CONTROLLING STEREOCHEMISTRY IN RADICAL ADDITION AND CYCLIZATION REACTIONS WITH OPPOLZER'S CAMPHOR SULTAM†

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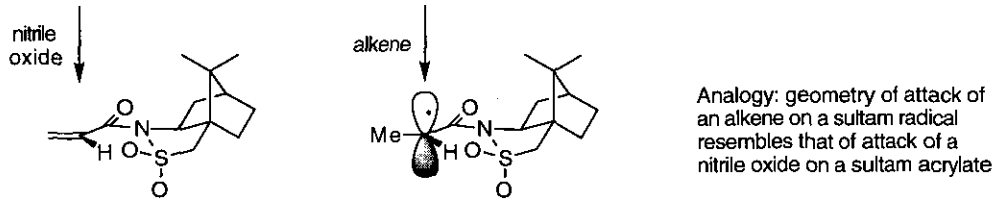
Abstract—Acrylate derivatives of Oppolzer's camphor sultam exhibit good to excellent levels of stereoselectivity in typical radical allylations and alkene and alkyne cyclizations.

Introduction. Over the past several years, the value of radical reactions in organic synthesis has become widely recognized.[1] Fertile ground for the productive use of radical reactions is now being located in areas that were formally considered as the exclusive turf of ionic and pericyclic reactions. Stereoselection with chiral auxiliaries is one such area.[2] As recently as a couple of years ago, only a few isolated examples of good stereoselection in chiral auxiliary controlled radical reactions had been observed. Of late, this situation has changed dramatically.

In the late 1980s, a number of researchers reached two general conclusions: 1) that there was every reason to believe that high levels of acyclic stereoselection could be attained in radical reactions, and 2) that such stereoselective reactions could be designed by drawing judicious analogies between radical intermediates and related closed shell molecules.[2,3] In our labs, we had been studying the asymmetric thermal reactions of Oppolzer's camphor sultam, and we had discovered preparatively useful nitrile oxide cycloaddition reactions.[4] These results led us to develop a hypothesis that rationalized how and why Oppolzer's sultam controlled stereochemistry, and we have detailed and generalized our ideas in a recent review.[5] We have postulated that the geometric features of the heterocyclic sultam ring are crucial for promoting good to excellent levels of stereoselection. According to this hypothesis, the same basic features that make acrylate derivatives of Oppolzer's sultam good chiral auxiliaries in reactions like nitrile oxide cycloadditions should promote good levels of stereocontrol in radical reactions of appropriate sultam analogs (see Figure 1).

Figure 1. Analogies between Nitrile Oxide Cycloadditions and Radical Reactions



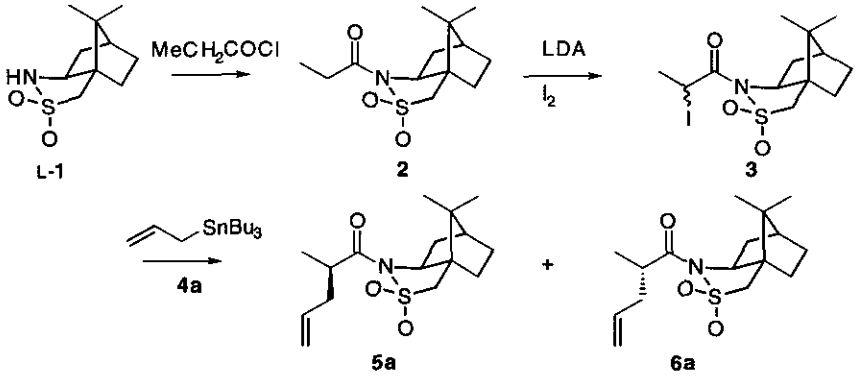
†Dedicated to Professor A. R. Katritzky on the occasion of his 65th birthday.

In 1990, we reported preliminary results showing that Oppolzer's camphor sultam possessed all the key features for use as a chiral auxiliary in asymmetric radical addition and cyclization reactions.[6a] In concurrent communications,[6b,c] Porter and Giese reported their observations on additions with the 2,5-dimethylpyrrolidine chiral auxiliary. In the wake of these reports, the use of chiral auxiliaries to control stereochemistry in radical reactions is quickly becoming an established synthetic tactic.[7] In this paper, we report full details of the reactions described in the preliminary communication,[6a] and we include a number of new examples of addition and cyclization reactions. These reactions all involve the use of Oppolzer's sultam to control the "face selectivity" of chiral radicals. Examples of "group selective" reactions of chiral sultam radicals are being reported separately.[8]

Results and Discussion. We selected Oppolzer's camphor sultam[9] with practicality in mind. Beyond the key feature of asymmetric induction, Oppolzer's sultam is an attractive auxiliary because both enantiomers are commercially available at equal price, because derivatives of the sultam are easy to make, are stable (and sometimes crystalline) and are easy to analyze and purify, and finally because the sultam auxiliary can be removed under mild conditions, reisolated, and reused. In the following text, the reactions are discussed by substrate: bimolecular radical allylations are followed by alkyne cyclizations and finally alkene cyclizations.

