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Stereoselective synthetic approach towards phytotoxic agent Agropyrenol

C S Rohith, T Anil, B Karunakar & A Venkat Narsaiah*

Organic Synthesis Laboratory, Fluoro-Agrochemicals Department, CSIR-Indian Institute of Chemical Technology, Hyderabad 500 007, India

E-mail: vnakkirala@iict.res.in; vnakkirala2001@yahoo.com

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A phytotoxic agent Agropyrenol is produced by *Ascochyta agropyrina* var. nana, in liquid culture. The synthetic approach has been commenced by using (−)-diethyl-D-tartrate and 2,3-di methyl phenol as building blocks. The key reactions involved are aromatic sulfone coupling under Julia-Kocienski olefination, selective acetonide protection, bromination, detosylation and selective oxidation.

Keywords: Agropyrenol, phytotoxic, bromination, detosylation, olefination

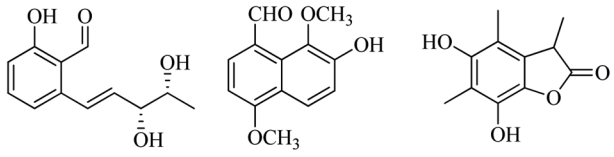
Agropyrenol (**1**), a naturally occurring phytotoxic agent, isolated from a fungal pathogen *Ascochyta agroyrina* var. nana, a perennial weed Elytriga repens (quack grass) along with other two secondary metabolites, Agropyerenal (**1a**) and Agropyrenone (**1b**) by Evidente group (Figure 1). The spectroscopic structural analysis of NMR, 2D-NMR indicates that Agropyrenol is a substituted salicylaldehyde with *trans* olefin and hydroxy functional groups[1,2]. The structural activity relationship studies shows that the diol system of 3,4-dihydropentyl side chain and primary aldehyde functional group at C-1 of phenolic ring, is responsible for phytotoxicity[3]. Further studies strengthen, the phytotoxic activity of Agropyrenol causing nerotic lesions, while performed assayed on several weedy plants [*M. annua* L, *C. album* L and *S. viridis* L][4] and recently Sudhakar group reported the synthesis[5].

Results and Discussion

As part of our regular research program, in synthesis of biologically active natural and synthetic molecules[6-10] herein we report, the stereoselective synthetic approach, towards Agropyrenol. As shown in the retrosynthetic analysis (Scheme I), target molecule **1** could be obtained from intermediate **17** and which could be obtained from **16** by deprotection of acetonide groups. The compound **16** could be obtained from sulfone **10** and aldehyde **15** by Julia-Kocienski olefination. The key building block sulfone **10** could be obtained from 2,3-dimethyl phenol **5** and the aldehyde fragment **15** could be obtained from (−)-diethyl-D-tartrate **11**.

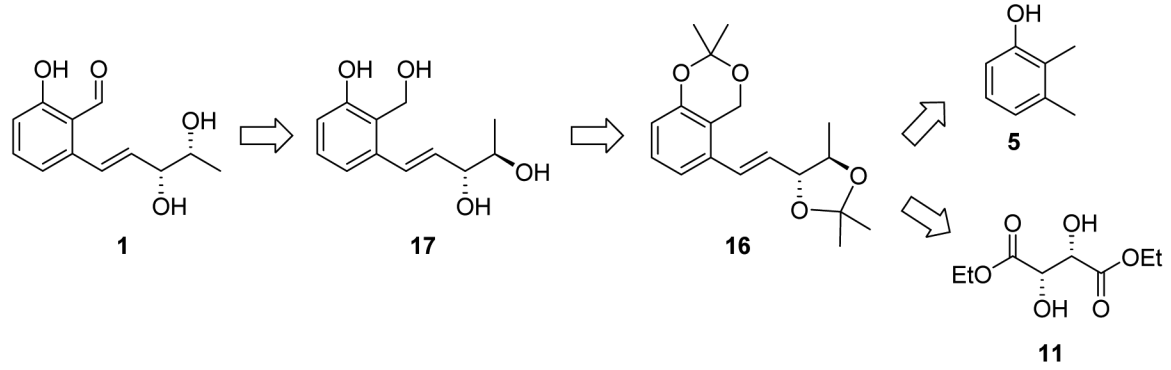
Synthesis started from commercially available, 2,3-dimethyl phenol **5**, which was subjected to acetylation of phenolic hydroxyl, dibromination of benzylic methyls followed by diacetylation and global reduction of triacetyls with $LiAlH_4$ in THF to give the corresponding triol compound **6** in 80% yield[11]. The selective protection of compound **6** as acetonide was carried out with *p*-TsOH in acetone to give, 5-hydroxymethyl-2,2-dimethyl-4-*H*-1,3-benzodioxin **7** in very good yields[12,13]. The primary alcohol compound **7** was reacted with CBr_4 and TPP in CH_2Cl_2 to afford, 5-(bromomethyl)-2,2-dimethyl-4*H*-benzo[1,3]dioxine **8** in excellent yields[14,15].

