Synthesis S. J. Gharpure et al. Special Topic

Cascade Radical Cyclization to Vinylogous Carbonates/Carbamates for the Synthesis of Oxa- and Aza-Angular Triquinanes: Diastereoselectivity Depends on the Ring Size of Radical Precursor

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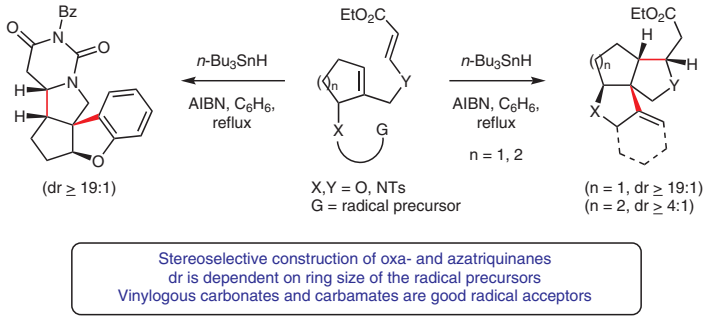
Dedicated to Professor Sambasivarao Kotha, IIT Bombay, on the occasion of his 60th birthday.



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Abstract An efficient strategy was developed for the stereoselective construction of oxa- and aza-angular triquinanes employing a cascade *5-exo-trig* radical cyclization to vinylogous carbonates and carbamates. The radical precursors are readily prepared from 2-(hydroxymethyl)cyclopentenone/cyclohexenones. High diastereoselectivity is observed for the formation of angular oxa- and azatriquinanes. Diastereoselectivity drops when six-membered radical precursors are used. The strategy is found to be useful to incorporate synthetically challenging moieties such as spiroindoline, lactone-bearing, and uracil-fused angular triquinanes in a concise manner.

Key words oxatriquinanes, azatriquinanes, vinylogous carbonates, vinylogous carbamates, cascade/tandem radical cyclization, stereoselective synthesis

Triquinanes have attracted considerable attention from organic chemists due to their unique and synthetically challenging framework, which is also present in many natural products.[1] Generally, triquinanes are classified into three types depending on the stereochemical arrangement of the five-membered rings present, namely, linear-, angular-, and propellane-type (Figure 1). In addition, many of these triquinanes display versatile biological activity. After the discovery and synthesis of the first polyquinane natural product, hirsutic acid C, significant progress has been made on the synthesis of carbocyclic polyquinanes. Substantial efforts have been directed towards the synthesis of carbocyclic triquinane frameworks as they constitute the core of many sesquiterpene natural products. In contrast, the heteroatom-substituted triquinanes have attracted considerably less attention from synthetic chemists.[2] The majority of the strategies developed in past few decades give access to either aza- or oxatriquinanes. Far less attention has been paid to develop strategies that would incorporate both oxygen and nitrogen in the same molecule.

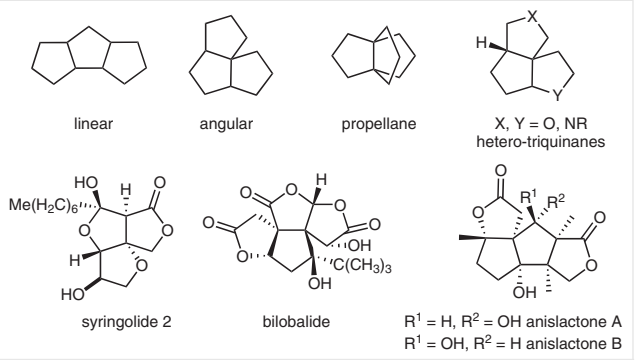

Figure 1 Carbocyclic and heterocyclic triquinanes and triquinane natural products

Such methods would be particularly useful as not only these heteroatom-substituted polyquinanes were thought to be more interesting from the point of view of their biological activity, but also many of these entities have proved to be useful intermediates for the synthesis of their carbocyclic analogues.[3] As a result, stereoselective synthesis of heteroatom-substituted angular triquinanes continues to be an important and interesting area of research. We disclose here full details of our approach to the synthesis of oxa- and azatriquinanes.[4j]

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In continuation of our interest on using vinylogous carbonates and carbamates in the synthesis of cyclic ethers and amines,[4] we envisioned that the heterocyclic angular triquinanes could be synthesized via a cascade radical cyclization (Figure 2). It was argued that a radical precursor such as iodide **1** could be rapidly assembled from the readily available cyclopentenone derivatives **2** via a short sequence involving: (i) hydroxymethylation of the enone **2** using Baylis–Hillman reaction, (ii) conversion of the resultant alcohol into the vinylogous carbonate, (iii) Luche reduction of the enone moiety to the allyl alcohol, and (iv) Mitsunobu reaction of the resultant alcohol.

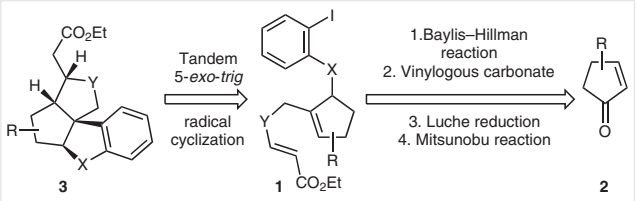
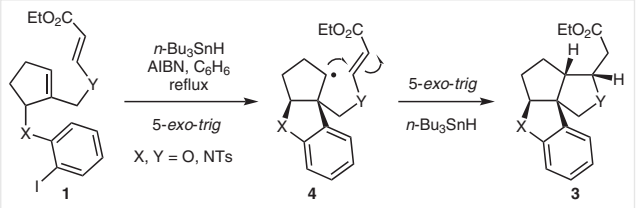


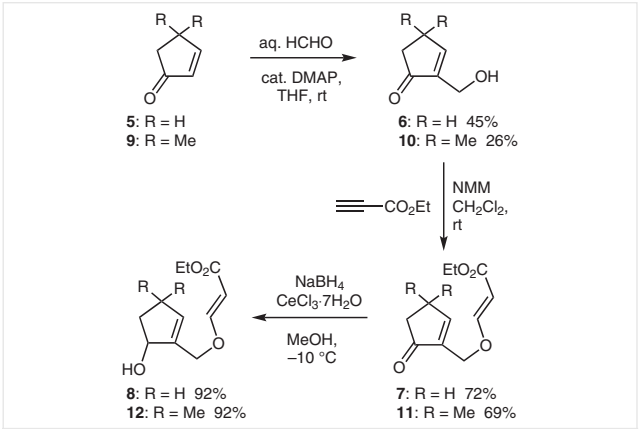
Figure 2 Retrosynthesis for heterocyclic angular triquinanes **3**

It was expected that the intramolecular radical cyclization of iodide **1** would lead to the formation of oxa-angular triquinane **3** through a cascade process. The reaction would involve initial formation of a radical from the iodide radical precursor **1**, which would undergo a 5-*exo*-*trig* radical cyclization to generate a new radical intermediate **4**. The radical intermediate **4** upon second 5-*exo*-*trig* cyclization to the vinylogous carbonate/carbamate moiety would generate a new radical, which on reduction with *n*-Bu_3SnH would give the heteroatom-substituted angular triquinane derivative **3** (Scheme 1).



Scheme 1 Rationale for proposed cascade radical cyclization for the formation of heterocyclic angular triquinanes

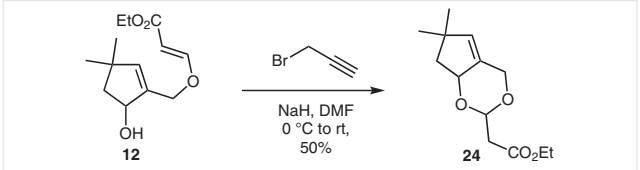
We initiated our studies with the synthesis of the required radical precursors. To expand the scope, three points of structural variations were considered, namely, modification in cyclopentenone structure, nature of radical precursor, and final acceptor as vinylogous carbonate or carbamate. Baylis–Hillman reaction of readily available cyclopent-2-enone (**5**) and formalin using 4-(dimethylamino)pyridine as the catalyst following literature protocol furnished 2-(hydroxymethyl)cyclopent-2-enone (**6**).[5,6] Reaction of the Baylis–Hillman adduct **6** with ethyl propynoate in the presence of *N*-methylmorpholine (NMM) in dry CH_2Cl_2 gave the vinylogous carbonate **7** in 72% yield (Scheme 2). The alcohol **8** could be readily obtained from the enone **7** by Luche reduction using $NaBH_4$ and $CeCl_3{\cdot}7H_2O$ in methanol.[7] Repetition of this three-step sequence on the known cyclopentenone derivative **9** furnished the alcohol **12**, through the intermediacy of the alcohol **10** and the keto-vinylogous carbonates **11**.[8,9]



Scheme 2 Synthesis of alcohol precursors

With the cyclopentenol derivatives **8** and **12** in hand, introduction of the radical precursor moiety was carried out by Mitsunobu reaction.[10,11] Thus, the alcohol **8** upon reaction with diisopropyl azodicarboxylate (DIAD), PPh_3, and 2-iodophenol (**13**), led to the corresponding iodide **17** in 72% yield (Table 1, entry 1). Similarly, alcohols **8** and **12** with various nucleophiles such as 2-iodophenol (**13**), 1-iodo-2-naphthol (**14**), and 2-iodo-*N*-tosylaniline (**15**) furnished the corresponding iodides **17–21** in good yields (Table 1, entries 2–5). On the other hand, Mitsunobu reaction of the alcohols **8** and **12** using *N*-tosylpropargylamine (**16**) gave the alkyne tethered precursors **22** and **23**, respectively, in good yield (Table 1, entries 6 and 7).

To synthesize an *O*-propargyl-tethered vinylogous carbonate substrate, the alcohol **12** was reacted with NaH and propargyl bromide. However, rather than the requisite propargyl ether, acetal **24** was obtained as the major product (Scheme 3). The product was formed by the base-promoted oxa-Michael addition of the hydroxy group to the vinylogous carbonate moiety.



Scheme 3 Acetal formation by oxa-Michael addition

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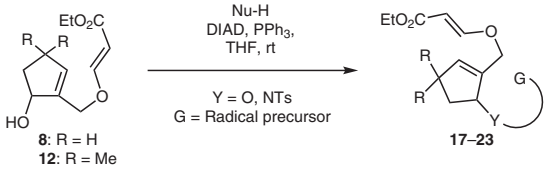
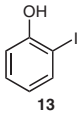
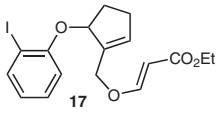
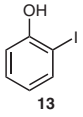
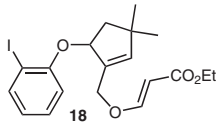
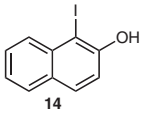
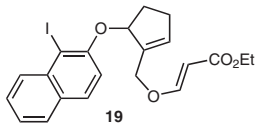
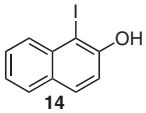
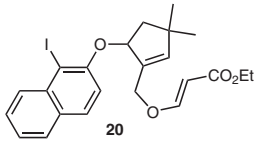
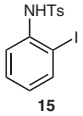
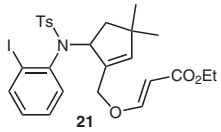
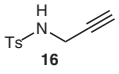
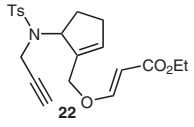
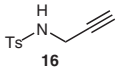
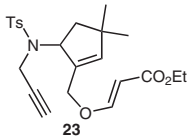
Table 1 Synthesis of Iodides and Alkynes for Radical Cyclization



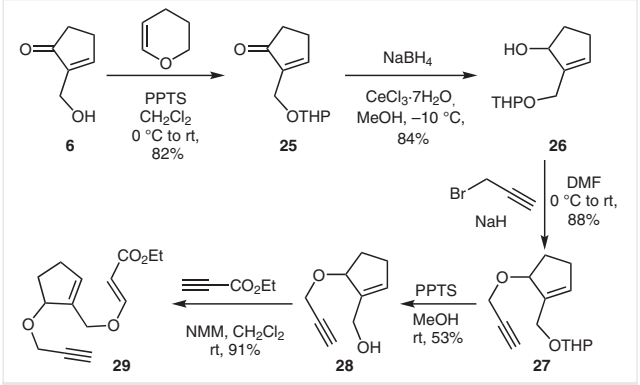
8: R = H
12: R = Me

17–23

Entry	Substrate	Nucleophile	Yield (%)[a]	Iodides and alkynes
1	**8**	 **13**	72	 **17**
2	**12**	 **13**	54	 **18**
3	**8**	 **14**	62	 **19**
4	**12**	 **14**	65	 **20**
5	**12**	 **15**	59	 **21**
6	**8**	 **16**	65	 **22**
7	**12**	 **16**	80	 **23**

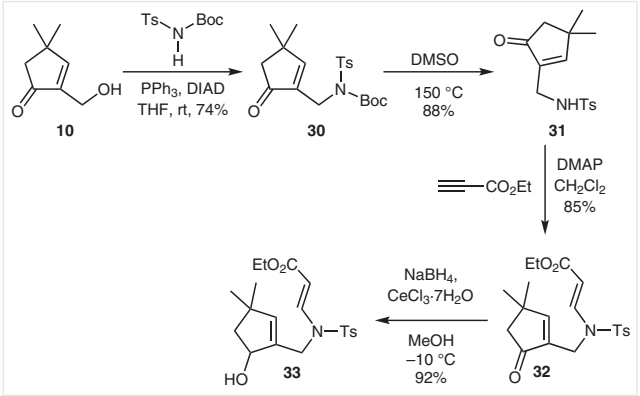
[a] Isolated yield.

