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Preparation of complex bridged bicyclic ring systems from 3,3-diacetoxy-2-phenylsulfonylpropene and β-keto esters

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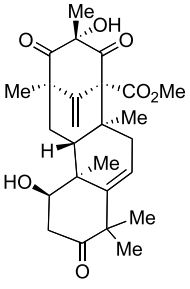
Abstract—The reaction of beta-keto esters with 3,3-diacetoxy-2-phenylsulfonylpropene affords bicyclic keto esters in good yields.

1. Introduction

The number of natural products bearing a phloroglucinol subunit has significantly increased in recent years.[1] Berkeleytrione (**1**) was isolated from *Penicillium* sp. found in the Berkeley Pit Lake in Butte, Montana and exhibits inhibitory activity against matrix metalloproteinase-3 and caspase-1.[2] Preaustinoid A (**2**) was isolated from *Melia azedarach* (Meliaceae) and exhibits broad bacteriostatic effects.[3] Nemorosone (**3**) was recently isolated and shows cytotoxic activity against epithelioid carcinoma (HeLa), epidermoid carcinoma (Hep-2), prostate cancer (PC-3) and central nervous system cancer (U251).[4] As part of a program to synthesize phloroglucinol-containing natural products,[5] we describe a useful synthesis of bridged bicyclic compounds.



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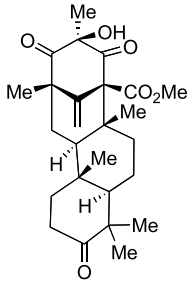

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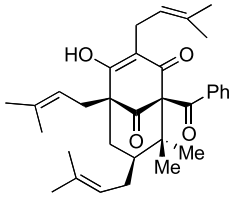

3

In a recent report[6] we described the preparation of bicyclic keto ester **5a** from **4a** by way of the versatile manganese mediated chemistry developed by Snider.[7] Bromination of **5a** with 3.5 equiv of NBS led to the isolation of bromo enone **6** in 55% yield. This reaction involves the intermediacy of a tribromide. Unfortunately, all attempts to produce **5b** from **4b** led only to undesired products (Scheme 1).

Michael addition of acrolein to **4c** led mainly to recovered **4c** plus polymeric products. The use of lower temperatures and radical inhibitors[8] failed to generate a bicyclic compound. This is in contrast to the successful Michael addition/intramolecular aldol reaction with acrolein and carbomethoxy cyclohexanone and is undoubtedly due to the steric hindrance of the geminal dimethyl group. Padwa has developed innovative methodology using sulfones as Michael acceptors.[9] We prepared annulation reagent **7** with the idea of performing two successive Michael additions to form a bridged bicyclic system followed by reductive elimination of the sulfone to generate a double bond. The three-step synthesis of **7** began with commercially available 3,3-diacetoxypropene. Addition of phenylsulfenyl chloride followed by oxidation of the sulfide with 2 equiv of MCPBA and elimination using diisopropylethylamine provided sulfone **7** in 80% overall yield on a 50 mmol scale (Scheme 2).

The Michael addition reaction of **7** was investigated with **4c**. Reaction of **4c** with 1 equiv of sodium hydride in THF at 25 °C followed by the addition of sulfone **7** furnished a 71% isolated yield of adduct **8** as one diastereomer by proton NMR. The stereochemistry of the methyl group relative to the quaternary center was not established since the next step would generate a bicyclic keto ester. Similarly, adducts **9–13** were generated. The *E*-stereochemistry of beta-acetoxy sulfone **8** was determined by a NOESY experiment (Scheme 3).