Radical Allylations: The general features of asymmetric radical carbon-carbon bond forming reactions with Oppolzer's sultam were probed through the use of standard radical allylation reactions (eq 1). Acylation of L-camphor sultam (**1**) with propionoyl chloride provided sulfonimide (**2**) in nearly quantitative yield. Deprotonation of (**2**) with LDA at –78°C, followed by slow addition of the resulting enolate to a solution of molecular iodine in THF,[10] provided the α-iodosultam (**3**) as a mixture of diastereomers in 78% isolated yield. The diastereomer ratio varied somewhat from one experiment to the next, ranging from 6/1 to 9/1. These diastereomers were generally used in the radical allylations without separation; however, they were partially separable and we did secure differentially enriched samples to conduct a pair of radical allylations. Ratios of the allylated products(**5/6**)were identical in these two experiments,[11] thus showing that the stereochemistry of the allylated products is independent of the stereochemistry of the iodide precursors. We did not attempt to prove configurations of iodides (**3**), but by analogy with the results of Oppolzer it seems likely that the major isomer has the *S* absolute configuration (iodide β in **3**).[12]

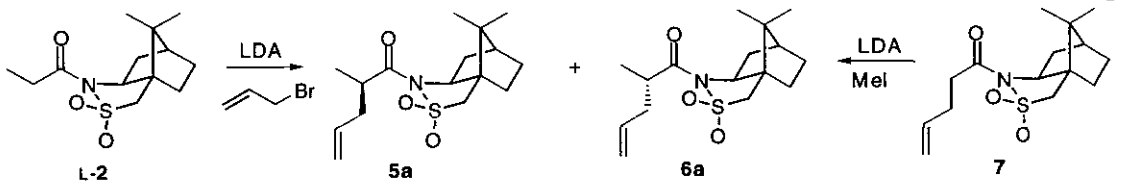
eq 1



Preliminary allylations of **3** were conducted by the standard thermal procedure of Keck (eq 1).[13] Heating of an 0.5M solution of **3** in benzene with **2** equiv of allyltributylstannane (**4a**) and 10% AIBN at 80°C for 5 h resulted in complete consumption of starting material. Analysis of the crude reaction mixture by gc or ^{1}H nmr showed that two new products (**5a**) and (**6a**) formed in a ratio of 92/8. These stereoisomers could not be separated by flash chromatography, and the purified 92/8 mixture was isolated in >95% yield.

The configuration of the new stereocenter was assigned with reference to the enolate alkylations of **2** that Oppolzer and coworkers conveniently reported[12] during the course of our studies (eq 2). Deprotonation of **2** with LDA and allylation with allyl bromide at –78°C provided **5a** and **6a** in a ratio of 96/4. This result compares favorably with that of the Oppolzer group; they reported alkylation of *ent*-**2** with allyl bromide (with lithium isopropylcyclohexylamide as the base) provided *ent*-**5a** and *ent*-**6a** in a ratio of 98/2. They conducted a complete series of alkylations and assigned configurations by solving X-ray crystal structures. For purposes of characterization and analysis, we also methylated the pentenyl analog (**7**) to provide **5a/6a** in a reversed ratio of 4/96 (Oppolzer reports that a similar experiment in the enantiomeric series gives a 2/98 ratio).

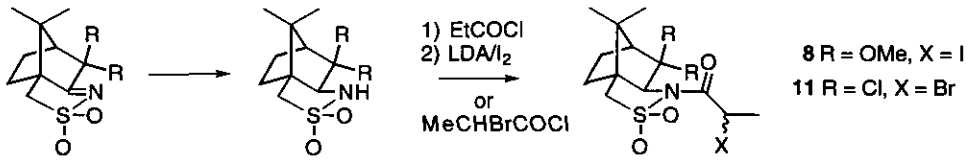
eq 2



The level of selectivity in the radical allylation of **3** (92/8) is quite good; indeed it is only a little bit lower than the selectivity of the ionic allylation (96/4), which was conducted at a temperature of 160°C lower. At comparable temperatures, the selectivity of the radical allylation actually marginally exceeds that of the ionic allylation (see Table 1 below[14]). Experiments like this help to erase any notions that radical reactions should be fundamentally less selective than their ionic counterparts.

