Available online at www.sciencedirect.com
SCIENCE DIRECT
Tetrahedron 60 (2004) 9093–9097
Tetrahedron

Synthesis of potassium 2,3,4-trihydroxy-2-methylbutanoate: a leaf-closing substance of *Leucaena leucocephalam*☆

Sanjib Gogoi and Narshinha P. Argade*

Division of Organic Chemistry (Synthesis), National Chemical Laboratory, Pune 411 008, India

Received 4 May 2004; revised 5 July 2004; accepted 28 July 2004

Available online 27 August 2004

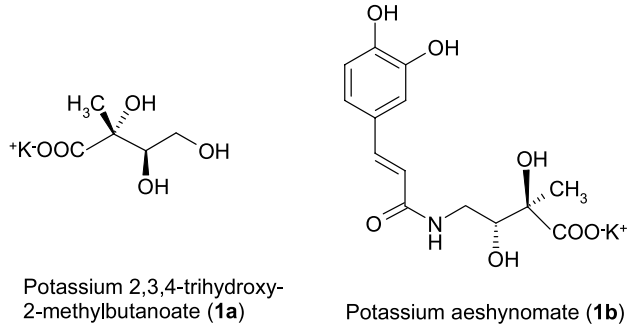
Abstract—Starting from citraconic anhydride (**2**), a six step synthesis of leaf closing substance (±)-*erythro* potassium 2,3,4-trihydroxy-2-methyl-butanoate (**1**) has been described with 29% overall yield via diesterification, OsO_4-dihydroxylation, acetonide protection, regioselective mono hydrolysis of unhindered ester moiety, borane–dimethylsulfide induced chemoselective reduction of carboxylic group and hydrolysis pathway. Surprisingly, the sodium borohydride reduction of monoester **5** and lithium borohydride reduction of **11** furnished the undesired regioisomer **7**.

1. Introduction

Most leguminosae plants close their leaves in the evening and open them in the morning.[1] This circadian rhythmic movement of the leaves is called nyctinasty and has been controlled by their biological clocks.[2] Recently, Ueda et al. have authoritatively identified several bioactive substances that regulate this leaf-movement and revealed that nyctinastic movement of the plants is dependent on the interaction between leaf-opening and leaf-closing substances. Moreover, they have demonstrated that these leaf movements are essential for the survival of legumes and they envisioned that the plant-specific leaf-movement factors could be useful as a herbicides.[3–5] Very recently, Ueda et al. have isolated potassium 2,3,4-trihydroxy-2-methyl-butanoate (**1a**) as a leaf-closing substance of *Leucaena leucocephalam*[3] and potassium aeshynomate (**1b**) as a leaf-opening substance of *Aeshynomene indica* L[5] (Fig. 1). The saccharinic acid lactone [(2*R*, 3*R*)-2,3-dihydroxy-2-methyl-γ-butyrolactone] is a potential precursor of leaf-closing substance **1** and it has also been isolated earlier as a natural product from *Astragalus lusitanicus* L.[6] and *Cicer arietinum* L.[7] To date, three syntheses of *erythro*-saccharinic acid lactone are known starting from 2-methyl-D-erythrose,[8] D-mannitol[9] and methyl pyruvate (via asymmetric aldol reaction).[10] In continuation of our on-going studies[11] on synthesis of bioactive natural products using cyclic anhydrides as potential precursors, starting from citraconic anhydride (**2**), now we herein report the synthesis of (±)-*erythro* potassium 2,3,4-trihydroxy-2-methylbutanoate (**1**) via the corresponding γ-butyrolactone **14** (Scheme 2).

