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Total synthesis of the putative structure of the novel triquinane based sesquiterpenoid natural product dichomitol

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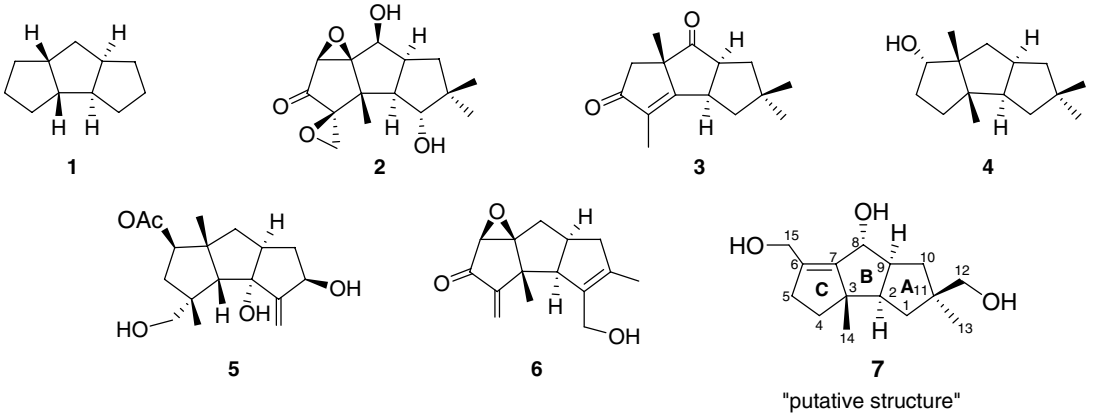
Abstract—A total synthesis of the recently reported triquinane natural product dichomitol, isolated from the fermentation broth of *Dichomitus squalens*, has been accomplished from the commercially available 1,5-cyclooctadiene through a series of unambiguous synthetic steps. A complete mismatch between the spectral characteristics of the synthetic product and that of the natural product warrants a revision of the structure of dichomitol.

Natural products incorporating either a linearly fused or angularly fused triquinane framework as the core structural entity continue to be unveiled at regular intervals from diverse sources like marine organisms, microbial and fungal broths and terrestrial plants.[1] However, it is particularly among sesquiterpenoids based on the *cis*, *anti*, *cis*-tricyclo[6.3.0.0^{2,6}]undecane skeleton **1** (linearly fused triquinane) that one encounters an impressive skeletal and functional diversity, constituting a significant synthetic challenge that has drawn considerable attention from synthetic chemists for the past several decades.[2] Until recently, five different skeletal types represented by coriolin **2** (hirsutane type), cucumin E **3** (isohirsutane type), ceratopicanol **4** (ceratopicane type), 3β-acetoxycapnellene-8β,10α,14β-triol **5** (capnellane type) and pleurotellol **6** (pleurotellane type), differing in the disposition of the methyl groups and functionalization pattern on the basic framework **1**, were known among naturally occurring sesquiterpenoids. Besides exhibiting diverse biological activity profiles, these linear triquinane natural products share a common biogenetic origin that can be traced to the farnesyl pyrophosphate derived humulenyl cation and further 1,2-methyl shifts.

In 2004, a group of Chinese researchers[3] reported the isolation of a novel sesquiterpenoid natural product, dichomitol **7** from *Dichomitus squalens*, a commonly found white-rot Basidiomycete fungus. The structural



