Use of the Composite Material $RuO_2/BaTi_4O_9$ as an Environmentally Benign Solid Catalyst for the Oxidative Cleavage of Olefins

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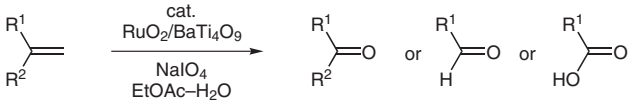
Abstract: Catalytic use of a composite material, $RuO_2/BaTi_4O_9$, in combination with $NaIO_4$ in EtOAc–H_2O has been shown to efficiently cleave alkenes, affording ketones, aldehydes and/or carboxylic acids in high yields.

Key words: ruthenium, green chemistry, oxidation, cleavage, heterogeneous catalysis

Cleavage of carbon–carbon double bonds is a fundamental reaction utilized to generate carbonyl functional groups such as with ketones, aldehydes and carboxylic acids. Besides ozonolysis, metal-catalyzed oxidation plays a principal role particularly in delicate synthetic manipulations.[1] Although various metals have been used,[2] ruthenium offers several advantages given its reasonable cost, low toxicity and controllable reactivity.[3] On the other hand, use of heterogeneous catalytic systems offers advantages from an environmental aspect since the solid can be readily separated, recovered and recycled.[3] Although use of immobilized Ru reagents has achieved promising results,[4] most of the immobilized Ru oxidants have been employed in the oxidation of alcohols,[5] and not in the cleavage of double bonds.

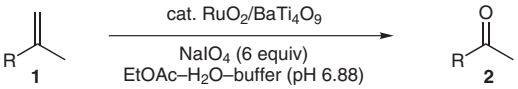
Our interests concern the development of an operationally benign catalyst for the cleavage of carbon–carbon double bonds in the context of the synthesis of bioactive compounds derived from sugars.[6] A report[7] detailing the preparation of ceramics utilizing $RuO_2/BaTi_4O_9$ prompted us to examine its potential use as a heterogeneous oxidizing agent of alkenes (Scheme 1).

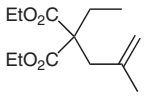
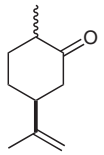
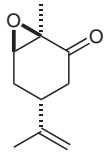
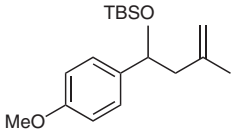
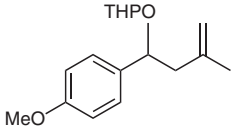
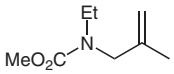
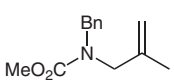
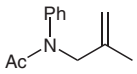


Scheme 1

Following the preparation of ceramics with variable Ru content, 1%, 3% and 5%, we initially investigated oxidative capacity in combination with typical co-oxidants. On the basis of these preliminary experiments, $NaIO_4$ was selected as a reoxidant based on yield, catalyst turnover and reaction time. The two reagents comprising 3% and 5% Ru did not show any distinct differences. Use of the 3% reagent in lieu of the 1% reagent often improved the yield and reaction time, especially for highly substituted olefins. Use of 1% $RuO_2/BaTi_4O_9$ (10 mg) was sufficient to consume 1 mmol of the substrate. The turnover of Ru exceeded 1000, being markedly superior to the conventional procedure.[8] Previous methods were usually performed using 3–5 mol% of $RuCl_3$ or RuO_2 since some deterioration of activity is unavoidable.[3,8]

Table 1 Oxidation of alkylidene group



Alkene **1**		Cat. (% Ru)	Yield (%)
1a		3 1	89 78
1b		3 1	84 79
1c		3	81
1d		3	71
1e		3	73
1f		3	80
1g		3	93
1h		3	88

