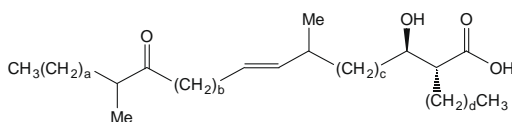




**Table 1**

Typical chain lengths of major  $\beta$ -methyl-*trans*-alkene-containing mycobacterial ketomycolic acids (**1**)

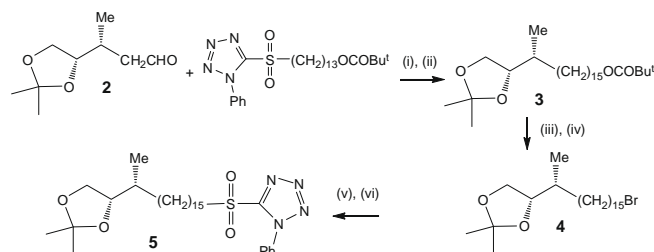


Species	a	b	c	d	Ref.
<i>Mycobacterium tuberculosis</i> , <i>Mycobacterium bovis</i> , <i>M. bovis</i> BCG, <i>Mycobacterium microti</i>	17	19	15	23	3
<i>M. tuberculosis</i> , <i>M. bovis</i> , <i>M. bovis</i> BCG, <i>M. microti</i>	17	19	13	23	3
<i>M. tuberculosis canetti</i>	17	17	17	23	3
<i>Mycobacterium avium</i> , complex (MAC)	17	17	17	21	3
<i>Mycobacterium marinum</i>	17	15	17	21	3
<i>Mycobacterium scrofulaceum</i>	15	17	17	21	3
<i>Mycobacterium aurum</i>	15	13	19	19	8
<i>M. aurum</i>	15	13	17	19	8

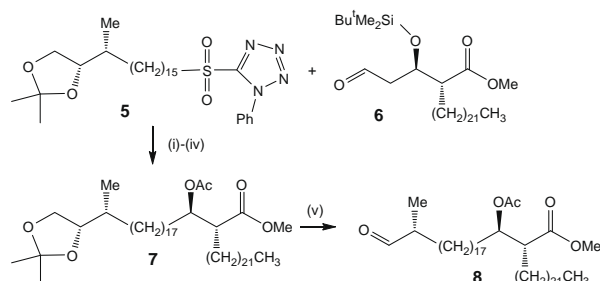
is then cyclopropanated by the CmaA2 gene, again with SAM, to give the  $\alpha$ -methyl-*trans*-cyclopropane.<sup>11–15</sup> Inactivation of CmaA2 causes the accumulation of unsaturated derivatives in both methoxy- and keto-MA and the lack of *trans*-cyclopropanes.<sup>16</sup> It should be noted, however, that there are alternative models for the creation of these functional groups.<sup>17</sup> It is also interesting that the labelling pattern of an  $\alpha$ -methyl-*trans*-cyclopropane-containing keto-MA of *M. tuberculosis* derived from [1-<sup>13</sup>C]acetic acid places a labelled carbon at the cyclopropane carbon nearest to the methyl group, while in an unsaturated  $\alpha$ 2-MA from *M. smegmatis*, the label in the proximal  $\alpha$ -methyl-*trans*-alkene is on the carbon adjacent to the methyl group – consistent with biochemical alkylation at opposite ends of a *cis*-alkene.<sup>18</sup> Another type of mycolic acid isolated from *M. smegmatis* and *Mycobacterium aurum*,<sup>8</sup> *Mycobacterium chelonae*,<sup>19</sup> and *Mycobacterium fortuitum*,<sup>20</sup> contains an  $\alpha$ -methyl-*trans*-alkene at the proximal position and a *cis*-alkene at the distal position.<sup>21–23</sup> Examples with a *cis*-cyclopropane or an  $\alpha$ -methyl-*trans*-oxirane at the distal position have also been reported.<sup>3</sup> In the former case the specific rotation of its methyl ester has been reported to be +1.4 (CHCl<sub>3</sub>),<sup>24</sup> while that of the acetoxy methyl ester is reported as +3 (CHCl<sub>3</sub>), and that of a deacetoxy derivative of a mycolate containing only an  $\alpha$ -methyl-*trans*-alkene chiral centre corresponds to a molecular rotation ( $M_D$ ) of –19.5.<sup>24</sup> In addition, the specific rotation of a wax ester containing the  $\alpha$ -methyl-*trans*-alkene unit has been reported to be +4.3 (CHCl<sub>3</sub>).<sup>8,25,26</sup> This allows the contribution to the molecular rotation from the  $\alpha$ -methyl-*trans*-alkene unit to be calculated, as the only other chiral centres in these molecules are at the hydroxy-acid position, the contribution of which to the molecular rotation is known (+40), leading to a value of –25 for the  $\alpha$ -methyl-*trans*-alkene (for 30% of methyl branched molecules); this in turn suggests that this subunit has an (*R*)-stereochemistry based on model compounds.<sup>9</sup>