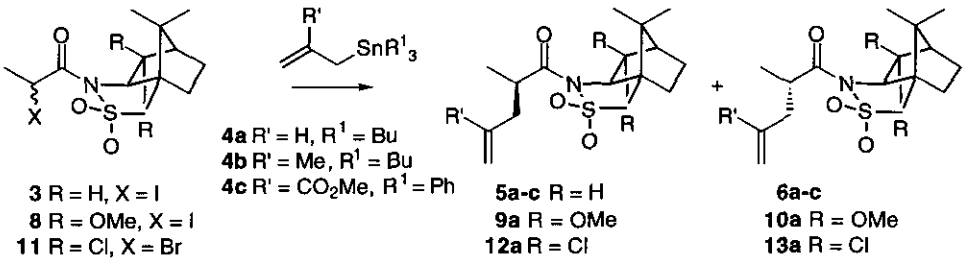
With this backdrop, we conducted a series of allylation experiments, the results of which are summarized in Table 1. In each allylation, we determined the stereoisomer ratio in the crude product mixture by integration of the gc. Most reactions were very clean, and isolated yields were determined in nearly all cases. With a few exceptions (see below), these yields routinely exceeded 90%. In this series, we changed experimental variables including the temperature (–80°C to +80°C), the solvent (benzene, toluene, dichloromethane), and the method of initiation (chemical initiation with AIBN or Et_3B/O_2,[15] or photochemical initiation with a Hanovia lamp). We also varied the allylstannane partner and the chiral auxiliary attached to the radical precursor. In addition to allyltributylstannane itself (**4a**), we tried a few experiments with methallyltributylstannane (**4b**) and 2-carbomethoxy-allyltriphenylstannane (**4c**). Oppolzer's sultam was the most well studied auxiliary, but we also conducted a few experiments with the dimethoxy- (**8**) and dichloro-sulfonimides (**11**). The appropriate substituted sultams (in the "D" series) were prepared by reduction of the known imines (eq 3). These imines have been prepared and used by Davis[16a-c] as precursors for chiral sulfox-aziridines. Dimethoxy analog (**8**) was prepared by analogy to the parent sultam precursor, but this

eq 3



standard acylation/iodination sequence worked poorly in the dichloro series. Instead, the dichlorosultam was acylated with 2-bromopropionoyl chloride, and the resulting bromide (**11**) was used in the allylation.[16c]

Table 1. Radical Allylations with Sultams 3, 8, and 11



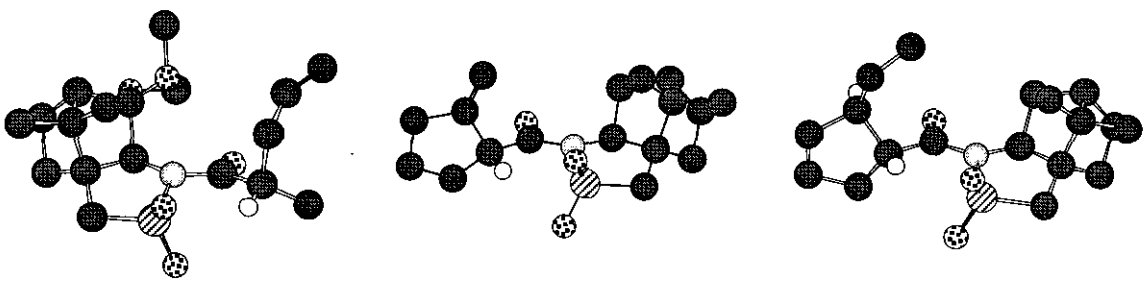
Entry	Sultam	Allyltin	Solvent	Initiation	Temp (°C)	Products[1]	Ratio[2]
1	**3**	**4a**	C_6D_6	AIBN	80	**5a/6a**	92/8
2	**3**	**4a**	CH_2Cl_2	AIBN	80	**5a/6a**	92/8
3	**3**	**4a**	CH_2Cl_2	Et_3B	80[3]	**5a/6a**	92/8
4	**3**	**4a**	C_6D_6	hν	25	**5a/6a**	91/9
5	**3**	**4a**	C_6D_6	Et_3B	25	**5a/6a**	93/7
6	**3**	**4a**	CH_2Cl_2	Et_3B	25	**5a/6a**	93/7
7	**3**	**4a**	CH_2Cl_2	Et_3B	0	**5a/6a**	95/5
8	**3**	**4a**	CH_2Cl_2	Et_3B	–20	**5a/6a**	96/4
9	**3**	**4a**	$PhCH_3$	hν	–20[4]	**5a/6a**	93/7
10	**3**	**4a**	CH_2Cl_2	Et_3B	–78[5]	**5a/6a**	>97/3
11	**3**	**4a**	$PhCH_3$	hν	–78[6]	**5a/6a**	97/3
12	**3**	**4b**	C_6D_6	Et_3B	25	**5b/6b**	93/7
13	**3**	**4c**	C_6D_6	Et_3B	25	**5c/6c**	94/6
14	**3**	**4c**	C_6D_6	hν	25	**5c/6c**	90/10
15	**8**[7]	**4a**	C_6D_6	AIBN	80	**9a/10a**[7]	98.5/1.5
16	**11**[7]	**4a**	C_6D_6	AIBN	80	**12a/13a**[7]	97/3

1) Isolated yields were ≥ 90% unless indicated. 2) Determined by capiliary gc. 3) Conducted in a sealed tube. 4) Starting material consumed, but yield not determined. 5) Et_3B added in 4 portions over 24 h, yield 34%, starting material remains. 6) Reaction mixture contains unidentified impurities, yield not determined. 7) Actual experiment used the enantiomer (see eq 3).