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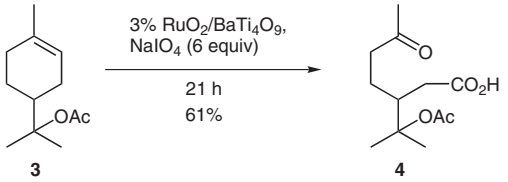
The cleavage of 1,1-disubstituted alkenes **1** giving rise to ketones **2** is summarized in Table 1. Treatment of **1** in an aqueous medium resulted in formation of the expected methyl ketones **2** in satisfactory yields. The oxidation could be performed under very mild conditions without any special techniques. When a buffer solution was added, the acid-labile functional groups such as epoxide, TBS and THP were tolerated under the reaction conditions. Compounds containing nitrogen atoms have been reported to undergo Ru-mediated oxidation.[3] Aniline and benzylamine moieties are known to be particularly reactive. However, the present ceramic-catalyzed method worked efficiently in the cleavage of double bonds to produce aminoketone compounds **2f**, **2g** and **2h** in excellent yields.

The activity of the prepared ceramic reagents towards double bond cleavage was mild compared with the conventional $RuO_2/NaIO_4$ method.[8] Although reaction with the 3-substituted olefin **3** produced the corresponding ketocarboxylic acid **4** in 61% yield after 21 hours (Scheme 2), the oxidation of tetrasubstituted olefin did not proceed to any appreciable extent.



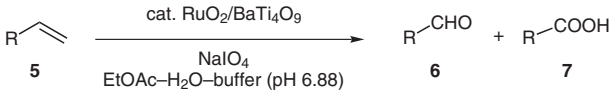
Scheme 2 Oxidation of terpinyl acetate

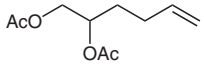
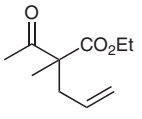
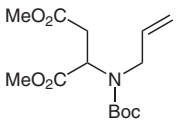
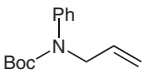
Subsequent investigations dealt with the oxidative cleavage of terminal olefins **5** affording aldehydes **6** and/or carboxylic acids **7**. The results are shown in Table 2.

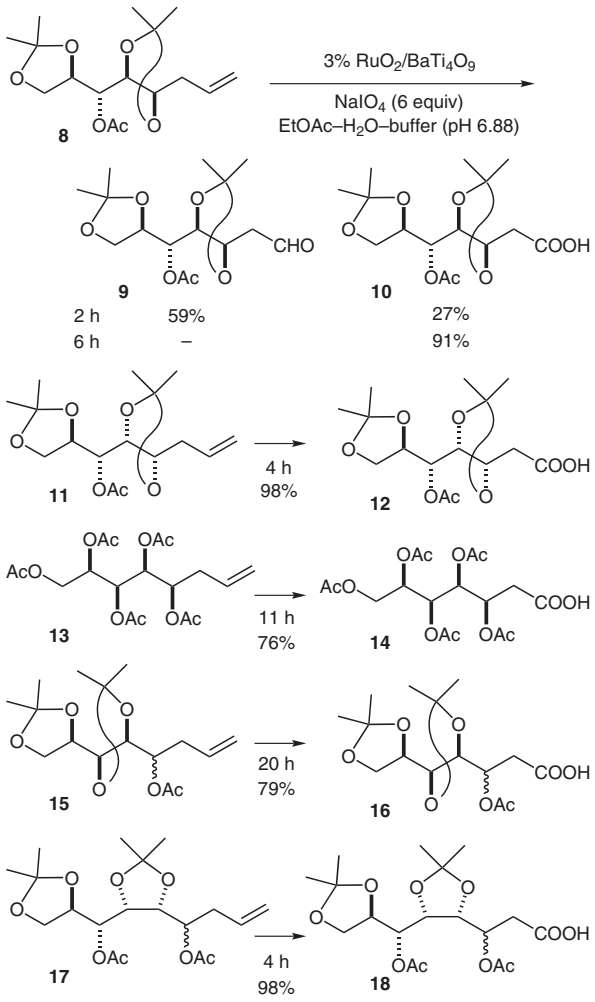
The monosubstituted olefins **5** could readily be cleaved to give the appropriate products depending on the conditions employed. Predominant formation of the aldehydes **6** was achieved as depicted for **5a** and **5b**, while the selectivity decreased in the case of nitrogen-containing compounds **5c** and **5d**. Although Ru-mediated reactions have been developed that control the oxidation state of the olefin,[9] preventing oxidation at intermediary stages in the RuO_2/RuO_4 redox system remains problematic.[8] The common Ru oxidant is powerful enough to convert the aldehydes **6** into the final carboxylic acids **7**. The choice of Ru content with respect to $BaTi_4O_9$ was important in the selective production of the aldehydes **6** and the carboxylic acids **7**. In a similar manner to the results illustrated in Table 1, reactions with phenyl ether **5e** and the nitrogen-containing compounds **5c** and **5d** led to formation of 2-phenoxycarboxylic acid **7e** and amino acid derivatives **7c** and **7d**, respectively, notwithstanding the possibility of Ru-mediated oxidation.[1,3,8]