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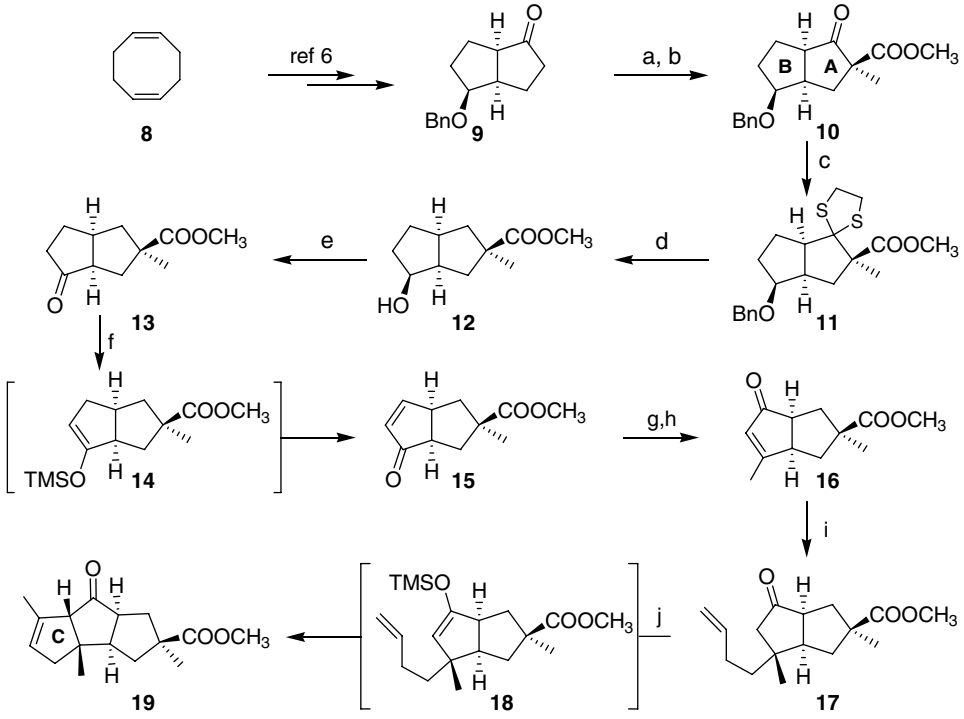
elucidation of dichomitol **7** was accomplished on the basis of complementary evidence garnered from HRTOFMS, ^{1}H and ^{13}C NMR (COSY, HMBC, NOESY) spectral data.[3] The triquinane triol based formulation of dichomitol **7**, not only represented a novel skeletal type among triquinane sesquiterpenoids but was also biogenetically intriguing as it was suggested to be related to the hirsutanes (e.g., **2**) through quite an unusual repositioning (shift) of methyl groups. As part of our long standing interest in the syntheses of triquinane natural products,[4,5] dichomitol **7** attracted our instant attention as a synthetic target on account of its complex and challenging structure. In this letter, we delineate a synthetic strategy that has led to the acquisition of structure **7**, assigned to the natural product dichomitol.[3] However, it was found that the spectral characteristics of compound **7**, synthesized through an unambiguous protocol, did not match those reported for the natural product dichomitol and necessitate a revision of the structure of the natural product.[3]

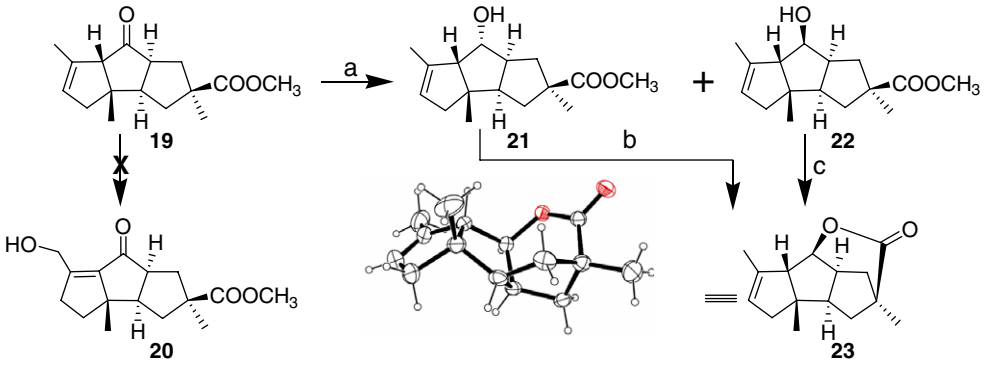
Our synthesis commenced from the bicyclic ketone **9**, readily accessible from commercially available 1,5-cyclooctadiene **8** as described by us in another context.[6] Succesive α-carbomethoxylation and α-methylation on **9** proceeded with predicted regio- and stereoselectivity to furnish **10** and correctly install the C11-quaternary centre. The carbonyl group in the AB ring precursor **10** was protected as thioketal **11** and reductive desulfurization led to simultaneous deprotection of the benzyl group to furnish **12**, which was oxidized to the required ketone **13** (Scheme 1). The regioselective formation of TMS–enol ether **14** and Pd^{+2}-mediated dehydrosilylation according to the Saegusa co-workers[8] procedure furnished enone **15** (Scheme 1). The enone functionality in **15** was subjected to a two-step alkylative transposition through the addition of methyllithium and PCC oxidation to deliver the requisite transposed enone **16**. The Cu-mediated 1,4-conjugate addition[9] of butenylmagnesium bromide to **16** was stereoselective, from the convex face, and delivered **17**[7] with the desired stereochemistry at the newly created quaternary centre. Kinetically controlled deprotonation in **17** and capture of the resultant enolate delivered the TMS–enol ether **18**, which was directly subjected to Pd-catalyzed Kende et al.[10] cyclization to generate the third five-membered ring, C, and furnish **19** (Scheme 1).[7] In the triquinane **19**, we had realized the complete carbon framework of the target.

At this stage, two key transformations that needed to be implemented were the relocation of the C5–C6 double bond to the required C6–C7 tetrasubstituted position, and the oxidation of the allylic C15-methyl group to furnish **20** (Scheme 2).

