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An Improved Procedure for the Preparation of the *O*,2-Dianion of Allyl Alcohol

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Abstract: An improved procedure for the preparation of the *O*,2-dianion of allyl alcohol is described. The use of the magnesium alkoxide of 2-bromopropen-1-ol instead of the known lithium salt, suppresses dehydrohalogenation upon treatment with *tert*-butyl lithium and furnishes the dianion. Addition of this dianion to a variety of carbonyl compounds affords the expected products in good yield.

The *O*,2-dianion of allyl alcohol, originally developed by Corey,[1] is a highly versatile reagent that has been used for the preparation of a variety of structures.[2,3] Synthetic equivalents of this anion have also been developed.[4] The Corey protocol for the metalation of 2-bromopropen-1-ol[5] uses 2.5 equivalents of *t*-butyllithium to achieve both deprotonation and halogen metal exchange. In general, this process proceeds smoothly to afford the desired dianion **3**. We have found that occasionally this procedure leads to formation of not only the desired vinyl anion **3** but also varying amounts of propargyl alcohol dianion **5**.[6] Both of these dianions add smoothly to ketones and aldehydes to afford the expected allylic and propargylic alcohols **4** and **6**.

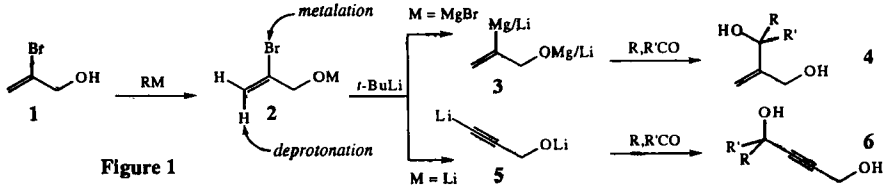
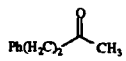
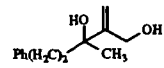
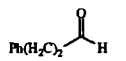
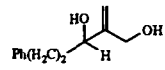
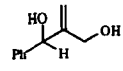
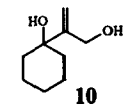
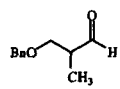
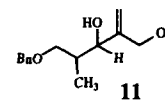
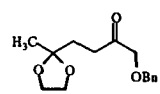
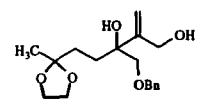


Figure 1

We have found that the undesired elimination reaction that leads to the formation of propargyl alcohol dianion **5** can be avoided by treating 2-bromopropen-1-ol sequentially with methylmagnesium bromide, to achieve deprotonation, followed by *t*-butyllithium to effect halogen metal exchange. To test the generality of this procedure, we prepared several allylic alcohols by treatment of a variety of aldehydes and ketones with the dianion of allyl alcohol (Table). The efficiency of the addition of anion **3** to carbonyl compounds is comparable to the published protocol. Only modest selectivity (1.3:1) was observed with a chiral aldehyde (entry 5).

Entry	Carbonyl	Product	% Yield
1		 **7**	58
2		 **8**	72
3		 **9**	71
4		 **10**	73
5		 **11**	62 (1.3:1)
6		 **12**	45

In summary, we have developed an improved synthesis of the *O*,2-dianion of allyl alcohol. The new procedure avoids the formation of undesired products and is amenable on a multigram scale. Addition products **7-12** are easily transformed into a variety of structures including poly-ols and α-hydroxy ketones etc. We are applying this methodology to the synthesis of zaragozic acids.[7] A typical procedure for the preparation of anion **3** is given below.

NMR spectra were recorded on a Bruker ARX-400 spectrometer operating at 400 MHz and 100 MHz for ^{1}H and ^{13}C, respectively. Solvents were purified according to standard procedures.