Thus obtained bromo compound **8** was treated with 1-phenyl-1*H*-tetrazole and triphenyl phosphine in THF to furnish, 5-{[(2,2-dimethyl-4*H*-benzo[1,3]dioxin-5-yl]thio}-2-phenyl-2*H*-tetrazole **9**, in quantitative yields. The tetrazole compound **9** was oxidized with ammonium molybdate and H_2O_2 (30%) in ethanol to give, 5-{[(2,2-dimethyl-4*H*-benzo[1,3]dioxin-5-yl) methyl]sulfonyl}-2-phenyl-

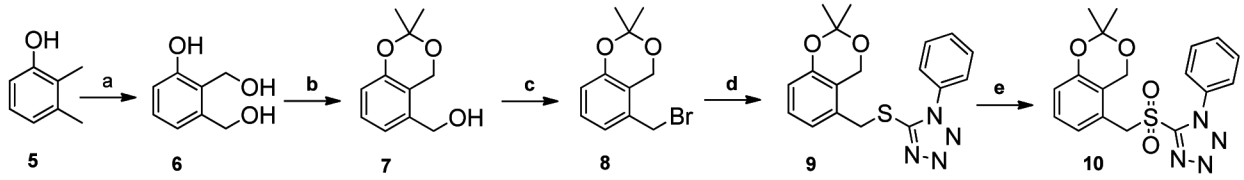


Agropyrenol (1) **Agropyerenal (1a)** **Agropyrenone (1b)**

Figure 1

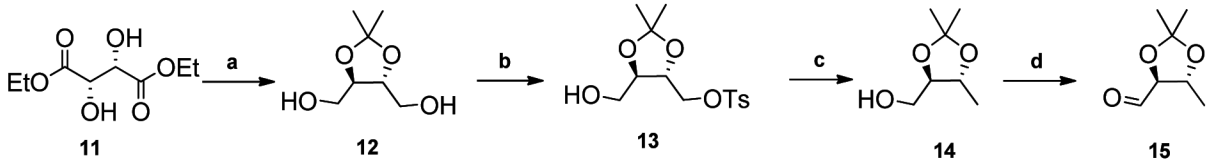


Scheme I — Retrosynthetic analysis



Reagents and Conditions: (a) Ref. 5, (b) *p*-TsOH, acetone, RT, 12 h, 75%, (c) CBr_4, TPP, CH_2Cl_2,, 0°C, 2 h, 92%, (d) 1-Phenyl-1*H*-tetrazole-5-thiol, TPP, THF, reflux, 6 h, 85%, (e) Ammonium molybdate, 30% H_2O_2, ethanol, 12 h, 86%.

Scheme II



Reagents and Conditions: (a) Ref. 9, (b) TsCl, *n*-BuLi, THF, −15°C, RT, 90%, (c) $NaBH_4$, DMSO, reflux, 2 h, 90%, (d) DMP, $NaHCO_3$, CH_2Cl_2, 0°C - RT, 2 h, 80%.

Scheme III

2*H*-tetrazole **10**, in 86% yield as shown in Scheme II (Ref. 16).

The second fragment aldehyde **15** was synthesized from commercially available, (−)-diethyl-D-tartrate **11**, which was subjected to acetonide protection and complete reduction of ester by following from known reported procedures to give, [(4*S*,5*S*)-2-dimethyl-1,3-dioxolane-4,5-dyl]di menthanol **12**, in good yields. The selective monotosylation of compound **12**, was smoothly carried out with *n*-BuLi and *p*-toluene sulfonyl chloride in DMSO-THF (1:4) mixture to achieve, [(4*S*,5*S*)-5-(hydroxymethyl)-2,2-dimethyl-1,3-dioxolan-4-yl]methyl-4-methylbenzene sulfonate **13**, in 90% yield[17].