The oxidation process was then utilized with various sugar derivatives.[10] The oxidation proceeded cleanly and stepwise to afford the aldehyde followed by the corresponding carboxylic acid (Scheme 3). It was possible to isolate the aldehyde in moderate yield by careful monitoring of the reaction using TLC. For example, oxidation of **8** could be interrupted at two hours to afford the aldehyde **9** in 59% yield together with the carboxylic acid **10** in 27% yield. In this case, strict control leading to exclusive formation of the aldehyde **9** was not achieved even when 1% $RuO_2/BaTi_4O_9$ was used. When the reaction was continued for six hours, the carboxylic acid **10** was generated in 91% yield as the only product. A similar sugar derivative **11** prepared from D-arabinose underwent smooth oxidation, and quantitative production of the acid **12** was achieved in four hours. The other products **14**, **16** and **18** contain an acetylated aldol moiety, which is considerably labile to both acid- and base-driven elimination. Our pro-

Table 2 Cleavage of terminal olefins



Alkene **5**		Cat. (% Ru)	$NaIO_4$ (equiv)	Time (h)	Yield (%) of **6**	Yield (%) of **7**
5a		1	4	21	98	–
		3	6	21	–	87
5b		1	4	24	98	–
		3	4	24	12	87
5c		1	4	12	64	8
		3	6	3	–	95
5d		1	4	29	47	33
		3	6	21	–	90
5e		3	6	72	–	78



Scheme 3 Oxidative cleavage of sugar derivatives

tocol was shown to be effective in the presence of this sensitive array of functional groups.[11]

Further experiments investigating the possibility of reusing the ceramics were performed with the alkene **5a** using 1% $RuO_2/BaTi_4O_9$ and $NaIO_4$ (4 equiv). After most of the starting material **5a** was consumed, the solid reagent was removed by filtration and utilized again in another round of catalysis. This process was repeated twice. The aldehyde **6a** was isolated from each filtrate by the usual procedure. The yields in the second and third rounds of catalysis decreased slightly to ca. 75%, with the reaction taking longer to complete. An alternative strategy was also employed as follows. When the first round of catalysis was completed, the stirring was stopped and the supernatant was removed by decantation to isolate the product. To the remaining aqueous phase containing inorganic materials was added the requisite amount of $NaIO_4$ followed by an organic solution of the olefin **5a**. The second round of catalysis also generated the aldehyde **6a** in ca. 75% yield. These results indicate that although the reagent deteriorated somewhat, it remained active and could be reused without the use of any extraneous procedures.

In conclusion, the composite material $RuO_2/BaTi_4O_9$ was shown to act as an efficient and reusable oxidant.[12] Further experiments are in progress in an effort to develop protocols under a variety of oxidation conditions that reflect environmentally friendly conditions such as the use of oxygen in lieu of $NaIO_4$, and avoiding the use of chemical reoxidants.

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(1) Backvall, J.-E. *Modern Oxidation Methods*; Wiley-VCH: Weinheim, **2004**.

(2) For recent works describing transition-metal-mediated cleavage with Os reagent, see: (a) Ley, S. V.; Ramarao, C.; Lee, A.; Ostergaard, N.; Smith, S. C.; Shirley, I. M. *Org. Lett.* **2003**, *5*, 185. (b) Travis, B. R.; Narayan, R. S.; Borhan, B. *J. Am. Chem. Soc.* **2002**, *124*, 3824. (c) With AuCl reagent, see: Xing, D.; Guan, B.; Cai, G.; Fang, Z.; Yang, L.; Shi, Z. *Org. Lett.* **2006**, *8*, 693.