The data in Table 1 reveal a number of trends. There is no significant dependence of the ratio of **5a/6a** on the solvent (for example, compare Entries 1/2 and 5/6). According to the accepted radical mechanism, there should also be no dependence of the **5a/6a** ratio on the initiation method; however, data on this point are less clear cut. At identical temperatures, initiation with AIBN or Et_3B/O_2 did indeed give identical product ratios (Entries 1/2/3). But photochemical initiation appeared to give slightly lower ratios than either method of chemical initiation (compare 8/9, 10/11, 13/14). Though the trend towards lower ratios in the photochemical initiation seems real, the differences are sufficiently small so as not to warrant further investigation or discussion. From the standpoint of experimental convenience, the chemical methods of initiation are preferred and were adapted for all further experiments. These bimolecular reactions show a common temperature dependence pattern: selectivity gradually increases as the temperature is lowered. A **5a/6a** ratio of 92/8 increases to >97/3 on cooling from +80°C to –80°C (compare Entries 2/7/8/10). In practice, the experiment conducted at –80°C is not very useful since only ~40% conversion was obtained after 24 h. However, the reaction does proceed smoothly at –20°C by using the Et_3B/O_2 initiation method. The reaction is complete after 6 h, and provides a 96/4 ratio of **5a/6a** in an isolated yield of 95% (Entry 8).

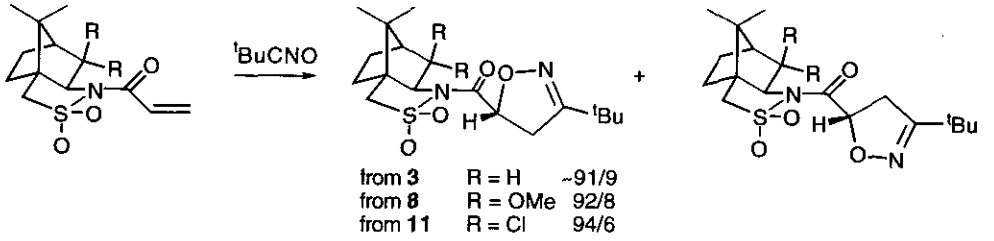
Allylstannane (**4b**) should be slightly more electron rich than **4a**, and **4c** should be significantly more electron poor. These electronic changes had little effect on the stereoisomer ratio in the reactions with **3** (compare entries 5 and 12/13/14). In contrast, the modified chiral auxiliaries (**8**) and (**11**) both gave noticeably better ratios of the allylated products. With the dichloro analog (**11**),[16c] the ratio of **12a/13a** was 97/3 at 80°C (Entry 16), while dimethoxy analog (**8**) provided **9a** and **10a** in a ratio of 98.5 /1.5 (Entry 15). The crystal structure of **9a** was solved (see Figure 2), thus proving that the sense of asymmetric induction is the same with **8** as with the parent sultam.

Figure 2. Crystal Structures of 9a (left), 19 (center) and 25b (right)



Based on the results in Table 1, Entries 15 and 16, we initially hoped that the dimethoxy and dichloro analogs of Oppolzer's sultam might be generally superior chiral auxiliaries to the parent. This did not prove to be the case. In benchmark nitrile oxide cycloadditions (see eq 4), the modified auxiliaries behaved only marginally better than the parent. And in several radical cyclizations, they actually provided lower stereoisomer ratios than the parent (see below). In short, our brief survey did not identify an obvious trend, and we decided that the improvements in stereoselectivity that might sometimes attend the use of **8** and **11** were not potentially significant enough to offset the extra steps required to prepare them.

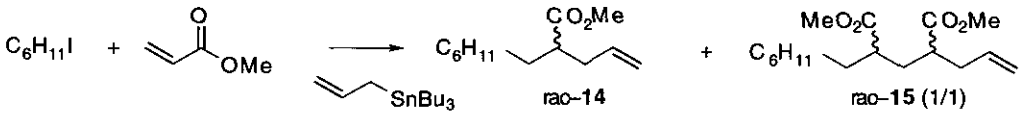
eq 4



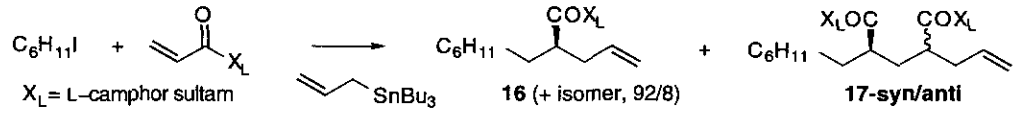
from **3**	R = H	~91/9
from **8**	R = OMe	92/8
from **11**	R = Cl	94/6