As part of a study to determine the biological significance of individual MAs and particularly of their stereochemistry, we have reported routes to  $\alpha$ -, methoxy- and keto-MAs as single stereoisomers, as well as to related wax esters.<sup>27–31</sup> We now report the first synthesis of type-2 hydroxy-MA **16** (R = R' = H) and **18** and the related keto-MA (**21**).

In order to fix the (*R*)-stereochemistry of the  $\beta$ -methyl-*trans*-alkene fragment, aldehyde **2**,<sup>32–34</sup> was chain-extended using a modified Julia–Kocienski reaction,<sup>35</sup> followed by hydrogenation of the derived alkenes to give **3**. The pivalate group was removed and the primary alcohol was converted into sulfone **5** via bromide **4** (Scheme 1).



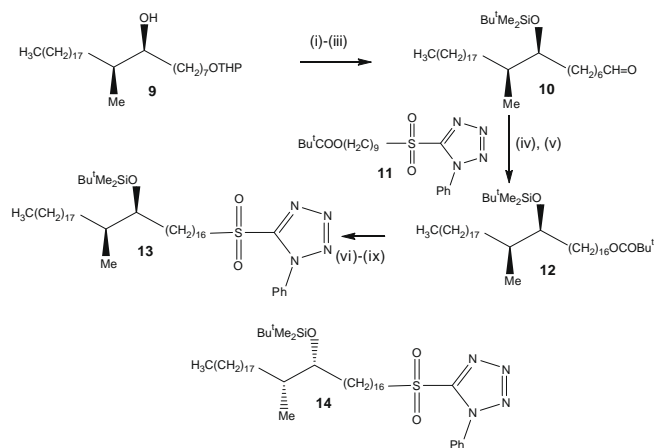
**Scheme 1.** Reagents: (i) LiHMDS, THF (86%); (ii) H<sub>2</sub>, Pd/C, EtOAc/EtOH (96%); (iii) KOH, THF, MeOH, H<sub>2</sub>O (97%); (iv) N-bromosuccinimide, PPh<sub>3</sub>, NaHCO<sub>3</sub>, CH<sub>2</sub>Cl<sub>2</sub> (92%); (v) 1-phenyl-1H-tetrazole-5-thiol, K<sub>2</sub>CO<sub>3</sub>, acetone (95%); (vi) H<sub>2</sub>O<sub>2</sub>, (NH<sub>4</sub>)<sub>6</sub>Mo<sub>7</sub>O<sub>24</sub>·4H<sub>2</sub>O, THF/IMS (81%).



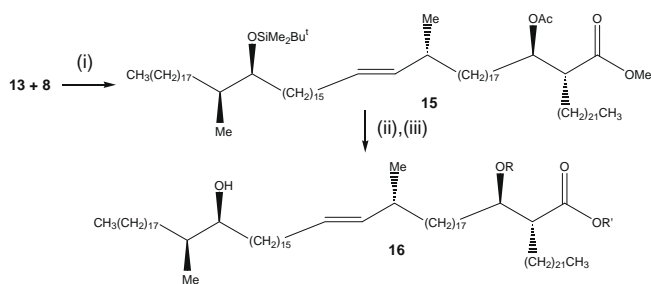
**Scheme 2.** Reagents: (i) LHMDS (86%); (ii) Pd/C, EtOAc (96%); (iii) HF-pyridine (83%); (iv) Ac<sub>2</sub>O, pyridine (94%); (v) periodic acid (80%).