An alternate sequence for the synthesis of the alkyne **29** was conceived to circumvent this problem. Towards this end, the hydroxy group of the Baylis–Hillman adduct **6** was protected as its THP ether **25** using dihydropyran and PPTS. Luche reduction of the enone using $CeCl_3{\cdot}7H_2O$ and $NaBH_4$ to the alcohol **26**, followed by propargylation using NaH and propargyl bromide gave the ether **27**. THP protection of the ether **27** was removed using PPTS and MeOH to yield the alcohol **28**. The alcohol **28** thus obtained was treated with ethyl propynoate in the presence of *N*-methylmorpholine in dry CH_2Cl_2 to furnish the corresponding vinylogous carbonate **29** in 91% yield (Scheme 4).



Scheme 4 Synthesis of *O*-propargyl tethered vinylogous carbonate **29**

For the synthesis of substrates bearing a vinylogous carbamate moiety, the Baylis–Hillman adduct **10** was envisaged to be an appropriate starting material. Thus, reaction of the alcohol **10** with DIAD, PPh_3, and N-Boc protected sulfonamide gave the amino enone **30** in 74% yield. The Boc group in enone **30** was deprotected using DMSO at 150 °C to yield the amine **31**.[12] Treatment of the amine **31** with ethyl propynoate and DMAP in dry CH_2Cl_2 furnished the keto-vinylogous carbamate **32** in 85% yield. Chemoselective reduction of the enone **32** using $NaBH_4$ and $CeCl_3{\cdot}7H_2O$ in methanol at –10 °C gave the desired alcohol **33** in excellent yield (Scheme 5).



Scheme 5 Synthesis of alcohol bearing vinylogous carbamate **33**

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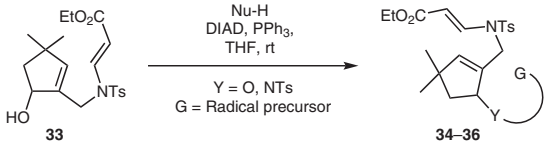
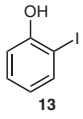
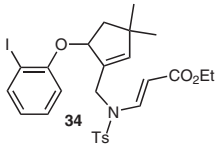
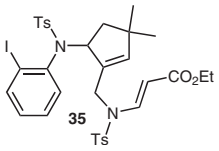
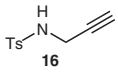
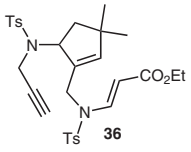
Table 2 Synthesis of Iodide/Alkyne Tethered Vinylogous Carbamates **34–36**

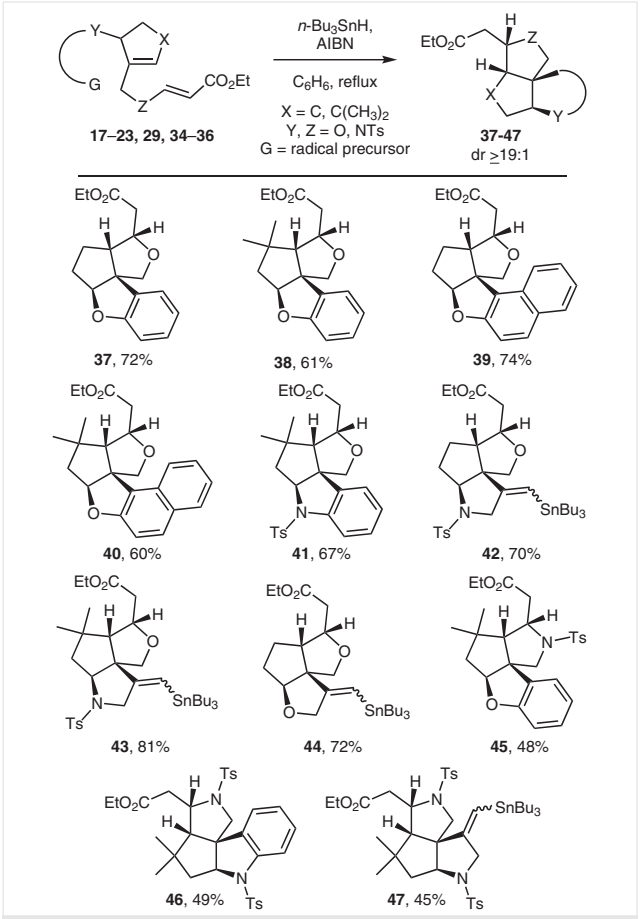


Entry	Substrate	Nucleophile	Yield (%)[a]	Iodides and alkynes
1	**33**	 **13**	62	 **34**
2	**33**	 **15**	65	 **35**
3	**33**	 **16**	73	 **36**

[a] Isolated yield.

For the installation of a radical precursor, the alcohol **33** was subjected to Mitsunobu reaction with different nucleophiles. Thus, Mitsunobu reaction of the alcohol **33** with 2-iodophenol (**13**), 2-iodo-*N*-tosylaniline (**15**), and *N*-tosylpropargylamine (**16**) furnished the products **34**, **35**, and **36**, respectively, in good yields (Table 2, entries 1–3).

Having the requisite radical precursors **17–23**, **29**, **34–36** in hand, attention was turned towards the tandem radical cyclization reaction of these precursors.[13,14] The results are summarized in the Scheme 6.[4j] Slow addition of a solution of *n*-Bu_3SnH and AIBN in benzene using syringe pump to a refluxing solution of the iodide **17** and AIBN in benzene, gratifyingly yielded the oxatriquinane **37** in 72% yield as the only detectable diastereomer.[4j] The structure of the triquinane **37** rests secured from its spectral data (see the Supporting Information to ref 4j). Similarly, various radical precursors were successfully employed in this reaction. Thus, the iodide derived from iodophenol, iodonaphthol, and protected iodoaniline also participated efficiently in this tandem radical cyclization giving triquinanes **38–45** and **46**. Not only aryl iodides but also the alkynes could act as radical precursors and furnished the triquinanes **42–44** and **47** bearing tributylstannyl substitution. Having a *gem*-dimethyl substitution on the cyclopentene ring did not affect the reactivity and oxa- and azatriquinanes were formed in comparable efficiencies with a variety of radical precursors. In general, vinylogous carbonates proved to be better acceptors in this tandem radical cyclization process than the vinylogous carbamates and thus the yields were better in the former cases.



Scheme 6 Synthesis of heteroatom-substituted angular triquinanes

Heteroatom-substituted triquinanes **41**, **45**, and **46** are particularly noteworthy as they incorporate spirocyclic indoline moiety, which is part structure of many bioactive molecules.[15–17] In all the cases, the triquinane formation proceeded with good to moderate yields and excellent diastereoselectivity.

To further confirm the structure of the triquinanes **42–44**, **47** they were subjected to proto-destannylation reaction (Scheme 7). Thus, treatment of angular triquinanes **42–44** with silica gel in CH_2Cl_2 furnished the heteroatom substituted angular triquinane **48–50**, respectively, in good yield. Alternatively, proto-destannylation of the vinylstannanes **47** could also be achieved using 4-toluenesulfonic acid (PTSA) in MeOH to furnish angular triquinane **51**.[4j]

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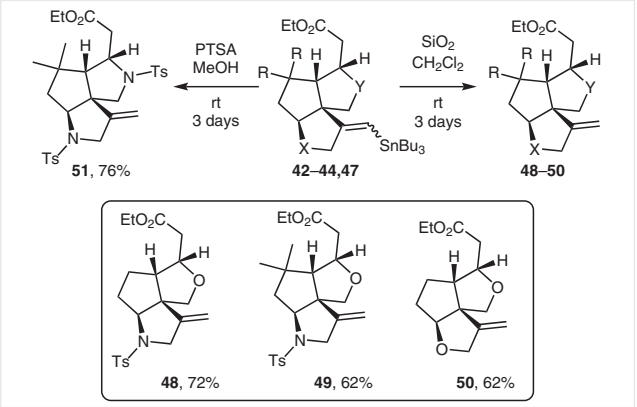

Scheme 7 Proto-destannylation of heteroatom substituted angular triquinanes

Stereochemical outcome of the radical cyclization reaction was established based on the ^{1}H NMR data. Further, single crystal X-ray diffraction studies on the heteroatom substituted triquinanes **38**, **41**, **46**, **49**, and **51**[4j] (Figure 3) unambiguously confirmed the assigned stereochemistry of the products. As can be noticed, the product oxa- and aza-triquinanes **38**–**47** had the hydrogens on carbons *cis* to each other.[20]

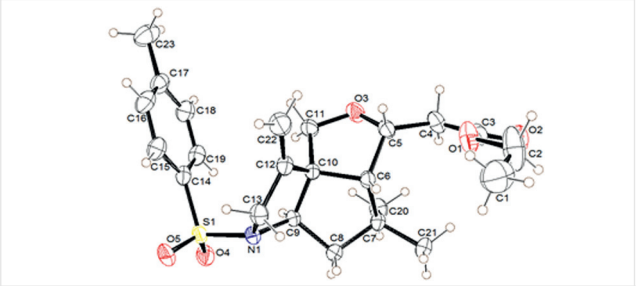

Figure 3 ORTEP picture of the oxatriquinane **49**[4j]

The stereochemical outcome of this reaction can be rationalized as follows.[4j] The first *5-exo-trig* radical cyclization happens on the cyclopentene moiety generating the *cis*-diquinane as expected. The next step of the tandem radical cyclization is the diastereoselectivity determining step. The two diastereomers can arise from two possible transition state structures **A** and **B**. We reasoned that the transition state structure **B** leading to the *trans*-product suffers from steric interaction between the aryl ring or the olefin moiety and the incipient (ethoxycarbonyl)methyl group (Figure 4). On the other hand, the transition state structure **A** is free from such an interaction and hence of lower energy. Naturally, it would lead to the *cis* product preferentially. We believed that the pronounced difference in the interactions in transition state structures **A** and **B** could be an outcome of the smaller five-membered rings present in the structure, which are devoid of significant conformational flexibility.

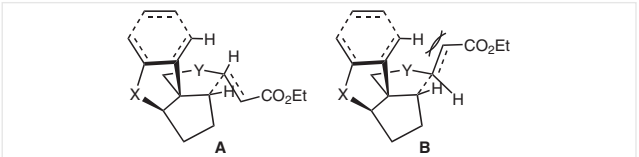

Figure 4 Transition state structures for the tandem radical cyclization reaction

To test this hypothesis, two types of substrates for radical cyclization were envisaged. To ascertain the importance of olefin or aryl ring for getting high stereoselectivity, a substrate devoid of olefin or aryl ring on the radical precursor was prepared. On the other hand, to check the effect of conformational flexibility, instead of starting with Baylis–Hillman adducts of cyclopentenone derivative, it was decided to prepare substrates starting from cyclohexenone derivatives. It was argued that not only these substrates will help us to understand the stereochemical outcome better but also expand the scope of this strategy.

The bromide **52** was thought to be a useful substrate to test the importance of olefin or aryl ring to impart higher stereoselectivity. The bromide **52** was readily assembled by reacting the alcohol **12** with ethyl vinyl ether and *N*-bromosuccinimide (NBS) in dry CH_2Cl_2. Reaction of the bromide **52** using *n*-Bu_3SnH and AIBN in refluxing benzene, however, furnished predominantly the simple reduction product without cyclization. Hence, the tandem radical cyclization was attempted using modified radical cyclization conditions, which rely on generating *n*-Bu_3SnH in situ. Reaction of the bromide **52** with sodium cyanoborohydride, tributyltin chloride, and catalytic AIBN in refluxing *t*-BuOH indeed furnished a diastereomeric mixture of ether **53**. Crude sample of the ether **53** was subjected to Jones oxidation to furnish the dioxatriquinane **54** as a 4:1 mixture of diastereomers in 56% yield over two steps (Scheme 8). Outcome of this experiment clearly suggests that the steric interaction between aryl ring/olefin moiety and the incipient (ethoxycarbonyl)methyl group arising from vinylogous carbonates/carbamates is important for getting good diastereoselectivity. The triquinane **54** is also particularly interesting as it gave an entry into lactone-bearing oxatriquinanes.[4j]

To test the effect of conformational flexibility on the stereochemical outcome of the tandem radical cyclization, synthesis of the iodides **59** and **60** was undertaken. Baylis–Hillman reaction of cyclohex-2-enone (**55**) using formalin and catalytic amount of DMAP in THF furnished 2-(hydroxymethyl)cyclohex-2-enone (**56**). The alcohol **56** was treated with ethyl propynoate in the presence of *N*-methylmorpholine in dry CH_2Cl_2 to obtain the corresponding viny-

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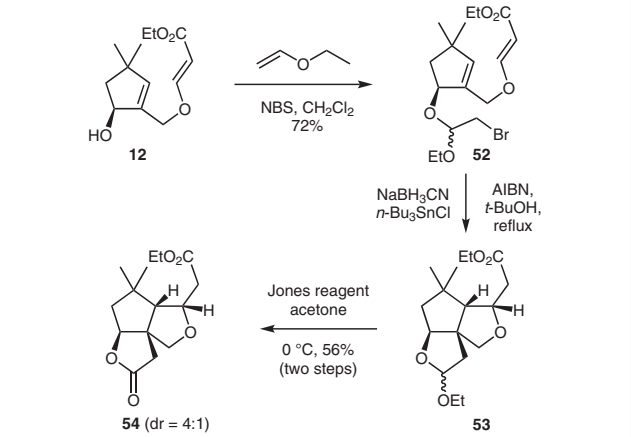
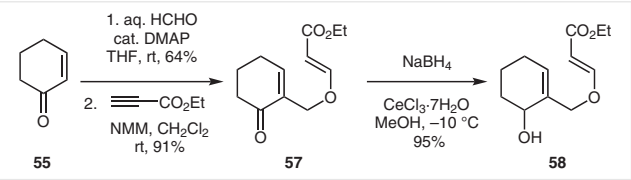


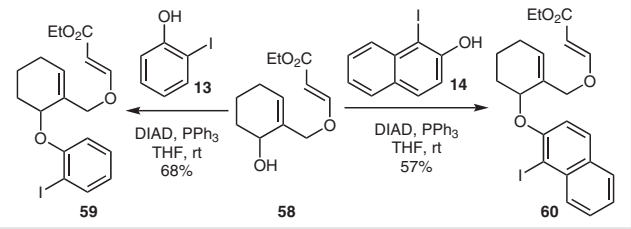
Scheme 8 Synthesis of lactone bearing oxatriquinane **54**

logous carbonate **57** in 91% yield. Luche reduction of the enone **57** using $NaBH_4$ and $CeCl_3{\cdot}7H_2O$ in methanol at –10 °C gave the corresponding alcohol **58** in 95% yield (Scheme 9).