Cyclization of keto sulfone **8** using 1 equiv of potassium *tert*-butoxide at ambient temperature produced three

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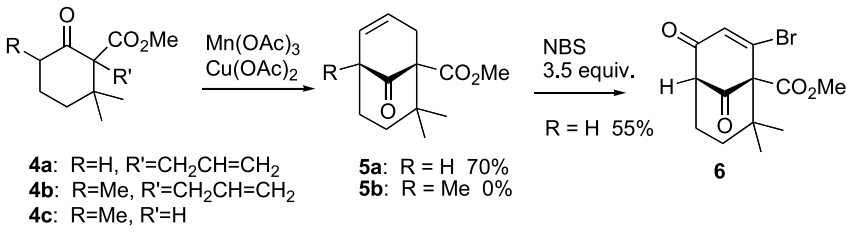
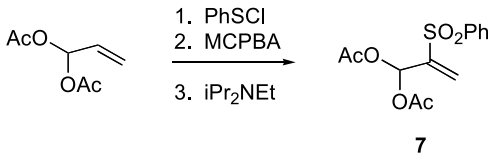


Scheme 1.

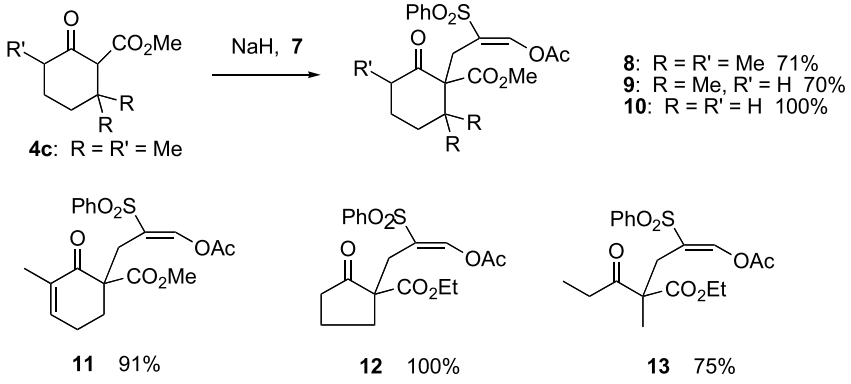


Scheme 2.

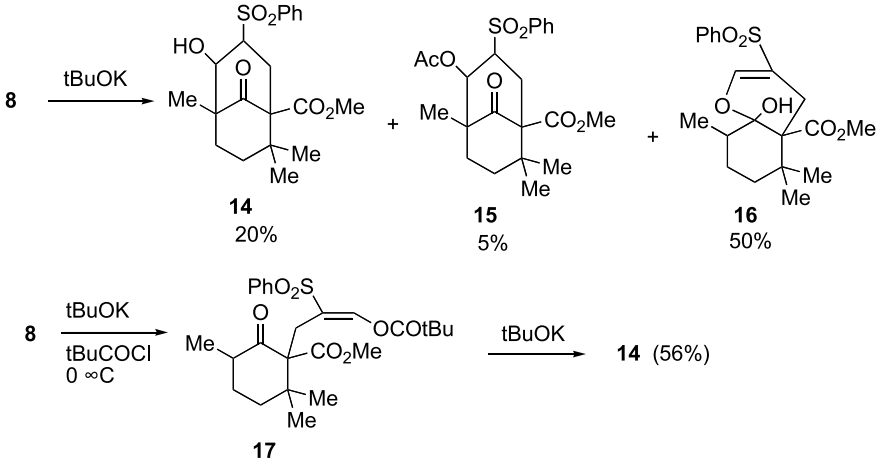
products, esters **14**, **15** and **16** in 20, 5 and 50% yields, respectively. The major product **16** was derived from the deacetylation of **8**. In order to enhance the yield of the cyclization products, acetate **8** was converted into pivalate **17** with potassium *tert*-butoxide followed by pivaloyl chloride at 0 °C in 80% yield. Reaction of **17** with potassium *tert*-butoxide in THF from 0 °C to room temperature afforded a 56% isolated yield of **14**, as a 1:0.8 mixture of hydroxy sulfone diastereomers (Scheme 4).