Towards this objective, **19** was exposed to a variety of double bond isomerization protocols ($RhCl_3$, PTSA, DBU, KO^{t}Bu, etc.) for a seemingly straightforward relocation of the C5–C6 double bond to the conjugated C6–C7 position, but without any success. Considering that the installation of three consecutive sp^2 centres at C6, C7 and C8 involving the bridgehead position might be causing excessive strain, it was decided to reduce the



Scheme 1. Reagents and conditions: (a) $CO(OCH_3)_2$, NaH, THF, reflux, 2 h, 82%; (b) MeI, DBU, THF, 0 °C, 15 min, 90%; (c) ethanedithiol, PTSA, C_6H_6, reflux, 36 h, 75%; (d) Raney–Ni, EtOH, reflux, 12 h, 90%; (e) PCC, DCM, 0 °C–rt, 3 h, 90%; (f) (i) LHMDS, TMSCl, THF, −78 °C, 30 min; (ii) $Pd(OAc)_2$, CH_3CN, rt, 2 h, 86%; (g) MeLi, ether, −80 °C, 10 min; (h) PCC, DCM, 0 °C–rt, 12 h, 84%; (i) (i) Mg, 4-bromobutene, CuBr–DMS, TMSCl, HMPA, THF, −78 °C to rt, 8 h; (ii) AcOH, 95% and (j) (i) LHMDS, TMSCl, THF, −78 °C, 30 min; (ii) $Pd(OAc)_2$, CH_3CN, rt, 2 h, 80%.

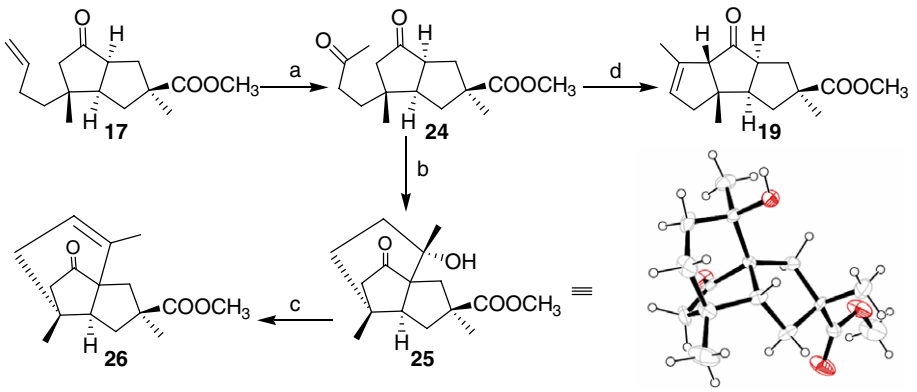


Scheme 2. Reagents and conditions: (a) $NaBH_4$, MeOH, 0 °C, 30 min, 68% and 23%, respectively; (b) PTSA, C_6H_6, reflux, 12 h, 95% and (c) $RhCl_3$, EtOH, reflux, 8 h, 96%.

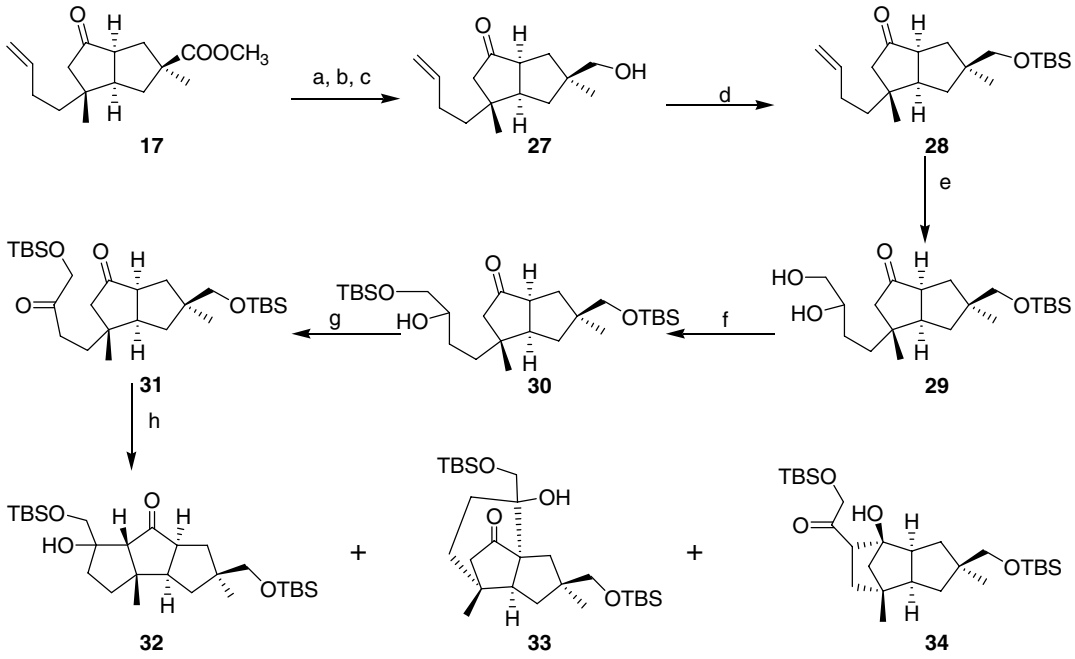
carbonyl group prior to attempting the double bond isomerization. Consequently, the carbonyl group in **19** was reduced to furnish a 3:1 mixture of diastereomers **21** and **22** (Scheme 2). Interestingly, when **21** and **22** were exposed to PTSA and $RhCl_3$, respectively, they furnished the same tetracyclic lactone **23** whose formulation was secured through a single crystal X-ray structure determination (Scheme 2).[11] However, during none of these manoeuvres was the double bond isomerization product detected.

