Cross-metathesis transformation of terpenes in dialkyl carbonate solvents

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Supplementary data

General remarks : All the reactions were conducted under an inert atmosphere of argon using standard Schlenck tube techniques. Solvent were dried by distillation prior to use. CH_2Cl_2, was dried over CaH_2, toluene over Na. Dimethyl carbonate was distilled under atmospheric pressure and stored under argon over activated 3Å molecular sieves. All terpenoids were purchased from Acros organics and used as received. Citronellal (93%), citronellol (95%), citral (95%, cis+trans mixt.). Methyl acrylate and methyl methacrylate were purchased from Acros Organics and stored under argon over 3Å molecular sieves prior to use. The key reactions were double checked.

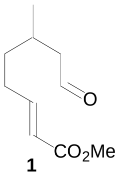
General procedure for the cross-metathesis reactions with methyl acrylate

A dry and degassed Schlenck tube was loaded under argon with 100 mg of terpenoid (~ 0.65 mmol), 8.0-8.3 mg of Hoveyda catalyst **A** (~13.10^{-3} mmol, 2 mol%), 115-118 µl of methyl acrylate (~1.3 mmol, 2 equiv.) and 2 ml of solvent. The reaction was stirred under the mentioned conditions. After solvent evaporation, the products were purified by column chromatography on silica gel using of EtOAc/petroleum ether mixtures.

General procedure for the cross-metathesis reactions with methyl methacrylate

A dry and degassed Schlenck tube was loaded under argon with 100 mg of terpenoid (~ 0.65 mmol), 8.0-8.3 mg of Hoveyda catalyst **A** (~13.10^{-3} mmol, 2 mol%) and 2 ml of methyl methacrylate (19 mmol, 29 equiv.). The reaction was stirred under the mentioned conditions. If necessary, the reaction mixture was slightly diluted with $CHCl_3$ and poured into 50 ml of MeOH or petroleum ether to precipitate the poly-MMA formed. After filtration and evaporation the products were purified by column chromatography on silica gel using of EtOAc/petroleum ether mixtures.

Synthesis of methyl 8-oxo-6-methyl-2-(*E*)-octenoate **1**

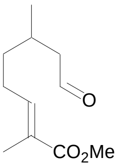


1

NMR Data were consistent with reported data.[1]

^{1}H NMR (200 MHz, $CDCl_3$, ppm): 1.00 (d, 6.0 Hz, 3H, CH_3) 1.2-1.6 (m, 2H), 2.0-2.5 (m, 5H), 3.74 (s, 3H, OCH_3), 5.85 (d, 16.0 Hz, 1H, CH), 6.97 (m, 1H, CH_2), 9.77 (s, 1H, CHO). ^{13}C NMR (75 MHz, $CDCl_3$, ppm): 20.0 (CH_3), 27.9 (CH), 30.0 (CH_2), 35.4 (CH_2), 51.2 (CH_2), 51.9 (OCH_3), 121.7 (CH), 149.2 (CH), 167.4 (CO_2CH_3), 202.7 (CHO).