A second method to generate radicals adjacent to carbonyls is by a prior radical addition reaction to an alkene, and eqs 5a and 5b show a pair of tandem reactions in which a radical addition precedes an asymmetric allylation. In the achiral model experiment, we heated a mixture of cyclohexyl iodide (1 equiv), methyl acrylate (1 equiv), allylstannane (**4a**) (5 equiv) and AIBN (10%) at 80°C in benzene for 6 h. From this mixture we isolated the (racemic) double adduct (**14**) in 58% yield and the triple adduct (**15**) in 19% yield. In addition to being racemic, adduct (**15**) is a 1/1 mixture of diastereomers. The complementary experiment substituting the sultam acrylate for methyl acrylate is illustrated in eq 5b. From this experiment, we isolated the double adduct (**16**) as a 92/8 mixture of isomers (only major isomer shown) in 81% yield. The formation of adduct (**16**) once again shows the ability of the chiral auxiliary to dictate absolute stereochemistry; excision[5,9] of the auxiliary from **16** prior to diastereomer separation would provide the product as a 92/8 ratio of enantiomers (84% ee).

eq 5a



eq 5b

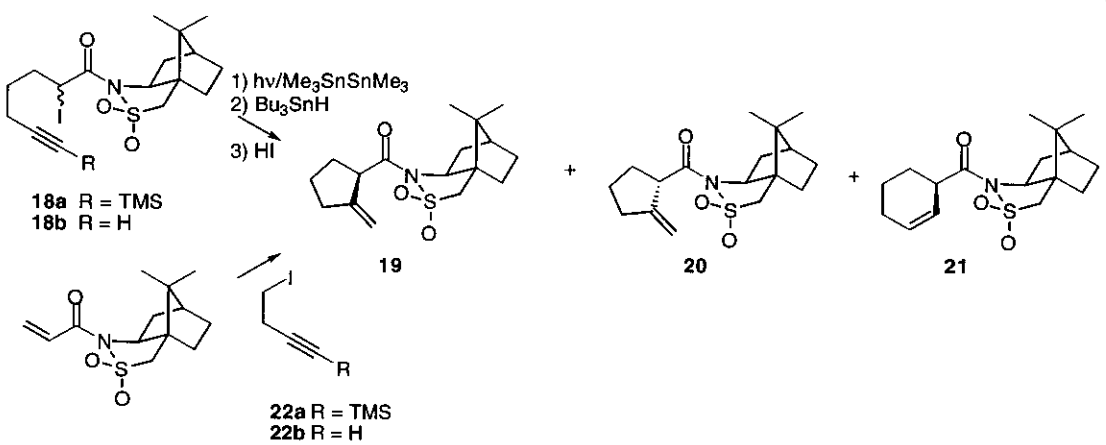


In our original communication,[6a] we also reported the isolation of a minor double adduct (**17-syn**) from the experiment in eq 5b, and suggested based on the stereochemical model that this was formed selectively over **17-anti**. Recent results of Porter and coworkers[17a] have questioned this suggestion. They found that Oppolzer's sultam does a poor job of controlling tacticity when its acrylate derivative is polymerized, and that double adducts related to **17** were not formed stereoselectivity. In contrast, amide- and oxazolidine-based auxiliaries control stereochemistry in single, double, and multiple additions.[7f,17a] These observations prompted us to repeat the experiment in eq 5b with higher concentrations of the sultam acrylate to increase the yield of **17**. In line with Porter's results, we observed that both **17-syn** and **17-anti** are formed in a ratio not far from unity.[17b] We are now conducting a series of experiments designed to probe why the sultam controls stereochemistry in a single addition but not double or multiple ones, and details of the formation and characterization of **17-syn** and **17-anti** will be contained in a paper describing this work.

Radical Cyclizations and Annulations: Much of the synthetic power of radical reactions rests in the expanded scope of intramolecular additions relative to their bimolecular counterparts. It is thus important to study the potential of the camphor sultam to control stereochemistry in representative radical cyclizations, so we prepared and cyclized a number of substrates containing both alkyne and alkene acceptors. Chiral radicals were generated either from traditional halide precursors or by a prior addition of another radical to the acrylimide (a radical annulation). The halides for the traditional route were prepared by a sequence of acylation of the appropriate acid chloride with the sultam followed by iodination, as in eq 1 (full details in the Experimental Section).