The hydroxy-acid unit was introduced in the form of **6**, prepared as described earlier from l-aspartic acid.<sup>36</sup> A further modified Julia reaction between the aldehyde **6** and sulfone **5** gave a mixture of alkenes which was hydrogenated. The silyl ether was changed to acetyl to avoid the presence of two identical protecting groups at a later stage to yield **7**, and the acetal group was converted into aldehyde **8** with periodic acid (Scheme 2).

The alcohol **9**<sup>28</sup> was protected as a TBDMS ether, the THP-group was removed and the resulting alcohol was oxidized to the aldehyde **10** (Scheme 3). A Julia–Kocienski reaction between **10** and the sulfone **11**<sup>37</sup> gave an *E/Z*-alkene mixture which was hydrogenated to give **12**. This was converted into the sulfone **13**. In the same way the enantiomer of **9** was converted into the enantiomer **14**.



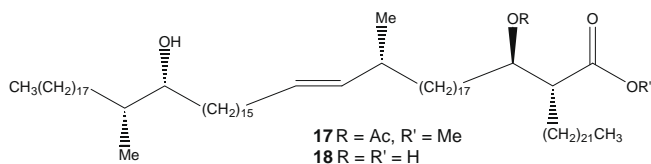
**Scheme 3.** Reagents: (i) TBDMSCl, imidazole, DMF (91%); (ii) PPTS, THF/MeOH (80%); (iii) PCC, CH<sub>2</sub>Cl<sub>2</sub> (94%); (iv) LiHMDS, THF (76%); (v) H<sub>2</sub>, Pd/C, THF/IMS (70%); (vi) LiAlH<sub>4</sub>·THF (90%); (vii) N-bromosuccinimide, PPh<sub>3</sub>, CH<sub>2</sub>Cl<sub>2</sub> (81%); (viii) 1-phenyl-1H-tetrazole-5-thiol, K<sub>2</sub>CO<sub>3</sub>, acetone (99%); (ix) H<sub>2</sub>O<sub>2</sub>, (NH<sub>4</sub>)<sub>6</sub>Mo<sub>7</sub>O<sub>24</sub>·4H<sub>2</sub>O, THF/IMS (85%).



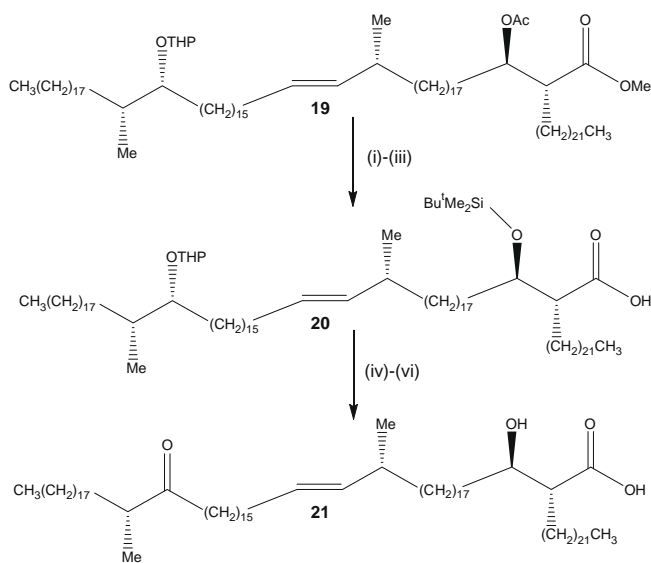
**Scheme 4.** Reagents: (i) KHMDS, 1,2-dimethoxyethane (44%); (ii) HF-pyridine, THF [**16** (R = Ac, R' = Me), 91%]; (iii) LiOH, MeOH, THF, H<sub>2</sub>O [**16** (R = H, R' = H), 65%].