Synthesis of methyl 8-oxo-2,6-dimethyl-2-(*E*)-octenoate **2**



2

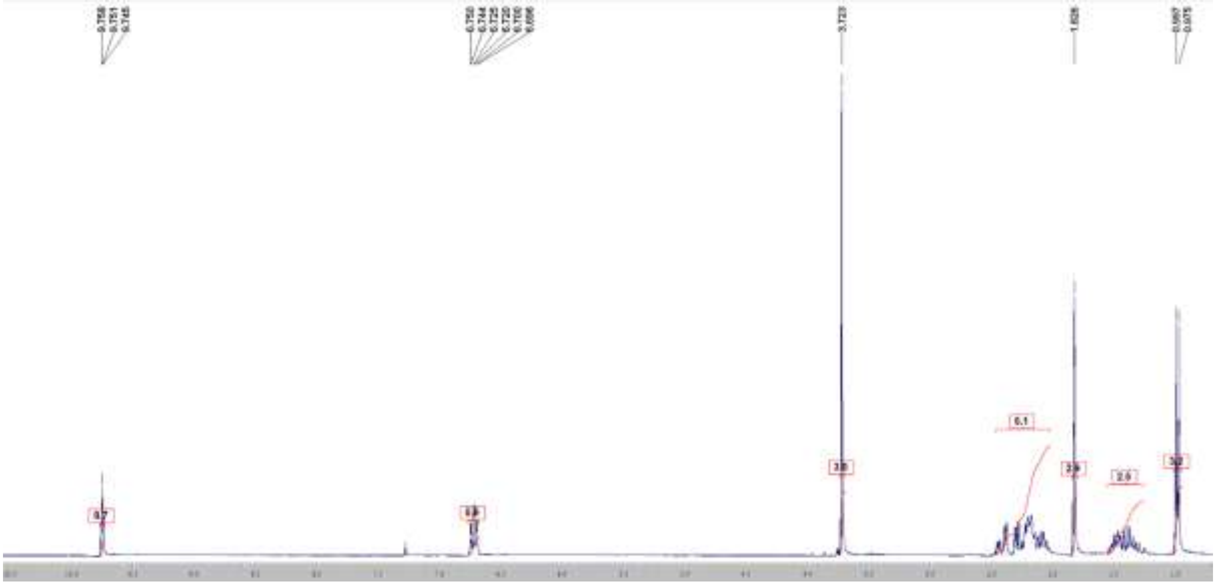
^{1}H NMR (300 MHz, $CDCl_3$, ppm): 0.98 (d, 6.0 Hz, 3H, CH_3), 1.25-1.55 (m, 2H, CH_2), 1.83 (s, 3H, CH_3), 2.05-2.45 (m, 5H, CH_2, CH), 3.72 (s, 3H), 6.72 (m, 1H, CH), 9.75 (t, 2.4 Hz, 1H, CHO).

^{13}C NMR (75 MHz, $CDCl_3$, ppm): 11.4 (CH_3), 18.8 (CH_3), 25.1 (CH_2), 26.8 (CH), 34.5 (CH_2), 49.9 (CH_2), 50.7 (CH), 126.8 (C), 140.5 (CH), 167.5 (CH), 201.4 (CHO).

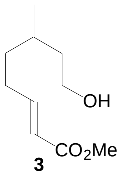
The *E* configuration was determined by 2D NOESY (500 MHz). This experiment did not show any cross-peak between the CH_3 at 1.83 ppm and the *H* at 6.72 ppm whereas a cross-peak was detected between the CH_3 at 3.72 ppm (CO_2CH_3) and the *H* at 6.72 ppm.

HRMS (ESI): $[M+Na]^+$ calculated for ($C_{11}H_{18}O_3Na$) = 221.1153. Measured: 221.1152

300 MHz ^{1}H NMR of **2**



Synthesis of methyl 8-hydroxy-6-methyl-2-(*E*)-octenoate **3**

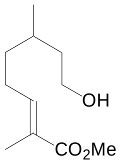


3

NMR Data were consistent with reported data.[2]

^{1}H NMR (200 MHz, $CDCl_3$, ppm): 0.93 (d, 6.0 Hz, 3H, CH_3) 1.20-1.80 (m, 6H, CH_2, CH, OH), 2.25-2.40 (m, 2H, CH_2, CH), 3.67-3.70 (m, 2H, CH_2), 3.74 (s, 3H, OCH_3), 5.84 (d, 16.0 Hz, 1H, CH), 6.97 (m, 1H, CH_2). ^{13}C NMR (50 MHz, $CDCl_3$, ppm): 19.7, 29.4, 30.1, 35.6, 40.0, 51.8, 61.2, 121.2, 150.1, 167.6.