Diol **10**: A flame dried 50 mL round bottom flask equipped with a magnetic stir bar is charged with 2-bromopropen-1-ol (320 mg, 2.34 mmole) followed by diethyl ether (16 mL) and cooled to 0°C in an ice bath. A solution of MeMgBr (3.82 M in ether, 0.61 mL, 2.34 mmol) is then added dropwise over *ca.* 1 minute. During the addition, a colorless precipitate forms. The suspension is stirred for 30

min., during which time the suspension slowly dissolves. The solution is then cooled to -78°C in a dry ice/acetone bath. To the solution is then added over 1 h via syringe pump a solution of *t*-butyl lithium (1.7 M in pentane, 2.75 mL, 4.68 mmole). The mixture is then allowed to warm to 0°C and stirred at that temperature for 2.5 hours. The flask is then cooled to -78°C and a solution of cyclohexanone (0.78 M in Et_2O, 1.0 mL, 0.78 mmole) is added. After stirring at -78°C for 2 hours, the mixture is allowed to warm to room temperature and stirred for *ca.* 12 h. Excess anion is quenched by addition of a few drops of methanol and the resulting suspension is added to a mixture of Na/K tartrate (saturated in water) and ethyl acetate. The phases are then separated and the aqueous (lower) phase is extracted with ethyl acetate (2X). The combined organic phases are then washed with brine, dried over sodium sulfate and concentrated under reduced pressure. The resulting oil is purified by silica-gel chromatography (3:2 hexane/ethyl acetate) to furnish diol **10** (88.4 mg, 73%). ^{1}H-NMR ($CDCl_3$, 400 MHz): ppm δ 5.08 (d, 1H, *J*= 0.92 Hz, -C=C*H*$_2$), 5.07 (d, 1H, *J*= 0.92 Hz, -C=C*H*$_2$), 4.22 (s, 2H, -C*H*$_2$OH), 3.34 (s(br), 1H, -O*H*), 2.90 (s(br), 1H, -O*H*), 1.41-1.82 (m, 9H, -(C*H*$_2$)-), 1.01-1.31 (m, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 153.6, 111.3, 73.9, 64.4, 36.8, 25.6, 21.9; IR (thin film) ν 3354 (br), 2934, 2859, 1644, 1449, 1256, 1152, 1030, 963, 907, 851; HRMS (EI) calc'd for $C_9H_{16}O_2$, 156.1150, found 156.1144.

Data for Compounds 7-12:

7: ^{1}H-NMR ($CDCl_3$, 400 MHz) ppm δ 7.16-7.26 (m, 5H, H$_{arom}$), 5.20 (d, 1H, *J*= 0.91 Hz, -C=C*H*$_2$), 5.13 (s(br), 1H, -C=C*H*$_2$), 4.30 (d, 1H, *J*= 13.0 Hz, -C*H*$_2$OH), 4.25 (d, 1H, *J*= 13.0 Hz, -C*H*$_2$OH), 2.59-2.66 (m, 4H), 1.90-2.04 (m, 2H, -C*H*$_2$CH$_2$Ph), 1.43 (s, 3H, -C*H*$_3$-); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 152.6, 142.2, 128.4, 128.4, 125.8, 111.8, 75.6, 64.8, 43.8, 30.5, 28.7; IR (thin film) ν 3359 (br), 3087, 3063, 3027, 2932, 2867, 1643, 1603, 1497, 1454, 1402, 1372, 1103, 1042, 912, 739, 698.

8: ^{1}H-NMR ($CDCl_3$, 400 MHz) ppm δ 7.17-7.31 (m, 5H, H$_{arom}$), 5.14 (d, 1H, *J*= 0.95 Hz, -C=C*H*$_2$), 5.11 (s(br), 1H, -C=C*H*$_2$), 4.31 (d, 1H, *J*= 13.1 Hz, -C*H*$_2$OH), 4.25 (m, 1H, *H*(OH)C-), 4.16 (d, 1H, *J*= 13.1 Hz, -C*H*$_2$OH), 2.76 (m, 1H, -CH$_2$C*H*$_2$Ph), 2.66 (m, 1H, -CH$_2$C*H*$_2$Ph), 2.27-2.60 (m, 2H, O*H*), 1.88-2.03 (m, 2H, -C*H*$_2$CH$_2$Ph); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 149.6, 141.7, 128.4, 125.9, 112.8, 73.9, 64.0, 37.3, 32.0; IR (thin film) ν 3341 (br), 3086, 3063, 3027, 2926, 2863, 1655, 1603, 1497, 1454, 1312, 1030, 914, 748, 700; HRMS (EI) calc'd for $C_{12}H_{16}O_2$, 192.1150, found 193.1227 $(M+H)^+$.