2. Results and discussion

The reaction of citraconic anhydride (**2**) with methanol at 0 °C was fairly regioselective at the unhindered carbonyl[12] and furnished the mixture of regioisomers of esters **3** and **4** in 86:14 ratio (by ^{1}H NMR) in nearly 100% yield (Scheme 1). In the above reaction the major isomer **3** is probably a kinetically controlled product as the ^{1}H NMR spectrum of above mixture after one-month time revealed the presence of **3** and **4** to be 1:1 and the migration of methoxy group might be taking place via the intermediate cyclic anhydride **2**. The OsO_4-induced *cis*-dihydroxylation



Potassium 2,3,4-trihydroxy-2-methylbutanoate (**1a**)

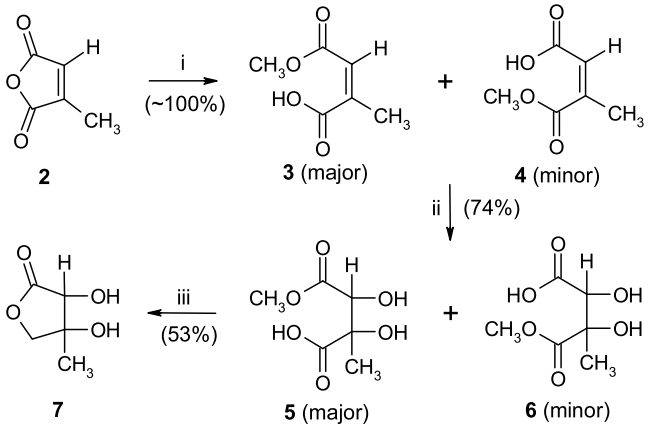
Potassium aeshynomate (**1b**)

Figure 1. Leaf-closing and leaf-opening substances.

☆ NCL Communication No. 6667.

Keywords: Citraconic anhydride; Regioselective hydrolysis; Chemoselective reduction; Leaf-closing substance; Potassium 2,3,4-trihydroxy-2-methylbutanoate; Synthesis.
* Corresponding author. Tel./fax: +91-20-25893153;
e-mail: argade@dalton.ncl.res.in

0040–4020/$ - see front matter © 2004 Elsevier Ltd. All rights reserved.
doi:10.1016/j.tet.2004.07.081



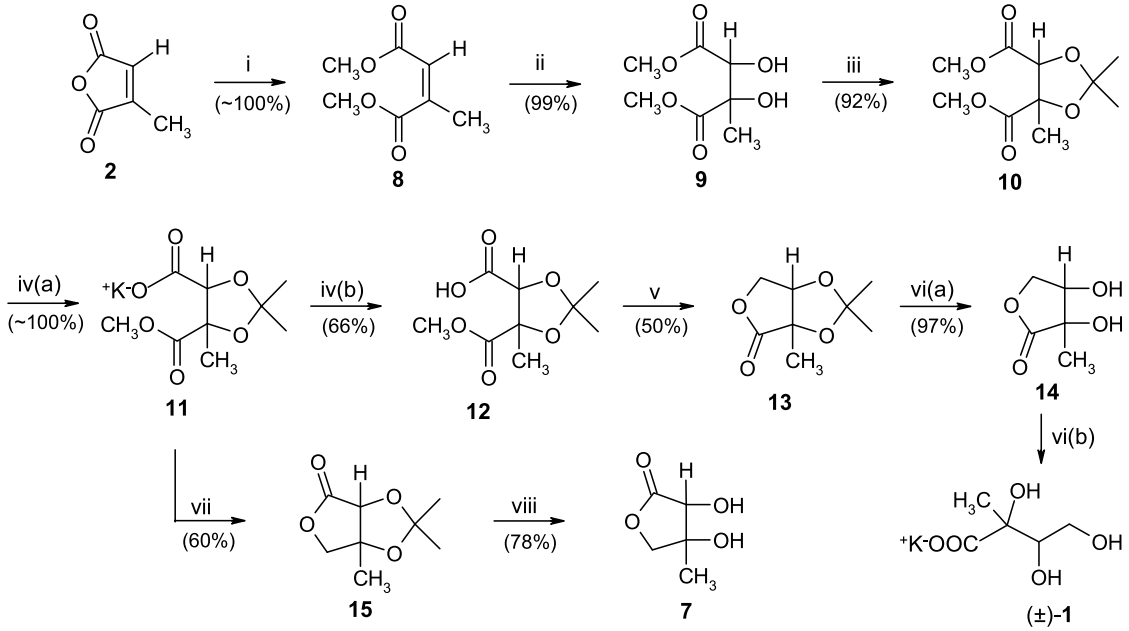
Scheme 1. Reagents, conditions and yields: (i) CH_3OH, 0 °C, 60 h (~100%, **3**:**4**=86:14); (ii) OsO_4, NMO, *t*-BuOH, CH_3COCH_3, rt, 72 h (74%, **5**:**6**=85:15), (two recrystallizations of **5** plus **6** mixture with ethyl acetate furnished pure **5** in 50% yield); (iii) $NaBH_4$, CH_3OH, reflux, 12 h, (53%).