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(4) For recent typical examples, see: (a) Kim, W.; Park, I.; Park, J. *Org. Lett.* **2006**, *8*, 2543. (b) Zhan, B.; White, M. A.; Sham, T.; Pincock, J. A.; Doucet, R.; Rao, K. V. R.; Robertson, K. N.; Cameron, T. S. *J. Am. Chem. Soc.* **2003**, *125*, 2195. (c) Cheung, W.; Yu, W.; Yip, W.; Zhu, N.; Che, C. *J. Org. Chem.* **2002**, *67*, 7716. (d) Yamaguchi, K.; Mori, K.; Mizugaki, T.; Ebitani, K.; Kaneda, K. *J. Am. Chem. Soc.* **2000**, *122*, 7144; and references cited therein.

(5) For an excellent work detailing control of the oxidation stage with immobilized Ru species, see: Ho, C.; Yu, W.; Che, C. *Angew. Chem. Int. Ed.* **2004**, *43*, 3303.

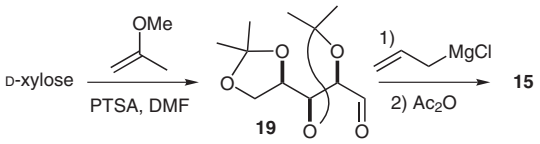
(6) (a) Okumoto, H.; Katto, H. *Synlett* **2003**, 1521. (b) Fukusaki, F.; Takeno, S.; Takeshi Bamba, T.; Okumoto, H.; Katto, H.; Kajiyama, S.; Kobayashi, A. *Biosci., Biotechnol., Biochem.* **2004**, *68*, 1988.

(7) Tada, M.; Yamashita, Y.; Petrykin, V.; Osada, M.; Yoshida, K.; Kakihana, M. *Chem. Mater.* **2002**, *14*, 2845.

(8) Carlsen, P. H. J.; Katsuki, T.; Martin, V. S.; Sharpless, K. B. *J. Org. Chem.* **1981**, *46*, 3936.

(9) For oxidation using $RuCl_3$ leading to aldehyde, see: (a) Yang, D.; Zhang, C. *J. Org. Chem.* **2001**, *66*, 4814. For oxidation using $RuCl_3$ leading to diol, see: (b) Tiwari, P.; Misra, A. K. *J. Org. Chem.* **2006**, *71*, 2911. (c) Plietker, B.; Niggemann, M. *J. Org. Chem.* **2005**, *70*, 2402. (d) Plietker, B.; Niggemann, M. *Org. Lett.* **2003**, *5*, 3353. (e) For oxidation using $RuCl_3$ leading to acyloin, see: Plietker, B. *J. Org. Chem.* **2004**, *69*, 8287.

(10) The sugar derivatives **8**, **11** and **13** were prepared from D-ribose, D-arabinose and D-xylose, respectively, according to the literature, followed by usual acetylation: (a) Shing, T. K. M.; Wong, W. F.; Ikeno, T.; Yamada, T. *Org. Lett.* **2007**, *9*, 207. (b) Lievens, S. C.; Molinski, T. F. *J. Am. Chem. Soc.* **2006**, *128*, 11764. (c) Prenner, R. H.; Binder, W. H.; Schmid, W. *Liebigs Ann. Chem.* **1994**, 73. (d) The acetate **15** was synthesized by reaction of the aldehyde **19** and allyl Grignard reagent, followed by acetylation as illustrated in



Scheme 4

Scheme 4. For preparation of the intermediate aldehyde **19**, see ref. 10a and: Calinaud, P.; Gelas, J. In *Preparative Carbohydrate Chemistry*; Hanessian, S., Ed.; Marcel Dekker: New York, **1996**, p15. (e) The diacetonide **17** is readily accessible from D-mannose: Shing, T. K. M.; Wong, W. F.; Cheng, H. M.; Kwok, W. S.; So, K. H. *Org. Lett.* **2007**, *9*, 753.