Synthesis of methyl 8-hydroxy-2,6-dimethyl-2-(*E*)-octenoate **4**



4

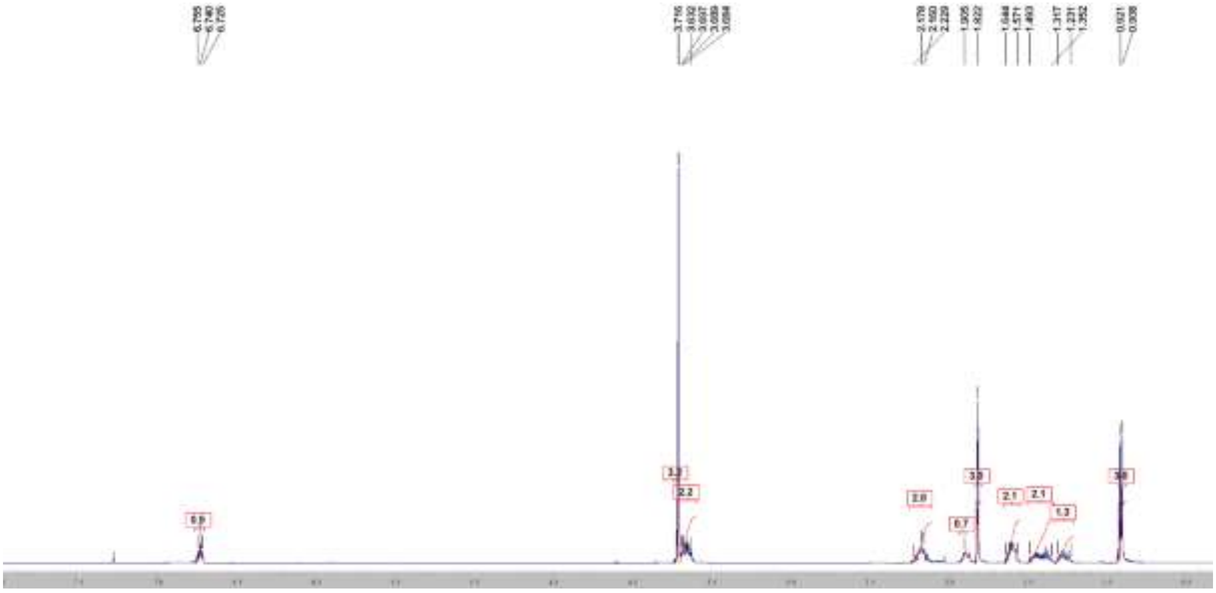
NMR data were consistent with partially reported data[3]

^{1}H NMR (500 MHz, $CDCl_3$, ppm): 0.95 (d, 6.7 Hz, 3H, CH_3), 1.23-1.31 (m, 1H, CH), 1.35-1.49 (m, 2H, CH_2), 1.57-1.64 (m, 2H, CH_2), 1.82 (s, 3H, CH_3), 1.90 (bs, 1H, OH), 2.15-2.25 (m, 2H, CH_2), 3.62-3.70 (m, 2H, CH_2), 3.72 (s, 3H, CH_3), 6.74 (tq, 7.5 Hz, 1.5 Hz, 1H, CH). ^{13}C NMR (50 MHz, $CDCl_3$, ppm): 12.7, 19.7, 26.5, 29.7, 36.2, 40.0, 52.1, 61.2, 127.7, 143.1, 169.2.

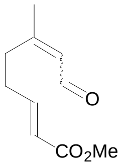
The *E* configuration was determined by 2D NOESY (500 MHz) experiments. This experiment did not show any cross-peak between the C*H*$_3$ at 1.82 ppm and the *H* at 6.74 ppm whereas a cross-peak was detected between the C*H*$_3$ at 3.72 ppm (CO$_2$C*H*$_3$) and the H at 6.74 ppm.

HRMS (ESI): $[M+Na]^+$ calculated for ($C_{11}H_{20}O_3Na$) = 223.1300. Measured: 223.1308

500 MHz ^{1}H NMR of **4**



Synthesis of methyl 8-oxo-6-(*Z*,*E*)-ene-6-methyl-2-(*E*)-octenoate **5**



5

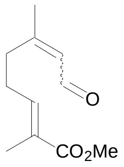
NMR Data were consistent with reported data.[4]

^{1}H NMR (300 MHz, CDCl$_3$, ppm): 1.97, 2.16 (2s, 3H, CH$_3$, cis+trans), 2.33-2.50 and 2.68-2.72(m, 4H, CH$_2$ cis + trans), 3.71 (s, 3H, CH$_3$), 5.80-5.89 (n, 2H, CH), 6.86 (m, 1H, CH), 9.91, 9.98 (2d, 8Hz, 1H, CHO cis + trans)

^{13}C NMR (50 MHz, CDCl$_3$, ppm) : 18.0, 25.1 (CH$_3$, cis + trans),* 29.8, 31.4 (CH$_2$, cis + trans), 38.9 (CH$_2$), 51.9 (OCH$_3$), 122.4, 122.7 (CH, cis + trans), 128.0, 129.3 (CH, cis + trans), 147.0, 147.3 (CH, cis + trans), 162.0, 162.2 (CO$_2$Me, cis + trans), 166.9, 167.0 (C, cis + trans), 190.6, 191.4 (CHO, cis + trans).