The resulted compound **13** was detosylated with $NaBH_4$ in DMSO at reflux to afford, [(4*S*,5*S*)-2,2,5-trimethyl-1,3-dioxolan-4-yl]methanol **14**, in 90% yield[18]. Oxidation of compound **14**, with Dess-Martin periodinane in presence of $NaHCO_3$ in CH_2Cl_2 furnished, respective aldehyde **15**, in very good yields as shown in the Scheme III (Ref. 19).

The intermediates, [(2,2-dimethyl-4*H*-benzo[*d*][1,3]dioxin-5-yl)methyl]triphenylphosphonium chloride **10a** and (4*S*,5*R*)-2,2,5-trimethyl-1,3-dioxalane-4-carbaldehyde **15** were coupled using Wittig protocol[20], in presence of *n*-BuLi in ether at low temperature to achieve *trans* olefin product, but the obtained olefin in 2:8 ratio of *trans* and *cis*-

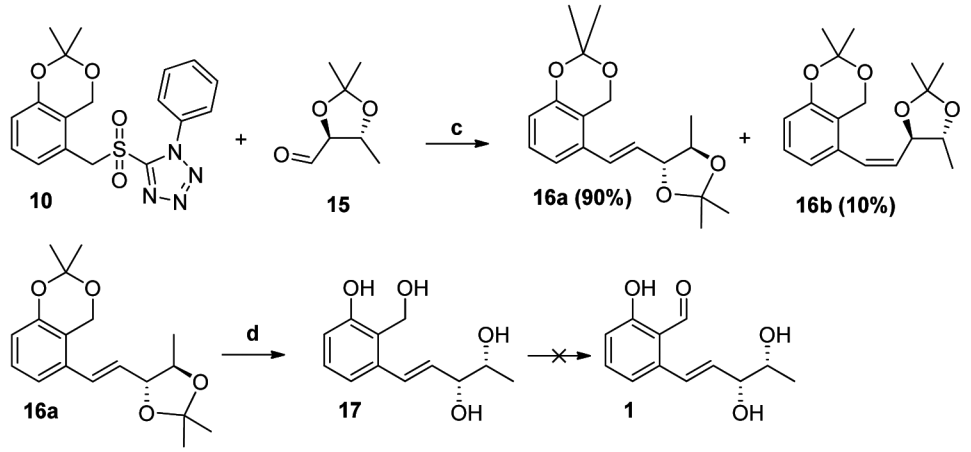
isomers, whereas, the natural product is a *trans* isomer. Then, adopted Horner-Wadsworth-Emmons protocol to couple the intermediates, diethyl-[(2,2-dimethyl-4*H*-benzo[d][1,3]dioxin-5-yl)methyl] phosphonate **10b** and aldehyde **15** under different conditions to yield olefin product[21]. Unfortunately, not only product, even starting material also could not be recovered.

Finally, we reacted, 5-{[(2,2-dimethyl-4*H*-benzo[*d*][1,3]dioxin-5-yl)methyl]sulfonyl}-1-phenyl-1*H*-tetrazole **10** with aldehyde **15** using Julia-Kocienski protocol in presence of KHM DS and 18-Crown-6 in DME at −78°C to afford, 2,2-dimethyl-5{[(4*S*,5*S*)-2,2,5-trimethyl-1,3-dioxolan-4 -yl]vinyl}-4*H*-benzo-[1,3] dioxine **16** in very good yields, with excellent *trans* selectivity[22]. The product *trans* olefin **16** was confirmed by ^{1}H NMR spectral analysis. The selectivity variation was observed with solvents. Among, diethylether, dimethoxyethane and THF, the dimethoxyethane was found as more appropriate solvent. The compound **16** was subjected to deprotection with *p*-TsOH in methanol at 0°C to give, (2*R*,3*R*,*E*)-5-(3-hydroxy methyl) phenyl) pent-4-ene-2,3-diol **17** in 86% yield as shown in the Scheme IV (Ref. 23-25).

Finally, the compound **17** was subjected to oxidation with various catalysts and conditions as shown in Table I. Unfortunately, we could not oxidized the benzylic alcohol to afford the target molecule Agropyrenol.

Experimental Section

All the air and moisture sensitive reactions were carried out under nitrogen atmosphere. Oven-dried glass apparatus were used to perform all the reaction. Freshly distilled anhydrous solvents were used for air and moisture sensitive reactions. Commercially available reagents were used as such. Purification of compounds was carried out *via* column chromatography by using silica gel (60-120 mesh) packed in glass columns. ^{1}H and ^{13}C NMR were recorded in $CDCl_3$ on 400 MHz and 500 MHz spectrometer, using TMS as an internal standard. IR spectra were recorded on a Perkin-Elmer FT-RT 240-c Spectrophotometer using KBr / Thin Film optics. Mass spectra were recorded on a Finnigan MAT 1020 mass spectrometer operating at 70eV. Optical rotation values were recorded on Horibasepa 300 Polari meter. High resolution mass spectra (HRMS) [ESI+] were obtained using either a TOF or a double focusing spectrometer.