Cyclization of **9** also suffered from the labile acetoxy group. Initially, sulfone **9** was converted into tosylate **18** using potassium *tert*-butoxide and *para*-toluenesulfonyl chloride at 0 °C. Cyclization of **18** with potassium *tert*-butoxide afforded divinyl ether **20** in 90% yield. Sulfone **9** was then converted into pivalate ester **19** and cyclized to **21** (one diastereomer based on proton NMR) in 57% yield with KH in THF at 0 °C (Scheme 5).

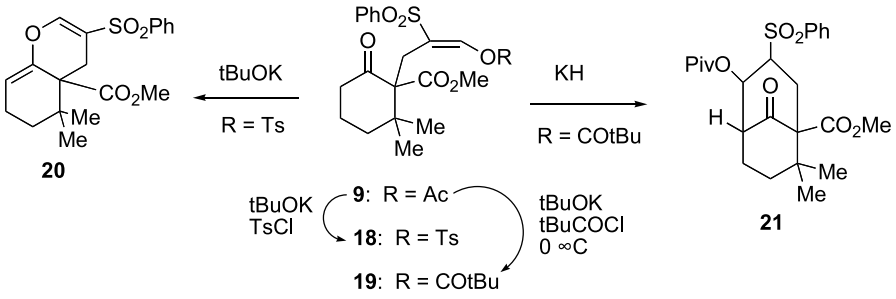
In view of the problems with acetate **9** and tosylate **18**, sulfones **10** and **11** were transformed directly into the pivalates and cyclized with potassium hydride in 40 and 83% yields, respectively. Interestingly, the reaction of the pivalate derived from **11** with potassium hydride gave a product derived from hydride addition to the enone system followed by cyclization to pivalate **23**, as one diastereomer based on proton NMR, in 83% yield (Scheme 6).



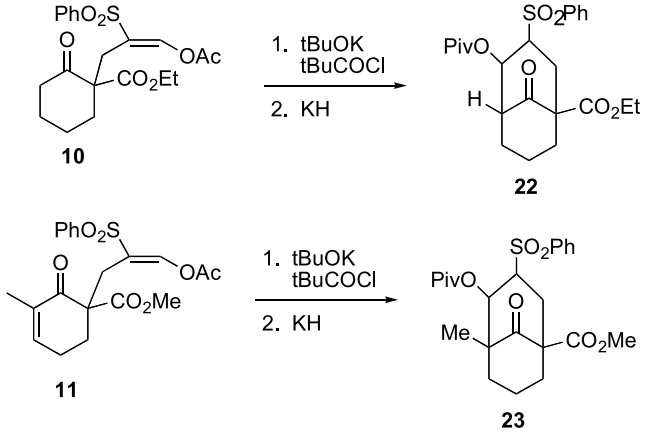
Scheme 3.



Scheme 4.

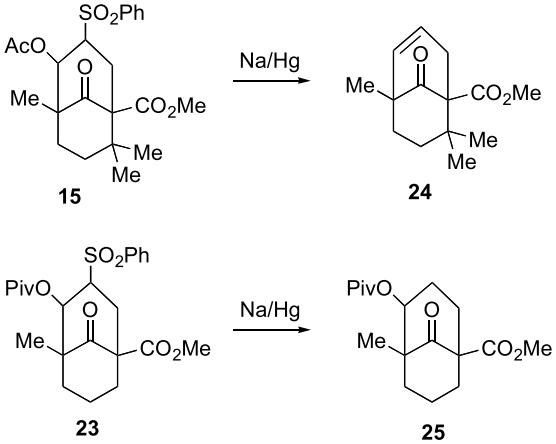


Scheme 5.



Scheme 6.

Acetoxy sulfone **15**, produced from alcohol **14** in 95% yield by acetylation with acetic anhydride and DMAP in methylene chloride at 25 °C, can be converted into the alkene **24** using sodium amalgam in MeOH in 57% yield.[10] Product **24** contains the bridgehead methyl group and bridgehead ester group present in **1** and **2**. Interestingly, pivalate **23** provided only desulfonated product **25** in 80% yield (Scheme 7).