(11) **General Experimental Procedure**: To a solution of olefin (0.5 mmol) in EtOAc (3 mL), H_2O (5 mL) and phosphate buffer (pH 6.88, 1 mL) were added 3% $RuO_2/BaTi_4O_9$ (10 mg) and then $NaIO_4$ (3 mmol) at r.t. The reaction mixture was stirred for the indicated times. Solids were filtered and washed with H_2O. Filtrates were extracted with EtOAc and the organic layer was dried and concentrated. The residue was then chromatographed on silica gel to give the product.

(12) **2a**: ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.85 (t, *J* = 7.6 Hz, 3 H), 1.25 (t, *J* = 7.2 Hz, 6 H), 2.05 (q, *J* = 7.6 Hz, 2 H), 2.17 (s, 3 H), 3.10 (s, 2 H), 4.19 (q, *J* = 7.0 Hz, 4 H). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 8.8, 13.7, 26.2, 30.0, 45.2, 55.6, 61.1, 170.5, 204.9.
2b: a mixture of separable diastereomers in a ratio of ca. 4:1. Major product: ^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.04 (d, *J* = 6.4 Hz, 3 H), 1.43 (ddd, *J* = 3.3, 13.1, 26.3 Hz, 1 H), 1.73 (ddd, *J* = 3.4, 13.1, 25.6 Hz, 1 H), 2.19 (s, 3 H), 2.08–2.25 (m, 2 H), 2.35–2.45 (m, 1 H), 2.45–2.52 (m, 2 H), 2.77–2.86 (m, 1 H). ^{13}C NMR (126 MHz, $CDCl_3$): δ = 14.2, 27.7, 28.2, 34.5, 42.6, 44.5, 52.1, 208.1, 211.4. Minor product: ^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.09 (d, *J* = 7.0 Hz, 3 H), 1.50–1.58 (m, 1 H), 1.91–2.10 (m, 3 H), 2.18 (s, 3 H), 2.30–2.42 (m, 2 H), 2.65 (ddd, *J* = 1.2, 6.1, 15.0 Hz, 1 H), 3.06–3.12 (m, 1 H). ^{13}C NMR (126 MHz, $CDCl_3$): δ = 15.2, 24.8, 28.1, 30.9, 40.5, 44.2, 50.1, 209.2, 211.3.
2c: ^{1}H NMR (500 MHz $CDCl_3$): δ = 1.42 (s, 3 H), 2.00 (ddd, *J* = 1.2, 11.0, 14.9 Hz, 1 H), 2.19 (s, 3 H), 2.25 (dd, *J* = 11.0, 18.0 Hz, 1 H), 2.51 (dt, *J* = 3.0, 14.9 Hz, 1 H), 2.63 (ddd, *J* = 1.2, 4.9, 18.0 Hz, 1 H), 3.10–3.18 (m, 1 H), 3.48 (dd, *J* = 0.9, 3.0 Hz, 1 H). ^{13}C NMR (126 MHz, $CDCl_3$): δ = 15.1, 25.8, 28.2, 37.5, 41.8, 59.0, 60.6, 203.8, 208.2.
2d: ^{1}H NMR (500 MHz, $CDCl_3$): δ = –0.29 (s, 3 H), –0.10 (s, 3 H), 0.73 (s, 9 H), 2.03 (s, 3 H), 2.42 (dd, *J* = 4.3, 14.6 Hz, 1 H), 2.81 (dd, *J* = 8.8, 14.6 Hz, 1 H), 3.68 (s, 3 H), 5.00 (dd, *J* = 4.3, 8.8 Hz, 1 H), 6.74 (d, *J* = 8.3 Hz, 2 H), 7.14 (d, *J* = 8.3 Hz, 2 H). ^{13}C NMR (126 MHz, $CDCl_3$): δ = –5.3, –4.7, 18.0, 25.7, 31.8, 54.4, 55.2, 71.6, 113.6, 126.9, 136.6, 158.8, 207.3.