Thwarted in our efforts to position the C6–C7 double bond, we ventured to explore an aldol-based approach for the construction of ring C (Scheme 3). For this purpose, the butenyl side arm in the bicyclic ketone **17** was subjected to Wacker-type oxidation employing Tsuji conditions[12] to furnish diketone **24** smoothly (Scheme 3). Aldol cyclization in **24** was attempted under a variety of acid and base catalysis conditions. The basic conditions yielded a stable aldol product **25** and its bridged structure was elucidated on the basis of single crystal X-ray studies.[11] Dehydration in **25** furnished an interesting tricyclic olefin **26** bearing a tricyclo[4.3.2.$0^{1,5}$]undecane framework reminiscent of the bioactive sesquiterpenoids quadrone and terrecyclic acid A.[13] On the other hand, when **24** was subjected to the acid catalyzed aldol cyclization, ketone **19** was once again produced as the only product with no trace of the requisite C6–C7 double bond isomer (Scheme 3).

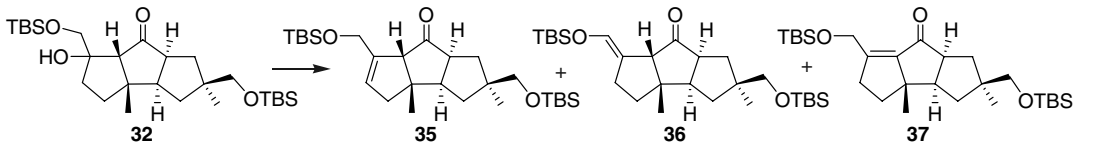
The foregoing observations and outcomes mandated tactical modifications of our approach and towards this end the carbonyl group in **17** was protected as its ethylene ketal and the ester group was reduced with LAH and then further ketal deprotection furnished **27** (Scheme 4). Primary hydroxyl group protection in **27** as the TBS derivative led to **28**. The butenyl arm was dihydroxylated using catalytic OsO_4 oxidation to give diol **29**[7] and the primary hydroxyl group was selectively protected as TBS derivative **30**, Scheme 4. The oxidation of **30** using IBX[14] led to dione **31** now set for the aldol cyclization. For the aldol reaction on **31**, several conditions were explored and the most consistent result was with LHMDS as the base to furnish a mixture (~3:1:1) of three aldol products **32**–**34** (Scheme 4). Among these, the major product **32** was serviceable for further elaboration to the target structure **7**. In the event, the tertiary hydroxy group in **32** was subjected to dehydration under several conditions (Scheme 5) with the expectation of installing the required C6–C7 double bond. The results displayed in Scheme 5 were far from satisfactory but still considered as manageable. Three regioisomeric olefins **35**–**37** were obtained[7,15] from the dehydration of **32** depending upon the conditions



Scheme 3. Reagents and conditions: (a) CuCl, $PdCl_2$, O_2, DMF–H_2O, rt, 5 h, 92%; (b) 2% KOH in MeOH, rt, 5 min, 90%; (c) $SOCl_2$, Py, DCM, −10 °C, 15 min, 85% and (d) PTSA, C_6H_6, reflux, 10 h, 90%.



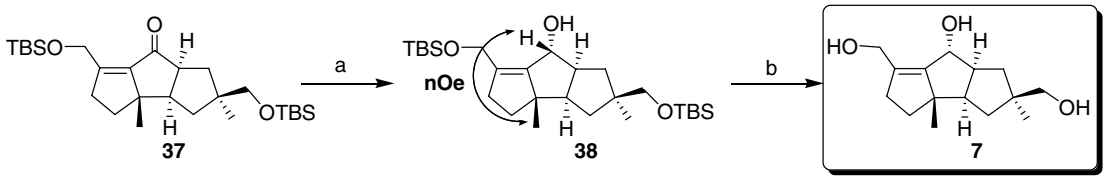
Scheme 4. Reagents and conditions: (a) ethylene glycol, PTSA, C_6H_6, reflux, 10 h, 97%; (b) LAH, THF, 0 °C–rt, 30 min, 96%; (c) Amberlyst-15, acetone, rt, 2 h, 95%; (d) TBSCl, imidazole, DCM, reflux, 1 h, 98%; (e) OsO_4, NMMO, acetone–H_2O, rt, 2 h, 90%; (f) TBSCl, imidazole, DCM, reflux, 1 h, 86%; (g) IBX, DMSO–toluene, rt, 10 h, 78% and (h) LHMDS, THF, −78 °C, 20 min (3:1:1) 40%, 15% and 15%, respectively.