* Citral consists in a mixture of neral and geranial

Synthesis of methyl 8-oxo-6-(*Z*,*E*)-ene-2,6-dimethyl-2-octenoate **6**



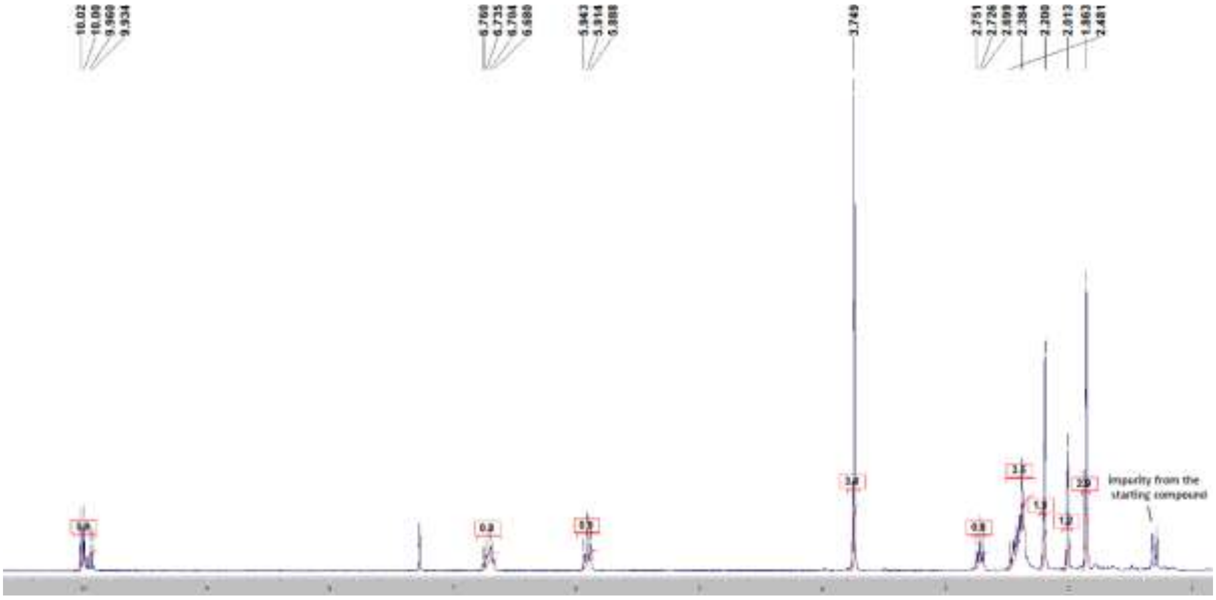
6

^{1}H NMR (300 MHz, $CDCl_3$, ppm):1.86 (s, 3H, CH_3), 2.01, 2.20 (2s, 3H, CH_3, cis+trans), 2.30-2.50 and 2.68-2.75 (m, 4H, CH_2, cis + trans), 2.72 (m, 1H, CH_2) 3.75 (s, 3H, CH_3), 5.89-5.94 (m, 1H, CH), 6.68-6.76 (m, 1H, CH), 9.91, 9.98 (2d, 8. 0 Hz, 1H, CHO cis + trans). ^{13}C NMR (50 MHz, $CDCl_3$, ppm) : 12.8 (CH_3), 18.0, 25.3 (CH_3, cis + trans) 26.5 (CH_2), 28.0 (CH_2), 31.7 (CH_2), 39.4 (CH_2), 52.2 (CH_3), 127.9, 129.2 (CH, cis + trans), 129.3 (C), 139.8, 140.2 (CH, cis + trans), 162.5, 162.7 (CH, cis + trans), 168.7 (CO), 190.7, 191.5 (CHO, cis + trans).

2D NOESY (500 MHz) experiments showed that the new C=C double bond was obtained as a mixture of isomers. However, it was not possible to determine if both isomers of citral led to *E* + *Z* configuration of this new bond. Experiments performed on pure neral and geranial will elucidate this point.

HRMS (ESI): $[M+Na]^+$ calculated for ($C_{11}H_{16}O_3Na$) = 219.0997. Measured: 219.0995.

300 MHz ^{1}H NMR of **6**



References

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