2e: ^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.40–1.80 (m, 6 H), 2.12, 2.20 (s, 3 H), 2.60–2.70 (m, 1 H), 3.00–3.10 (m, 1 H), 3.20–3.30 (m, 0.5 H), 3.40–3.60 (m, 1 H), 3.78 (s, 3 H), 3.70–3.90 (m, 0.5 H), 4.39, 4.84 (t, *J* = 3.3 Hz, 1 H), 5.01 (dd, *J* = 4.6, 8.5 Hz, 0.5 H), 5.14 (dd, *J* = 4.9, 8.9 Hz, 0.5 H), 6.80–6.90 (m, 2 H), 7.25–7.35 (m, 2 H). ^{13}C NMR (126 MHz, $CDCl_3$): δ = 19.1, 19.1, 25.2, 30.4, 31.0, 31.0, 51.4, 51.6, 55.0, 55.1, 61.9, 62.0, 72.7, 75.2, 94.5, 98.9, 113.5, 113.8, 127.4, 128.0, 132.7, 134.6, 158.7, 159.2, 206.6.
2f: ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.10 (t, *J* = 7.05 Hz, 3 H), 2.15 (s, 3 H), 3.20–3.45 (m, 2 H), 3.65 (s, 1.5 H), 3.72 (s, 1.5 H), 3.98, 4.04 (s, 2 H). ^{13}C NMR (126 MHz, $CDCl_3$): δ = 12.9, 13.3, 26.5, 26.7, 42.8, 43.4, 52.5, 52.6, 56.3, 56.6, 156.1, 156.8, 204.0, 204.1.
2g: ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.03 (s, 1.5 H), 2.06 (s, 1.5 H), 3.71 (s, 1.5 H), 3.77 (s, 1.5 H), 3.90 (s, 1 H), 3.99 (s, 1 H), 4.52 (s, 1 H), 4.54 (s, 1 H), 7.15–7.40 (m, 5 H). ^{13}C NMR (126 MHz): δ = 26.6, 26.8, 51.0, 51.5, 52.9, 52.9, 55.4, 55.7, 127.4, 127.5, 128.0, 128.5, 128.5, 136.7, 156.8, 157.0, 203.5, 203.6.
2h: ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.90 (s, 1.5 H), 1.92 (s, 1.5 H), 2.15 (s, 1.5 H), 2.16 (s, 1.5 H), 4.43 (s, 1 H), 4.44 (s, 1 H), 7.25–7.50 (m, 5 H). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 21.8, 26.9, 59.1, 127.6, 127.9, 129.6, 143.3, 170.5, 202.3.
4: ^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.35–1.47 (m, 1 H), 1.44 (s, 3 H), 1.53 (s, 3 H), 1.82–1.90 (m, 1 H), 1.95 (s, 3 H), 2.16 (s, 3 H), 2.15–2.23 (m, 1 H), 2.31–2.37 (m, 1 H), 2.48–2.59 (m, 3 H). ^{13}C NMR (126 MHz, $CDCl_3$): δ = 22.2, 22.3, 24.0, 24.3, 30.1, 35.0, 42.0, 43.9, 84.4, 170.3, 179.0, 208.3.
6a: ^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.80–2.02 (m, 2 H), 2.067 (s, 3 H), 2.071 (s, 3 H), 2.54 (t, *J* = 7.1 Hz, 2 H), 4.06 (dd, *J* = 6.1, 11.9 Hz, 1 H), 4.24 (dd, *J* = 3.7, 11.9 Hz, 1 H), 5.05–5.20 (m, 1 H), 9.77 (s, 1 H). ^{13}C NMR (126 MHz, $CDCl_3$): δ = 20.6, 20.8, 23.1, 39.4, 64.6, 70.5, 170.4, 170.6, 200.6.
7a: ^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.90–2.00 (m, 2 H), 2.07 (s, 6 H), 2.43 (dt, *J* = 1.5, 7.6 Hz, 2 H), 4.06 (dd, *J* = 5.9, 11.9 Hz, 1 H), 4.25 (dd, *J* = 3.7, 11.9 Hz, 1 H), 5.09–5.20 (m, 1 H). ^{13}C NMR (126 MHz, $CDCl_3$): δ = 20.7, 20.9, 25.8, 29.7, 64.7, 70.4, 170.6, 170.8, 178.1.