The modified Julia–Kocienski reaction using a 1-phenyl-1*H*-tetrazole sulfone and an aldehyde with potassium bis (trimethylsilyl)amide in 1,2-dimethoxyethane is known to lead to an *E*-alkene with good stereoselectivity, especially if the sulfone or aldehyde is  $\alpha$ -substituted.<sup>38–40</sup> Reaction of the sulfone **13** with aldehyde **8** gave the *trans*-alkene **15** (Scheme 4). It is also clearly essential that no epimerization occurs adjacent to the aldehyde during this process. There is considerable precedent for the retention of the chirality.<sup>39,41–44</sup> Removal of the silyl group gave **16** (R = Ac, R' = Me) and hydrolysis of the two esters produced the free hydroxy-acid **16** (R = H, R' = H).<sup>45</sup> The  $[\alpha]_D^{21}$  of this,  $-2.07$  (CHCl<sub>3</sub>, 0.743  $\mu$ mol), corresponding to  $M_D -26$ , is in agreement with that reported for the hydroxymycolates of *M. smegmatis* ( $M_D -16$ , though it must be noted that these only contain 30% *trans*-alkene).<sup>9</sup>

In the same way the enantiomer **14** was converted into **17** and free hydroxy-MA **18** (Fig. 2).<sup>46</sup> The <sup>1</sup>H NMR spectra of each of these in the alkene region were identical to those reported in the litera-



**Figure 2.**



**Scheme 5.** Reagents: (i) LiOH, MeOH, H<sub>2</sub>O, THF (72%); (ii) TBDMSCl, imidazole, DMF; (iii) K<sub>2</sub>CO<sub>3</sub>, MeOH/H<sub>2</sub>O, then KHSO<sub>4</sub>, (70%); (iv) PPTS, MeOH, H<sub>2</sub>O, THF (73%); (v) PCC (89%); (vi) HF-pyridine (44%).

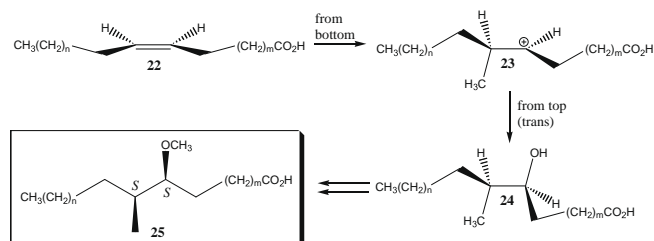
ture,<sup>10,14</sup> and to minor signals in fractions of  $\alpha$ -mycolates derived from *M. tuberculosis*.<sup>46</sup>

Oxidation of either **16** (R = Ac, R' = Me) or **17** gave the corresponding protected keto-MAs.<sup>47</sup> However, attempted deprotection of these using LiOH led to epimerization at the position adjacent to the ketone. In order to avoid this, the alcohol **17** was first protected as THP-ether **19**, followed by hydrolysis of the esters and then reprotection at the alcohol group as a silyl ether **20**. Removal of the THP-group, oxidation, and then deprotection now proceeded without epimerization,<sup>48</sup> leading to the free acid **21** (Scheme 5), matching the major *trans*-alkene ketomycolate reported for *M. marinum*.<sup>49</sup>

