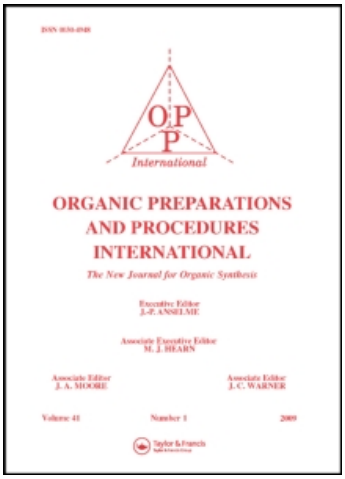

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trans-1-CHLORO-5(ETHOXYETHOXY)-2-PENTENE

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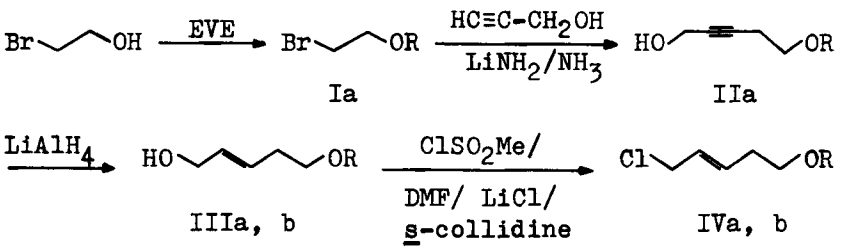
Ongoing synthetic investigations[1] required substantial amounts of a pure trans-2-pentenyl unit suitable for subsequent carbanion alkylations at C-1 and C-5. These prerequisites are met by title compound IVa, which possesses a reactive C-1 allylic halide in addition to featuring potential electrophilicity at C-5. We hereby describe a convenient procedure for preparing this synthon.

In contrast to frequently cited 1,5-disubstituted-cis-2-pentenyl systems,[2] scant attention has been paid to their trans counterparts. For example, trans-1,5-pentene-2-diol has been described only once via a short, but operationally cumbersome methodology, centering on sodium borohydride reduction of glutacondialdehyde;[2a] the dihalides derived from IIIb seem to have been passed over altogether. For large-scale purposes, trans-alkenols are best prepared by lithium tetrahydroaluminate (LAH) reduction of acetylenic carbinols,[3] suggesting IIa as logical precursor for IVa. Such alkynyl fragments are in principle accessible via hydroxymethylation of 3-butyne-1-ol [2b,d] or hydroxyethylation (ethylene oxide) of propargyl alcohol.[2c,4] In practice, these routes proceed via acetylenic an-

ions, so that blocking of base consuming hydroxy functions is often advisable.

SCHEME I



a, R = CH(Me)OEt

b, R = H EVE = ethyl vinyl ether

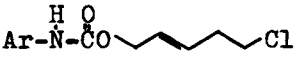
We chose to prepare IVa as shown in Scheme I. 2-Bromoethanol, on acid-promoted treatment with ethyl vinyl ether, gave the O-protected Ia.[5] Our preference for the ethoxyethoxy rather than the more conventional tetrahydropyranyl blocking group derived from the greater ease of hydrolysis or methanolysis of the ethoxyethoxy group to yield readily removable breakdown fragments;[6] moreover, the ethoxyethoxy group displays clearly distinguishable CH_3 NMR signals at 1.21 and 1.29 ppm (t and d resp.). Propargyl alcohol dianion, generated in $LiNH_2$-containing liquid NH_3, reacted rapidly with Ia to provide, after 1 hr, 77% of IIa. Reduction thereof to IIIa gave optimal yields on using 1.25 equivs of LAH in refluxing THF (1 hr); characterization of IIIa was based on ^{13}C NMR inspection and also by hydrolysis to IIIb and its subsequent conversion to the earlier reported bis-phenylcarbamate.[2a] Transformation of IIIa to IVa was realized *via* the method of Collington and Meyers.[7] This involved the system $MeSO_2Cl$ and LiCl in

collidine containing DMF and gave, just as in the cited examples, unrearranged chloride IVa of at least 95% homogeneity.[8]

The potential of IVa was briefly examined. It reacted in DMF with potassium phthalimide and with sodium p-toluenesulfinate to give, after mild hydrolysis, pentenols Va and Vb. Deblocking of IVa gave trans-5-chloro-3-penten-1-ol IVb, derivatized by conversion to solid carbamates VIa and VIb. Our main application of IVa in natural product synthesis will be reported in due course.

V

a, X = N-phthalimide
b, X = p-$SO_2C_6H_4CH_3$



VI

a, Ar = C_6H_5
b, Ar = α-naphtyl

EXPERIMENTAL

Melting points, taken on a Fisher-Johns block, and boiling points are uncorrected. ^{1}H-NMR spectra were obtained on a Varian EM 360 spectrometer; ^{13}C- MR spectra were recorded on a Varian HA 100 equipped with a Digilab FTS-NMR-3. GLC data were obtained on a carbowax column of 30 meter and 0.3 mm diameter at 170°C. We thank Messrs P. van den Bosch and H. Eding for providing the microanalytical data.