of above **3** plus **4** mixture (86:14) again furnished the mixture of diols **5** and **6** in 85:15 ratio (by ^1H NMR) in 74% yield. Two recrystallizations of mixture of diols **5** plus **6** with ethyl acetate gave the pure diol **5** in 50% yield. Surprisingly, the $NaBH_4$-reduction of mixture of **5** plus **6** or pure **5** in methanol, exclusively furnished the undesired lactone **7** in 53% yield. The structural assignment of lactone **7** was done on the basis of three clean singlets in the ^1H NMR spectrum and ^{13}C NMR spectra. Thus our first straightforward approach to obtain **1** met with failure and then we planned for synthesis **1** using a different synthetic route as depicted in Scheme 2.

The citraconic anhydride (**2**) on treatment with methanol and catalytic amount of conc. H_2SO_4 under reflux, furnished the diester **8** in nearly 100% yield. The OsO_4-induced *cis*-dihydroxylation of **8** gave the diol **9** in 99% yield. The *cis*-diol moiety in compound **9** was protected as an acetonide using 2,2-dimethoxypropane and catalytic amount of *para*-toluenesulfonic acid (*p*-TSA) to obtain compound **10** in 92% yield. The highly regioselective hydrolysis of unhindered ester moiety in compound **10** using 1 equiv. of KOH in methanol at room temperature followed by acidification gave the desired monoacid **12** in 66% yield. The borane–dimethylsulfide complex induced chemoselective reduction of carboxylic group in compound **12** furnished the desired diol-protected lactone **13** in 50% yield.[13–15] The deprotection of the acetonide moiety using catalytic amount of TFA in water gave the desired lactone **14** in 97% yield. The treatment of lactone-diol **14** with aqueous KOH at room temperature gave the desired leaf-closing compound (±)-*erythro* potassium 2,3,4-trihydroxy-2-methylbutanoate (**1**).[16] The analytical and spectral data obtained for lactones **13** and **14** and leaf-closing compound **1** were in complete agreement with reported data.[3,8–10,17] As expected the $LiBH_4$-reduction of compound **11** gave the undesired diol-protected lactone **15** in 60% yield, which on deprotection of acetonide moiety gave the undesired lactone **7** in 78% yield.

3. Conclusion

In summary, starting from citraconic anhydride (**2**), we have demonstrated a new six-step route to leaf-closing compound **1** with 29% overall yield. In the present approach the regioselective hydrolysis of unhindered ester moiety in compound **10** and chemoselective reduction of carboxylic group in compound **12** are the key conversions. The Sharpless asymmetric dihydroxylation reactions of **8** could provide an easy access to both the enantiomers of **1**. During



Scheme 2. Reagents, conditions and yields: (i) CH_3OH, H_2SO_4, reflux, 12 h (~100%); (ii) OsO_4, NMO, *t*-BuOH, CH_3COCH_3, rt, 60 h (99%); (iii) $(CH_3)_2C(OCH_3)_2$, *p*-TSA, benzene, reflux, 3 h (92%); (iv) (a) KOH, CH_3OH, rt, 2 h (~100%); (iv) (b) 2 N HCl, (66%); (v) $BH_3(CH_3)_2S$, THF, −8 °C to rt, 36 h (50%); (vi) (a) CF_3COOH, H_2O, 0 °C to rt, 24 h (97%); (vi) (b) KOH, rt, 10 min; (vii) (a) $LiBH_4$, THF, 0 °C to rt, 6 h; (b) dil. HCl (60%); (viii) CF_3COOH, THF, H_2O, 0 °C to rt, 3 h (78%).

the $NaBH_4$-reduction of **5** the migration of –OMe group from unhindered to hindered site followed by its reduction to generate the undesired regioisomer **7** is noteworthy.