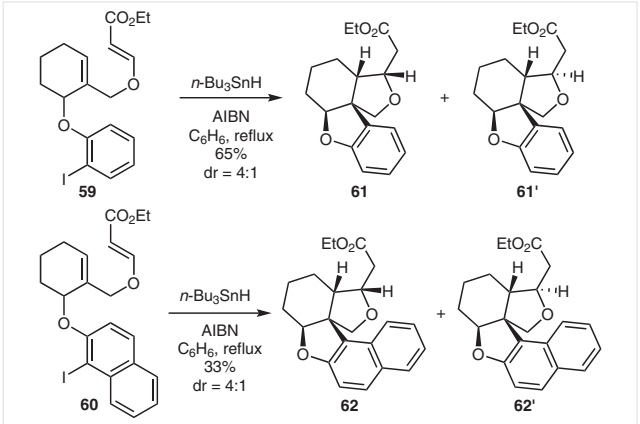
Scheme 9 Synthesis of vinylogous carbonate **58** from cyclohexenone

The alcohol **58** was converted into the iodide **59** by the Mitsunobu reaction using DIAD, PPh_3, and 2-iodophenol (**13**). On the other hand, when 1-iodo-2-naphthol (**14**) was used as the nucleophile, the iodide **60** was obtained in 57% yield (Scheme 10).



Scheme 10 Synthesis of radical precursors **59** and **60**

The iodides **59** and **60** were then subjected to the standardized tandem radical cyclization conditions. Thus, a slow addition of a solution of *n*-Bu_3SnH and AIBN in benzene to a refluxing solution of the iodide **59** and AIBN in benzene yielded the cyclized product **61** in 65% yield, albeit with lower diastereoselectivity (dr = 4:1). The diastereoselectivity was determined based on ^1H NMR analysis of the crude reaction mixture. Similarly, radical cyclization on the iodide **60** bearing a bigger naphthyl ring rather than the phenyl ring did not improve the diastereoselectivity and the product **62** was obtained in moderate yield and diastereoselectivity (dr = 4:1) (Scheme 11).



Scheme 11 Tandem radical cyclization of iodides **59** and **60**

To further expand the scope of this tandem radical cyclization, it was decided to change the acceptor from vinylogous carbonate/carbamate to vinylogous urea. It was thought that the iodide **66** would be an appropriate precursor to test this strategy.[18,19] The synthesis of the iodide began with the Baylis–Hillman adduct **6**. Protection of the hydroxy group of the alcohol **6** using acetic anhydride furnished the acetate **63**. Luche reduction of the enone **63** gave the alcohol **64**, which on Mitsunobu reaction using 2-iodophenol (**13**) gave rise to the corresponding ether and subsequent hydrolysis of the acetate group using K_2CO_3 gave yielded the alcohol **65**. Mitsunobu reaction of the alcohol **65b** using *N*-benzoyluracil furnished the requisite iodide **66** in good overall yield. When the iodide **66** was subjected to standard radical cyclization condition, the uracil-fused oxatriquinane **67** was obtained in good yield and excellent diastereoselectivity (Scheme 12).[4j] This demonstrated that vinylogous urea could also be used as a radical acceptor in tandem radical cyclization for the synthesis of angular triquinane.

In conclusion, a tandem 5-*exo*-*trig* radical cyclization-based strategy for the construction of novel heterocyclic angular triquinanes was developed. The heterocyclic angular triquinanes were obtained in moderate to good yields and excellent diastereoselectivity. This method gave access to lactone-bearing oxatriquinanes. It was observed that the diastereoselectivity of cascade radical cyclization was affected by the ring size, with less flexible smaller rings giving higher selectivity. Further, this method has been utilized for the synthesis of conformationally constrained uracil-fused angular triquinane.

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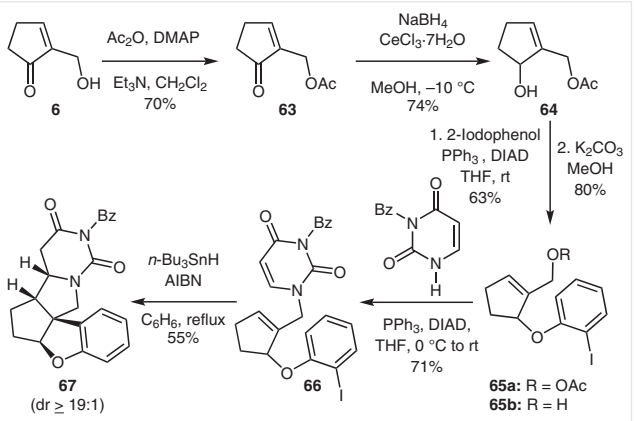

Scheme 12 Synthesis of uracil-fused oxatriquinane **67**

Melting points are recorded using sigma melting point apparatus in capillary tubes and are uncorrected. IR spectra were recorded on Nicolet 6700 spectrophotometer and Jasco FT-IR-4100 spectrophotometer. ^{1}H (400 MHz) and ^{13}C (100 MHz) spectra were recorded on Bruker Avance 400 spectrometer and ^{1}H (500 MHz) and ^{13}C (125 MHz) spectra were recorded on Bruker Avance 500 spectrometer both referenced to residual $CHCl_3$. In the ^{13}C NMR spectra, the nature of the carbons (C, CH, CH_2 or CH_3) was determined by recording the DEPT-135 experiment and is given in parentheses. CHN analysis was carried out using Elemental analyser VSM-VT. HRMS measurements were carried out using MicromassQ-ToF instrument using direct inlet mode. Analytical TLC was performed on glass plates (7.5 × 2.5 and 7.5 × 5.0 cm) coated with Merck silica gel G containing 13% $CaSO_4$ as binder or on pre-coated 0.2 mm thick Merck 60 F245 silica plates and various combinations of EtOAc and hexane were used as eluent. Visualization of spots was accomplished by exposure to I_2 vapor and UV light. All compounds were purified using silica gel [Acme silica gel (100–200 mesh)] column chromatography. All small-scale dry reactions were carried out using standard syringe septum technique. Dry THF was obtained by distillation over Na/benzophenone ketyl. Dry CH_2Cl_2 and DMF were prepared by distilling over CaH_2. AIBN obtained from spectrochem was recrystallized from Et_2O and stored at 0–5 °C in the dark. All the commercial reagents were used as such without further purification. Compounds **7**, **8**, **17**, **37**–**47**, **53**, **54**, **67**, were previously reported by us.[4j]

Ethyl (*E*)-3-{[(5*S**)-5-(2-bromo-1-ethoxyethoxy)-3,3-dimethylcyclopent-1-en-1-yl]methoxy}acrylate (52)

To a magnetically stirred solution of the *N*-bromosuccinimide (166 mg, 0.92 mmol) in dry CH_2Cl_2 (5 mL) was added ethoxyethene (152 µL, 2.1 mmol), and cooled the reaction mixture to 0 °C. To this, alcohol **34** (202 mg, 0.84 mmol) in dry CH_2Cl_2 (5 mL) was added dropwise and allowed to stir for 6 h. Evaporation of the solvent and purification of the residue on a silica gel column using ethyl acetate/hexanes (1:9) as eluent furnished the bromoacetal **52** (238 mg, 73%) as a colorless liquid; R_f = 0.6 (EtOAc/hexanes, 1:9).

IR (neat): 3089, 3033, 2960, 2931, 2870, 1710, 1627, 1459, 1373, 1326, 1284, 1234, 1198, 1131, 1049 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.58 (d, *J* = 12.8 Hz, 1 H), 5.76–5.70 (m, 1 H), 5.23 (d, *J* = 12.8 Hz, 1 H), 4.80–4.78 (m, 1 H), 4.73–4.67 (m, 1 H), 4.53–4.40 (m, 2 H), 4.15 (q, *J* = 7.2 Hz, 2 H), 3.67–3.53 (m, 2 H), 3.47–3.32 (m, 2 H), 2.10 (ABX, *J* = 13.6, 7.2 Hz, 1 H), 1.79 (ABX, *J* = 13.6, 4.4 Hz, 1 H), 1.30–1.18 (m, 6 H), 1.14 (m, 3 H), 1.06 (m, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$, DEPT): δ = 167.90 (C), 162.15 (CH), 144.39 (CH), 135.82 (C), 102.63 (CH), 97.19 (CH), 80.38 (CH), 67.54 (CH_2), 61.68 (CH_2), 59.93 (CH_2), 46.24 (CH_2), 43.90 (C), 32.13 (CH_2), 29.63 (CH_3), 28.82 (CH_3), 15.38 (CH_3), 14.47 (CH_3).

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{17}H_{28}O_5Br$: 391.1120; found: 391.1121.

2-(Hydroxymethyl)-4,4-dimethylcyclopent-2-enone (10)

Reaction of 4,4-dimethylcyclopent-2-enone (**9**; 800 mg, 7.27 mmol) with aq HCHO (2.2 mL, 29.08 mmol) and DMAP (89 mg, 0.73 mmol) in THF (20 mL) at rt as described for the alcohol **6**[4j] followed by purification of the residue by column chromatography (silica gel, EtOAc/hexanes, 1:4) gave the alcohol **10** (260 mg, 26%) as a colorless liquid; R_f = 0.5 (EtOAc/hexanes, 1:4).

IR (neat): 3414, 2960, 2928, 2868, 1699, 1641, 1463, 1409, 1364, 1347, 1294, 1206, 1154, 1084, 1003 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.25 (t, *J* = 1.6 Hz, 1 H), 4.30 (d, *J* = 1.2 Hz, 2 H), 2.31 (br s, 1 H), 2.30 (s, 2 H), 1.21 (s, 6 H).

^{13}C NMR (100 MHz, $CDCl_3$, DEPT): δ = 209.70 (C), 168.26 (CH), 141.84 (C), 57.34 (CH_2), 50.90 (CH_2), 39.49 (C), 28.12 (2 CH_3).

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_8H_{13}O_2$: 141.0916; found: 141.0912.

Ethyl (*E*)-3-[(3,3-Dimethyl-5-oxocyclopent-1-enyl)methoxy]acrylate (11); Typical Procedure 1 (TP1)

Following the procedure for **7**.[4j] To a magnetically stirred solution of **10** (230 mg, 1.64 mmol) in CH_2Cl_2 (5 mL) were added ethyl propynoate (183 µL, 1.81 mmol) and NMM (197 µL, 1.81 mmol) at rt and the mixture was stirred for 4 h (TLC control). Evaporation of the solvent and purification of the residue by column chromatography (silica gel, EtOAc/hexanes, 1:9) gave the vinylogous carbonate **11** (265 mg, 69%) as a colorless liquid; R_f = 0.5 (EtOAc/hexanes, 1:5).

IR (neat): 2960, 1707, 1624, 1462, 1405, 1367, 1325, 1284, 1204, 1132, 1049 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.57 (d, *J* = 12.4 Hz, 1 H), 7.35 (t, *J* = 1.2 Hz, 1 H), 5.25 (d, *J* = 12.4 Hz, 1 H), 4.50 (d, *J* = 1.2 Hz, 2 H), 4.15 (q, *J* = 7.2 Hz, 2 H), 2.32 (s, 2 H) 1.27 (s, 3 H), 1.25 (s, 3 H), 1.23 (s, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$, DEPT): δ = 206.99 (C), 169.58 (CH), 167.55 (C), 161.77 (CH), 137.78 (C), 97.86 (CH), 64.59 (CH_2), 59.97 (CH_2), 50.66 (CH_2), 39.78 (C), 28.11 (2 CH_3), 14.44 (CH_3).

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{13}H_{19}O_4$: 239.1283; found: 239.1286.