Reagents and Conditions: (a) *n*-BuLi (1.1 eq), ether, 0°C, (b) (i) *n*-BuLi, THF, 0°C, (ii) *n*-BuLi, THF, −78°C, (iii) KHMDS, THF, 0°C, (iv) KHMDS, THF, −78°C, (v) NaHMDS, THF, −78°C, (c) KHMDS, DME, 18-Crown-6, −78°C, 80%, (d) *p*-TsOH, methanol, 0°C - RT, 80%.

Scheme IV

Table I — Various conditions tried for selective oxidation of benzylic alcohol

S.No.	Oxidizing reagent	Catalyst	Solvent	Result
1	Iodobenzene diacetate (0.5 eq)	TEMPO (0.1 eq)	CH_2Cl_2 (5 mL)	No product
2	Iodobenzene diacetate (0.5 eq)	TEMPO (0.1 eq)	CH_2Cl_2 (12 mL)	No product
3	Active MnO_2 (5 eq)	–	CH_2Cl_2 (5 mL)	No product
4	Active MnO_2 (5 eq)	–	*n*-Hexane(5 mL)	No product

3-Bis(hydroxymethyl)phenol, 6

Compound **6** was prepared from compound **5** *via* the procedure reported in the literature (Ref.5).

To a suspension of $LiAlH_4$ (2.5 g, 65 mmol) in dry THF (20 mL) was added drop wise the solution of triacetyls compound (7.0 g, 25 mmol) in dry THF (15 mL) with stirring at 0°C. After completing the addition, the reaction mixture was refluxed for 6 h and then cooled. The mixture was diluted with EtOAc (15mL) and quenching with water, acidified with dil.H_2SO_4, saturated with NaCl, solvent was removed under reduced pressure and the residue was extracted with EtOAc (2×20 mL), the combine organic layers were washed with $NaHCO_3$, brine, and then dried over anhydrous Na_2SO_4. Evaporation of the solvent under reduced pressure to afforded a crystalline residue, which was recrystalized from EtOAc-hexane to give compound **6**, 3.0 g (80%), as a white solid.

m.p.110 - 112°C. IR (neat): 3377, 3333, 2923, 1560, 1465, 1361, 1209, 1132, 1051, 993, 772 cm^{-1}; ^1H NMR (400 MHz, Acetone-d_6): δ 8.70 (brs, 1H), 7.10 (t, 1H, *J* = 7.8 Hz), 6.86 (d, 1H, *J* = 7.3 Hz), 6.78 (d, 1H, *J* = 7.5 Hz), 4.90 - 4.85 (m, 2H), 4.65 - 4.62 (m, 2H), 4.59 (t, 1H, *J* = 5.1 Hz), 4.30 (t, 1H, *J* = 5.6 Hz); ^{13}C NMR (100 MHz, Acetone-d_6): δ 158.0, 143.2, 129.8, 126.7, 121.6, 117.0, 64.5, 58.8; ESI-MS: *m/z* 153 $[M-H]^+$.

5-Hydroxymethyl-2,2-dimethyl-4*H*-1,3-benzodioxin, 7

To a stirred mixture of triol **6** (3.0 g, 19.4 mmol) in dry acetone (20 mL) was added catalytic amount of *p*-TsOH at RT and stirred for 12h. The reaction mixture was quenched by adding $NaHCO_3$ solution and solvent was removed under reduced pressure and the residue extract with ether (2×20 mL). The organic layers were washed with brine, dried over Na_2SO_4 and evaporated the solvent under reduced pressure, the crude product was purified by column chromatography using silica gel (60-120 mesh) by eluting with EtOAc-Hexane (4:6) mixture to afforded, alcohol **7**, 2.8 g (75%), as a colorless liquid.

IR (neat): υ 3379, 2989, 1590, 1470, 750 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 7.15 (t, 1H, *J* = 7.8 Hz), 6.90 (d, 1H, *J* = 7.4 Hz), 6.78 (d, 1H, *J* = 7.5 Hz), 4.92 (s, 2H), 4.56 (s, 2H), 1.54 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 151.4, 136.4, 127.9, 119.7, 117.9, 116.9, 99.0, 62.7, 59.1, 24.6; ESI-MS: *m/z* 195 $[M]^+$.