9: ^{1}H-NMR ($CDCl_3$, 400 MHz) ppm δ 7.23-7.37 (m, 5H, H$_{arom}$), 5.24 (s(br), 1H, -*H*(OH)C-), 5.14 (s(br), 2H, -C=C*H*$_2$), 4.04 (d, 1H, *J*= 13.3 Hz, -C*H*$_2$OH), 3.90 (d, 1H, *J*= 13.3 Hz, -C*H*$_2$OH), 3.80 (s, 1H, O*H*), 3.28 (s, 1H, O*H*); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 149.4, 141.8, 128.4, 127.7, 126.4, 113.1, 75.9, 63.6; IR (thin film) ν 3358 (br), 3088, 3063, 3030, 2926, 2874, 1661, 1603, 1493, 1452, 1406, 1323, 1240, 1190, 1020, 912, 841, 735, 700; HRMS (EI) calc'd for $C_{10}H_{12}O_2$, 164.0837, found 164.0794.

11: ^{1}H-NMR ($CDCl_3$, 400 MHz) (inseparable mixture of diastereomers) ppm δ 7.27-7.40 (m, 10H, H$_{arom}$), 5.05-5.20 (m, 4H, -C=C*H*$_2$), 4.54 (s, 2H, -OC*H*$_2$Ph), 4.51 (s, 2H, -OC*H*$_2$Ph), 4.22-4.36 (m, 2H, -*H*(OH)C-), 4.03-4.21 (m, 4H, -C*H*$_2$OH), 3.67 (dd, 1H, *J*= 3.92, 9.20 Hz, -C*H*$_2$OBn), 3.47-3.59 (m, 3H, -C*H*$_2$OBn), 2.08-2.18 (m, 1H, *H*(CH$_3$)C-), 1.98-2.08 (m, 1H, *H*(CH$_3$)C-), 0.97 (d, 3H, *J*= 7.0 Hz, -C*H*$_3$), 0.79 (d, 3H, *J*= 7.0 Hz, -C*H*$_3$); ^{13}C NMR ($CDCl_3$, 100 MHz) (inseparable mixture of

diastereomers) δ 149.1, 147.7, 137.9, 137.4, 128.6, 128.5, 128.0, 127.8, 127.7, 114.8, 112.0, 81.7, 75.7, 75.4, 74.4, 73.7, 73.4, 64.6, 63.9, 37.3, 36.4, 14.0, 11.1; IR (thin film) ν 3341 (br), 3389, 3065, 3031, 2922, 2861, 1655, 1497, 1454, 1364, 1208, 1096, 1073, 1028, 912, 737, 698; HRMS (EI) calc'd for $C_{14}H_{20}O_3$, 236.1412, found 237.1486 $(M+H)^+$.

12: ^{1}H-NMR ($CDCl_3$, 400 MHz) ppm δ 7.2-7.4 (m, 5H, H_{arom}), 5.22 (d, 1H, *J*= 0.89 Hz, -C=C*H*$_2$), 5.07 (d, 1H, *J*= 0.78 Hz, -C=C*H*$_2$), 4.55 (s, 2H, -OC*H*$_2$Ph), 4.12 (d, 2H, *J*= 5.32 Hz, -C*H*$_2$OH), 3.85-3.95 (m, 4H, -O(CH$_2$)$_2$O-), 3.50 (d, 1H, *J*= 9.13 Hz, -C*H*$_2$OBn), 3.39 (d, 1H, *J*= 9.14 Hz, -C*H*$_2$OBn), 3.24 (s, 1H, tertiary OH), 2.77 (t, 1H, *J*= 5.82 Hz, -CH$_2$O*H*), 1.66-1.86 (m, 4H, -C*H*$_2$CH$_2$-), 1.29 (s, 3H, -C*H*$_3$); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 149.9, 137.6, 128.5, 127.9, 127.8, 113.3, 110.0, 77.4, 76.8, 73.6, 64.9, 64.6 (2 lines), 32.4, 31.2, 23.9; IR (thin film) ν 3447 (br), 3063, 3030, 2982, 2936, 2878, 1645, 1497, 1454, 1377, 1217, 1076, 1042, 947, 700; HRMS (EI) calc'd for $C_{18}H_{26}O_5$, 322.1780, found 322.1772.

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