Scheme 7.

In summary, the reaction of diacetoxy sulfone **7** with beta-keto esters provides a useful synthetic method for the preparation of complex bicyclic systems. The reactions are operationally convenient and amenable to scale up to produce gram quantities of bicyclic compounds.

2. Experimental

2.1. General

2.1.1. 3,3-Diacetoxy-2-phenylsulfonylpropene (7). To a mechanically stirred suspension of 6.8 g (0.05 mol) of *N*-chlorosuccinimide in 60 mL of dry methylene chloride at room temperature in a 250 mL flask equipped with a pressure-equalizing dropping funnel and an efficient condenser was added about 0.5 g of a total of 5.5 g (0.05 mol) of thiophenol. The mixture was then gently heated on a steam bath for 1–2 min until sulfenyl chloride formation commenced as evidenced by the intense orange coloration of the suspension. Once initiated, the remaining thiophenol was added dropwise at a rate sufficient to maintain the solvent at reflux. When the addition was complete (usually about 30 min were required), the homogeneous orange solution was stirred at room temperature for an additional 30 min. The suspension was then cooled to 0 °C and 8.7 g (0.055 mol) of 1,1-diacetoxy-2-propene was added in one portion. The mixture was then maintained at 0 °C until complete decoloration of the sulfenyl chloride suspension was observed (2 h). After warming to room temperature, the colorless suspension was filtered to remove the majority of the succinimide. Concentration of the combined filtrate and wash left a pale yellow oil which was diluted with 30 mL of hexane to precipitate the remainder of the succinimide. This suspension was let stand 1 h and then filtered, and the filtrate was evaporated to dryness which was pure enough to be used without further purification ^{1}H NMR (300 MHz, $CDCl_3$) 7.53–7.49 (m, 2H), 7.38–7.31 (m, 3H), 7.14 (d, $J=3.6$ Hz, 1H), 3.84–3.68 (m, 2H), 3.63–3.58 (m, 1H), 2.09 (s, 3H), 2.08 (s, 3H).

To a stirred solution of 4.4 g (0.02 mol) of chloro sulfide prepared above in 25 mL of dry methylene chloride, cooled to 0 °C under nitrogen, a solution of 2.2 equiv of *m*-chloroperbenzoic acid in 50 mL of methylene chloride was added dropwise. When the addition was complete, the mixture was stirred an additional 20 min and then filtered to remove the majority of the chlorobenzoic acid, which was washed with 30 mL of methylene chloride. The combined filtrate and wash was diluted with 50 mL of methylene chloride and then washed successively with 10% NaHCO3 (50 mL), 10% NaHSO3 (50 mL), 10% NaHCO3 again (50 mL), and saturated brine and finally dried (MgSO4), which was pure enough to be used without further purification.

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.98–7.94 (m, 2H),

7.76–7.60 (m, 3H), 7.23 (d, $J=3.0$ Hz, 1H), 4.17–3.94 (m, 2H), 3.88–3.83 (m, 1H), 2.07 (s, 3H), 2.02 (s, 3H).

A solution of 1.3 mL (7.5 mmol) of diisopropylethylamine in 50 mL of dry methylene chloride was added dropwise, under a nitrogen atmosphere, to a stirred solution of 2.3 g (6.9 mmol) of chlorosulfone at -10 °C. The reaction temperature was maintained at 0 °C for 2 h, then diluted with 40 mL of methylene chloride, washed with 25 mL each of chilled 1 N HCl, water, and brine, and finally dried over anhydrous magnesium sulfate. Crystallization with diethyl-ether/hexane gave compound **7** as a white solid, mp 72–73 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.92–7.89 (m, 2H), 7.69–7.54 (m, 3H), 7.39 (s, 1H), 6.75 (s, 1H), 6.36 (s, 1H), 1.96 (s, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 167.95, 145.84, 139.68, 134.05, 129.53, 129.43, 128.55, 84.90, 20.61; HRMS (EI) *m/z* ($M-CH_3CO_2$) calcd for 239.03781, found 239.03830.