5-(Bromomethyl)-2,2-dimethyl-4*H*-benzo[1,3] dioxine, 8

To a stirred solution of primary alcohol **7** (2.5g, 12.8 mmol) in CH_2Cl_2 (20 mL) was added CBr_4 (6.4g, 19.3 mmol) and triphenyl phosphine (5.1g, 19.3 mmol) at 0°C and stirred for 2h. After completion of reaction (confirmed by monitoring TLC), quench with cold water. The reaction mixture was extracted with CH_2Cl_2 (2×20 mL). The combined organic layers were washed with brine and dried over Na_2SO_4 and concentrated under reduced pressure. The residue was purified by column chromatography using silica gel (60-120 mesh) by eluting with EtOAc-hexane (1:9) mixture to afford, bromo compound **8**, in 3.1g (92%), as a colorless oil.

IR (neat) : υ 2924, 1733, 1587, 1272, 1028, 680 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 7.15 (t, 1H, *J* = 7.5 Hz), 6.92 (d, 1H, *J* = 8.3 Hz), 6.80 (d, 1H, *J* = 8.3 Hz), 4.96 (s, 2H), 4.36 (s, 2H), 1.55 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 151.7, 133.4, 128.2, 121.9, 118.5, 117.8, 99.2, 58.8, 29.8, 24.6; ESI-MS: *m/z* 275 $[M+H_2O]^+$.

5-{[(2,2-Dimethyl-4*H*-benzo[1,3]dioxin-5-yl]thio}-2-phenyl-2*H*-tetrazole, 9

To a stirred solution of 1-phenyl-1*H*-tetrazole-5-thiol (2.6g, 14.5 mmol) in dry THF (20 mL) was added triethylamine (2 mL, 14.5 m mol) and the reaction mixture was stirred at RT for 40 min. The bromo compound **8** (2.5g, 9.7 mmol) was added to reaction mixture and the reaction was refluxed for 6h and then the resulting mixture was quenching by adding cold water. The solvent was removed under reduced pressure and extracted with EtOAc (2×20 mL), the organic layer was washed with brine and dried over Na_2SO_4 and concentrated under reduced pressure. The crude compound was purified by column chromatography using silica gel (60-120 mesh) by eluting with EtOAc-hexane (2:8) mixture to afford, tetrazole **9**, in 2.9 g (85%), as colorless liquid.

IR (neat): 2926, 1737, 1215, 1003, 746, 665cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 7.54 - 7.48 (m, 5H), 7.15 - 7.10 (t, 1H, *J* = 7.1 Hz), 7.01 - 6.90 (m, 1H), 6.75 - 7.80 (m, 1H), 4.96 (s, 2H), 4.50 (s, 2H), 1.53 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 153.5, 151.7, 133.5, 130.4, 130.2, 129.8, 128.3, 123.7, 122.3, 118.5, 117.6, 117.1, 99.2, 59.1, 34.2, 24.6; ESI-MS: *m/z* 355 $[M-H]^+$.

5-{[(2,2-Dimethyl-4*H*-benzo[d][1,3]dioxin-5-yl)methyl] sulfonyl}-2-phenyl-2*H*-tetrazole, 10

To a stirred solution of tetrazole compound **9** (1.5g, 4.2 mmol) in ethanol (15 mL) was added ammonium molybdate [$(NH_4)_6 MO_7O_{24}. H_2O$] (0.52g, 0.42 mmol) and H_2O_2 (4.8 mL, 42.3 mmol, 30%) at RT and stirred for 12h. The completion of reaction confirmed by TLC and quenched with H_2O and concentrated under reduced pressure. The residue was extracted with EtOAc (2×20 mL) and the combined organic layer was washed with brine, dried over Na_2SO_4, and concentrated under reduced pressure. Purification of the crude product by column chromatography using silica gel (60-120 mesh) by eluting with EtOAc-hexane; (1:9) mixture to obtain compound **10**, in 1.4g (86%), as a white solid.

m.p.130 - 133°C; IR (neat): υ 2923, 1732, 1246, 1005, 750 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 7.60 - 7.45 (m, 3H), 7.38 - 7.30 (m, 2H), 7.15 (t, 1H, *J* = 7.8 Hz), 6.90 (d, 1H, *J* = 8.1 Hz), 6.75 (d, 1H, *J* = 8.0 Hz), 4.92 (s, 2H), 4.82 (s, 2H), 1.48 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 152.3, 132.7, 131.4, 129.4, 128.4, 125.2, 124.4, 120.8, 120.5, 119.2, 99.5, 59.4, 58.9, 24.5; ESI-MS: *m/z* 404 $[M+H_2O]^+$.