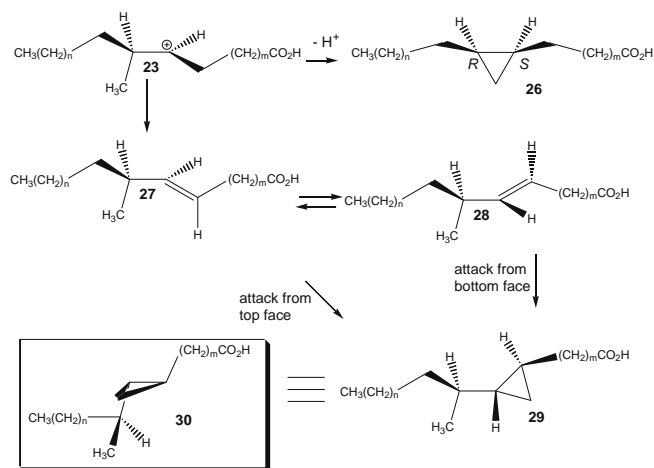
These results provide the first synthetic approaches to both keto and hydroxy-MAs containing a proximal (*R*)- $\alpha$ -methyl-*trans*-alkene unit, and a comparison of molecular rotations with those in the literature confirmed the stereochemistry of this subunit. It has been proposed that alkylation of a *cis*-alkene by SAM (S-adenosylmethionine) provides a common intermediate cation leading to each of the other MA functionalities.<sup>50</sup> Although the actual mechanism may well be different, this does provide a model by which to analyse the stereochemistry of the various classes of MA. It is known that the stereochemistry at the distal groups in methoxy-MA is (*S,S*);<sup>7,11</sup> using **22** as a model for a MA precursor, formal addition of a methyl cation to the distal carbon of the alkene from the bottom face would produce cation **23**; trapping could lead to **24** and hence to the (*S,S*)-molecule **25** (Scheme 6).

If the same species were involved at the proximal position, this would be consistent with the stereochemistry proposed for the proximal  $\alpha$ -methyl-*trans*-cyclopropane unit **30** (Scheme 7).<sup>28</sup>

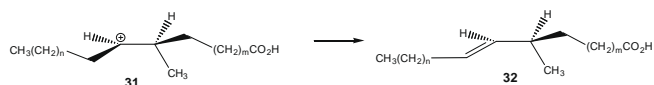
In applying this to the stereochemistry of *trans*-alkene mycolates, one possibility is that alkylation again occurs from the bottom face, this time to the proximal carbon of the alkene, leading



**Scheme 6.**



**Scheme 7.**



Scheme 8.

formally to **31**; elimination of a proton would then lead to the (*R*)- $\alpha$ -methylalkene **32** (Scheme 8).

The *trans*-MA content of the cell wall is linked to its permeability and growth *in vitro*.<sup>18</sup> The keto- and hydroxy-MAs described above are currently being tested to determine whether or not they show specific effects in a range of appropriate biological screens.