Scheme 5. Reagents and conditions: (a) $SOCl_2$, Py, DCM, −10 °C, 15 min. **35** (66%) **36** (14%) **37** (5%); (b) Martin Sulfurane, $CHCl_3$, rt, 30 min. **35** (40%) **36** (40%) **37** (5%) and (c) MsCl, NEt_3, DCM, rt, 45 min **35** (42%) **36** (42%).

employed and among them the very minor product **37** was the desired one with the long sought C6–C7 double bond in position. For the purpose of accessing **37**, both classical thionyl chloride and Martin sulfurane[16] were acceptable for effecting the dehydration reaction. Despite its formation in near trace amounts, scaling up the sequence leading to **37** made it possible to carry out the final few steps.

DIBAL–H reduction on **37** was expectedly stereoselective to deliver the α-hydroxy compound **38** and its pectral data,[7] particularly the observation of a key NOE, secured its structure (Scheme 6). Deprotection of the two TBS protecting groups delivered triol **7** corresponding to the assigned structure of the natural product dichomitol.[3] However, we observed that the spectral data[7] of our synthetic material **7** were very different from that reported for the natural product dichomitol, with some of the ^{13}C resonances varying by as much as 10 ppm, (Table 1). To further strengthen our arrival at structure **7** we carried out high field NMR (700 MHz) studies (^1H–^1H COSY, HSQC and NOESY) on our synthetic material and the key features are depicted in Figure 1.



Scheme 6. Reagents and conditions: (a) DIBAL–H, DCM, −78 °C, 90% and (b) TBAF, THF, rt, 12 h, 85%.

Table 1. Comparison of the ^{13}C resonances (175 MHz) of synthetic **7** and the natural product dichomitol

Dichomitol[3]	145.8	129.1	74.3	72.1	59.0	50.5	45.9	45.5	45.1	40.8	36.1	36.0	25.1	22.7	20.3
7	153.3	130.0	75.8	71.7	61.6	55.8	55.6	50.4	48.5	41.8	41.6	36.3	35.7	22.7	22.4

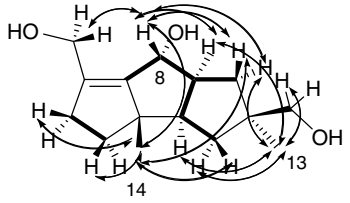


Figure 1. ^{1}H–^{1}H COSY and HSQC (bold lines) NOE (arrows) of C8–H, C13–Me and C14–Me.

In summary, we have achieved a total synthesis of tricyclic triquinane triol framework **7**, corresponding to the structure assigned to the recently isolated natural product dichomitol, from commercially available 1,5-cyclooctadiene. Significant variations in the spectral characteristics of **7** and those reported for dichomitol necessitate a reinvestigation of the structure of the natural product.

Acknowledgements

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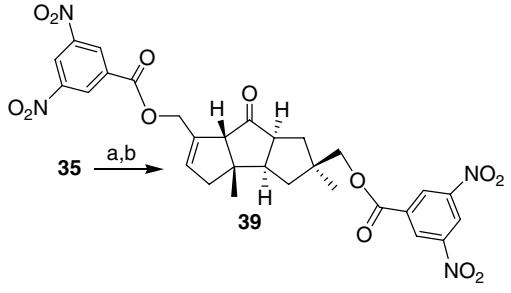
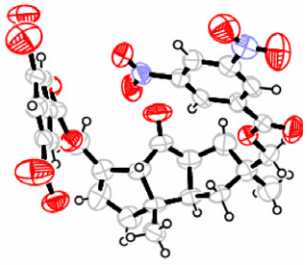
References and notes