Ethyl (*E*)- 3-[(5-Hydroxy-3,3-dimethylcyclopent-1-enyl)methoxy]acrylate (12); Typical Procedure 2 (TP2)

Following the procedure for **8**.[4j] To a cold –10 °C, magnetically stirred solution of **11** (265 mg, 1.11 mmol) and $CeCl_3·7H_2O$ (438 g, 1.34 mmol) in MeOH (10 mL) was added $NaBH_4$ (51 mg, 1.34 mmol) portionwise. The solvent was removed under reduced pressure and the residue was extracted with EtOAc. The organic layer was washed with brine and dried (anhyd Na_2SO_4). The solvent was evaporated under

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reduced pressure and the residue was purified by column chromatography (silica gel, EtOAc/hexanes, 1:5) to furnish the alcohol **12** (245 mg, 92%) as a colorless liquid; R_f = 0.5 (EtOAc/hexanes, 1:5).

IR (neat): 3434, 2955, 2868, 1703, 1629, 1457, 1373, 1324, 1288, 1197, 1137, 1047 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 7.59 (d, *J* = 12.8 Hz, 1 H), 5.72 (s, 1 H), 5.25 (d, *J* = 12.4 Hz, 1 H), 4.83 (dd, *J* = 7.2, 4.4 Hz, 1 H), 4.48 (q, *J* = 12.4 Hz, 2 H), 4.15 (q, *J* = 7.2 Hz, 2 H), 2.17 (ABX, *J* = 13.6, 7.2 Hz, 1 H), 1.62 (ABX, *J* = 13.6, 4.0 Hz, 1 H), 1.26 (t, *J* = 7.2 Hz, 3 H), 1.54 (s, 3 H), 1.05 (s, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$, DEPT): δ = 167.98 (C), 162.25 (CH), 143.58 (CH), 137.35 (C), 97.23 (CH), 76.72 (CH), 67.97 (CH_2), 59.99 (CH_2), 49.64 (CH_2), 43.60 (CH_2), 29.96 (CH_3), 28.88 (CH_3), 14.46 (CH_3).

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{13}H_{21}O_4$: 241.1440; found: 241.1435.

Ethyl (*E*)- 3-{[5-(2-Iodophenoxy)-3,3-dimethylcyclopent-1-enyl]methoxy}acrylate (18); Typical Procedure 3 (TP3)

Following the procedure for **17**.[4j] To a magnetically stirred solution of the alcohol **12** (146 mg, 0.60 mmol) in THF (5 mL) were added successively PPh_3 (319 mg, 1.22 mmol) and 2-iodophenol (**13**; 161 mg, 0.72 mmol), followed by dropwise addition of DIAD (239 µL, 1.22 mmol) over a period of 10 min at rt. The mixture was stirred at rt for 6 h (TLC control). The solvent was evaporated under reduced pressure and the residue was purified by column chromatography (silica gel, EtOAc/hexanes, 1:9) to furnish the iodide **18** (138 mg, 54%) as a colorless liquid; R_f = 0.5 (EtOAc/hexanes, 1:9).

IR (neat): 2957, 2865, 1709, 1628, 1584, 1468, 1369, 1322, 1280, 1238, 1131, 1045 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 7.76 (dd, *J* = 7.6, 1.6 Hz, 1 H), 7.59 (d, *J* = 12.4 Hz, 1 H), 7.29–7.25 (m, 2 H), 6.79 (dd, *J* = 8.4, 1.2 Hz, 1 H), 6.70 (td, *J* = 7.6, 1.2 Hz, 1 H), 5.90 (s, 1 H), 5.28 (d, *J* = 12.4 Hz, 1 H), 5.26 (dd, *J* = 6.8, 3.2 Hz, 1 H), 4.60 (s, 1 H), 4.14 (q, *J* = 7.2 Hz, 2 H), 2.26 (ABX, *J* = 13.6, 7.2 Hz, 1 H), 1.91 (ABX, *J* = 13.6, 3.2 Hz, 1 H), 1.25 (t, *J* = 7.2 Hz, 3 H), 1.22 (s, 3 H), 1.15 (s, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$, DEPT): δ = 167.93 (C), 162.19 (CH), 156.95 (C), 145.10 (CH), 139.73 (CH), 134.72 (C), 129.49 (CH), 122.66 (CH), 113.23 (CH), 97.45 (CH), 87.49 (C), 83.27 (CH), 67.73 (CH_2), 59.93 (CH_2), 46.33 (CH_2), 44.56 (C), 29.72 (CH_3), 28.98 (CH_3), 14.49 (CH_3).

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{19}H_{24}O_4I$: 443.0719; found: 443.0712.

Ethyl (*E*)- 3-{[5-(1-Iodonaphthalen-2-yloxy)cyclopent-1-enyl]methoxy}acrylate (19)

Reaction of the alcohol **8** (151 mg, 0.72 mmol) with PPh_3 (374 mg, 1.43 mmol), 1-iodo-2-naphthol (**14**; 211 mg, 0.78 mmol), and DIAD (281 µL, 1.43 mmol) in THF (4 mL) at rt for 6 h as described TP3 and purification of the residue by column chromatography (silica gel, EtOAc/hexanes, 1:9) furnished the iodide **19** (206 mg, 62%) as a colorless liquid; R_f = 0.5 (EtOAc/hexanes, 1:9).

IR (neat): 3063, 2976, 2929, 2864, 1781, 1703, 1625, 1499, 1457, 1388, 1328, 1270, 1235, 1129, 1046 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 8.13 (d, *J* = 8.8 Hz, 1 H), 7.80 (d, *J* = 8.8 Hz, 1 H), 7.74 (d, *J* = 8.0 Hz, 1 H), 7.60 (d, *J* = 12.4 Hz, 1 H), 7.54 (t, *J* = 7.2 Hz, 1 H), 7.38 (t, *J* = 7.2 Hz, 1 H), 7.19 (d, *J* = 8.8 Hz, 1 H), 6.15 (s, 1 H), 5.44 ((t, *J* = 4.8 Hz, 1 H),) 5.30 (d, *J* = 12.8 Hz, 1 H), 4.75 (AB, *J* = 12.8 Hz, 1 H), 4.71 (AB, *J* = 12.8 Hz, 1 H), 4.16 (q, *J* = 7.2 Hz, 2 H), 2.72–2.63 (m, 1 H), 2.56–2.42 (m, 2 H), 2.19–2.10 (m, 1 H), 1.23 (t, *J* = 7.2 Hz, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$, DEPT): δ = 167.91 (C), 162.19 (CH), 155.59 (C), 137.74 (C), 135.88 (CH), 135.37 (C), 131.47 (CH), 130.41 (CH), 130.10 (C), 128.31 (CH), 128.24 (CH), 124.63 (C), 115.31 (CH), 97.51 (CH), 89.54 (C), 84.95 (CH), 67.88 (CH_2), 59.93 (CH_2), 31.24 (CH_2), 30.91 (CH_2), 14.46 (CH_3).

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{21}H_{22}O_4I$: 465.0563; found: 465.0573.

Ethyl (*E*)- 3-{[5-(1-Iodonaphthalen-2-yloxy)-3,3-dimethylcyclopent-1-enyl]methoxy}acrylate (20)

Reaction of the alcohol **12** (108 mg, 0.45 mmol) with PPh_3 (236 mg, 0.90 mmol), 1-iodo-2-naphthol (**14**; 182 mg, 0.68 mmol), and DIAD (177 µL, 0.90 mmol) in THF (3 mL) at rt for 6 h as described for TP3 and purification of the residue by column chromatography (silica gel, EtOAc/hexanes, 1:9) furnished the iodide **20** (135 mg, 65%) as a colorless liquid; R_f = 0.5 (EtOAc/hexanes, 1:9).

IR (neat): 2954, 2865, 1703, 1620, 1592, 1554, 1499, 1459, 1427, 1323, 1260, 1235, 1122, 1040, 1019, 1005 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 8.13 (d, *J* = 8.8 Hz, 1 H), 7.79 (d, *J* = 9.2 Hz, 1 H), 7.73 (d, *J* = 8.0 Hz, 1 H), 7.61 (d, *J* = 12.8 Hz, 1 H), 7.53 (t, *J* = 8.0 Hz, 1 H), 7.38 (t, *J* = 8.0 Hz, 1 H), 7.15 (d, *J* = 8.8 Hz, 1 H), 5.94 (s, 1 H), 5.44 (dd, *J* = 7.2, 3.2 Hz, 1 H),) 5.30 (d, *J* = 12.4 Hz, 1 H), 4.70 (AB, *J* = 12.8 Hz, 1 H), 4.65 (AB, *J* = 12.8 Hz, 1 H), 4.12 (q, *J* = 7.2 Hz, 2 H), 2.31 (ABX, *J* = 14.0, 7.2 Hz, 1 H), 2.02 (ABX, *J* = 13.6, 3.2 Hz, 1 H), 1.26 (s, 3 H), 1.23 (t, *J* = 7.2 Hz, 3 H), 1.17 (s, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$, DEPT): δ = 167.87 (C), 162.14 (CH), 155.58 (C), 145.18 (CH), 135.90 (CH), 134.84 (C), 131.44 (CH), 130.32 (CH), 130.00 (C), 128.29 (CH), 128.22 (CH), 124.54 (C), 114.98 (CH), 97.46 (CH), 89.21 (C), 84.19 (CH), 67.79 (CH_2), 59.90 (CH_2), 46.65 (CH_2), 44.55 (C), 29.69 (CH_3), 28.99 (CH_3), 14.44 (CH_3).

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{23}H_{26}O_4I$: 493.0876; found: 493.0886.

Ethyl (*E*)- 3-({5-[*N*-(2-Iodophenyl)-4-methylphenylsulfonamido]-3,3-dimethylcyclopent-1-enyl}methoxy)acrylate (21)

Reaction of the alcohol **12** (106 mg, 0.44 mmol) with PPh_3 (231 mg, 0.88 mmol), 2-iodo-*N*-tosylaniline (**15**; 181 mg, 0.49 mmol), and DIAD (174 µL, 0.88 mmol) in THF (5 mL) at rt for 6 h as described for TP3 and purification of the residue by column chromatography (silica gel, EtOAc/hexanes, 1:9) furnished the iodide **21** (155 mg, 59%) as a colorless liquid; R_f = 0.4 (EtOAc/hexanes, 1:9).

IR (neat): 2981, 2958, 2868, 2306, 1705, 1624, 1577, 1493, 1464, 1398, 1367, 1347, 1327, 1266, 1200, 1161, 1137, 1092, 1049, 1021 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 7.93 (dd, *J* = 6.4, 1.2 Hz, 1 H), 7.62 (d, *J* = 6.8 Hz, 2 H), 7.55 (d, *J* = 10.4 Hz, 1 H), 7.35 (td, *J* = 6.4, 1.2 Hz, 1 H), 7.27 (d, *J* = 7.2 Hz, 2 H), 7.10–7.05 (m, 2 H), 5.69 (br s, 1 H), 5.27 (dd, *J* = 7.2, 4.4 Hz, 1 H), 5.05 (d, *J* = 10.0 Hz, 1 H), 4.26–4.14 (m, 4 H), 2.43 (s, 3 H), 2.20 (ABX, *J* = 11.6, 7.6 Hz, 1 H), 2.05 (ABX, *J* = 11.6, 4.4 Hz, 1 H), 1.30 (t, *J* = 5.6 Hz, 3 H), 0.96 (s, 3 H), 0.48 (s, 3 H).

^{13}C NMR (125 MHz, $CDCl_3$, DEPT): δ = 167.84 (C), 162.04 (CH), 145.56 (CH), 144.21 (C), 143.85 (CH), 141.09 (CH), 139.64 (C), 138.07 (C), 134.15 (C), 133.04 (CH), 130.38 (CH), 129.78 (2 CH), 128.95 (CH), 128.43 (2 CH), 106.49 (C), 97.14 (CH), 68.14 (CH_2), 59.97 (CH_2), 43.17 (CH_2), 42.65 (C), 29.51 (CH_3), 27.90 (CH_3), 21.69 (CH_3), 14.54 (CH_3).

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{26}H_{31}NO_5SI$: 596.0968; found: 596.0957.

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Ethyl (*E*)- 3-({5-[4-Methyl-*N*-(prop-2-ynyl)phenylsulfonamido]cyclopent-1-enyl}methoxy)acrylate (22)

Reaction of the alcohol **8** (60 mg, 0.28 mmol) with PPh_3 (148 mg, 0.57 mmol), *N*-tosylpropargylamine (**16**; 71 mg, 0.34 mmol), and DIAD (108 µL, 0.57 mmol) in THF (2 mL) at rt for 6 h as described for TP3 and purification of the residue by column chromatography (silica gel, EtOAc/hexanes, 1:4) furnished the alkyne **22** (74 mg, 65%) as a colorless liquid; R_f = 0.5 (EtOAc/hexanes, 1:4).