4. Experimental

4.1. General

Melting points are uncorrected Column chromatographic separations were carried out on ACME silica gel (60–120 mesh). Commercially available citraconic anhydride, osmium tetraoxide, *N*-methylmorpholine *N*-oxide, sodium borohydride, 2,2-dimethoxypropane, *p*-toluenesulfonic acid, borane–methyl sulfide complex, trifluroacetic acid were used.

4.1.1. 2-Methyl-but-2-enedioic acid 4-methyl ester and 2-methyl-but-2-enedioic acid 1-methyl ester (3 and 4). A solution of citraconic anhydride (1.00 g, 8.93 mmol) in CH_3OH (6 mL) was stirred at 0 °C for 60 h under an argon atmosphere. The reaction mixture was then concentrated and dried in vacuo to obtain compounds **3** and **4** in the ratio 86:14, respectively. The obtained compounds **3** and **4** were used for the next step without any further purification.

Compounds **3** and **4** (mixture). 1.28 g (~100% yield); colourless thick oil; ^{1}H NMR ($CDCl_3$, 500 MHz), major isomer: δ 2.09 (s, 3H), 3.82 (s, 3H), 5.90 (s, 1H), 9.43 (bs, 1H), minor isomer: δ 2.12 (s, 3H), 3.79 (s, 3H), 6.08 (s, 1H), 9.43 (bs, 1H); ^{13}C NMR ($CDCl_3$, 125 MHz), major isomer: δ 20.8, 52.6, 121.0, 147.4, 169.1, 169.2, minor isomer: δ 21.3, 52.5, 122.6, 145.5, 166.1, 166.8; IR (neat) ν_{max} 1771, 1728, 1651, 1448 cm^{-1}.

4.1.2. 2,3-Dihydroxy-2-methyl-succinic acid 4-methyl ester and 2,3-dihydroxy-2-methyl-succinic acid 1-methyl ester (5 and 6). To a solution of olefins **3** and **4** (1.00 g, 6.94 mmol) in *t*-BuOH (12 mL) and acetone (3 mL) was added OsO_4 (0.5 mL, 0.08 mmol, 4% solution in *t*-BuOH) and NMO (7 mL, 60% aqueous solution) with constant stirring at room temperature. Reaction mixture was further stirred for 72 h and then quenched with addition of solid Na_2SO_3 (1.6 g). The reaction mixture was stirred for 1 h at room temperature and then concentrated and dried in vacuo. The crude product was purified by silica gel column chromatography using a mixture of ethyl acetate and methanol (95:5) to furnish **5** and **6**. Analytically pure **5** was obtained in 50% yield by two recrystallizations from ethyl acetate.

Compounds **5** and **6** (mixture). 915 mg (74% yield); white solid; mp 120–125 °C; ^{1}H NMR (mixture), ($CDCl_3$+ CD_3COCD_3, 500 MHz), major isomer: δ 1.46 (s, 3H), 3.71 (s, 3H), 4.32 (s, 1H), 4.71 (bs, 2H), minor isomer: δ 1.48 (s, 3H), 3.66 (s, 3H), 4.38 (s, 1H), 4.71 (bs, 1H); IR (Nujol), mixture ν_{max} 3352, 1753, 1728, 1454 cm^{-1}.

Compound **5**. 618 mg (50% yield); white crystalline solid; mp 153–154 °C; ^{1}H NMR ($CDCl_3$ +CD_3COCD_3, 500 MHz) δ 1.45 (s, 3H), 3.71 (s, 3H), 4.33 (s, 1H); ^{13}C NMR ($CDCl_3$ +CD_3COCD_3, 125 MHz) δ 21.7, 51.4, 74.3, 75.6, 171.3, 173.7; IR (Nujol) ν_{max} 3389, 3340, 2700–2500, 1738, 1703, 1452 cm^{-1}. Anal. Calcd for $C_6H_{10}O_6$: C, 40.45; H, 5.66. Found: C, 40.51; H, 5.72.