[(4*S*,5*S*)-2-Dimethyl-1,3-dioxolane-4,5-dyl] dimenthanol, 12

To a stirring mixture of dry THF (20 mL) was added $LiAlH_4$ (0.61g, 16.3 mmol) in fractions at 0°C under nitrogen atmosphere, after some time was added the solution of dimethyl-2,3,-*O*-isopropylidene-D-tartrate (4g, 16.3 mmol), which was dissolved in dry THF (10 mL) and the reaction mixture was refluxed for 5 h. The completion of reaction confirmed (TLC), then cooled to 0°C and diluted with EtOAc (20 mL). The mixture was quenched with water, NaOH (20%, 4 mL) and allowed to stir for 4h at RT and solvent was removed under reduced pressure and the residue was extracted with EtOAc (3×15 mL). The combined organic layers were washed with brine, dried over Na_2SO_4 and concentrated under reduced pressure. The crude product was purified by column chromatography using silica gel (60-120mesh) by eluting with EtOAc-hexane (2:1) mixture to afford, diol compound **12**, in 2.6g (97%), as colorless oil. Optical rotation: $[\alpha]_D^{27}$ +5.5° (c = 1, $CHCl_3$).

IR (neat): υ 2986, 1737, 1443, 1237, 1044, 848 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): 4.03 - 3.98 (m, 2H), 3.83 - 3.77 (m, 2H), 3.74 - 3.69 (m, 2H), 2.46 (brs, 2H), 1.44 (s ,6H);^{13}C NMR (100 MHz, $CDCl_3$): 109.2, 77.9, 61.9, 26.9; ESI-MS: *m/z* 163 $[M+H]^+$.

[(4*S*,5*S*)-5-(Hydroxymethyl)-2,2-dimethyl-1,3-dioxolan-4-yl]methyl-4-methyl benzene sulfonate, 13

To a stirred solution of diol **12** (2.5 g, 15.2 mmol) in dry THF (20 mL) and DMSO (5 mL) was added *n*-BuLi (1.58 M, hexane, 6.42 mL) at −15°C and the resulting reaction mixture was stirred at RT for 15 min and then cooled to 0°C and added a solution *p*-toluene sulfonyl chloride (2.9g, 15.2 mmol), which was dissolved in THF (5 mL) and the reaction mixture was stirred at RT for 1h. The completion of reaction confirmed by TLC and quenched with water. The solvent was removed under reduced pressure and extracted with EtOAc (2×20 mL), the organic layer was washed with brine, dried over Na_2SO_4 and concentrated under reduced pressure, the crude product was purified by column chromatography using silica gel (60-120) mesh by eluting with EtOAc-hexane (1:2) mixture to afford, compound **13**, in 4.1 g (90%) as colorless oil.

Optical rotation: $[\alpha]_D^{27}$+10.3° (c = 1, $CHCl_3$); IR (neat): υ 3378, 2923, 1710, 1231, 1006, 682 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 7.79 (d, 2H, *J* = 8.2 Hz), 7.36 (d, 2H, *J* = 8.1 Hz), 4.19 - 4.07 (m, 3H), 3.99 - 3.94 (m, 1H), 3.81 - 3.75 (m, 1H), 3.61 - 3.65 (m, 1H), 2.45 (s, 3H), 2.30 (brs, 1H, OH), 1.40 (s, 3H), 1.35 (s, 3H); ^{13}C NMR (100MHz, $CDCl_3$): δ 145.1, 132.5, 129.9, 127.9, 109.9, 77.9, 74.3, 68.7, 61.6, 26.9, 26.7, 21.6; ESI-MS: *m/z* 317 $[M+H]^+$.

[(4S,5S)-2,2,5-Trimethyl-1,3-dioxolan-4-yl]methanol, 14

To a stirred suspension of sodium borohydride (1.9g, 50.3 mmol) in dry DMSO (25 mL) was added a solution of monotosyled compound **13** (3g, 10 mmol), which was dissolved in dry DMSO (10 mL) at RT under nitrogen atmosphere, and the resulting reaction mixture was stirred at 50°C for 2h. The mixture was quenched by adding ice-cold water and extracted with ether (2×40 mL). The organic layer was washed with brine, dried over Na_2SO_4 and concentrated under reduced pressure. The crude product was purified by column chromatography using (60-120) mesh by eluting with EtOAc-hexane (3:2) mixture to afford, alcohol compound **14**, in 1.32 g (87%), as colorless oil.