IR (neat): 3303, 2982, 2934, 1714, 1631, 1504, 1462, 1381, 1331, 1235, 1154, 1120, 1043 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 7.79 (d, *J* = 8.4 Hz, 2 H), 7.46 (d, *J* = 12.4 Hz, 1 H), 7.28 (d, *J* = 8.4 Hz, 2 H), 6.05 (s, 1 H), 5.06 (d, *J* = 12.8 Hz, 1 H), 5.00–4.97 (m, 1 H), 4.24–4.12 (m, 5 H), 3.91 (d, *J* = 2.4 Hz, 2 H), 2.49–2.43 (m, 1 H), 2.42 (s, 3 H), 2.17–2.10 (m, 2 H), 1.93–1.89 (m, 1 H), 1.28 (t, *J* = 7.2 Hz, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$, DEPT): δ = 167.79 (C), 161.99 (CH), 143.76 (C), 137.51 (C), 135.99 (CH), 129.70 (2 CH), 127.61 (2 CH), 97.10 (CH), 79.81 (C), 72.29 (C), 67.32 (CH_2), 63.68 (CH), 59.97 (CH_2), 32.24 (CH_2), 31.14 (CH_2), 27.62 (CH_2), 21.95 (CH), 21.65 (CH_3), 14.48 (CH_3).

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{21}H_{26}NO_5S$: 404.1532; found: 404.1535.

Ethyl (*E*)- 3-({3,3-Dimethyl-5-[4-methyl-*N*-(prop-2-ynyl)phenylsulfonamido]cyclopent-1-enyl}methoxy)acrylate (23)

Reaction of the alcohol **12** (108 mg, 0.45 mmol) with PPh_3 (236 mg, 0.90 mmol), *N*-tosylpropargylamine (**16**; 141 mg, 0.68 mmol), and DIAD (177 µL, 0.90 mmol) in THF (3 mL) at rt for 6 h as described for TP3 and purification of the residue by column chromatography (silica gel, EtOAc/hexanes, 1:4) furnished the alkyne **23** (155 mg, 80%) as a colorless liquid; R_f = 0.4 (EtOAc/hexanes, 1:4).

IR (neat): 3273, 2956, 2868, 1754, 1704, 1621, 1454, 1333, 1281, 1199, 1163, 1126, 1092, 1065, 1046, 1017 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 7.78 (d, *J* = 8.4 Hz, 2 H), 7.44 (d, *J* = 12.4 Hz, 1 H), 7.28 (d, *J* = 8.4 Hz, 2 H), 5.77 (d, *J* = 1.2 Hz, 1 H), 5.08–5.02 (m, 2 H), 4.20–4.10 (m, 4 H), 4.01 (ABX, *J* = 18.4, 2.4 Hz, 1 H), 3.89 (ABX, *J* = 18.4, 2.4 Hz, 1 H), 2.42 (s, 3 H), 2.18 (t, *J* = 2.4 Hz, 1 H), 1.97 (ABX, *J* = 14.4, 8.8 Hz, 1 H), 1.78 (ABX, *J* = 14.4, 6.4 Hz, 1 H), 1.27 (t, 3 H), 1.12 (s, 3 H), 1.02 (s, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$, DEPT): δ = 167.73 (C), 161.92 (CH), 145.11 (CH), 143.72 (C), 137.54 (C), 133.26 (C), 129.67 (2 CH), 127.57 (2 CH), 97.06 (CH), 79.90 (C), 72.80 (C), 67.23 (CH_2), 64.08 (CH), 59.93 (CH_2), 43.40 (C), 42.24 (CH_2), 32.28 (CH_2), 29.24 (CH), 21.82 (CH_3), 21.63 (CH_3), 14.48 (CH_3).

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{23}H_{30}NO_5S$: 432.1845; found: 432.1853.

2-[(Tetrahydro-2*H*-pyran-2-yloxy)methyl]cyclopent-2-enone (25)

To a magnetically stirred solution of 2-(hydroxymethyl)cyclopent-2-enone (**6**; 109 mg, 0.97 mmol) in CH_2Cl_2 (5 mL) was added PPTS (49 mg, 0.19 mmol) at 0 °C followed by addition of dihydropyran (155 µL, 1.71 mmol) and the mixture was stirred for 12 h (TLC control). Evaporation of the solvent and purification of the residue by column chromatography (silica gel, EtOAc/hexanes, 1:9) furnished the product **25** (156 mg, 82%) as a colorless liquid; R_f = 0.5 (EtOAc/hexanes, 1:9).

IR (neat): 2943, 2868, 1700, 1641, 1559, 1540, 1523, 1453, 1442, 1356, 1288, 1257, 1200, 1123, 1076, 1025 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 7.04 (s, 1 H), 4.61–4.58 (m, 2 H), 4.21–4.17 (m, 1 H), 3.83–3.77 (m, 1 H), 3.40–3.36 (m, 1 H), 1.93–1.90 (m, 2 H), 1.82–1.79 (m, 2 H), 1.76–1.67 (m, 1 H), 1.59–1.55 (m, 2 H), 1.38–1.32 (m, 1 H), 1.31–1.21 (m, 2 H).

^{13}C NMR (100 MHz, $CDCl_3$, DEPT): δ = 206.52 (C), 157.75 (CH), 143.80 (C), 98.54 (CH), 61.69 (CH_2), 61.46 (CH_2), 34.62 (CH_2), 30.81 (CH_2), 26.52 (CH_2), 25.76 (CH_2), 19.55 (CH_2).

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{11}H_{17}O_3$: 197.1178; found: 197.1168.

2-[(Tetrahydro-2*H*-pyran-2-yloxy)methyl]cyclopent-2-enol (26)

Reduction of **25** (120 mg, 0.61 mmol) using $NaBH_4$ (28 mg, 0.73 mmol) and $CeCl_3{\cdot}7H_2O$ (241 mg, 0.73 mmol) in MeOH (10 mL) at –10 °C as described for TP2 followed by purification of the residue by column chromatography (silica gel, EtOAc/hexanes, 1:9) furnished the alcohol **26** (99 mg, 84%) as a colorless liquid; R_f = 0.5 (EtOAc/hexanes, 1:9).

IR (neat): 3418, 2941, 2859, 1656, 1448, 1386, 1351, 1321, 1267, 1204, 1125, 1030 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 5.62–5.61 (m, 1 H), 4.81–4.93 (m, 1 H), 4.62 (t, *J* = 3.2 Hz, 1 H), 4.52–4.49 (m, 1 H), 4.46–4.42 (m, 1 H), 4.12 (dd, *J* = 12.4, 5.2 Hz, 1 H), 3.82–3.73 (m, 1 H), 3.38–3.31 (m, 1 H), 2.10–2.09 (m, 1 H), 2.08–1.96 (m, 2 H), 1.83–1.76 (m, 1 H), 1.68–1.61 (m, 1 H), 1.53–1.49 (m, 2 H), 1.33–1.27 (m, 1 H), 1.26–1.22 (m, 2 H).

^{13}C NMR (100 MHz, $CDCl_3$, DEPT): δ = 143.87 (C), 130.60 (CH), 98.50 (CH), 78.00 (CH), 64.99 (CH_2), 62.18 (CH_2), 34.05 (CH_2), 30.97 (CH_2), 30.32 (CH_2), 25.74 (CH_2), 19.82 (CH_2).

HRMS (ESI): *m*/*z* [M + Na]$^+$ calcd for $C_{11}H_{18}O_3Na$: 221.1154; found: 221.1146.

2-{[5-(Prop-2-ynyloxy)cyclopent-1-enyl]methoxy}tetrahydro-2*H*-pyran (27)

To a cold (0 °C) magnetically stirred suspension of NaH (85 mg 60% in mineral oil, 1.29 mmol) in dry DMF (2 mL), a solution of the alcohol **26** (235 mg, 1.19 mmol) in dry DMF (3 mL) was added and the mixture was stirred at rt for 30 min. 80% Propargyl bromide in toluene (264 µL, 2.37 mmol) was added slowly over a period of 15–20 min and the mixture was stirred overnight at rt. The reaction was quenched with water at 0 °C and extracted with Et_2O. The combined organic layer was washed with brine and dried (anhyd Na_2SO_4). Evaporation of the solvent under reduced pressure and purification of the residue by column chromatography (silica gel, EtOAc/hexanes, 1:19) furnished the propargyl ether **27** (245 mg, 88%) as a colorless liquid; R_f = 0.5 (EtOAc/hexanes, 1:19).

IR (neat): 3287, 3260, 2941, 2855, 2115, 1450, 1353, 1263, 1202, 1179, 1120, 1075, 1029 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 5.77 (t, *J* = 2.8 Hz, 1 H), 4.73 (t, *J* = 2.8 Hz, 1 H), 4.69–4.58 (m, 2 H), 4.58–4.52 (m, 1 H), 4.19 (t, *J* = 10.8 Hz, 1 H), 4.03–3.90 (m, 2 H), 3.89–3.78 (m, 2 H), 3.44–3.63 (m, 1 H), 2.02–2.01 (m, 1 H), 1.96–1.86 (m, 1 H), 1.84–1.72 (m, 2 H), 1.67–1.58 (m, 2 H), 1.42–1.35 (m, 1 H), 1.34–1.22 (m, 2 H).

^{13}C NMR (100 MHz, $CDCl_3$, DEPT): δ = 142.35 (C), 130.78 (CH), 98.39 (CH), 83.94 (CH), 81.15 (C), 73.84 (CH), 64.22 (CH_2), 63.50 (CH_2), 61.39 (CH_2), 56.34 (CH_2), 30.92 (CH_2), 30.33 (CH_2), 25.90 (CH_2), 19.49 (CH_2).

HRMS (ESI): *m*/*z* [M + Na]$^+$ calcd for $C_{14}H_{20}O_3Na$: 259.1310; found: 259.1320.

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[5-(Prop-2-ynyloxy)cyclopent-1-enyl]methanol (28)

To a magnetically stirred solution of **27** (140 mg, 0.59 mmol) in MeOH (5 mL) was added PPTS (140 mg, 0.59 mmol) at rt and the mixture was stirred for overnight (TLC control). Evaporation of the solvent and purification of the residue by column chromatography (silica gel, EtOAc/hexanes, 1:4) furnished the product **28** (48 mg, 53%) as a colorless liquid; R_f = 0.5 (EtOAc/hexanes, 1:4).

IR (neat): 3633, 3551, 3466, 2987, 2087, 1559, 1451, 1376, 1243, 1051 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 5.87 (s, 1 H), 4.79–4.75 (m, 1 H), 4.27 (br s, 2 H), 4.24 (ABX, *J* = 15.6, 2.4 Hz, 1 H), 4.12 (ABX, *J* = 15.6, 2.0 Hz, 1 H), 2.52–2.45 (m, 1 H), 2.42 (t, *J* = 2.4 Hz, 1 H), 2.30–2.29 (m, 1 H), 2.26–2.18 (m, 1 H), 1.94–1.85 (m, 1 H), 1.70–1.67 (m, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$, DEPT): δ = 143.06 (C), 131.48 (CH), 84.96 (CH), 80.37 (C), 74.25 (C), 60.54 (CH_2), 56.36 (CH_2), 30.34 (CH_2), 30.14 (CH_2).

HRMS (ESI): *m*/*z* [M + Na]$^+$ calcd for $C_9H_{12}O_2Na$: 175.0735; found: 175.0741.

Ethyl (*E*)- 3-{[5-(Prop-2-ynyloxy)cyclopent-1-enyl]methoxy}acrylate (29)

Reaction of **28** (45 mg, 0.30 mmol) with ethyl propynoate (33 µL, 0.33 mmol) and NMM (35 µL, 0.33 mmol) in CH_2Cl_2 (3 mL) at rt as described TP1 followed by purification of the residue by column chromatography (silica gel, EtOAc/hexanes, 1:9) gave the vinylogous carbonate **29** (70 mg, 91%) as a colorless liquid; R_f = 0.5 (EtOAc/hexanes, 1:9).

IR (neat): 2986, 2944, 2909, 2085, 1889, 1742, 1642, 1626, 1448, 1374, 1301, 1243, 1098, 1048 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 7.59 (d, *J* = 12.4 Hz, 1 H), 5.97 (br s, 1 H), 5.26 (d, *J* = 12.4 Hz, 1 H), 4.69 (t, *J* = 3.6 Hz, 1 H), 4.50 (br s, 2 H), 4.21–4.09 (m, 4 H), 2.54–2.46 (m, 1 H), 2.42 (m, 1 H), 2.35–2.29 (m, 1 H), 2.26–2.17 (m, 1 H), 1.95–1.87 (m, 1 H), 1.26 (t, *J* = 7.2 Hz, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$, DEPT): δ = 167.98 (C), 162.43 (CH), 138.60 (C), 134.33 (CH), 97.28 (CH), 83.40 (CH), 80.32 (C), 74.24 (C), 67.83 (CH_2), 59.91 (CH_2), 56.59 (CH_2), 30.53 (CH_2), 29.89 (CH_2), 14.50 (CH_3).

HRMS (ESI): *m*/*z* [M + Na]$^+$ calcd for $C_{14}H_{18}O_4Na$: 273.1103; found: 273.1109.

***tert*-Butyl [(3,3-Dimethyl-5-oxocyclopent-1-enyl)methyl](tosyl)carbamate (30)**

Reaction of the alcohol **10** (225 mg, 1.61 mmol) with PPh_3 (842 mg, 3.21 mmol), *tert*-butyl tosylcarbamate (479 mg, 1.77 mmol), and DIAD (633 µL, 3.21 mmol) in THF (5 mL) at rt for 12 h as described for TP3 and purification of the residue by column chromatography (silica gel, EtOAc/hexanes, 1:4) furnished the carbamate **30** (423 mg, 74%) as a colorless solid; R_f = 0.5 (EtOAc/hexanes, 1:4); mp 92–94 °C.