4.1.3. 3,4-Dihydroxy-4-methyl-dihydro-furan-2-one (7). To a solution of ester **5** (100 mg, 0.56 mmol) in CH_3OH (5 mL) was added $NaBH_4$ (85 mg, 2.25 mmol) and the reaction mixture was refluxed for 12 h. The reaction mixture was then concentrated and dried in vacuo. The residue was acidified with minimum amount of dilute HCl and then extracted with ethyl acetate (15 mL×3). The organic layer was washed with brine, dried over Na_2SO_4, concentrated and dried in vacuo to obtain pure **7**.

Compound **7**. 39 mg (53% yield); faint yellow thick oil; ^{1}H NMR (D_2O, 500 MHz) δ 1.34 (s, 3H), 4.22 (s, 2H), 4.38 (s, 1H); ^{13}C NMR (D_2O, 125 MHz) δ 19.6, 73.3, 75.0, 76.0, 178.5; IR (neat) ν_{max} 3415–3360, 1778, 1117, 1007 cm^{-1}. Anal. Calcd for $C_5H_8O_4$: C, 45.46; H, 6.10. Found: C, 45.63; H, 6.22.

4.1.4. Dimethyl methylmaleate (8). A solution of citraconic anhydride (4.48 g, 40 mmol) in methanol (40 mL) and H_2SO_4 (4 mL) mixture was refluxed for 12 h under nitrogen atmosphere. The reaction mixture was concentrated in vacuo. The residue was diluted with water and extracted with ethyl acetate (20 mL×3). The combined organic layer was washed with aqueous solution of $NaHCO_3$, brine, and dried over Na_2SO_4. Concentration of organic layer in vacuo gave pure diester **8**.

Compound **8**. 5.65 g (~100% yield); thick oil; ^{1}H NMR ($CDCl_3$, 200 MHz) δ 2.04 (bs, 3H), 3.70 (s, 3H), 3.81 (s, 3H), 5.84 (bs, 1H); IR (neat) ν_{max} 1736, 1726, 1655 cm^{-1}.

4.1.5. 2,3-Dihydroxy-2-methyl-succinic acid dimethyl ester (9). To a stirred solution of diester **8** (4.00 g, 28.17 mmol) in *t*-BuOH (16 mL) and acetone (4 mL) was added OsO_4 (1.5 mL, 0.24 mmol, 4% solution in *t*-BuOH) and NMO (14 mL, 60% aqueous solution) at room temperature. The reaction mixture was further stirred for 60 h and then quenched with solid Na_2SO_3 (3.0 g). After addition of Na_2SO_3 the reaction mixture was further stirred for 1 h at room temperature, and then concentrated and dried in vacuo. The crude product was purified by silica gel column chromatography using a mixture of ethyl acetate and petroleum ether (1:1) to furnish **9**.

Compound **9**. 5.35 g (99% yield); white crystalline solid; mp 94–96 °C; ^{1}H NMR ($CDCl_3$, 200 MHz) δ 1.54 (s, 3H), 3.24 (bs, 1H), 3.45 (bs, 1H), 3.76 (s, 3H), 3.82 (s, 3H), 4.37 (s, 1H); ^{13}C NMR ($CDCl_3$, 50 MHz) δ 22.4, 52.5, 52.9, 75.5, 76.5, 171.7, 174.6; IR ($CHCl_3$) ν_{max} 3491, 3348, 1735, 1726 cm^{-1}. Anal. Calcd for $C_7H_{12}O_6$: C, 43.75; H, 6.29. Found: C, 43.69; H, 6.21.