6b: ^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.27 (t, *J* = 7.0 Hz, 3 H), 1.52 (s, 3 H), 2.26 (s, 3 H), 2.90 (d, *J* = 17.7 Hz, 1 H), 3.00 (d, *J* = 17.7 Hz, 1 H), 4.22 (q, *J* = 7.0 Hz, 2 H), 9.71 (s, 1 H). ^{13}C NMR (126 MHz, $CDCl_3$): δ = 13.8, 20.4, 26.0, 39.4, 48.5, 56.9, 61.9, 171.6, 199.1, 204.7.
7b: ^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.27 (t, *J* = 7.0 Hz, 3 H), 1.51 (br s, 3 H), 2.23 (br s, 3 H), 2.92 (br s, 2 H), 4.21 (q, *J* = 7.0 Hz, 2 H), 9.5 (br, 1 H). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 13.8, 39.4, 61.8, 171.6.
6c: ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.42 (s, 4.5 H), 1.45 (s, 4.5 H), 2.85–3.25 (m, 2 H), 3.69 (s, 1.5 H), 3.71 (s, 1.5 H), 3.75 (s, 1.5 H), 3.76 (s, 1.5 H), 3.90–4.25 (m, 2 H), 4.45–4.52 (m, 0.5 H), 4.80–4.90 (m, 0.5 H), 9.56 (m, 0.5 H), 9.58 (s, 0.5 H). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 28.3, 35.5, 52.1, 57.4, 57.5, 58.6, 58.6, 58.7, 58.7, 81.9, 99.2, 157.8, 154.8, 170.7, 170.7, 170.8, 170.8, 171.5, 171.5, 171.6, 171.6, 171.6, 171.9, 199.0.
7c: ^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.43 (s, 4.5 H), 1.44 (s, 4.5 H), 2.90–3.20 (m, 2 H), 3.69 (s, 1.5 H), 3.70 (s, 1.5 H), 3.75 (s, 1.5 H), 3.76 (s, 1.5 H), 3.95–4.11 (m, 1.5 H), 4.32 (d, *J* = 18.4 Hz, 0.5 H), 4.53 (t, *J* = 6.4 Hz, 0.5 H), 4.80 (t, *J* = 6.4 Hz, 0.5 H), 6.35 (br, 1 H). ^{13}C NMR (126 MHz, $CDCl_3$): δ = 27.9, 28.1, 34.9, 35.8, 49.8, 50.4, 52.0, 52.6, 52.9, 57.1, 58.3, 60.4, 82.0, 82.2, 154.3, 170.9, 171.5, 171.7, 171.7, 173.5, 173.7.
6d: ^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.44 (s, 9 H), 4.33 (s, 2 H), 7.20–7.40 (m, 5 H), 9.70 (s, 1 H). ^{13}C NMR (126 MHz): δ = 28.2, 60.1, 81.5, 126.4, 128.9, 142.5, 198.1.
7d: ^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.42 (s, 9 H), 4.30 (s, 2 H), 6.00 (br, 1 H), 7.20–7.40 (m, 5 H). ^{13}C NMR (126 MHz, $CDCl_3$): δ = 28.1, 52.2, 81.3, 126.3, 128.7, 142.5, 154.9, 175.2.
7e: ^{1}H NMR (300 MHz, $CDCl_3$): δ = 4.30–5.00 (br, 1 H), 4.68 (s, 2 H), 6.90–7.40 (m, 5 H). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 64.8, 72.6, 114.7, 122.1, 129.6, 157.4. 174.3.
9: ^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.35 (s, 3 H), 1.40 (s, 9 H), 2.11 (s, 3 H), 2.65–2.82 (m, 2 H), 3.87–3.94 (m, 2 H), 4.05–4.09 (m, 1 H), 4.25–4.30 (m, 1 H), 4.48–4.54 (m, 1 H), 5.16–5.21 (m, 1 H), 9.81 (s, 1 H). ^{13}C NMR (126 MHz, $CDCl_3$): δ = 20.9, 25.3, 26.4, 26.7, 27.1, 47.0, 66.1, 71.7,