IR (neat): 2961, 2928, 2868, 1732, 1708, 1644, 1596, 1458, 1362, 1303, 1247, 1163, 1092, 1024 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 7.81 (d, *J* = 8.0 Hz, 2 H), 7.31 (d, *J* = 8.0 Hz, 2 H), 7.20 (s, 1 H), 4.57 (d, *J* = 1.6 Hz, 2 H), 2.44 (s, 3 H), 2.34 (s, 2 H), 1.35 (s, 9 H), 1.22 (s, 6 H).

^{13}C NMR (100 MHz, $CDCl_3$, DEPT): δ = 207.30 (C), 167.87 (CH), 150.63 (C), 144.58 (C), 139.67 (C), 136.90 (C), 129.40 (2 CH), 128.37 (2 CH), 84.54 (C), 50.80 (CH_2), 42.53 (CH_2), 39.27 (C), 28.16 (CH_3), 28.05 (CH_3), 28.02 (CH_3), 27.92 (2 CH_3), 21.73 (CH_3).

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{20}H_{28}NO_5S$: 394.1688; found: 394.1691.

***N*-[(3,3-Dimethyl-5-oxocyclopent-1-enyl)methyl]-4-methylbenzenesulfonamide (31)**

A magnetically stirred solution of the carbamate **30** (140 mg, 0.36 mmol) in DMSO (3 mL) was heated at 150 °C and the mixture was stirred for 1.5 h (TLC control). The mixture was diluted with water and extracted with Et_2O. The organic layer was washed with brine and dried (anhyd Na_2SO_4). The solvent was evaporated under reduced pressure and purification of the residue by column chromatography (silica gel, EtOAc/hexanes, 3:7) furnished the amine **31** (94 mg, 88%) as a colorless solid; R_f = 0.5 (EtOAc/hexanes, 3:7); mp 76–78 °C.

IR (neat): 3270, 2959, 2921, 2866, 1690, 1641, 1598, 1495, 1435, 1409, 1326, 1306, 1289, 1207, 1185, 1155, 1093, 1019 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 7.71 (d, *J* = 8.0 Hz, 2 H), 7.29 (d, *J* = 8.0 Hz, 2 H), 7.11 (s, 1 H), 3.77 (d, *J* = 5.6 Hz, 2 H), 2.41 (s, 3 H), 2.16 (s, 2 H), 1.10 (s, 6 H).

^{13}C NMR (100 MHz, $CDCl_3$, DEPT): δ = 208.75 (C), 169.35 (CH), 143.59 (C), 137.82 (C), 137.05 (C), 129.81 (2 CH), 127.24 (2 CH), 50.42 (CH_2), 39.37 (C), 38.84 (CH_2), 27.80 (2 CH_3), 21.54 (CH_3).

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{15}H_{20}NO_3S$: 294.1164; found: 294.1169.

Ethyl (*E*)- 3-{*N*-[(3,3-Dimethyl-5-oxocyclopent-1-enyl)methyl]-4-methylphenylsulfonamido}acrylate (32)

Reaction of **31** (92 mg, 0.31 mmol) with ethyl propynoate (35 µL, 0.34 mmol) and DMAP (7 mg, 0.06 mmol) in CH_2Cl_2 (3 mL) at rt as described for TP1 followed by purification of the residue by column chromatography (silica gel, EtOAc/hexanes, 1:9) gave the vinylogous carbonate **32** (110 mg, 85%) as a colorless liquid; R_f = 0.5 (EtOAc/hexanes, 1:9).

IR (neat): 2959, 2922, 2869, 1702, 1620, 1597, 1493, 1447, 1364, 1283, 1255, 1152, 1089, 1062 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 8.12 (d, *J* = 14.0 Hz, 1 H), 7.70 (d, *J* = 8.4 Hz, 2 H), 7.33 (d, *J* = 8.4 Hz, 2 H), 7.02 (d, *J* = 1.2 Hz, 1 H), 4.90 (d, *J* = 14.0 Hz, 1 H), 4.18–4.12 (m, 4 H), 2.43 (s, 3 H), 2.29 (s, 2 H), 1.26 (t, *J* = 7.2 Hz, 3 H), 1.13 (s, 6 H).

^{13}C NMR (100 MHz, $CDCl_3$, DEPT): δ = 207.46 (C), 169.53 (CH), 167.03 (C), 145.26 (C), 141.08 (CH), 135.75 (C), 135.10 (C), 130.41 (2 CH), 127.41 (2 CH), 99.05 (CH), 60.35 (CH_2), 50.63 (CH_2), 41.47 (CH_2), 39.59 (C), 28.05 (2 CH_3), 21.73 (CH_3), 14.46 (CH_3).

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{20}H_{26}NO_5S$: 392.1532; found: 392.1515.

Ethyl (*E*)- 3-{*N*-[(5-Hydroxy-3,3-dimethylcyclopent-1-enyl)methyl]-4-methylphenylsulfonamido}acrylate (33)

Reduction of **32** (85 mg, 0.21 mmol) using $NaBH_4$ (10 mg, 0.26 mmol) and $CeCl_3{\cdot}7H_2O$ (85 g, 0.26 mmol) in MeOH (5 mL) at –10 °C as described for TP2 followed by purification of the residue by column chromatography (silica gel, EtOAc/hexanes, 3:7) furnished the alcohol **33** (80 mg, 92%) as a colorless liquid; R_f = 0.5 (EtOAc/hexanes, 3:7).

IR (neat): 3424, 2954, 2924, 2861, 1706, 1620, 1446, 1361, 1308, 1286, 1258, 1154, 1089, 1054 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 8.10 (d, *J* = 14.0 Hz, 1 H), 7.70 (d, *J* = 8.0 Hz, 2 H), 7.33 (d, *J* = 8.0 Hz, 2 H), 5.44 (s, 1 H), 5.14 (d, *J* = 14.0 Hz, 1 H), 4.72 (dd, *J* = 7.6, 4.4 Hz, 1 H), 4.23–4.14 (m, 3 H), 3.95 (d, *J* = 16.8 Hz, 1 H), 2.42 (s, 3 H), 2.12 (ABX, *J* = 13.6, 7.2 Hz, 2 H), 1.60 (ABX, *J* = 13.6, 4.4 Hz, 1 H), 1.27 (t, *J* = 7.2 Hz, 3 H), 1.07 (s, 3 H), 0.97 (s, 3 H).

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^{13}C NMR (100 MHz, $CDCl_3$, DEPT): δ = 167.23 (CH), 145.15 (C), 143.29 (CH), 141.53 (CH), 135.46 (C), 135.06 (C), 130.33 (2 CH), 127.41 (2 CH), 99.45 (CH), 76.07 (CH), 60.31 (CH_2), 48.79 (CH_2), 44.51 (CH_2), 43.50 (C), 29.80 (CH_3), 28.97 (CH_3), 21.74 (CH_3), 14.49 (CH_3).

HRMS (ESI): *m*/*z* [M + Na]$^+$ calcd for $C_{20}H_{27}NO_5NaS$: 416.1508; found: 416.1504.

Ethyl (*E*)- 3-(*N*-{[5-(2-Iodophenoxy)-3,3-dimethylcyclopent-1-enyl]methyl}-4-methylphenylsulfonamido)acrylate (34)

Reaction of the alcohol **33** (61 mg, 0.16 mmol) with PPh_3 (81 mg, 0.31 mmol), 2-iodophenol (**13**; 38 mg, 0.17 mmol), and DIAD (61 µL, 0.31 mmol) in THF (3 mL) at rt for 6 h as described for TP3 and purification of the residue by column chromatography (silica gel, EtOAc/hexanes, 1:4) furnished the iodide **34** (57 mg, 62%) as a colorless liquid; R_f = 0.5 (EtOAc/hexanes, 1:4).

IR (neat): 2955, 2923, 2865, 1704, 1620, 1581, 1568, 1468, 1439, 1363, 1308, 1273, 1236, 1152, 1089, 1056, 1016 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.13 (d, *J* = 14.0 Hz, 1 H), 7.74–7.71 (m, 3 H), 7.28–7.20 (m, 3 H), 6.67 (d, *J* = 8.0 Hz, 2 H), 5.37 (s, 1 H), 5.31 (d, *J* = 14.0 Hz, 1 H), 5.03 (dd, *J* = 7.2, 2.8 Hz, 1 H), 4.25 (q, *J* = 18.0 Hz, 2 H), 4.11 (q, *J* = 7.2 Hz, 2 H), 2.38 (s, 3 H), 2.11 (ABX, *J* = 14.0, 6.8 Hz, 1 H), 1.77 (ABX, *J* = 13.6, 2.8 Hz, 1 H), 1.21 (t, *J* = 7.2 Hz, 3 H), 1.01 (s, 3 H), 0.97 (s, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$, DEPT): δ = 167.50 (C), 156.48 (C), 144.89 (C), 143.73 (CH), 141.30 (CH), 139.74 (CH), 135.58 (C), 131.60 (C), 130.24 (2 CH), 129.43 (CH), 127.56 (2 CH), 122.54 (CH), 112.72 (CH), 99.63 (CH), 87.36 (C), 83.49 (CH), 60.14 (CH_2), 46.05 (CH_2), 44.88 (CH_2), 44.39 (C), 29.69 (CH_3), 28.92 (CH_3), 21.72 (CH_3), 14.51 (CH_3).

HRMS (ESI): *m*/*z* [M + Na]$^+$ calcd for $C_{26}H_{30}NO_5SINa$: 618.0787; found: 618.0798.

Ethyl (*E*)- 3-[*N*-({5-[*N*-(2-Iodophenyl)-4-methylphenylsulfonamido]-3,3-dimethylcyclopent-1-enyl}methyl)-4-methylphenylsulfonamido]acrylate (35)

Reaction of the alcohol **34** (109 mg, 0.28 mmol) with PPh_3 (145 mg, 0.55 mmol), 2-iodo-*N*-tosylaniline (**15**; 124 mg, 0.33 mmol), and DIAD (109 µL, 0.55 mmol) in THF (5 mL) at rt for 6 h as for described TP3 and purification of the residue by column chromatography (silica gel, EtOAc/hexanes, 3:7) furnished the iodide **35** (135 mg, 65%) as a colorless solid; R_f = 0.5 (EtOAc/hexanes, 3:7); mp 82–84 °C.

IR (neat): 2979, 2955, 2930, 2867, 1736, 1709, 1625, 1597, 1464, 1451, 1363, 1319, 1285, 1260, 1164, 1090, 1057, 1019 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.02 (d, *J* = 13.6 Hz, 1 H), 7.84–7.86 (m, 3 H), 7.53 (dd, *J* = 8.0, 1.2 Hz, 1 H), 7.44 (d, *J* = 8.4 Hz, 2 H), 7.40–7.36 (m, 1 H), 7.16 (br s, 1 H), 7.24 (d, *J* = 8.0 Hz, 2 H), 7.11 (d, *J* = 8.4 Hz, 2 H), 6.98–6.94 (m, 1 H), 5.07–5.02 (m, 2 H), 4.96 (d, *J* = 13.6 Hz, 1 H), 4.96 (AB, *J* = 13.6 Hz, 1 H), 4.10–4.05 (m, 1 H), 3.91 (AB, *J* = 13.6 Hz, 1 H), 2.32 (s, 3 H), 2.29 (s, 3 H), 2.05 (ABX, *J* = 14.0, 9.2 Hz, 1 H), 1.78 (ABX, *J* = 14.0, 6.0 Hz, 1 H), 1.18 (t, *J* = 7.2 Hz, 3 H), 0.74 (s, 3 H), 0.33 (s, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$, DEPT): δ = 167.40 (C), 144.94 (C), 144.13 (C), 142.60 (CH), 141.76 (CH), 140.55 (CH), 139.13 (C), 137.23 (C), 135.52 (C), 134.69 (CH), 131.63 (C), 130.57 (CH), 130.32 (2 CH), 129.57 (2 CH), 129.40 (CH), 128.79 (2 CH), 128.47 (CH), 128.40 (C), 127.58 (2 CH), 99.32 (CH), 69.35 (CH), 60.26 (CH_2), 47.07 (CH_2), 43.13 (CH_2), 42.33 (C), 29.46 (CH_3), 28.03 (CH_3), 21.76 (CH_3), 14.52 (CH_3).

HRMS (ESI): *m*/*z* [M + Na]$^+$ calcd for $C_{33}H_{37}N_2O_6S_2INa$: 771.1036; found: 771.1028.

Ethyl (*E*)- 3-[*N*-({3,3-Dimethyl-5-[4-methyl-*N*-(prop-2-ynyl)phenylsulfonamido]cyclopent-1-enyl}methyl)-4-methylphenylsulfonamido]acrylate (36)

Reaction of the alcohol **33** (92 mg, 0.15 mmol) with PPh_3 (123 mg, 0.47 mmol), *N*-tosylpropargylamine (**16**; 59 mg, 0.28 mmol), and DIAD (92 µL, 0.0.47 mmol) in THF (3 mL) at rt for 6 h as described for TP3 and purification of the residue by column chromatography (silica gel, EtOAc/hexanes, 1:4) furnished the iodide **36** (100 mg, 73%) as a colorless liquid; R_f = 0.5 (EtOAc/hexanes, 1:4).