4.1.6. 2,2,4-Trimethyl-[1,3]dioxolane-4,5-dicarboxylic acid dimethyl ester (10). To a solution of dihydroxy compound **9** (2.00 g, 10.42 mmol) in benzene (15 mL) was added 2,2-dimethoxypropane (2.17 g, 20.84 mmol) and *p*-toluenesulfonic acid monohydrate (2 mg, 0.01 mmol) and the reaction mixture was refluxed for 3 h using Dean and Stark apparatus containing freshly conditioned 4 Å molecular sieves (5.0 g). The reaction mixture was concentrated

and dried in vacuo. The residue was purified by silica gel column chromatography using a mixture of ethyl acetate and petroleum ether (1:4) to furnish **10**.

Compound **10**. 2.22 g (92% yield); faint yellow thick oil; ^{1}H NMR ($CDCl_3$, 200 MHz) δ 1.41 (s, 3H), 1.55 (s, 3H), 1.66 (s, 3H), 3.70 (s, 3H), 3.78 (s, 3H), 4.40 (s, 1H); ^{13}C NMR ($CDCl_3$, 50 MHz) δ 22.2, 26.1 (2 *gem*-methyl carbons), 51.8, 51.9, 81.5, 82.9, 111.0, 167.2, 171.1; IR ($CHCl_3$) ν_{max} 1761, 1744 cm^{-1}. Anal. Calcd for $C_{10}H_{16}O_6$: C, 51.72; H, 6.95. Found: C, 51.66; H, 6.89.

4.1.7. Potassium 2,2,4-trimethyl-[1,3]dioxolane-4-carbmethoxy-5-carboxylate (11). To a solution of diester **10** (2.00 g, 8.62 mmol) in methanol (15 mL) was added a solution of KOH (484 mg, 8.62 mmol) in methanol (10 mL) in a drop wise fashion with constant stirring at room temperature. The reaction mixture was stirred for 1 h and concentrated in vacuo. The residue obtained was washed with $CHCl_3$ (10 mL$\times$2) to obtain pure **11**.

Compound **11**. 2.20 g ($\sim$100% yield); white solid; mp 234–236 °C; ^{1}H NMR (D_2O, 200 MHz) δ 1.33 (s, 3H), 1.46 (s, 3H), 1.55 (s, 3H), 3.59 (s, 3H), 4.33 (s, 1H); ^{13}C NMR (D_2O, 50 MHz) δ 24.9, 28.2, 28.4, 55.3, 85.7, 86.6, 113.3, 175.7, 176.5; IR (KBr) ν_{max} 1736, 1628 cm^{-1}.

4.1.8. 2,2,4-Trimethyl-[1,3]dioxolane-4,5-dicarboxylic acid 4-methyl ester (12). The salt **11** (2.00 g, 7.81 mmol) was acidified to pH 5 with minimum amount of 2 N HCl and extracted with ethyl acetate. The organic layer was washed with brine, dried over Na_2SO_4 and concentrated in vacuo to obtain **12**.

Compound **12**. 1.12 g (66% yield); colourless thick oil; ^{1}H NMR ($CDCl_3$, 200 MHz) δ 1.37 (s, 3H), 1.48 (s, 3H), 1.62 (s, 3H), 3.66 (s, 3H), 4.36 (s, 1H), 9.15 (bs, 1H); ^{13}C NMR ($CDCl_3$, 50 MHz) δ 22.5, 26.5, 26.6, 52.3, 81.5, 83.5, 111.7, 171.3, 171.7; IR ($CHCl_3$) ν_{max} 1744, 1720 cm^{-1}. Anal. Calcd for $C_9H_{14}O_6$: C, 49.54; H, 6.47. Found: C, 49.39; H, 6.51.

4.1.9. 2,2,3*a*-Trimethyl-dihydro-furo[3,4-*d*][1,3]dioxol-4-one (13). To a solution of acid **12** (100 mg, 0.46 mmol) in THF (5 mL) was added borane–dimethylsulfide complex (38.3 mg, 0.50 mmol) in THF (1 mL) in a drop wise fashion with constant stirring at -8 °C. The reaction mixture was then allowed to warm up to room temperature and further stirred at room temperature for 36 h. The reaction was quenched with water (3 mL), and the reaction mixture was concentrated in vacuo. The obtained residue was stirred with diethyl ether (40 mL). The organic layer was washed with brine and dried over Na_2SO_4, concentrated and dried in vacuo. The crude product was purified by silica gel column chromatography using a mixture of ethyl acetate and petroleum ether (1:4) to furnish **13**.