## References and notes

- For a review see: Barry, C. E.; Lee, R. E.; Mduli, K.; Sampson, A. E.; Schroeder, B. G.; Slayden, R. A.; Yuan, Y. *Prog. Lipid Res.* **1998**, *37*, 143–179.
- Ojha, A. K.; Baughn, A. D.; Sambandan, D.; Hsu, T.; Trivelli, X.; Guerardel, Y.; Alahari, A.; Kremer, L.; Jacobs, W. R.; Hatfull, G. F. *Mol. Microbiol.* **2008**, *69*, 164–174.
- Watanabe, M.; Aoyagi, Y.; Mitome, H.; Fujita, T.; Naoki, H.; Ridell, M.; Minnikin, D. E. *Microbiology* **2002**, *148*, 1881–1902.
- Watanabe, M.; Aoyagi, Y.; Ridell, M.; Minnikin, D. E. *Microbiology* **2001**, *147*, 1825–1837.
- For example, see: Glickman, M. S.; Cox, J. S.; Jacobs, W. R. *Mol. Cell* **2000**, *5*, 717–727.
- Rao, V.; Gao, F.; Chen, B.; Jacobs, W. R.; Glickman, M. S. *J. Clin. Invest.* **2006**, *116*, 1660–1667.
- Asselineau, C.; Tocanne, G.; Tocanne, J. F. *Bull. Soc. Chim. Fr.* **1970**, 1455–1459.
- Lanéelle, M.-A.; Lacave, C.; Daffé, M.; Lanéelle, G. *Eur. J. Biochem.* **1988**, *177*, 631–635.
- Quémard, A.; Lanéelle, M.-A.; Marrakchi, H.; Promé, D.; Daffé, M. *Eur. J. Biochem.* **1997**, *250*, 758–763.
- Yuan, Y.; Barry, C. E. *Proc. Natl. Acad. Sci. U.S.A.* **1996**, *93*, 12828–12833.
- Dubnau, E.; Lanéelle, M.-A.; Soares, S.; Bénichou, A.; Vaz, T.; Promé, D.; Promé, J.-C.; Daffé, M.; Quémard, A. *Mol. Microbiol.* **1997**, *23*, 313–322.
- Yuan, Y.; Mead, D.; Schroeder, B. G.; Zhu, Y. Q.; Barry, C. E. *J. Biol. Chem.* **1998**, *273*, 21282–21290.
- Takayama, K.; Wang, C.; Besra, G. S. *Clin. Microbiol. Rev.* **2005**, *18*, 81–101.
- George, K. M.; Yuan, Y.; Sherman, D. R.; Barry, C. E. *J. Biol. Chem.* **1995**, *270*, 27292–27298.
- Mikusova, K.; Mikus, M.; Besra, G. S.; Hancock, I.; Brennan, P. J. *J. Biol. Chem.* **1996**, *271*, 7820–7828.
- Glickman, M. S.; Cahill, S. M.; Jacobs, W. R. *J. Biol. Chem.* **2001**, *276*, 2228–2233.
- Asselineau, C.; Asselineau, J.; Lanéelle, G.; Lanéelle, M.-A. *Prog. Lipid Res.* **2002**, *41*, 501–523.
- Schroeder, B. G.; Barry, C. E. *Bioorg. Chem.* **2001**, *29*, 164–177.
- Minnikin, D. E.; Minnikin, S. M.; Goodfellow, M.; Stanford, J. L. *J. Gen. Microbiol.* **1982**, *128*, 817–822.
- Lacave, C.; Lanéelle, M.-A.; Daffé, M.; Montrozier, H.; Rols, M.-P. *Eur. J. Biochem.* **1987**, *163*, 369–378.
- Etemadi, A. H. *Bull. Soc. Chim. Fr.* **1967**, 195–199.
- Wong, M. Y. H.; Gray, G. R. *J. Biol. Chem.* **1979**, *254*, 5741–5744.
- Danielson, S. J.; Gray, G. R. *J. Biol. Chem.* **1982**, *257*, 12196–12203.
- Etemadi, A. H. *Bull. Soc. Chim. Fr.* **1964**, 868–870.
- Kusamram, K.; Polgar, N.; Minnikin, D. E. *J. Chem. Soc., Chem. Commun.* **1972**, 111.
- Markovits, J.; Pinte, F.; Etemadi, A. H. *Compt. Rend. Hebd. Acad. Sci. Ser. C* **1966**, *263*, 960.