2.2. General procedure for Michael addition to 7

Keto ester (1 mmol) was added dropwise to the solution of sodium hydride (1 mmol) in THF (10 mL). After 20 min sulfone **7** (1 mmol) was added in one portion and stirred for another 1 h. The resulting mixture was neutralized with AcOH, which was dissolved in 20 mL of ether. The ether layer was washed with brine and dried over anhydrous $MgSO_4$. The crude material was purified by column chromatography.

2.2.1. Compound 8. ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.29 (d, $J=3.3$ Hz, 1H), 7.88 (d, $J=7.8$ Hz, 2H), 7.67–7.52 (m, 3H), 3.67 (s, 3H), 3.31 (d, $J=16.8$ Hz, 1H), 2.90 (d, $J=16.8$ Hz, 1H), 2.23 (s, 3H), 1.87–1.34 (m, 4H), 0.92 (s, 6H), 0.74 (d, $J=6.3$ Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 206.44, 169.59, 166.20, 145.45, 139.58, 133.78, 129.58, 128.27, 123.20, 65.43, 51.43, 42.46, 40.53, 36.20, 30.56, 28.73, 26.28, 25.55, 20.75, 15.27; HRMS (EI) *m/z* calcd for 436.15558, found 436.15630.

2.2.2. Compound 9. ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.14 (s, 1H), 7.91 (d, $J=7.5$ Hz, 2H), 7.64–7.51 (m, 3H), 3.46 (s, 3H), 2.65–2.50 (m, 2H), 2.33–1.21 (m, 6H), 2.02 (s, 3H), 0.91 (s, 3H), 0.72 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 207.50, 170.76, 165.72, 142.24, 139.73, 133.47, 129.16, 128.04, 125.55, 66.73, 51.65, 44.17, 39.17, 36.25, 26.72, 26.62, 22.75, 22.53, 20.37; HRMS (EI) *m/z* calcd for 422.13993, found 422.14080.

2.2.3. Compound 10. ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.47 (s, 1H), 7.87–7.83 (m, 2H), 7.63–7.50 (m, 3H), 4.26–4.17 (m, 2H), 2.90–2.76 (m, 2H), 2.52–1.56 (m, 8H), 2.20 (s, 3H), 1.32–1.24 (m, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 206.27, 170.67, 165.89, 146.91, 139.82, 133.49, 129.30, 128.07, 124.08, 61.69, 59.98, 40.62, 35.11, 28.89, 27.07, 22.39, 20.59, 13.98; HRMS (EI) *m/z* calcd for 408.12428, found 408.12500.

2.2.4. Compound 11. ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.40 (s, 1H), 7.81–7.76 (m, 2H), 7.58–7.43 (m, 3H), 6.57 (br s, 1H), 3.62 (s, 3H), 3.99 (d, $J=15.6$ Hz, 1H), 2.75 (d, $J=15.6$ Hz, 1H), 2.45–2.19 (m, 2H), 2.13 (s, 3H), 1.95–1.88 (m, 2H), 1.73 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 194.93, 171.22, 166.06, 146.92, 144.91, 139.65, 134.81, 133.71, 129.46, 128.30, 124.10, 56.08, 52.81, 30.20, 28.93, 23.67, 20.69, 16.84, 14.34.