1-Bromo-2-(ethoxyethoxy)ethane (Ia).- The following directions are based on those of Brandsma.[9] To 180 g. (2.50 moles) of ethyl vinyl ether were added at 0° and with stirring 175 mg. of p-toluenesulfonic acid (TSA) and 15.7 g. (0.125 mole) of 2-bromoethanol. The cooling bath was removed, resulting in a rapid temperature-rise to 6°; the mixture was recooled to 0° whereupon another 140.6 g. (1.125 moles) of 2-bromoethanol and 120 mg. of TSA were added. The mixture was slowly allowed to

come to room temperature (1 hr) and was then first basified by addition of 12.5 ml. of saturated K_2CO_3 solution and thereafter rendered water-free by introduction of anhydrous K_2CO_3. On bubbling NH_3 through the mixture for 10 seconds, the solids were removed by filtration and were rinsed with ether. The low-boiling components were removed from the filtrate at aspirator pressure below 50°; fractionation of the residue from anhydrous K_2CO_3 in NH_3-flushed equipment afforded 220 g. (92%) of Ia, bp. 63-64°/10 mm. ^{1}H-NMR δ (CCl_4): 1.14 (t, 3, $OCCH_3$), 1.25 (d, 3, O_2CCH_3), 3.16-3.91 (m, 6, 3 x CH_2), 4.62 (q, 1, OCHO).

5-(Ethoxyethoxy)-2-pentyn-1-ol (IIa).- To a stirred, refluxing mixture of 1.1 mole of freshly prepared $LiNH_2$ (from 7.7 g. of Li wire and 0.10 g. of $Fe(NO_3)_3$ in 1000 ml. of liquid NH_3) was added dropwise 28.0 g. (0.50 mole) of propargyl alcohol. Stirring was continued for 15 min. at which point 98.2 g. (0.50 mole) of Ia was introduced. After 1 hr the solvent was expelled (warm water bath) and the residue was taken up in ice water -ether and filtered through Hy-Flow (Celite 545) to remove bothersome solids. The filtrate was then thoroughly extracted with 400 ml. of ether. Drying and evaporation of the organic phase left a residue which, on fractionation from anhydrous K_2CO_3, provided 66.8 g. (77%) of product, bp. 86-89°/0.15 mm. ^{1}H-NMR δ (CCl_4): 1.21 (t, 3, $OCCH_3$), 1.29 (d, 3, O_2CCH_3), 2.20 -2.62 (m, 2, $\equiv CCH_2CO$), 3.08-3.91 (m, 5, OH and CH_2OCOCH_2), 3.91-4.25 (t, 2, OCH_2C), 4.63 (q, 1, OCHO).

trans-5-(Ethoxyethoxy)-2-penten-1-ol (IIIa).- To a stirred mixture of 6.25 g. (0.164 mole) of LAH in 150 ml. of dry THF

was introduced dropwise 43.0 g. (0.25 mole) of IIa in 50 ml. of THF. The mixture was refluxed for 1 hr and was then decomposed by consecutive addition of 6.25 ml. of water, 4.7 ml. of 5N NaOH and 20.3 ml. of water. Filtration and filtrate-solvent removal gave a residue which was fractionated to furnish 37.8 g. (87%) of product, bp. 77-78°/0.1 mm. ^{1}H-NMR δ (CCl_4): 1.21 (t, 3, $OCCH_3$), 1.27 (d, 3, O_2CCH_3), 2.08-2.56 (m, 2, $=CCH_2$), 3.14-4.32 (m, 7, $HOCH_2$ and CH_2OCOCH_2), 4.64 (q, 1, OCHO), 5.23 -5.97 (m, 2, CH=CH). ^{13}C-NMR δ (neat): 63.32 (C_1), 33.29 (C_4).[10]

For purposes of literature comparison and ^{13}C-NMR ascertainment of the proper trans-geometry, IIIa was hydrolyzed to IIIb which was then derivatized to the known bis-phenylcarbamate.[2a]

trans-1,5-Pentene-2-diol (IIIb).- A solution of 8.7 g. (0.05 mole) of IIIa in 100 ml. of methanol containing 0.15 ml. of sulfuric acid was kept at room temperature for 18 hr. Sodium methoxide in methanol, equivalent to the acid used, was added and the solvent was removed and replaced with chloroform. The solids were filtered; removal of the solvent and fractionation of the residual oil provided 4.8 g. (93%) of diol IIIb, bp. 88-89°/0.7 mm. ^{1}H-NMR δ ($CDCl_3$): 2.10-2.50 (m, 2, CH_2CO), 3.57 (t, 2, CCH_2O), 3.85-4.38 (m, 2, $OCH_2C=$ and 2 x OH), 5.22-5.97 (m, 2, CH=CH). ^{13}C-NMR δ (neat): 63.82 (C_1), 36.29 (C_4).[10] This material was GLC-compared with authentic cis-isomer.[2d] It was 99% pure and contained none of the cis-isomer.