1. For a recent entrant to the triquinane based natural products family, see: Roncal, T.; Cordobes, S.; Ugalde, U.; He, Y.; Sterner, O. *Tetrahedron Lett.* **2002**, *43*, 6799–6802.
2. Recent reviews: (a) Mehta, G.; Srikrishna, A. *Chem. Rev.* **1997**, *97*, 671–719; (b) Singh, V.; Thomas, B. *Tetrahedron* **1998**, *54*, 3647–3692.
3. Huang, Z.; Dan, Y.; Huang, Y.; Lin, L.; Li, T.; Ye, W.; Wei, X. *J. Nat. Prod.* **2004**, *67*, 2121–2123.
4. For some of the recent accomplishments in the area of linear triquinane natural product syntheses from other groups, see: (a) Banwell, M. G.; Edwards, A. J.; Harfoot, G. J.; Jolliffe, K. A. *Tetrahedron* **2004**, *60*, 535–547; (b) Wang, J. C.; Krische, M. J. *Angew. Chem., Int. Ed.* **2003**, *42*, 5855–5857; (c) Singh, V.; Vedantham, P.; Sahu, P. K. *Tetrahedron Lett.* **2002**, *43*, 519–522; (d) Mukai, C.; Kobayashi, M.; Kim, I. J.; Hanaoka, M. *Tetrahedron* **2002**, *58*, 5225–5230; (e) Shindo, M.; Sato, Y.; Shishido, K. *Tetrahedron Lett.* **2002**, *43*, 5039–5041; (f) Harrowven, D. C.; Lucas, M. C.; Howes, P. D. *Tetrahedron* **2001**, *57*, 9157–9162.
5. (a) Mehta, G.; Reddy, A. V. *J. Chem. Soc., Chem. Commun.* **1981**, 756–757; (b) Mehta, G.; Reddy, A. V.; Murty, A. N.; Reddy, D. S. *J. Chem. Soc., Chem. Commun.* **1982**, 540–541; (c) Mehta, G.; Reddy, D. S.; Murty, A. N. *J. Chem. Soc., Chem. Commun.* **1983**, 824–825; (d) Mehta, G.; Murthy, A. N.; Reddy, D. S.; Reddy, A. V. *J. Am. Chem. Soc.* **1986**, *108*, 3443–3452; (e) Mehta, G.; Karra, S. R. *J. Chem. Soc., Chem. Commun.* **1991**, 1367–1368; (f) Mehta, G.; Umarye, J. D. *Tetrahedron Lett.* **2001**, *42*, 1991–1993; (g) Mehta, G.; Murthy, A. S. K.; Umarye, J. D. *Tetrahedron Lett.* **2002**, *43*, 8301–8305; (h) Mehta, G.; Murthy, A. S. K. *Tetrahedron Lett.* **2003**, *44*, 5243–5246.
6. (a) Mehta, G.; Sreenivas, K. *Chem. Commun.* **2001**, 1892–1893; (b) Mehta, G.; Sreenivas, K. *Tetrahedron Lett.* **2002**, *43*, 703–706.
7. All new compounds reported here were racemic and characterized on the basis of spectroscopic data (IR, ^{1}H and ^{13}C NMR and mass). Spectral data for some of the key compounds are as follows: Compound **17**: IR (thin film): ν_{max} 2956, 1736 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ 5.79–5.66 (m, 1H), 4.96 (dd, $J = 17.1$, 1.8 Hz, 1H), 4.89 (dd, $J = 10.2$, 1.8 Hz, 1H), 3.61 (s, 3H), 2.80–2.72 (m, 1H), 2.64–2.54 (m, 1H), 2.23 (1/2ABq, $J = 18.6$ Hz, 1H), 2.09 (1/2ABq, $J = 18.6$ Hz, 1H), 2.09–1.89 (m, 4H), 1.87–1.76 (m, 1H), 1.70–1.64 (m, 1H), 1.37 (t, $J = 8.4$ Hz, 2H), 1.18 (s, 3 H), 1.03 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 221.4, 177.3, 138.3, 114.6, 51.9, 51.1, 50.4, 49.9, 48.2, 41.8, 39.7, 39.0, 38.5, 28.7, 23.7, 21.8. HRMS (ES) *m/z* calcd for $C_{16}H_{24}O_3Na$, $[M+Na]^+$: 287.1623, found: 287.1628. Compound **19**: IR (thin film): ν_{max} 2954, 2849, 1732 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ 5.32 (s, 1H), 3.66 (s, 3H), 2.80–2.75 (m, 1H), 2.62–2.31 (m, 5H), 1.84–1.70 (m, 2H), 1.76 (s, 3H), 1.57–1.47 (m, 1H), 1.25 (s, 3H), 1.16 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 218.0, 177.8, 136.0, 125.6, 67.1, 52.8, 52.0, 50.6, 49.5, 49.2, 47.5, 40.5, 38.2, 25.3, 24.7, 15.3. HRMS (ES) *m/z* calcd for $C_{16}H_{22}O_3Na$, $[M+Na]^+$: 285.1467, found: 285.1463. Compound **35**: IR (thin film): ν_{max} 2954, 2856, 1735 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ 5.58 (d, $J = 1.8$ Hz, 1H), 4.28 (1/2ABq, $J = 15.6$ Hz, 1H), 4.19 (1/2ABq, $J = 15.6$ Hz, 1H), 3.28 (s, 2H), 2.76–2.70 (m, 1H), 2.63 (s, 1H), 2.63–2.50 (m, 1H), 2.45–2.33 (m, 2H), 1.94 (dd, $J = 13.8$, 3.0 Hz, 1H), 1.57–1.40 (m, 3H), 1.14 (s, 3H), 0.95 (s, 3H), 0.90 (s, 9H), 0.88 (s, 9H), 0.07 (s, 3H), 0.06 (s, 3H), 0.01 (s, 6H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 219.3, 139.9, 124.8, 71.2, 63.5, 60.9, 53.3, 50.5, 48.4, 47.9, 45.6, 39.9, 36.6, 25.9(3C), 25.7(3C), 24.7, 24.6, 18.4, 18.3, −5.4(2C), −5.5(2C). HRMS (ES) *m/z* calcd for $C_{27}H_{50}O_3Si_2Na$, $[M+Na]^+$: 501.3196, found: 501.3216. Compound **36**: IR (thin film): ν_{max} 2927, 1737 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ 6.37 (s, 1H), 3.35 (1/2ABq, $J = 11.4$ Hz, 1H), 3.33 (1/2ABq, $J = 11.4$ Hz, 1H), 3.15 (s, 1H), 2.88–2.82 (m, 1H), 2.68–2.61 (m, 1H), 2.33–2.22 (m,3H), 2.05–2.01 (m, 1H), 1.77–1.72 (m, 1H), 1.64–1.47 (m, 2H), 1.44–1.41 (m, 1H), 1.06 (s, 3H), 0.93 (s, 9H), 0.92 (s, 3H), 0.88 (s, 9H), 0.16 (s, 3H), 0.13 (s, 3H), 0.02 (s, 6H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 220.8, 135.4, 119.8, 70.1, 58.5, 51.6, 48.4, 47.9, 46.5, 39.4, 38.9, 37.9, 31.9, 26.2, 25.9(3C), 25.7(3C), 23.2, 18.3, 18.2, −5.2, −5.3, −5.5(2C). HRMS (ES) *m/z* calcd for $C_{27}H_{50}O_3Si_2Na$, $[M+Na]^+$: 501.3196, found: 501.3196. Compound **37**: IR (thin film): ν_{max} 2927, 2855, 1703 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ 4.77 (d, $J = 15.0$ Hz, 1H), 4.19 (d, $J = 15.0$ Hz, 1H), 3.37 (s, 2H), 3.25–3.11 (m, 1H), 2.91–2.63 (m, 3H), 1.93–1.81