2.2.5. Compound 12. ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.48 (s, 1H), 7.87–7.83 (m, 2H), 7.64–7.51 (m, 3H), 4.19–4.08 (m, 2H), 3.09 (d, $J=15.6$ Hz, 1H), 2.63 (d, $J=15.6$ Hz, 1H), 2.39–2.30 (m, 2H), 2.22 (s, 3H), 2.03–1.91 (m, 2H), 1.21 (t, $J=6.9$ Hz 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 214.17, 171.14, 166.03, 146.31, 138.85, 133.79, 129.42, 128.49, 124.00, 62.00, 59.04, 37.53, 31.92, 27.70, 20.65, 19.86, 14.11.

2.2.6. Compound 13. ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.48 (s, 1H), 7.84–7.81 (m, 2H), 7.63–7.49 (m, 3H), 4.28–4.09 (m, 2H), 3.05 (d, $J=15.6$ Hz, 1H), 2.84 (d, $J=15.6$ Hz, 1H), 2.61–2.2.45 (m, 2H), 2.20 (s, 3H), 1.33 (s, 3H), 1.27 (t, $J=7.2$ Hz, 3H), 1.06 (t, $J=7.2$ Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 207.45, 172.38, 166.02, 146.66, 139.27, 133.68, 129.38, 128.37, 124.22, 61.95, 58.62, 31.64, 28.75, 20.69, 18.64, 14.08, 8.365.

2.3. Procedure for cyclizations using *t*-BuOK

To a stirred solution of keto ester (1 mmol) in THF (10 mL) was added *t*-BuOK (1 mmol) in one portion at 0 °C. The mixture was stirred overnight at room temperature and dissolved in 20 mL of ether. The ether layer was washed with 10% aq. HCl, brine and dried over anhydrous $MgSO_4$. The crude material was purified by column choromatography.

2.3.1. Compound 14. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.95–7.89 (m, 2H), 7.76–7.54 (m, 3H), 4.52 (d, $J=10.5$ Hz, 1H), 3.85 (s, 1H), 3.48 (s, 3H), 3.13–3.03 (m, 1H), 2.05–1.25 (m, 6H), 1.12 (s, 6H), 1.04 (s, 3H), 0.93(s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 208.94, 170.13, 136.07, 134.92, 129.81, 129.35, 74.31, 66.17, 64.63, 52.29, 51.27, 42.93, 37.81, 29.30, 28.41, 26.48, 25.54, 20.90; HRMS (EI) *m/z* calcd for 394.14501, found 394.14570.

2.3.2. Compound 15. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.88–7.83 (m, 2H), 7.71–7.56 (m, 3H), 5.62 (d, $J=11.4$ Hz, 1H), 3.68 (s, 3H), 3.45–3.33 (m, 1H),), 2.76 (dd, $J=14.7$, 4.8 Hz, 1H), 2.47 (d, $J=14.4$ Hz, 1H), 2.17–1.96 (m, 2H), 1.77–1.71 (m, 1H), 1.64 (s, 3H), 1.31–1.26 (m, 1H), 1.13 (s, 3H), 1.11 (s, 3H), 0.86 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 209.80, 170.86, 169.78, 139.47, 134.07, 129.50, 128.33, 74.83, 62.99, 61.07, 52.31, 49.84, 43.76, 38.08, 33.74, 26.59, 24.58, 22.87, 20.30, 17.63.

2.3.3. Compound 16. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.88 (m, 2H), 7.62–7.49 (m, 3H), 7.49 (d, $J=1.8$ Hz, 1H), 6.88 (d, $J=2.1$ Hz, 1H), 3.19 (s, 3H), 2.82–2.61 (m, 2H), 1.82–1.23 (m, 5H), 1.11–0.89 (m, 9H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 174.63, 152.20, 140.44, 132.87, 129.11, 127.55, 112.56, 105.36, 52.65, 52.22, 38.37, 36.04, 34.54, 27.70, 27.46, 25.60, 24.99, 13.39; HRMS (EI) *m/z* calcd for 394.14501, found 380.97603.