Optical rotation: $[\alpha]_D^{27}$ +2° (c = 2, $CHCl_3$); IR (neat): υ 3325, 2943, 2831, 1449, 1027, 629 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 4.06 - 3.99 (m, 1H),

3.84 - 3.79 (m, 1H), 3.68 - 3.58 (m, 2H), 1.43 (s, 3H), 1.41 (s, 3H), 1.30 (d, 3H, *J* = 5.9 Hz); ^{13}C NMR (100 MHz, $CDCl_3$): δ 108.4, 82.7, 72.7, 61.3, 27.4, 26.9, 17.6; ESI-MS: *m/z* 147 $[M+H]^+$.

Trimethyl-1,3-dioxolane-4-carbaldehyde, 15

To a stirred solution of alcohol **14** (0.4 g, 2.1 mmol) in dry CH_2Cl_2 (10 mL) was added Dess-Martin periodianae (1.3g, 3.1 mmol) and $NaHCO_3$ (0.2g, 2.2 mmol) slowly at 0°C and stirred for 45 min. The completion of reaction was confirmed by TLC. The reaction mixture was diluted with water (20 mL) and extracted with CH_2Cl_2 (2×40 mL). The combined organic layers were washed with brine, dried over Na_2SO_4 and concentrated to give crude aldehyde **15** as yellowish oil which was used in the next step without further purification, 0.3 g (80%).

2,2-Dimethyl-5-{[(4*S*,5*S*)-2,2,5-trimethyl-1,3-dioxolan-4-yl]vinyl}-4*H*-benzo-[1,3]dioxine, 16

To a stirred solution of sulfone compound **10** (0.09g, 0.23 mmol) in dry DME (10 mL) under argon atmosphere was added KHMDS (0.32 mL, 1M, 0.32 mmol) and catalytic amount 18-crown-6 ether, at −78°C and stirred for 10 minutes then added aldehyde **15** (0.03g, 0.208 mmol), which was dissolved in dry DME (3 mL) and stirred for 30 min at same temperature. The reaction mixture was allowed to RT and stirring was continued for 1 h, then the reaction was quenched with saturated NH_4Cl (5 mL) and extracted with EtOAc (2×10 mL). The combined organic layers were washed with H_2O, brine, dried over Na_2SO_4 and concentrated under reduced pressure. The crude product was purified by flash column chromatography using silica gel (60-120 mesh) by eluting with EtOAc-hexane (1:9) mixture to give, compound **16** as colorless liquid, 0.5g (80%).

Optical rotation: $[\alpha]_D^{27}$ +12.3° (c = 0.1, $CHCl_3$); IR (neat): υ 2986, 1734, 1675, 1373, 728, 644 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.18 - 7.03 (m, 2H), 6.83 - 6.72 (m, 1H), 6.62 - 6.52 (m, 1H), 6.05 (dd, 1H, *J* = 15.6, 7.3 Hz), 4.88 (s, 2H), 4.22 - 4.04 (m, 1H), 3.93 - 3.80 (m, 1H), 1.54 (s, 6H), 1.46 (s, 3H), 1.45 (s, 3H), 1.31 (d, 3H, *J* = 6.0 Hz); ^{13}C NMR (100 MHz, $CDCl_3$): δ 151.3, 129.9, 128.9, 128.7, 127.9, 121.0, 118.2, 116.9, 116.7, 108.6, 98.9, 83.8, 59.8, 27.4, 26.9, 24.7, 24.5, 16.5; ESI-MS: *m/z* 305 $[M+H]^+$.

(2*R*,3*R*,*E*)-5-(3-Hydroxymethyl)phenyl)pent-4-ene-2,3-diol, 17

To a stirred solution of diacetonide **16** (0.3g, 0.9 mmol) in dry methanol (10 mL) was added a catalytic amount of *p*-TsOH at 0°C and stirred at RT for 1h. After completion of reaction (monitored by TLC), quenched with adding aq.$NaHCO_3$ in small amounts, and concentrated under reduced pressure. The residue was extracted with EtOAc (2×15 mL) and the combined organic layer was washed with brine, dried over Na_2SO_4 and concentrated under reduced pressure. The residue was purified by column chromatography using silica gel (60-120 mesh) by eluting with ethyl acetate-hexane (8:2) mixture to give a corresponding compound **17**, 0.017 g (80%), as a colorless liquid.