Compound **13**. 39 mg, (50% yield); colourless thick oil; ^{1}H NMR ($CDCl_3$, 200 MHz) δ 1.42 (s, 3H), 1.47 (s, 3H), 1.57 (s, 3H), 4.32 (dd, J=4, 10 Hz, 1H), 4.44 (dd, J=0, 10 Hz, 1H), 4.49 (dd, J=0, 4 Hz, 1H); ^{13}C NMR ($CDCl_3$, 50 MHz) δ 18.4, 26.6, 26.9, 68.9, 80.3, 81.4, 113.0, 176.7; IR ($CHCl_3$) ν_{max} 1788, 1379, 1105 cm^{-1}. Anal. Calcd for $C_8H_{12}O_4$: C, 55.81; H, 7.02. Found: C, 55.72; H, 6.97.

4.1.10. 3,4-Dihydroxy-3-methyl-dihydro-furan-2-one (14). To a stirred solution of lactone **13** (20 mg, 0.12 mmol) in water (1 mL) was added trifluroacetic acid (0.01 mL) at 0 °C. The reaction mixture was allowed to warm up to room temperature and further stirred at room temperature for 24 h. The reaction mixture was then concentrated and dried in vacuo to obtain pure **14**.

Compound **14**. 15 mg (97% yield); faint yellow thick oil; ^{1}H NMR (CD_3OD, 200 MHz) δ 1.37 (s, 3H), 4.04 (dd, J=2, 4 Hz, 1H), 4.13 (dd, J=2, 10 Hz, 1H), 4.43 (dd, J=4, 10 Hz, 1H); ^{13}C NMR (CD_3OD, 50 MHz) δ 21.6, 73.3, 74.4, 74.6, 180.4; IR ($CHCl_3$) ν_{max} 3421, 1778, 1215, 758 cm^{-1}. Anal. Calcd for $C_5H_8O_4$: C, 45.46; H, 6.10. Found: C, 45.45; H, 6.19.

4.1.11. Potassium 2,3,4-trihydroxy-2-methylbutanoate (1). To a solution of lactone **14** (10 mg, 0.08 mmol) in water (1 mL) was added KOH (4 mg, 0.08 mmol). The reaction mixture was stirred for 10 min and concentrated in vacuo to obtain **1**.[16]

Compound **1**. ^{1}H NMR (D_2O, 200 MHz) δ 1.34 (s, 3H), 3.57 (m, 2H), 3.80 (m, 1H); ^{13}C NMR (D_2O, 50 MHz) δ 25.0, 64.9, 78.5, 79.5, 183.5.

4.1.12. 2,2,6*a*-Trimethyl-dihydro-furo[3,4-*d*][1,3]dioxol-4-one (15). To the suspension of salt **11** (100 mg, 0.39 mmol) in THF (7 mL) was added $LiBH_4$ (34 mg, 1.56 mmol) at 0 °C. The reaction mixture was then stirred at room temperature for 6 h. The reaction was quenched with water and the reaction mixture was concentrated in vacuo. The aqueous layer was acidified with minimum amount of dilute HCl and extracted with ethyl acetate (15 mL$\times$3). The organic layer was washed with brine, dried over Na_2SO_4, concentrated and dried in vacuo to obtain pure **15**.