(m, 2H), 1.67–1.50 (m, 2H), 1.39–1.23 (m, 2H), 1.06 (s, 3H), 0.88 (s, 3H), 0.87 (s, 9H), 0.86 (s, 9H), 0.04 (s, 3H), 0.03 (s, 3H), 0.02 (s, 6H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 204.8, 149.1, 149.0, 70.0, 58.9, 57.3, 54.1, 49.2, 48.8, 43.7, 37.7, 35.7, 35.0, 25.9(3C), 25.8(3C), 23.8, 23.1, 18.3, 18.2, −5.3, −5.4, −5.5, −5.6. HRMS (ES) *m/z* calcd for $C_{27}H_{50}O_3Si_2H$, $[M+H]^+$: 479.3377, found: 479.3376. Compound **38**: IR (thin film): ν_{max} 3446, 2925, 2856 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$): δ 4.42 (d, $J = 15.5$ Hz, 1H), 4.38 (br s, 1H), 4.12 (d, $J = 15.5$ Hz, 1H), 3.38 (s, 2H), 2.81–2.74 (m, 1H), 2.58–2.57 (m, 1H), 2.55–2.49 (m, 1H), 2.23 (td, $J = 14.5$, 4.5 Hz, 1H), 1.72–1.68 (m, 3H), 1.62 (dd, $J = 12.5$, 9.5 Hz, 1H), 1.48 (t, $J = 11.5$, 1H), 1.20 (ddd, $J = 12.5$, 9.0, 1.5, 1H), 0.96 (s, 3H), 0.92 (s, 9H), 0.89 (s, 9H), 0.88 (s, 3H), 0.13 (s, 6H), 0.03 (s, 6H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 155.2, 127.7, 74.9, 70.7, 62.7, 56.4, 55.3, 50.5, 48.5, 41.7, 41.5, 36.1, 35.2, 25.9(3C), 25. 8(3C), 23.0, 22.4, 18.4, 18.3, −5.5(2C), −5.6(2C). HRMS (ES) *m/z* calcd for $C_{27}H_{52}O_3Si_2Na$, $[M+Na]^+$: 503.3353, found: 503.3351. Compound **7**: IR (thin film): ν_{max} 3436, 2935 cm^{-1}. ^{1}H NMR (700 MHz, $CDCl_3$): δ 4.48 (br s, 1H), 4.40 (d, $J = 15.4$ Hz, 1H), 4.15 (d, $J = 15.4$ Hz, 1H), 3.49 (s, 2H), 2.81–2.75 (m, 1H), 2.66–2.60 (m, 1H), 2.57 (q, $J = 9.1$ Hz, 1H), 2.29 (q, $J = 7.7$ Hz, 1H), 1.78 (ddd, $J = 12.6$, 8.4, 1.4 Hz, 1H), 1.75–1.70 (m, 2H), 1.53 (dd, $J = 12.6$, 9.8 Hz, 1H), 1.39 (t, $J = 11.2$ Hz, 1H), 1.33 (ddd, $J = 12.6$, 9.1,1.4 Hz, 1H), 0.98 (s, 3H), 0.97 (s, 3H). ^{13}C NMR (175 MHz, $CDCl_3$): δ 153.3, 130.0, 75.8, 71.7, 61.6, 55.8, 55.6, 50.4, 48.5, 41.8, 41.6, 36.3, 35.7, 22.7, 22.4. HRMS (ES) *m/z* calcd for $C_{15}H_{24}O_3Na$, $[M+Na]^+$: 275.1623, found: 275.1607.

