chem. Soc.*, **85**, 3964 (1963); G. W. Parshell, "Homogeneous Catalysis," Wiley-Interscience, New York, 1980; V. Janout and S. L. Regen, *J. Org. Chem.*, **47**, 3331 (1982).
5) M. Suzuki, Y. Kimura, and S. Terashima, *Chem. Lett.*, **1984**, 1543.
6) J. E. Baldwin, O. W. Lever, Jr., and N. R. Tzodikov, *J. Org. Chem.*,

41, 2312 (1976).
7) E. J. Corey and B. W. Erickson, *J. Org. Chem.*, **36**, 3553 (1971).
8) R. B. Boar, J. F. McGhie, M. Robinson, and D. H. R. Barton, *J. Chem. Soc., Perkin Trans. 1*, **1975**, 1242.
9) M. Fetizon, P. Goulaouic, and I. Hanna, *Tetrahedron Lett.*, **26**, 4925 (1985).
10) Y. Tamura, T. Yakura, J. Haruta, and Y. Kita, *Tetrahedron Lett.*, **26**, 3837 (1985).
11) T. Umemoto, Y. Kuriu, and O. Miyano, *Tetrahedron Lett.*, **23**, 3579 (1982).
12) E. B. Merkushev, L. G. Karpitskaya, and G. I. Novosel'tseva, *Dokl. Akad. Nauk SSSR*, **245**, 607 (1979) [*Chem. Abstr.*, **91**, 39072*d* (1979)].
13) P. Müller and J. Godoy, *Helv. Chim. Acta*, **64**, 2531 (1981); *idem*, *Tetrahedron Lett.*, **23**, 3661 (1982).
14) M. Ochiai, M. Kunishima, K. Sumi, Y. Nagao, E. Fujita, M. Arimoto, and H. Yamaguchi, *Tetrahedron Lett.*, **26**, 4501 (1985); M. Ochiai, M. Kunishima, Y. Nagao, K. Fuji, M. Shiro, and E. Fujita, *J. Am. Chem. Soc.*, **108**, 8281 (1986).
15) G. F. Koser, L. Rebrovic, and R. H. Wettach, *J. Org. Chem.*, **46**, 4324 (1981); L. Rebrovic and G. F. Koser, *ibid.*, **49**, 4700 (1984); A. J. Margida and G. F. Koser, *ibid.*, **49**, 4703 (1984); P. J. Stang and B. W. Surber, *J. Am. Chem. Soc.*, **107**, 1452 (1985); P. J. Stang, M. Boehshar, and J. Lin, *ibid.*, **108**, 7832 (1986); P. J. Stang, B. W. Surber, Z.-C. Chen, K. A. Roberts, and A. G. Anderson, *ibid.*, **109**, 228 (1987).
16) R. M. Moriarty, R. K. Vaid, M. P. Duncan, and B. K. Vaid, *Tetrahedron Lett.*, **28**, 2845 (1987).
17) F. M. Beringer and S. A. Galton, *J. Org. Chem.*, **30**, 1930 (1965).
18) Y. Tamura, M. Sasho, H. Ohe, S. Akai, and Y. Kita, *Tetrahedron Lett.*, **26**, 1549 (1985).
19) I. N. Nazarov, I. L. Kotlyarevskiĭ, and V. F. Ryabchenko, *Izv. Akad. Nauk SSSR, Otdel. Khim. Nauk*, **1956**, 960 [*Chem. Abstr.*, **51**, 5019*f* (1957)].
20) V. O. Illi, *Tetrahedron Lett.*, **1979**, 2431.
21) A. Nishida, M. Shibasaki, and S. Ikegami, *Tetrahedron Lett.*, **22**, 4819 (1981).
22) D. Reuschling, H. Pietsch, and A. Linkies, *Tetrahedron Lett.*, **1978**, 615.
23) A. M. El-Abbady and S. H. Doss, *J. Chem. U.A.R.*, **8**, 33 (1965) [*Chem. Abstr.*, **64**, 11139*a* (1966)].
24) T. Tsuji, *Tetrahedron Lett.*, **1966**, 2413.
25) G. A. Russell and G. J. Mikol, *J. Am. Chem. Soc.*, **88**, 5498 (1966).