Diol IIIb, 0.51 g. (0.005 mole) was treated with 1.19 g. (0.01 mole) of phenyl isocyanate for 4 hr in refluxing THF, to give, on solvent removal and trituration of residual solids

with isopropyl ether, 1.50 g. (91%), mp. 160-161°, lit.[2a] mp. 159-160°; the mp. did not change after crystallization from isopropyl ether.

trans-1-Chloro-5-(ethoxyethoxy)-pentene-2 (IVa).- To an ice-cold mixture of 2.26 g (0.055 mole) of LiCl, 7.25 g. (0.06 mole) of s-collidine and 8.7 g. (0.05 mole) of IIIa in 25 ml. of dry DMF was introduced, with stirring, 6.87 g. (0.06 mole) of methanesulfonyl chloride. After 1.5 hr at 0° the mixture was poured into 50 ml. of ice water. This was extracted with 100 ml. of 50% ether-petroleum ether. The combined organic layers were then scrubbed with 15 ml. of saturated copper nitrate solution and ultimately with water. Drying of the organic layer (K_2CO_3), solvent evaporation and fractionation of the residue from K_2CO_3 gave 7.7 g. (80%) of product, bp. 60-62°/0.3 mm.[11] ^{1}H-NMR δ (CCl_4): 1.14 (t, 3, $OCCH_3$, 1.26 (d, 3, O_2CCH_3), 2.07-2.50 (m, 2, $=CCH_2$), 3.05-3.79 (m, 4, CH_2OCOCH_2), 3.79-4.25 (m, 2, $ClCH_2$), 4.57 (q, 1, OCHO), 5.25-6.07 (m, 2, CH=CH). ^{13}C-NMR δ (neat): 45.32 (C_1), 33.20 (C_4).[10]

Compound IVa was converted to IVb according to the procedure IIIa→IIIb (see above). ^{1}H-NMR δ ($CDCl_3$): 2.07-2.35 (m, 2, CH_2CO), 3.62 (t, 2, CCH_2O), 4.04 (d, 2, $ClCH_2$), 4.20-4.53 (t, 1, OH), 5.29-6.06 (m, 2, CH=CH).

Treatment of IVb with one equiv of phenyl isocyanate, gave phenyl carbamate VIa, mp. 54-55° (isopropyl ether). Anal. Calcd. for $C_{12}H_{14}ClNO_2$: C, 66.32; H, 5.89; N, 5.85. Found: C, 60.25; H, 5.89; N, 5.81.

Similarly IVb, on treatment with α-naphtyl isocyanate, gave α-naphtyl carbamate VIb, mp. 91-92° (isopropyl ether).

Anal. Calcd. for $C_{16}H_{16}ClNO_2$: C, 66.32; H, 5.57; N, 4.84. Found: C, 66.54; H, 5.66; N, 4.76.

trans-5-(N-Phthalimido)-2-penten-1-ol (Va).- A mixture of 3.85 g. (0.02 mole) of IVa and 3.75 g. (0.02 mole) of potassium phthalimide in 15 ml. of DMF was kept at 135° for 10 min. It was poured into water from which the product was extracted into ether, which was dried and evaporated. Methanol, 50 ml., and 0.10 g. of sulfuric acid were added to the residue, which was kept at room temperature overnight and was then neutralized with sodium methoxide in methanol. Solvent was removed *in vacuo* and replaced with chloroform; the inorganics were filtered whereupon the chloroform was stripped *in vacuo* to leave solid product, 4.5 g. (97%). Recrystallization from ethanol gave white crystals melting at 83-84°.

Anal. Calcd. for $C_{13}H_{13}NO_2$: C, 67.52; H, 5.67; N, 6.06. Found: C, 67,24; H, 5.67; N, 5.93.

trans-5-(p-Toluenesulfonyl)-2-penten-1-ol (Vb).- Treatment of IVa with an equivalent amount of sodium p-toluenesulfinic acid in DMF as described above, led to sulfone Vb (71%), recrystallized from isopropyl alcohol to melt at 48-49°.

Anal. Calcd. for $C_{12}H_{16}O_3S$: C, 59.97; H, 6.71. Found: C, 60.11; H, 6.73.

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10. The trans geometry was confirmed by the chemical shifts of C_1 and C_4; see for instance J. W. de Haan and L. J. M. van de Ven, Org. Magn. Res., 5, 147 (1973).

11. Compound IVa, especially when crude, appears to be heat sensitive and has, in our hands, decomposed during distillation at bath temperatures exceeding 120°.

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