2.3.4. Compound 20. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.88–7.84 (m, 2H), 7.65–7.52 (m, 3H), 7.46 (d, $J=2.4$ Hz, 1H), 5.59 (t, $J=4.2$ Hz, 1H), 3.28 (s, 3H), 2.82 (d, $J=15.6$ Hz,

1H), 2.33 (dd, $J=15.6$, 2.4 Hz, 1H), 2.17–2.09 (m, 2H), 1.63–1.55 (m, 1H), 1.33–1.28 (m, 1H), 0.98 (s, 3H), 0.85 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 171.44, 150.63, 147.13, 140.34, 133.15, 129.22, 127.92, 115.84, 109.73, 52.19, 51.04, 35.47, 33.90, 25.63, 24.23, 20.29; HRMS (EI) *m/z* calcd for 362.11880, found 362.11940.

2.4. Procedure for cyclizations using KH

To a stirred solution of potassium hydride (1 mmol) in THF (10 mL) was added diketone (1 mmol). The mixture was stirred overnight at room temperature and dissolved in 20 mL of ether. The ether layer was washed with 10% aq. HCl, brine and dried over anhydrous $MgSO_4$. The crude material was purified by column choromatography.

2.4.1. Compound 21. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.89–7.86 (m, 2H), 7.72–7.56 (m, 3H), 5.40 (d, $J=10.8$ Hz, 1H), 4.12–4.00 (m, 2H), 3.49–3.39 (m, 1H),), 2.48–1.80 (m, 6H), 1.27–1.21 (m, 1H), 1.15–1.06 (m, 18H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 209.06, 177.39, 170.00, 138.41, 134.41, 129.68, 128.70, 73.82, 62.92, 61.18, 60.78, 54.22, 44.08, 38.71, 33.95, 28.62, 28.44, 27.00, 24.71, 22.73, 14.14; HRMS (EI) *m/z* calcd for 478.20253, found 478.20310.

2.4.2. Compound 22. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.94–7.89 (m, 2H), 7.73–7.57 (m, 3H), 5.54 (dd, $J=10.5$ Hz, 0.9 Hz, 1H), 4.27–4.11 (m, 3H), 3.46–3.36 (m, 1H), 3.01–2.75 (m, 2H), 2.32 (br s, 1H), 2.28–1.51 (m, 6H), 1.18 (t, $J=10.2$ Hz 3H), 1.12 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 209.27, 177.41, 171.28, 138.23, 134.44, 129.69, 128.82, 73.26, 61.97, 60.19, 56.39, 55.01, 38.73, 38.06, 34.17, 29.03, 26.99, 17.70, 14.23; HRMS (EI) *m/z* calcd for 450.17123, found 450.17200.

2.4.3. Compound 23. Mp 168–169 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.83 (d, $J=8.4$ Hz, 2H), 7.71–7.54 (m, 3H), 5.51 (d, $J=1.5$ Hz, 1H), 3.73 (s, 3H), 2.88 (br s, 1H), 2.67 (d, $J=$ 12.3 Hz, 1H), 2.49 (dd, $J=12.3$, 1.8 Hz, 1H), 2.31–1.81 (m, 6H), 1.27 (s, 3H), 0.90 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 207.59, 176.57, 170.40, 136.35, 134.57, 129.64, 129.48, 72.68, 65.73, 58.61, 55.46, 52.67, 39.45, 38.79, 31.21, 28.86, 26.81, 16.53, 15.14; HRMS (EI) *m/z* calcd for 450.17123, found 450.17190.

2.5. General procedure for pivaloyl group substitution

To a stirred solution of diketone (1 mmol) in THF (10 mL) was added *t*-BuOK (2 mmol) in one portion at 0 °C. The reaction temperature was maintained at 0 °C for 1 h, then trimethylacetyl chloride (2 mmol) was added. The resulting mixture was neutralized with AcOH, which was dissolved in 20 mL of ether. The ether layer was washed with brine and dried over anhydrous $MgSO_4$. The crude material was purified by column choromatography.