- Al Dulayymi, J. R.; Baird, M. S.; Roberts, E. *Tetrahedron* **2005**, *61*, 11939–11951.
- Al Dulayymi, J. R.; Baird, M. S.; Roberts, E.; Deysel, M.; Verschoor, J. *Tetrahedron* **2007**, *63*, 2571–2592.
- Al Dulayymi, J. R.; Baird, M. S.; Roberts, E.; Minnikin, D. E. *Tetrahedron* **2006**, *62*, 11867–11880.
- Koza, G.; Baird, M. S. *Tetrahedron Lett.* **2007**, *48*, 2165–2169.
- Baird, M. S.; Al-Dulayymi, J. R.; Mohammed, H.; Roberts, E.; Clegg, W. *Tetrahedron* **2006**, *62*, 4851–4862.
- Nilsson, K.; Ullenius, C. *Tetrahedron* **1994**, *50*, 13173–13180.
- Leonard, J.; Mohialdin, S.; Reed, D.; Ryan, G.; Swain, P. A. *Tetrahedron* **1995**, *51*, 12843–12858.
- Munakata, R.; Ueki, T.; Katakai, H.; Tako, K.-i.; Tadano, K.-i. *Org. Lett.* **2001**, *3*, 3029–3032.
- (a) Baudin, J. B.; Hareau, G.; Julia, S. A.; Ruel, O. *Tetrahedron Lett.* **1991**, *32*, 1175–1178; (b) Blakemore, J. R.; Kocienski, P. J.; Marzcek, S.; Wicha, J. *Synthesis* **1999**, 1209–1215; (c) Smith, N. D.; Kocienski, P. J.; Street, S. D. A. *Synthesis* **1996**, 652–666.
- Frick, J. A.; Klassen, J. B.; Bathe, A.; Abramson, J. M.; Rappoport, H. *Synthesis* **1992**, 621–623.
- This was obtained from 9-bromononanol by protection of the alcohol with trimethylacetyl chloride, Et<sub>3</sub>N, CH<sub>2</sub>Cl<sub>2</sub> (85%), then reaction with 1-phenyl-1*H*-tetrazole-5-thiol, K<sub>2</sub>CO<sub>3</sub>, acetone (91%), followed by oxidation of the derived sulfone [H<sub>2</sub>O<sub>2</sub>, (NH<sub>4</sub>)<sub>6</sub>Mo<sub>7</sub>O<sub>24</sub>·4H<sub>2</sub>O, THF/IMS (97%)].
- Blackemore, P. R.; Coke, W. J.; Kocienski, P. J.; Morley, A. *Synlett* **1998**, *1*, 26–28.
- Brandl, T.; Hoffmann, R. W. *Eur. J. Org. Chem.* **2004**, 4373–4378.
- Pospisil, J.; Marko, I. E. *Org. Lett.* **2006**, *8*, 5983–5986.
- Takano, D.; Nagamitsu, T.; Ui, H.; Shiomu, K.; Yamaguchi, Y.; Masuma, R.; Kuwajima, I.; Omura, S. *Org. Lett.* **2001**, *3*, 2289–2291.
- Lautens, M.; Colucci, J. T.; Hiebert, S.; Smith, N. D.; Bouchain, G. *Org. Lett.* **2002**, *4*, 1879–1882.
- Pollex, A.; Abraham, L.; Muller, J.; Hiersemann, M. *Tetrahedron Lett.* **2004**, *45*, 6915–6918.
- Kao, C.-L.; Bonsova, S. A.; Kim, H. J.; Liu, H.-w. *J. Am. Chem. Soc.* **2006**, *128*, 5600–5607.
- Compound **16** (R = R' = H):  $\delta_{\text{H}}$  (500 MHz, CDCl<sub>3</sub>): 5.33 (1H, dt, *J* 6.6, 15.45 Hz), 5.23 (1H, dd, *J* 7.55, 15.45 Hz), 3.70–3.69 (1H, m), 3.52–3.51 (1H, m), 2.45 (1H, br pent, *J* 4.7 Hz), 2.05–2.00 (1H, m), 1.97 (2H, q, *J* 6.9 Hz), 1.79–1.71 (1H, m), 1.66–1.59 (2H, m), 1.64–1.23 (139H, br m, including br s at 1.26), 0.94 (3H, d, *J* 6.6 Hz), 0.89 (6H, t, *J* 6.95 Hz), 0.86 (3H, d, *J* 7.25 Hz);  $\delta_{\text{C}}$ : 177.3, 136.5, 128.5, 75.4, 72.2, 50.5, 37.3, 36.7, 34.4, 33.4, 32.6, 31.9, 30.0, 29.7, 29.6, 29.52, 29.46, 29.4, 29.1, 27.4, 22.7, 21.0, 16.6, 14.1;  $\nu_{\text{max}}$ : 3534, 2922, 2854, 1751, 1466 cm<sup>-1</sup> [found M+Na<sup>+</sup>: 1234.39; C<sub>82</sub>H<sub>162</sub>NaO<sub>4</sub> requires: 1234.24];  $[\alpha]_{\text{D}}^{21}$  –2.07 (CHCl<sub>3</sub>, 0.743  $\mu\text{mol}$ ).