IR (neat): 3283, 2955, 2919, 2872, 1706, 1623, 1491, 1452, 1358, 1340, 1290, 1162, 1090, 1058 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.10 (d, *J* = 14.0 Hz, 1 H), 7.79 (d, *J* = 8.4 Hz, 2 H), 7.70 (d, *J* = 8.4 Hz, 2 H), 7.35 (d, *J* = 8.0 Hz, 2 H), 7.29 (d, *J* = 8.0 Hz, 2 H), 5.38 (d, *J* = 1.2 Hz, 1 H), 4.99 (t, *J* = 1.2 Hz, 1 H), 4.95 (d, *J* = 9.6 Hz, 1 H), 4.20–4.10 (m, 4 H), 3.80 (ABX, *J* = 18.4, 2.4 Hz, 1 H), 3.68 (ABX, *J* = 18.8, 2.4 Hz, 1 H), 2.44 (s, 3 H), 2.43 (s, 3 H), 2.21 (t, *J* = 2.4 Hz, 1 H), 1.80–1.69 (m, 2 H), 1.28 (t, *J* = 7.2 Hz, 3 H), 1.00 (s, 3 H), 0.91 (s, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$, DEPT): δ = 167.21 (C), 145.13 (C), 143.78 (C), 142.55 (CH), 141.59 (CH), 135.28 (C), 130.82 (C), 130.38 (2 CH), 129.67 (2 CH), 127.68 (CH), 127.34 (2 CH), 127.38 (2 CH), 98.96 (CH), 79.70 (C), 64.87 (CH), 60.30 (CH_2), 44.87 (CH_2), 43.30 (C), 41.58 (CH_2), 33.01 (C), 32.21 (CH_2), 29.39 (CH_3), 29.04 (CH_3), 21.85 (CH_3), 21.70 (CH_3), 14.50 (CH_3).

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{30}H_{37}N_2O_6S_2$: 465.0563; found: 465.0573.

2-(Hydroxymethyl)cyclohex-2-enone (56)

To a magnetically stirred solution of cyclohex-2-enone (**55**; 2 g, 20.81 mmol) in THF was added aq HCHO (4.3 mL, 41.61 mmol), followed by portionwise addition of catalytic amount of DMAP (254 mg, 2.08 mmol) and the mixture was stirred for 5 d. The mixture was diluted with CH_2Cl_2 and acidified with aq 1 M HCl. The organic layer was separated and washed with aq $NaHCO_3$ and brine and dried (anhyd Na_2SO_4). Evaporation of the solvent under reduced pressure and purification of the residue by column chromatography (silica gel, Et_2O/CH_2Cl_2, 3:7) furnished the alcohol **56** (1.65 g, 64%) as a colorless liquid; R_f = 0.5 (Et_2O/CH_2Cl_2, 3:7).

IR (neat): 3447, 2937, 2870, 1667, 1388, 1251, 1172, 1138, 1072, 911, 860, 803 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.93 (t, *J* = 4.0 Hz, 1 H), 4.22 (d, *J* = 5.2 Hz, 2 H), 2.75 (t, *J* = 6.4 Hz, 1 H), 2.45–2.36 (m, 3 H), 2.02–1.96 (m, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$, DEPT): δ = 200.83 (C), 147.20 (CH), 138.30 (C), 62.05 (CH_2), 38.30 (CH_2), 25.72 (CH_2), 22.80 (CH_2).

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_7H_{11}O_2$: 127.0759; found: 127.0759.

Ethyl (*E*)- 3-[(6-Oxocyclohex-1-enyl)methoxy]acrylate (57)

To a magnetically stirred solution of **56** (500 mg, 3.99 mmol) in dry CH_2Cl_2 (10 mL) were added NMM (427 µL, 4.36 mmol) and ethyl propynoate (440 µL, 4.36 mmol) at rt and the mixture was stirred for 4 h (TLC control). Evaporation of the solvent and purification of the residue by column chromatography (silica gel, EtOAc/hexanes, 1:4) furnished the alcohol **57** (811 mg, 91%) as a colorless liquid; R_f = 0.5 (EtOAc/hexanes, 1:4).

IR (neat): 2938, 1707, 1678, 1630, 1455, 1395, 1283, 1136, 1047 cm^{-1}.

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^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.58 (d, *J* = 12.4 Hz, 1 H), 7.03 (t, *J* = 4.02 Hz, 1 H), 5.26 (d, *J* = 12.4 Hz, 1 H), 4.53 (s, 2 H), 4.15 (q, *J* = 7.2 Hz, 2 H), 2.49–2.42 (m, 4 H), 2.03 (quin, *J* = 6.4 Hz, 2 H), 1.26 (t, *J* = 7.2 Hz, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$, DEPT): δ = 198.08 (C), 167.85 (C), 162.16 (CH), 148.33 (CH), 134.11 (C), 97.57 (CH), 67.98 (CH_2), 59.98 (CH_2), 38.15 (CH_2), 25.88 (CH_2), 22.73 (CH_2), 14.48 (CH_3).

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{12}H_{17}O_4$: 225.1127; found: 225.1122.

Ethyl (*E*)- 3-[(6-Hydroxycyclohex-1-enyl)methoxy]acrylate (58)

To a cold (–10 °C), magnetically stirred solution of **57** (751 mg, 3.35 mmol) and $CeCl_3·7H_2O$ (1.21 g, 3.69 mmol) in MeOH (10 mL) was added $NaBH_4$ (127 mg, 3.35 mmol) portionwise. The solvent was removed under reduced pressure and residue was extracted with EtOAc. The organic layer was washed with brine and dried (anhyd $NaSO_4$). The solvent was evaporated under reduced pressure and purification of the residue by column chromatography (silica gel, EtOAc/hexanes, 3:7) furnished the alcohol **58** (715 mg, 95%) as a colorless liquid; R_f = 0.5 (EtOAc/hexanes, 3:7).

IR (neat): 3412, 2935, 1690, 1619, 1453, 1373, 1324, 1282, 1123, 1044 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.58 (d, *J* = 12.8 Hz, 1 H), 5.92 (t, *J* = 3.6 Hz, 1 H), 5.25 (d, *J* = 12.4 Hz, 1 H), 4.53 (AB, *J* = 11.6 Hz, 1 H), 4.28 (AB, *J* = 11.6 Hz, 1 H), 4.21–4.19 (m, 1 H), 4.16 (q, *J* = 7.2 Hz, 2 H), 2.10–2.02 (m, 3 H), 1.84–1.74 (m, 2 H), 1.72–1.67 (m, 1 H), 1.63–1.58 (m, 1 H), 1.25 (t, *J* = 7.2 Hz, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$, DEPT): δ = 168.03 (C), 162.28 (CH), 134.28 (C), 131.61 (CH), 97.23 (CH), 73.64 (CH_2), 64.88 (CH), 59.96 (CH_2), 31.69 (CH_2), 25.37 (CH_2), 17.85 (CH_2), 14.41 (CH_3).

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{12}H_{19}O_4$: 227.1283; found: 227.1286.

Ethyl (*E*)- 3-{[6-(2-Iodophenoxy)cyclohex-1-enyl]methoxy}acrylate (59)

Reaction of the alcohol **58** (430 mg, 1.90 mmol) with PPh_3 (997 mg, 3.80 mmol), 2-iodophenol (**13**; 460 mg, 2.09 mmol), and DIAD (748 µL, 3.80 mmol) in THF (7 mL) at rt for 6 h as described for TP3 and purification of the residue by column chromatography (silica gel, EtOAc/hexanes, 1:9) furnished the iodide **59** (550 mg, 68%) as a colorless liquid; R_f = 0.5 (EtOAc/hexanes, 1:9).

IR (neat): 2936, 1702, 1623, 1575, 1463, 1373, 1320, 1273, 1232, 1122, 1045 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.77 (dd, *J* = 7.6, 1.2 Hz, 1 H), 7.57 (d, *J* = 12.8 Hz, 1 H), 7.30–7.26 (m, 1 H), 6.88 (d, *J* = 7.6 Hz, 1 H), 6.71 (td, *J* = 7.6, 1.2 Hz, 1 H), 6.13–6.12 (m, 1 H), 5.25 (d, *J* = 12.4 Hz, 1 H), 4.84 (br s, 1 H), 4.66 (dd, *J* = 11.6, 0.8 Hz, 1 H), 4.32 (d, *J* = 11.6 Hz, 1 H), 4.14 (q, *J* = 7.2 Hz, 2 H), 2.23–2.21 (m, 1 H), 2.13–2.12 (m, 1 H), 2.04–1.99 (m, 1 H), 1.89–1.76 (m, 2 H), 1.67–1.62 (m, 1 H), 1.25 (t, *J* = 7.2 Hz, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$, DEPT): δ = 167.92 (C), 162.14 (CH), 156.92 (C), 139.72 (CH), 133.27 (CH), 131.65 (C), 129.54 (CH), 122.95 (CH), 114.06 (CH), 97.33 (CH), 88.27 (C), 72.77 (CH_2), 71.73 (CH), 59.88 (CH_2), 27.57 (CH_2), 25.26 (CH_2), 17.99 (CH_2), 14.45 (CH_3).

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{18}H_{22}O_4I$: 429.0563; found: 429.0562.

Ethyl (*E*)- 3-{[6-(1-Iodonaphthalen-2-yloxy)cyclohex-1-enyl]methoxy}acrylate (60)

Reaction of the alcohol **58** (151 mg, 0.72 mmol) with PPh_3 (374 mg, 1.43 mmol), 1-iodo-2-naphthol (**14**; 211 mg, 0.78 mmol), and DIAD (281 µL, 1.43 mmol) in THF (4 mL) at rt for 6 h as described for TP3 and purification of the residue by column chromatography (silica gel, EtOAc/hexanes, 1:9) furnished the iodide **60** (206 mg, 57%) as a colorless liquid; R_f = 0.5 (EtOAc/hexanes, 1:9).

IR (neat): 2976, 2932, 2873, 1706, 1622, 1592, 1500, 1459, 1324, 1280, 1260, 1236, 1130, 1045, 1000 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.14 (d, *J* = 8.8 Hz, 1 H), 7.79 (d, *J* = 8.8 Hz, 1 H), 7.73 (d, *J* = 8.8 Hz, 1 H), 7.59 (d, *J* = 12.4 Hz, 1 H), 7.53 (t, *J* = 8.4 Hz, 1 H), 7.39 (t, *J* = 7. 6 Hz, 1 H), 7.21 (d, *J* = 8.8 Hz, 1 H), 6.16 (br s, 1 H), 5.27 (d, *J* = 12.4 Hz, 1 H), 5.00 (br s, 1 H), 4.75 (d, *J* = 11.6 Hz, 1 H), 4.36 (d, *J* = 11.6 Hz, 1 H), 4.11 (qd, *J* = 7.2, 2.0 Hz, 2 H), 2.26–2.25 (m, 1 H), 2.15–2.13 (m, 1 H), 2.10–2.03 (m, 1 H), 2.01–1.96 (m, 1 H), 1.82–1.76 (m, 1 H), 1.70–1.66 (m, 1 H), 1.23 (t, *J* = 7.2 Hz, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$, DEPT): δ = 167.91 (C), 162.14 (CH), 155.72 (C), 135.93 (C), 133.53 (CH), 131.88 (C), 131.65 (CH), 130.47 (CH), 130.34 (C), 128.29 (CH), 128.19 (CH), 124.76 (CH), 116.01 (CH), 97.53 (CH), 90.63 (C), 72.96 (CH), 72.94 (CH_2), 59.90 (CH_2), 28.15 (CH_2), 25.37 (CH_2), 18.13 (CH_2), 14.46 (CH_3).

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{22}H_{24}O_4I$: 479.0719; found: 479.0714.

Angularly-Fused Bis-ether 61; Typical Procedure 4 (TP4)

Following the procedure for **37**.[4j] To a magnetically stirred, refluxing solution of iodide **59** (707 mg, 1.48 mmol) and AIBN (48.5 mg, 0.3 mmol) in benzene (40 mL) was added a solution of with *n*-Bu_3SnH (796 µL, 2.96 mmol) and AIBN (48.5 mg, 0.3 mmol) in benzene (30 mL) over a period of 3 h under a nitrogen atmosphere. The mixture was further refluxed until completion (ca. 3 h, TLC control). It was then cooled, diluted with Et_2O, washed with 2% aq NH_3 and brine, and the organic layer was dried (anhyd Na_2SO_4). Evaporation of the solvent under reduced pressure gave a residue that was purified by column chromatography (silica gel, EtOAc/hexanes, 1:9) to furnish the angularly-fused bis-ether **61** (286 mg, 65%; dr = 4:1) as a colorless liquid; R_f = 0.5 (EtOAc/hexanes, 1:19).