2.5.1. Compound 17. ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.32 (d, $J=0.9$ Hz, 1H), 7.84 (d, $J=8.7$ Hz, 2H), 7.62–7.49 (m, 3H), 3.65 (s, 3H), 3.21 (dd, $J=15.6$, 0.9 Hz, 1H), 2.99 (d, $J=15.6$ Hz, 1H), 2.04–1.38 (m, 4H), 1.25 (s, 9H), 1.00–0.95 (m, 9H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 207.02, 173.77, 170.68, 147.20, 140.17133.47, 129.30, 128.09, 124.61, 66.63, 51.52, 41.98, 41.23, 39.11, 36.17, 29.92, 27.53, 26.69, 26.26, 25.45, 15.41; HRMS (EI) *m/z* calcd for 478.20253, found 478.20320.

2.5.2. Compound 19. ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.36 (s, 1H), 7.91 (d, $J=7.8$ Hz, 2H), 7.64–7.51 (m, 3H), 3.51 (s, 3H), 3.21–3.10 (m, 1H), 2.88 (dd, $J=15.9$, 1.2 Hz, 1H), 2.57 (d, $J=15.9$ Hz, 1H), 2.38–2.32 (m, 1H), 2.11–2.00 (m, 1H), 1.90–1.67 (m, 2H), 1.34–1.28 (m, 1H), 1.21 (s, 9H), 1.10 (s, 3H), 0.74 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 206.40, 174.50, 170.19, 145.62, 140.27, 133.29, 129.10, 128.18, 125.34, 67.25, 51.65, 43.79, 40.02, 39.13, 36.56, 26.74, 24.93, 22.86, 22.49; HRMS (EI) *m/z* calcd for 464.18688, found 464.18760.

2.6. Procedure for tosyl group substitution

To a stirred solution of diketone 9 (422 mg, 1 mmol) in THF (10 mL) was added *t*-BuOK (224 mg, 2 mmol) in one portion at 0 °C. The reaction temperature was maintained at 0 °C for 1 h, then *p*-toluenesulfonyl chloride (381 mg, 2 mmol) was added. The resulting mixture was neutralized with AcOH, which was dissolved in 20 mL of ether. The ether layer was washed with brine and dried over anhydrous $MgSO_4$. The crude material was purified by column choromatography.

2.6.1. Compound 18. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.92–7.39 (m, 10H), 3.49 (s, 3H), 2.49 (s, 3H), 2.09–1.53 (m, 6H), 1.26–1.11 (m, 2H), 0.86 (s, 3H), 0.67 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 207.06, 169.82, 146.56, 143.13, 139.22, 133.60, 131.51, 130.15, 129.14, 128.51, 127.98, 126.70, 66.52, 51.78, 43.93, 38.85, 36.05, 26.50, 26.48, 22.49, 22.42, 21.90; HRMS (EI) *m/z* calcd for 534.13821, found 534.13900.

2.7. Procedure for aceoxysulfone elimination

The diketone 15 (43.6 mg, 0.1 mmol) in methanol (1 mL) and ethylacetate (0.5 mL) was stirred at 0 °C with 5% sodium amalgam. After 3 h, the mixture was poured into water (5 mL) and extracted with ether three times. The combined organic layer washed with brine and dried over anhydrous $MgSO_4$. The crude material was purified by column choromatography.

2.7.1. Compound 24. ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.81 (dt, $J=9.3$, 3.6 Hz, 1H), 5.29 (d, $J=9.3$, 1H), 3.71 (s, 3H), 3.13–2.83 (m, 2H), 2.06–1.52 (m, 3H), 1.24–1.167 (m, 1H), 1.11 (s, 3H), 1.09 (s, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 210.70, 171.64, 132.74, 127.86, 64.83, 51.86, 46.23, 42.73, 36.89, 36.20, 35.02, 25.46, 25.06, 21.85; HRMS (EI) *m/z* calcd for 236.14124, found 236.14170.

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