8. Ito, Y.; Hirao, T.; Saegusa, T. *J. Org. Chem.* **1978**, *43*, 1011–1013.
9. (a) Horiguchi, Y.; Matsuzawa, S.; Nakamura, E.; Kuwajima, I. *Tetrahedron Lett.* **1986**, *27*, 4025–4028; (b) Nakamura, E.; Matsuzawa, S.; Horiguchi, Y.; Kuwajima, I. *Tetrahedron Lett.* **1986**, *27*, 4029–4032.
10. Kende, A. S.; Roth, B.; Sanfilippo, P. J. *J. Am. Chem. Soc.* **1982**, *104*, 1784–1785.
11. X-ray data: X-ray data were collected at 293 K on a SMART CCD–BRUKER diffractometer with graphite monochromated MoKα radiation ($\lambda = 0.71073$ Å). The structure was solved by direct methods (SIR92). Refinement was by full-matrix least-squares procedures on F^2 using SHELXL-97. Compound **23**: $C_{15}H_{20}O_2$, MW = 232.31, Crystal system: monoclinic, space group: $P2_1/c$, cell parameters: $a = 10.283(3)$ Å, $b = 11.266(4)$ Å, $c = 11.765(4)$ Å, $\beta = 106.654(6)°$, $V = 1305.8(7)$ Å^3, $Z = 4.0$, $D_c = 1.182$ g cm^{-3}, $F(000) = 504.0$, $\mu = 0.077$ mm^{-1}. Total number of l.s. parameters = 157, $R1 = 0.0516$ for 1777 $F_o > 4\sigma(F_o)$ and 0.0649 for all 2284 data. $wR2 = 0.1349$, GOF = 1.052, Restrained GOF = 1.052 for all data. CCDC 617717. Compound **25**: $C_{16}H_{24}O_4$, MW = 280.35, Crystal system: orthorhombic, space group: $P2_12_12_1$, cell parameters: $a = 9.1612(12)$ Å, $b = 12.8326(16)$ Å, $c = 12.9976(16)$ Å, $V = 1528.0(3)$ Å^3, $Z = 4.0$, $D_c = 1.219$ g cm^{-3}, $F(000) = 608.0$, $\mu = 0.086$ mm^{-1}. Total number of l.s. parameters = 186, R1 = 0.1048 for 1834 $F_o > 4\sigma(F_o)$ and 0.1565 for all 2696 data. $wR2 = 0.171$, GOF = 1.168, Restrained GOF = 1.168 for all data. CCDC 617718. Compound **39**: $C_{29}H_{26}O_{13}N_4$, MW = 638.5, Crystal system: Triclinic, space group: P-1 cell parameters: $a = 11.159(2)$ Å, $b = 15.112(3)$ Å, $c = 20.915(4)$ Å, $\alpha = 108.232(4)°$, $\beta = 90.660(4)°$, $\gamma = 95.137(4)°$, $V = 3333.7(12)$ Å^3, $Z = 4.0$, $D_c = 1.272$ g cm^{-3}, $F(000) = 1328.0$, $\mu = 0.102$ mm^{-1}. Total number of l.s. parameters = 833, $R1 = 0.0879$ for 5432 $F_o > 4\sigma(F_o)$ and 0.1611 for all 11330 data. $wR2 = 0.2555$, GOF = 1.048, Restrained GOF = 1.048 for all data. CCDC 617731.
12. Tsuji, J. *Synthesis* **1984**, 369–384.
13. (a) Ranieri, R. L.; Calton, G. J. *Tetrahedron Lett.* **1978**, *19*, 499–502; (b) Calton, G. J.; Ranieri, R. L.; Espenshade, M. A. *J. Antibiot.* **1978**, *31*, 38–45; (c) Nakagawa, M.; Hirota, A.; Sakai, H.; Isogai, A. *J. Antibiot.* **1982**, *35*, 778–782.
14. Frigerio, M.; Santagostino, M. *Tetrahedron Lett.* **1994**, *35*, 8019–8022.
15. As a matter of abundant precaution, it was considered important to further secure structures **35**–**37**. Towards this end, the major compound **35** from the dehydration of **32** was transformed to a crystalline derivative **39** as shown below and its structure was determined following the single crystal X-ray technique.[11]





Reagents and conditions: (a) TBAF, THF, rt, 10 h, 95%; (b) 3,5-dinitrobenzoyl chloride, NEt_3, DCM, 0 °C, 30 min., 95%.

16. Martin, J. C.; Arhart, R. J. *J. Am. Chem. Soc.* **1971**, *93*, 4327–4329.