Compound **15**. 40 mg, (60% yield); white crystalline solid; mp 42–44 °C; ^{1}H NMR ($CDCl_3$, 200 MHz) δ 1.41 (s, 3H), 1.49 (s, 3H), 1.54 (s, 3H), 4.15 (d, J=12 Hz, 1H), 4.45 (d, J=12 Hz, 1H), 4.46 (s, 1H); ^{13}C NMR ($CDCl_3$, 50 MHz) δ 21.9, 27.7, 28.5, 75.7, 79.6, 83.5, 114.1, 174.5; IR ($CHCl_3$) ν_{max} 1788, 1383, 1217 cm^{-1}. Anal. Calcd for $C_8H_{12}O_4$: C, 55.81; H, 7.02. Found: C, 56.01; H, 7.07.

4.1.13. 3,4-Dihydroxy-4-methyl-dihydro-furan-2-one (7). To a stirred solution of lactone **15** (20 mg, 0.12 mmol) in THF (2 mL) and water (0.5 mL) was added trifluroacetic acid (0.01 mL) at 0 °C. The reaction mixture was allowed to warm to room temperature and further stirred at room temperature for 3 h. The reaction mixture was then concentrated and dried in vacuo to obtain pure **7** in 78% yield. Analytical and spectral data matched with that of compound **7**, obtained from **5**.

Acknowledgements

S. G. thanks CSIR, New Delhi, for the award of a research

fellowship and N. P. A. thanks Department of Science and Technology, New Delhi, for financial support.

References and notes

1. Darwin, C. *The Power of Movement in Plants Third Thousand*; John Murray: London, 1882.
2. Bunning, E. *The Physiological Clock*. 3rd ed.; English University Press: London, 1973.
3. Ueda, M.; Sohtome, Y.; Ueda, K.; Yamamura, S. *Tetrahedron Lett.* **2001**, *42*, 3109.
4. Ueda, M.; Yamamura, S. *Angew. Chem., Int. Ed.* **2000**, *39*, 1400.
5. Ueda, M.; Hiraoka, T.; Niwa, M.; Yamamura, S. *Tetrahedron Lett.* **1999**, *40*, 6777 and references cited therein.
6. Teresa, J.d. P.; Aubanell, J. C. H.; Feliciano, A. S.; Corral, J. M. M.d. *Tetrahedron Lett.* **1980**, *21*, 1359.
7. Ford, C. W. *Phytochemistry* **1981**, *20*, 2019.
8. Yoshimura, J.; Hara, K.; Yamaura, M. *Carbohydr. Res.* **1982**, *101*, 343.
9. Kis, K.; Wungsintaweekul, J.; Eisenreich, W.; Zenk, M. H.; Bacher, A. *J. Org. Chem.* **2000**, *65*, 587.
10. (a) Kobayashi, S.; Horibe, M.; Saito, Y. *Tetrahedron* **1994**, *50*, 9629. (b) Mukaiyama, T.; Shiina, I.; Izumi, J.; Kobayashi, S. *Heterocycles* **1993**, *35*, 719.
11. (a) Mhaske, S. B.; Argade, N. P. *Tetrahedron* **2004**, *60*, 3417. (b) Kar, A.; Argade, N. P. *Tetrahedron* **2003**, *59*, 2991. (c) Kar, A.; Argade, N. P. *Tetrahedron Lett.* **2002**, *43*, 6563. (d) Kar, A.; Argade, N. P. *J. Org. Chem.* **2002**, *67*, 7131. (e) Mhaske, S. B.; Argade, N. P. *J. Org. Chem.* **2001**, *66*, 9038 and references cited therein.
12. Mangaleswaran, S.; Argade, N. P. *J. Chem. Soc., Perkin Trans. 1* **2000**, 3290 and references cited therein.
13. Musich, J. A.; Rapoport, H. *J. Am. Chem. Soc.* **1978**, *100*, 4865.
14. Ortuno, R. M.; Alonso, D.; Font, J. *Tetrahedron Lett.* **1986**, *27*, 1079.
15. Ortuno, R. M.; Alonso, D.; Cardellach, J.; Font, J. *Tetrahedron* **1987**, *43*, 2191.
16. The leaf-closing compound **1** is unstable around neutral or basic pH, and gradually decomposes to give lactate.[3]
17. In lactones **13** and **14**, the explanation for the low coupling constants between the methine proton and methylene protons has been given by Bacher et al.[9]