Initial experiments were conducted by the atom transfer method[18] with the iodide (**18a**) possessing a trimethylsilyl alkyne acceptor (eq 6). Sunlamp irradiation of **18a** (9/1 mixture of diastereomeric iodides) in a solution of benzene containing 15% hexamethylditin quickly (15 min, 80°C) afforded a mixture of cyclized products (diastereomers and E/Z vinyl iodide/silane isomers). This crude mixture was treated with tributyltin hydride to effect reductive deiodination and then with hydroiodic acid to effect desilylation. Analysis of the resulting crude product by gc and ^{1}H nmr spectroscopy showed that two products remained in a ratio of 90/10. Purification by flash chromatography did not separate these products, and we isolated a mixture of **19** and **20** in 61% overall yield after the three step sequence. Iodide (**18a**) also cyclized smoothly at 25°C by using the Et_3B/O_2 initiation procedure, but the improvement in selectivity was negligible: after deiodination and desilylation, we isolated a mixture of **19** and **20** in a ratio of 91/9. Crystallization of the mixture provided pure **19**, whose structure was solved by X-ray crystallography. Figure 2 shows this structure, and the configuration of the newly formed stereocenter is as predicted from the model in Figure 1.

eq 6



Desilylation of **18a** provided the terminal alkyne (**18b**), which we then subjected to a similar sequence of atom transfer cyclization and reductive deiodination. From this sequence, we obtained a mixture of three isomers in a ratio of 87/3/10 in 46% combined yield. The major and minor products were previously isolated 5-exo diastereomers (**19**) and (**20**), but the ratio of these isomers obtained from the terminal alkyne (**18b**) (96/4) was higher than that obtained from the trimethylsilylalkyne (**18a**) (90/10).

The intermediate product in the reaction of **18b** was a 6-*endo* product (**21**), whose configuration was not proven but can be assigned as that shown by applying the model. The 5-*exo*/6-*endo* ratio in this experiment (90/10) is typical for that of cyclizations of related terminal alkynes.[18] A minor diastereomeric 6-*endo* product is also expected, but assuming that the selectivity for formation of this product is in the vicinity of 10/1, its yield would be 1% or less. We did not attempt to locate this expected minor product.

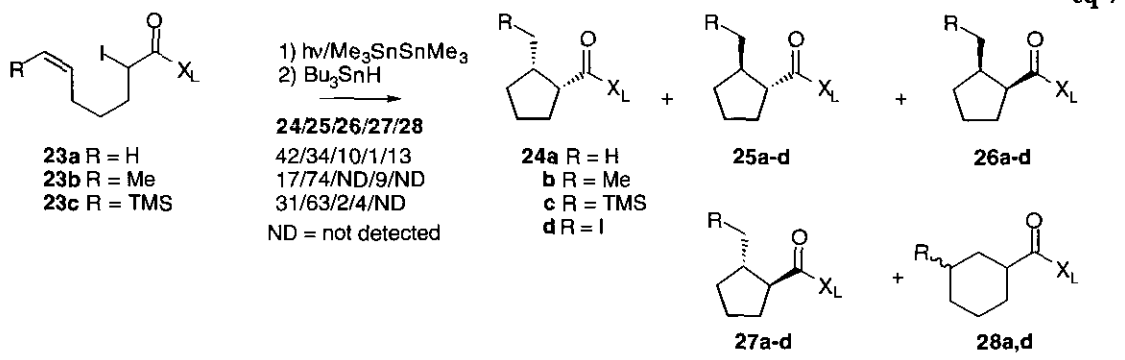
In principle, radicals derived from iodides (**18a,b**) can be formed more expeditiously by a prior radical addition reaction, and it was indeed through such radical annulations that we first probed the asymmetric radical reactions of Oppolzer's sultam. Atom transfer annulation of trimethylsilyl-1-iodobutyne (**22a**) and the sultam acrylate under our standard conditions[19] (hexamethylditin, sunlamp irradiation) gave a very complex mixture of products that we did not attempt to purify. We are puzzled by the failure of this reaction because iodide (**22a**) is quite a good partner in annulation reactions with methyl acrylate.[19a] In contrast, annulation with iodobutyne (**22b**) and the sultam acrylate worked as expected and provided a mixture of **19**, **20**, and **21** in 52% yield in a ratio virtually identical to that of the cyclization of **18b** (87/3/10). The identity of the ratios in these two experiments shows that the same radical intermediate is involved in both and that (as expected) the reactivity profile of this radical does not depend on its method of generation. We also conducted the annulation experiment at 25°C, and we isolated the product mixture (**19/20/21**) in 53% yield. The observed ratio (88/2.5/9.5) was little changed from the 80°C experiment.