IR (neat): 2932, 2865, 1733, 1596, 1469, 1370, 1271, 1229, 1181, 1136, 1024 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.32 (dd, *J* = 7.2, 0.8 Hz, 1 H), 7.17 (td, *J* = 7.6, 1.2 Hz, 1 H), 6.93 (t, *J* = 7.6 Hz, 1 H), 6.83 (d, *J* = 7.6 Hz, 1 H), 4.70 (dt, *J* = 8.0, 5.2 Hz, 1 H), 4.42 (t, *J* = 2.8 Hz, 1 H), 4.16 (q, *J* = 7.2 Hz, 2 H), 4.13 (AB, *J* = 8.8 Hz, 1 H), 3.93 (AB, *J* = 8.8 Hz, 1 H), 2.66 (ABX, *J* = 15.6, 8.0 Hz, 1 H), 2.47 (ABX, *J* = 15.6, 5.2 Hz, 1 H), 2.30 (dd, *J* = 16.8, 2.0 Hz, 1 H), 1.84–1.81 (m, 1 H), 1.71–1.65 (m, 1 H), 1.64–1.58 (m, 2 H), 1.56–1.52 (m, 1 H), 1.26 (t, *J* = 7.2 Hz, 3 H), 1.12 (dd, *J* = 13.2, 2.8 Hz, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$, DEPT): δ = 171.47 (C), 158.36 (C), 136.86 (C), 128.55 (CH), 122.92 (CH), 121.25 (CH), 109.93 (CH), 82.66 (CH), 72.62 (CH_2), 60.85 (CH_2), 53.74 (C), 47.24 (CH), 35.96 (CH_2), 26.21 (CH_2), 24.19 (CH), 22.37 (CH_2), 18.63 (CH_2), 14.31 (CH_3).

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{18}H_{23}O_4$: 303.1596; found: 303.1600.

Angularly-Fused Bis-ether 62

Reaction of the iodide **60** (105 mg, 0.22 mmol) with *n*-Bu_3SnH (118 µL, 0.44 mmol) and AIBN (14 mg, 0.09 mmol) in benzene (30 mL) as described TP4 followed by purification of the residue by column chro-

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matography (silica gel, EtOAc/hexanes, 1:9) furnished the angularly-fused bis-ether **62** (25 mg, 33%; dr = 4:1) as a colorless liquid; R_f = 0.7 (EtOAc/hexanes, 1:9).

IR (neat): 2978, 2932, 2867, 1735, 1623, 1592, 1519, 1480, 1461, 1373, 1348, 1300, 1260, 1185, 1164, 1134, 1120, 1049, 1029, 1010 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 8.22 (d, *J* = 8.4 Hz, 1 H), 7.81 (d, *J* = 8.4 Hz, 1 H), 7.72 (d, *J* = 8.4 Hz, 1 H), 7.52 (t, *J* = 8.4 Hz, 1 H), 7.31 (t, *J* = 7.6 Hz, 1 H), 7.15 (d, *J* = 8.8 Hz, 1 H), 4.92 (td, *J* = 8.4, 5.2 Hz, 1 H), 4.61 (AB, *J* = 8.8 Hz, 1 H), 4.52 (br s, 1 H), 4.14 (q, *J* = 7.2 Hz, 2 H), 4.05 (AB, *J* = 8.8 Hz, 1 H), 2.70 (ABX, *J* = 15.6, 8.4 Hz, 1 H), 2.50 (ABX, *J* = 15.6, 5.2 Hz, 1 H), 2.35 (dt, *J* = 14.0, 2.4 Hz, 1 H), 2.01 (dt, *J* = 12.8, 5.2 Hz, 1 H), 1.77–1.69 (m, 2 H), 1.64–1.60 (m, 3 H), 1.26 (t, *J* = 7.2 Hz, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$, DEPT): δ = 171.36 (C), 156.83 (C), 130.52 (2 C), 130.28 (CH), 129.38 (CH), 127.39 (CH), 126.54 (C), 122.99 (CH), 122.44 (CH), 112.57 (CH), 83.04 (CH), 79.46 (CH), 70.22 (CH_2), 60.76 (CH_2), 55.70 (C), 48.00 (CH), 36.39 (CH_2), 26.21 (CH_2), 22.62 (CH_2), 18.63 (CH_2), 14.39 (CH_3).

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{22}H_{25}O_4$: 353.1753; found: 353.1750.

(5-Oxocyclopent-1-enyl)methyl Acetate (63)

To a cold (0 °C) magnetically stirred solution of 2-(hydroxymethyl)cyclopent-2-enone (**6**; 249 mg, 2.22 mmol) in dry CH_2Cl_2 (5 mL) were added successively, Et_3N (728 µL, 0.67 mmol) and DMAP (54 mg, 0.44 mmol), followed by dropwise addition of Ac_2O (420 µL, 4.44 mmol) over a period of 15 min and the mixture was stirred overnight at rt. The mixture was diluted with EtOAc (50 mL) and organic layer was washed with water and brine and dried (anhyd $NaSO_4$). Evaporation of the solvent under reduced pressure and purification of the residue by column chromatography (silica gel, EtOAc/hexanes, 1:4) furnished the acetate **63** (342 mg, 70%) as a colorless liquid; R_f = 0.5 (EtOAc/hexanes, 1:4).

IR (neat): 2924, 2854, 1590, 1459, 1416, 1317, 1267, 1120, 1041 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 7.58–7.56 (m, 1 H), 4.74 (d, *J* = 1.2 Hz, 2 H), 2.65–2.63 (m, 2 H), 2.45–2.43 (m, 2 H), 2.07 (s, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$, DEPT): δ = 207.85 (C), 170.78 (C), 161.19 (CH), 141.28 (C), 57.99 (CH_2), 34.81 (CH_2), 26.99 (CH_2), 20.94 (CH_3).

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_8H_{11}O_3$: 155.0708; found: 155.0710.

(5-Hydroxycyclopent-1-enyl)methyl Acetate (64)

Reduction of **63** (140 mg, 0.91 mmol) using $NaBH_4$ (41 mg, 1.09 mmol) and $CeCl_3{\cdot}7H_2O$ (357 mg, 1.09 mmol) in MeOH (5 mL) at –10 °C as described TP2 followed by purification of the residue by column chromatography (silica gel, EtOAc/hexanes, 3:7) furnished the alcohol **64** (100 mg, 74%) as a colorless liquid; R_f = 0.5 (EtOAc/hexanes, 3:7).

IR (neat): 3410, 2930, 2846, 1732, 1630, 1584, 1446, 1412, 1373, 1242, 1123, 1039 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 5.89–5.88 (m, 1 H), 4.81 (AB, *J* = 12.8 Hz, 1 H), 4.74 (s, 1 H), 4.63 (AB, *J* = 12.8 Hz, 1 H), 2.50–2.42 (m, 1 H), 2.39 (br s, 1 H), 2.34–2.28 (m, 1 H), 2.08 (s, 3 H), 1.81–1.74 (m, 2 H).

^{13}C NMR (100 MHz, $CDCl_3$, DEPT): δ = 171.53 (C), 140.89 (C), 133.41 (CH), 76.72 (CH), 61.14 (CH_2), 33.31 (CH_2), 29.94 (CH_2), 20.97 (CH_3).

HRMS (ESI): *m*/*z* [M + Na]$^+$ calcd for $C_8H_{12}O_3Na$: 179.0684; found: 179.0684.

[5-(2-Iodophenoxy)cyclopent-1-enyl]methyl Acetate (65a)

Reaction of the alcohol **64** (160 mg, 1.03 mmol) with PPh_3 (537 mg, 2.05 mmol), 2-iodophenol (**13**; 226 mg, 1.03 mmol), and DIAD (403 µL, 2.05 mmol) in THF (5 mL) at rt for 6 h as described for TP3 and purification of the residue by column chromatography (silica gel, EtOAc/hexanes, 1:9) furnished the iodide **65a** (235 mg, 63%) as a colorless liquid; R_f = 0.5 (EtOAc/hexanes, 1:9).

IR (neat): 3058, 2934, 2854, 1741, 1580, 1568, 1469, 1439, 1365, 1306, 1275, 1239, 1160, 1119, 1051, 1033, 1017 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 7.81 (dd, *J* = 8.0, 1.2 Hz, 1 H), 7.35–7.30 (m, 1 H), 6.90 (d, *J* = 8.4 Hz, 1 H), 6.75 (t, *J* = 7.2 Hz, 1 H), 6.12 (s, 1 H), 5.33 (t, *J* = 4.4 Hz, 1 H), 4.93 (AB, *J* = 13.2 Hz, 1 H), 4.84 (AB, *J* = 13.2 Hz, 1 H), 2.70–2.60 (m, 1 H), 2.52–2.48 (m, 2 H), 2.09 (s, 3 H), 2.11–2.07 (m, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$, DEPT): δ = 170.93 (C), 157.10 (C), 139.75 (CH), 137.89 (C), 134.85 (CH), 129.46 (CH), 122.62 (CH), 113.46 (CH), 87.63 (C), 84.36 (CH), 61.18 (CH_2), 30.90 (CH_2), 30.77 (CH_2), 21.14 (CH_3).

HRMS (ESI): *m*/*z* [M + Na]$^+$ calcd for $C_{14}H_{15}O_3NaI$: 380.9964; found: 380.9954.

[5-(2-Iodophenoxy) cyclopent-1-enyl]methanol (65b)

To a magnetically stirred solution of **65a** (231 mg, 0.65 mmol) in MeOH (5 mL) was added K_2CO_3 (134 mg, 0.97 mmol) at rt and the mixture was stirred overnight (TLC control). Evaporation of the solvent and purification of the residue by column chromatography (silica gel, EtOAc/hexanes, 1:4) furnished the product **65b** (160 mg, 80%) as a colorless solid; R_f = 0.5 (EtOAc/hexanes, 1:4); mp 74–76 °C.

IR (neat): 3435, 2953, 2926, 2813, 2725, 1593, 1470, 1436, 1384, 1350, 1276, 1241, 1350, 1276, 1241, 1165, 1123, 1057, 1033, 1018 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 7.77 (d, *J* = 8.0 Hz, 1 H), 7.30 (t, *J* = 8.0 Hz, 1 H), 6.88 (d, *J* = 8.0 Hz, 1 H), 6.72 (t, *J* = 7.6 Hz, 1 H), 6.04 (t, *J* = 1.2 Hz, 1 H), 5.34 (t, *J* = 3.2 Hz, 1 H), 4.40 (s, 2 H), 2.60–2.42 (m, 3 H), 2.11 (t, *J* = 5.6 Hz, 1 H), 2.04–1.98 (m, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$, DEPT): δ = 156.84 (C), 141.90 (C), 139.67 (CH), 133.15 (CH), 129.55 (CH), 122.67 (CH), 113.34 (CH), 87.41 (C), 85.55 (CH), 60.39 (CH_2), 31.17 (CH_2), 30.72 (CH_2).

HRMS (ESI): *m*/*z* [M + Na]$^+$ calcd for $C_{12}H_{13}O_2NaI$: 338.9858; found: 338.9857.

3-Benzoyl-1-{[5-(2-iodophenoxy)cyclopent-1-enyl]methyl}pyrimidine-2,4(1*H*,3*H*)-dione (66)

Reaction of the alcohol **65b** (70 mg, 0.22 mmol) with PPh_3 (116 mg, 0.44 mmol), 3-benzoylpyrimidine-2,4(1*H*,3*H*)-dione (60 mg, 0.28 mmol), and DIAD (89 µL, 0.44 mmol) in THF (7 mL) at rt for 12 h as described for TP3 and purification of the residue by column chromatography (silica gel, EtOAc/hexanes, 2:3) furnished the iodide **66** (85 mg, 71%) as a colorless solid; R_f = 0.5 (EtOAc/hexanes, 2:3); mp 52–54 °C.

IR (neat): 3058, 2931, 2854, 1747, 1704, 1663, 1596, 1582, 1467, 1440, 1381, 1341, 1238, 1175, 1118, 1073, 1048, 1035, 1020 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 7.89 (d, *J* = 7.6 Hz, 2 H), 7.80 (dd, *J* = 7.6, 1.6 Hz, 1 H), 7.62 (t, *J* = 7.2 Hz, 1 H), 7.45–7.41 (m, 3 H), 7.29 (td, *J* = 8.4, 1.2 Hz, 1 H), 6.84 (dd, *J* = 8.4, 0.8 Hz, 1 H), 6.75 (td, *J* = 8.4, 1.2 Hz, 1 H), 6.05 (s, 1 H), 5.77 (d, *J* = 8.0 Hz, 1 H), 5.24 (d, *J* = 4.0 Hz, 1 H), 4.70 (AB, *J* = 15.6 Hz, 1 H), 4.62 (AB, *J* = 15.6 Hz, 1 H), 2.66–2.59 (m, 1 H), 2.54–2.44 (m, 2 H), 2.04–1.98 (m, 1 H).

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^{13}C NMR (100 MHz, $CDCl_3$, DEPT): δ = 168.91 (C), 162.58 (C), 156.27 (C), 149.90 (C), 144.59 (CH), 139.79 (CH), 136.71 (C), 135.60 (CH), 135.12 (CH), 131.52 (C), 130.53 (2 CH), 129.77 (CH), 129.21 (2 CH), 123.06 (CH), 113.53 (CH), 102.35 (CH), 87.38 (C), 84.43 (CH), 46.72 (CH_2), 30.81 (CH_2), 30.76 (CH_2).

HRMS (ESI): *m*/*z* [M + Na]$^+$ calcd for $C_{23}H_{19}N_2O_4NaI$: 534.0287; found: 537.0265.

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Supporting Information

Supporting information for this article is available online at https://doi.org/10.1055/s-0036-1589541.

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(20) ORTEP pictures for the other triquinanes **38**, **45**, **46**, and **51** are given in the Supporting Information.

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