Optical rotation: $[\alpha]_D^{27}$ +5.3° (c = 0.1, $CHCl_3$); IR (neat): υ 3377, 2926, 1467, 1119 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.18 - 7.14 (m, 1H), 6.93 (d, 1H, *J* = 7.6 Hz), 6.86 - 6.81 (m, 2H), 6.01 (dd, 2H, *J* = 15.5, 6.5 MHz), 4.80 (s, 2H), 4.05 - 4.01 (m, 1H), 3.74 (t, 1H, *J* = 6.5 Hz), 1.25 (d, 3H, *J* = 6.0 Hz); ^{13}C NMR (100 MHz, $CDCl_3$): δ 162.3, 131.9, 129.5, 129.1, 119.3, 118.6, 116.3, 70.9, 58.5, 19.1; MS (ESI) *m/z*: 223 $[M-H]^-$.

Conclusion

In conclusion, the stereoselective synthetic approach for phytotoxic agent Agropyrenol has been achieved by employing halogenation, Julia-Kocienski olefination, deprotection of acetonides as key steps. All the reactions are very clean, yields very good and all the products were confirmed by their NMR, IR and mass spectroscopic analysis.

Supplementary Information

Supplementary information is available in the website http://nopr.niscair.res.in/handle/123456789/58776.

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References

1 Carrieri A & Fano A, *Curr Top Med Chem*, 7 (2007) 195.
2 Evidente A, Berestetskiy A, Cimmion A, Tuzi A, Superchi S, Melck D & Andolfi A, *J Agric Food Chem*, 57 (2009) 11168.
3 Cimmino A, Zonno C M, Andolfi A, Troise C, Motta A, Vurro M & Evidente A, *J Agric Food Chem*, 61 (2013) 1779.
4 Andolfi A, Cimmino A, Vurro M, Berestetskiy A, Troise C, Zonno C M, Motta A & Evidente A, *Phytochemistry*, 79 (2012) 102.

5 Mahesh G, Raghavaiah J & Sudhakar G, *Tetrahedron*, 76 (2020) 131368.
6 Anil T, Karunakar B & Narsaiah A V, *Arkivoc*, v (2019) 307.
7 Anil T, Karunakar B & Narsaiah A V, *SynOpen*, 3 (2019) 49.
8 Karunakar B, Anil T & Narsaiah A V, *SynOpen*, 3 (2019) 26.
9 Karunakar B, Anil T & Narsaiah A V, *ChemistrySelect*, 4 (2019) 5531.
10 Ganesh NS, Nagalatha G & Narsaiah A V, *Nat Prod Res*, 34 (2020) 2173.
11 Suzuki M, Sugiyama T, Watanabe M, Murayama T & Yamashita K, *Agric Biol Chem*, 51 (1987) 1121.
12 Sugiyama T, Watanabe M, Sassa T & Yamashita K, *Agric Biol Chem*, 47 (1983) 2411.
13 Singh V & Das B, *Tetrahedron*, 56 (2015) 1982.
14 Furuta K, Tomokiyo K, Kuo T M, Ishikawa T & Suzuki M, *Tetrahedron*, 55 (1999) 7529.
15 Qi T, Yamamoto N, Meijler, M M, Altobell L J, Koob G F, Wirsching P & Janda K D, *J Med Chem*, 48 (2005) 7389.
16 Das S, Kuilya T K & Goswami R K, *J Org Chem*, 80 (2015) 6467.
17 Kotsuki H, Kadota I & Ochi M, *J Org Chem*, 55 (1990) 4417.
18 Kita Y, Itho F, Tamura O, Miki T, Ke Y Y, Takashi M & Tmaura Y, *Chem Pharm Bull*, 37 (1989) 1446.
19 Gardiner J M, Panchal N R, Stimpson W T, Herbert J M & Ellames G J, *Synlett*, 17 (2005) 2685.
20 Wei H, Li Y, Xiao K, Cheng B, Wang H, Hu L & Zhai H, *Org Lett*, 17 (2015) 5974.
21 Harris J M & O'Doherty G A, *Tetrahendron*, 57 (2001) 5161.
22 Ko H, Kim E, Park J E, Kim D & Kim S, *J Org Chem*, 69 (2004) 112.
23 Kiyota H, Rumi U, Takayuki O & Shigejumi K, *Synlett*, 2 (2003) 219.
24 Yadav J S, Vardhan V & Das S, *Synthesis*, 46 (2014) 2347.
25 Hoover J M, Steves J E & Stahl S S, *Nat Protocols*, 7 (2012) 1161.