We also studied the cyclization reactions of three iodoalkenes. Cyclization of the terminal alkene **23a** by the atom transfer method gave a mixture of isomeric iodides (**24d-28d**). The ratio of these iodides could not be determined accurately from the crude mixture, but we were able to separate the mixture into four fractions, two of which were reasonably pure (>85%) samples of the two major products. Each of the four fractions was then reductively deiodinated with tributyltin hydride to give **24a-28a**. We then estimated product ratios by correcting the isolated yields for each fraction (77% total isolated yield) by the contents of the fractions. In this way, we estimated the ratio of **24a-28a** to be 42/34/10/1/13. Structures of products were assigned by a combination of methods. The one 6-*endo* **28a** product was readily differentiated from the 5-*exo* products by spectroscopy. The 5-*exo* products were paired into *cis* (**24a** and **26a**) and *trans* (**25a** and **27a**) isomers by a series of independent syntheses of adducts and epimerization studies.[20] Finally, stereochemistry on the cyclopentane or cyclohexane ring relative to the auxiliary was designated by applying the stereochemical model in Figure 1. The cyclization data can be viewed in a number of ways. The 5-*exo*/6-*endo* ratio ([**24a-27a**]/**28a**) is 87/13, and this is typical for related cyclizations of esters.[18] Likewise, the low *cis*/*trans* selectivity (59/41) within the 5-*exo* manifold is typical. Within each pair of products, diastereoselectivity is somewhat variable. The diastereoselectivity in the 5-*exo cis* series (**24a**/**26a**) was somewhat lower than expected from the alkyl cyclizations (81/19) while that in the 5-*exo trans* series (**25**/**27**) was somewhat higher (96/4).

Eq 7 also summarizes the results cyclizations of the *cis*-methyl- (**23b**) and *cis*-trimethylsilyl-substituted (**23c**) alkenes. Direct analyses of the crude mixtures were again difficult due to overlapping, and for these substrates the crude iodide mixtures were reduced with tributyltin hydride

prior to separation. The selectivities shown in eq 7 were then calculated based on the yields and product ratios of the isolated fractions. In general, we obtained the major products (**24b,c**, **25b,c**) in pure form, but the minor products (**26b,c**, **27b,c**) could only be obtained partially enriched in mixed fractions. Therefore, these minor products are not well characterized. Structural assignments followed methods analogous to those described for the terminal alkenes. Ultimately, we succeeded in crystallizing **25b**, and its X-ray structure was solved. This structure, shown is Figure 2, is consistent with the assignments in eq 7.

eq 7



For substrates **23b,c**, we neither expected nor located any 6-*endo* products **28**. In the 5-*exo* series, the cyclizations occurred with moderate to good trans selectivities (**23c**, 67/33; **23b**, 83/17). Within each pair of *trans* isomers, face selectivity was good (**25c/27c**, 89/11; **25b/27b**, 94/6). The minor diastereomer (**26b**) paired with *cis* isomer (**24b**) could not be located, so we can not determine the face selectivity in this pair. The face selectivity of the other *cis* pair (**24c/26c**) was about 94/6. Due to the method of estimation, the exact selectivity numbers with all of these alkene substrates must be taken with a grain of salt since small weighing errors in determining isolated yields of minor products could lead to significant errors in our ratios. However, we believe that the trends identified by our estimated ratios are reliable.

EXPERIMENTAL

General Allylation Procedure A (80°C) A mixture of the α-iodosultam (**3**, **8**, or **11**) (1.0 equiv), allyltin (**4a-c**) (1.5 equiv) and AIBN (0.05-0.1 equiv) in benzene or benzene-d_6 (0.5 M for the substrate) was heated at 80°C until all the starting iodide was consumed. Then the solution was diluted with wet ether, followed by addition 2 to 5 drops of DBU. After 5 min, the solution was filtered through a layer of silica gel eluting with dry ether. The residue after concentrating the filtrate was purified by flash column chromatography.

Radical allylation procedure B (–78°C to 25°C) Using the same solution as in A (no AIBN), the initiation was carried out with triethylborane (0.05-0.2 equiv) by passing a slow, steady stream of air over the surface of the reaction mixture.

Radical allylation procedure C: No initiator was added, and the standard reaction mixture was irradiated with Hanovia UV lamp.

4-(1-Oxopropyl)-(7*R*)-10,10-dimethyl-5-thia-4-azatricyclo[5.2.1.0]decane-5,5-dioxide (2). To the suspension of sodium hydride (36.0 mg, 1.5 mmol) in THF (5 ml) was slowly added L-(+)-2,10-camphor sultam (215 mg, 1.0 mmol) in THF (5 ml). After 1 h, propanoyl chloride (185 mg, 2 mmol) was added *via* syringe. After 10 min, the reaction mixture was filtered through a plug of silica gel (2 g), and the residue was

washed with dry ether (20 ml). Evaporation of the filtrate afforded **2** (264 mg, 97%) with good purity: ^{1}H Nmr (300 MHz, $CDCl_3$) δ 3.86 (dd, 1 H, *J* = 5.3, 7.3 Hz), 3.51 (d, 1 H, *J* = 13.7 Hz), 3.42 (d, 1 H, *J* = 13.7 Hz), 2.76 (m, 2 H), 2.11 (m, 2 H), 1.88 (m, 3 H), 1.38 (m, 2 H), 1.16 (t, 3 H, *J* = 7.3 Hz), 1.17 (s, 3 H), 0.97 (s, 3 H).