72.4, 74.0, 79.5, 109.6, 110.1, 170.0, 199.4.

10: ^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.35 (s, 3 H), 1.40 (s, 9 H), 2.11 (s, 3 H), 2.63 (dd, *J* = 8.5, 16.1 Hz, 1 H), 2.76 (dd, *J* = 3.5, 16.1 Hz, 1 H), 3.88–3.96 (m, 2 H), 4.08 (dd, *J* = 6.4, 8.3 Hz, 1 H), 4.29 (dd, *J* = 6.4, 11.9 Hz, 1 H), 4.45 (dt, *J* = 3.6, 8.3 Hz, 1 H), 5.22 (t, *J* = 5.0 Hz, 1 H), 5.90–6.20 (br, 1 H). ^{13}C NMR (126 MHz, $CDCl_3$): δ = 21.1, 25.5, 26.5, 27.0, 27.3, 38.9, 66.2, 72.0, 74.1, 74.3, 79.5, 109.8, 110.4, 170.3, 175.6.

12: ^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.36 (s, 3 H), 1.40 (s, 6 H), 1.41 (s, 3 H), 2.14 (s, 3 H), 2.58–2.78 (m, 2 H), 3.82–3.92 (m, 1 H), 3.95–4.10 (m, 2 H), 4.10–4.20 (m, 1 H), 4.25–4.33 (m, 1 H), 5.08–5.11 (m, 1 H). ^{13}C NMR (126 MHz, $CDCl_3$): δ = 20.8, 25.3, 26.5, 26.5, 27.3, 37.5, 66.1, 70.2, 72.8, 75.0, 79.3, 109.5, 109.7, 170.4, 174.6.

14: ^{1}H NMR (500 MHz, $CDCl_3$): δ = 2.05 (s, 3 H), 2.102 (s, 3 H), 2.104 (s, 3 H), 2.11 (s, 6 H), 2.63 (dd, *J* = 6.1, 16.8 Hz, 1 H), 2.69 (dd, *J* = 6.1, 16.8 Hz, 1 H), 4.03 (dd, *J* = 6.1, 11.9 Hz, 1 H), 4.27 (dd, *J* = 4.3, 11.9 Hz, 1 H), 5.30–5.45 (m, 4 H). ^{13}C NMR (126 MHz, $CDCl_3$): δ = 20.5, 20.5, 20.6, 20.6, 20.7, 35.0, 61.8, 67.8, 68.9, 69.0, 70.4, 169.8, 170.0, 170.0, 170.2, 170.5, 173.7.

16: 2:1 mixture of diastereomers. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.33, 1.36, 1.37, 1.38 (s, 12 H), 2.03, 2.04 (s, 3 H), 2.60–2.85 (m, 2 H), 3.75–3.93 (m, 2 H), 3.96–4.20 (m, 3 H), 5.25–5.40 (m, 1 H), 6.50 (br, 1 H). ^{13}C NMR (126 MHz, $CDCl_3$): δ = 20.8, 20.9, 25.4, 25.4, 26.0, 26.1, 26.6, 26.9, 27.0, 27.0, 35.4, 35.9, 65.5, 65.6, 67.5, 70.3, 74.6, 75.4, 76.1, 77.5, 77.6, 78.4, 109.8, 109.8, 110.0, 110.5, 170.3, 170.4, 174.8, 175.0.

18: 3:2 mixture of diastereomers. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.35, 1.36, 1.38, 1.44, 1.49, 1.51 (s, 12 H), 2.05, 2.06, 2.09, 2.10, 2.11 (s, 6 H), 2.60–2.90 (m, 2 H), 3.75–4.45 (m, 5 H), 5.00–5.50 (m, 2 H). ^{13}C NMR (126 MHz, $CDCl_3$): δ = 20.8, 20.9, 21.0, 25.1, 25.3, 25.4, 25.6, 26.0, 26.3, 26.3, 36.2, 36.4, 65.9, 67.1, 67.9, 69.3, 69.5, 70.2, 75.3, 75.4, 75.8, 76.5, 76.6, 76.9, 109.0, 109.2, 110.2, 169.9, 170.0, 170.2, 170.4, 174.4, 174.9.