- Compound **18** showed  $[\alpha]_{\text{D}}^{20}$  +1.67 (CHCl<sub>3</sub>, 1.287  $\mu\text{mol}$ ); [Found M+Na<sup>+</sup>: 1234.18; C<sub>82</sub>H<sub>162</sub>NaO<sub>4</sub> requires: 1234.24].
- The protected ketone derived by PCC oxidation of **17** showed  $\delta_{\text{H}}$  (500 MHz, CDCl<sub>3</sub>): 5.33 (1H, dt, *J* 6.6, 15.1 Hz), 5.24 (1H, dd, *J* 7.25, 15.1 Hz), 5.09 (1H, dt, *J* 4.1, 8.15 Hz), 3.68 (3H, s), 2.62 (1H, ddd, *J* 4.45, 6.95, 11.05 Hz), 2.50 (1H, sext, *J* 6.95 Hz), 2.41 (2H, dt, *J* 2.25, 7.25 Hz), 2.03 (3H, s), 1.97 (2H, q, *J* 6.6 Hz), 1.63–1.18 (137H, m, including s at 1.26), 1.05 (3H, d, *J* 6.6 Hz), 0.94 (3H, d, *J* 6.6 Hz), 0.89 (6H, t, *J* 6.95 Hz);  $\delta_{\text{C}}$ : 215.2, 173.7, 170.3, 128.4, 74.1, 51.5, 49.6, 46.3, 41.2, 37.3, 36.7, 33.1, 32.6, 31.9, 31.7, 29.8, 29.7, 29.64, 29.59, 29.54, 29.51, 29.48, 29.43, 29.39, 29.3, 29.2, 28.1, 27.5, 27.4, 27.3, 25.0, 23.7, 22.7, 21.0, 16.4, 14.1;  $\nu_{\text{max}}$ : 2932, 2853, 1748, 1711, 1466 cm<sup>-1</sup>;  $[\alpha]_{\text{D}}^{22}$  +3.52 (CHCl<sub>3</sub>, 1.094  $\mu\text{mol}$ ); [found M+Na<sup>+</sup>: 1288.22; C<sub>85</sub>H<sub>164</sub>NaO<sub>5</sub> requires: 1288.25]. That from **16** (R = Ac, R' = Me),  $[\alpha]_{\text{D}}^{23}$  –2.39 (CHCl<sub>3</sub>, 0.55  $\mu\text{mol}$ ), showed essentially identical NMR spectra.
- Koza, G.; Al Dulayymi, J. R.; Theunissen, C.; Baird, M. S. *Tetrahedron* **2009**, *10214*–10229.
- The ketone **21** showed  $\delta_{\text{H}}$  (500 MHz, CDCl<sub>3</sub>): 5.32 (1H, td, *J* 6.65, 15.45 Hz), 5.24 (1H, dd, *J* 7.55, 15.45 Hz), 2.50 (1H, pent, *J* 6.6 Hz), 2.47 (1H, m), 2.42 (2H, dt, *J* 1.55, 6.95 Hz), 2.36 (1H, t, *J* 7.55 Hz), 1.97 (2H, q, *J* 6.95 Hz), 1.65–1.17 (139H, br m, including br s at 1.26), 1.05 (3H, d, *J* 6.95 Hz), 0.95 (3H, d, *J* 6.95 Hz), 0.89 (6H, t, *J* 6.65 Hz);  $\delta_{\text{C}}$ : 215.5, 177.9, 136.5, 128.4, 72.2, 50.6, 46.4, 41.2, 37.3, 36.7, 35.6, 33.1, 32.6, 31.9, 29.8, 29.7, 29.64, 29.59, 29.54, 29.51, 29.48, 29.43, 29.39, 29.3, 29.1, 28.9, 27.4, 27.3, 25.7, 23.7, 22.6, 21.0, 19.4, 16.4, 14.1;  $\nu_{\text{max}}$ : 3420, 3019, 2926, 2855, 1521, 1420, 1215 cm<sup>-1</sup>;  $[\alpha]_{\text{D}}^{23}$  +2.90 (CHCl<sub>3</sub>, 0.471  $\mu\text{mol}$ ); [found M+Na<sup>+</sup>: 1232.36; C<sub>82</sub>H<sub>160</sub>NaO<sub>4</sub> requires: 1232.22].
- Yuan, Y.; Crane, D. C.; Musser, J. M.; Sreevatsan, S.; Barry, C. E. *J. Biol. Chem.* **1997**, *272*, 10041–10049.