4-(2-Iodo-1-oxopropyl)-(7*R*)-10,10-dimethyl-5-thia-4-azatricyclo[5.2.1.0]decane-5,5-dioxide (3). To a solution of diisopropylamine (348.5 mg, 0.483 ml, 3.44 mmol) in THF (20 ml) at 0°C was slowly added BuLi (1.43 M, 2.22 ml, 2.22 mmol). After 10 min, the solution was cooled to –78°C, and a solution of **2** (718 mg, 2.65 mmol) in THF (5 ml) was slowly added. After 2 h, the solution was transferred dropwise into a solution of iodine (1.02 g, 4.0 mmol) in THF (25 ml) at –78°C *via* a canula. The reaction was kept at –78°C for 0.5 h, then at 0°C for 0.5 h. Then, 1 N HCl (3 ml) was added, followed by ether extraction and column chromatographic purification (2/1 hexane/CH_2Cl_2) to afford **3** (0.816 g, 78%): ^{1}H Nmr (300 MHz, $CDCl_3$) for the major diastereomer δ 5.12 (q, 1 H, *J* = 4.5 Hz), 3.97 (dd, 1 H, *J* = 5.4, 7.3 Hz), 3.50 (d, 1 H, *J* = 13.7 Hz), 3.45 (d, 1 H, *J* = 13.7 Hz), 2.07 (m, 2 H), 1.98 (d, 3 H, *J* = 4.5 Hz), 1.98-1.88 (m, 4 H), 1.40 (m, 2 H), 1.21 (s, 3 H), 0.99 (s, 3 H).

4-(2*R*)-2-Methyl-1-oxopent-4-enyl)-(7*R*)-10,10-dimethyl-5-thia-4-azatricyclo[5.2.1.0]-decane-5,5-dioxide (5a). See Table 1 for reaction conditions and results. Separation was performed with 10/1 hexane/ethyl acetate. ^{1}H Nmr (300 MHz, $CDCl)_3$, δ 5.75 (m, 1 H), 5.04 (d, 1 H, *J* = 16.6 Hz), 4.97 (d, 1 H, *J* = 9.8 Hz), 3.86 (t, 1 H, *J* = 6.3 Hz), 3.49 (d, 1 H, *J* = 16.2 Hz), 3.41 (d, 1 H, *J* = 16.2 Hz), 3.19 (sexet, 1 H, *J* = 6.7 Hz), 2.41 (m, 1 H), 2.22 (m, 1 H), 2.03 (m, 2 H), 1.85 (m, 3 H), 1.35 (m, 2 H), 1.14 (d, 3 H, *J* = 6.5 Hz), 1.14 (s, 3 H), 0.95 (s, 3 H); ^{13}C nmr (75 MHz, $CDCl_3$) δ 175.7, 135.0, 117.2, 65.3, 53.2, 48.2, 47.7, 44.7, 39.5, 39.3, 38.5, 32.9, 28.5, 20.9, 19.9, 16.2; ir (neat) 2965, 1688, 1458, 1414, 1393, 1329, 1269, 1161, 980, 916, 770, 739, 704 cm^{-1}; HRms calcd for $C_{16}H_{25}NO_3S$ (M^+) 311.1555, found 311.1555.

4-((2*R*)-2,4-Dimethyl-1-oxopent-4-enyl)-(7*R*)-10,10-dimethyl-5-thia-4-azatricyclo[5.2.1.0] decane-5,5-dioxide (5b). The reaction was run by Procedure B at 25°C to give 95% yield of **5b** mixed with **6b** (14/1). ^{1}H Nmr (300 MHz, $CDCl_3$) δ 4.71 (s, 2 H), 3.88 (t, 1 H, *J* = 16.2 Hz), 3.31 (m, 1 H), 2.50 (dd, 1 H, *J* = 8.3, 13.3 Hz), 2.00-2.09 (m, 3 H), 1.82-1.93 (m, 3 H), 1.74 (s, 3 H), 1.21-1.41 (m, 2 H), 1.14 (d, 3 H, *J* = 6.6 Hz), 1.13 (s, 3 H), 0.95 (s, 3 H); ^{13}C nmr (75 MHz, $CDCl_3$) δ 176.1, 142.7, 113.9, 65.4, 53.3, 48.3, 47.7, 38.5, 38.0, 32.9, 26.5, 22.0, 20.7, 20.0, 16.7; ir (neat) 2961, 1680, 1454, 1393, 1377, 1325, 1271, 1221, 1165, 1134, 1061, 895 cm^{-1}; HRms calcd for $C_{17}H_{27}NO_3S$ (M^+), 327.1712; found, 325.1712.

4-((2*R*)-4-Methoxycarbonyl-2-methyl-1-oxopent-4-enyl)-(7*R*)-10,10-dimethyl-5-thia-4-azatricyclo[5.2.1.0]decane-5,5-dioxide (5c). The reaction was run by procedure B at 25°C to give 95% yield of **5c** mixed with **6c** (16/1). ^{1}H Nmr (300 MHz, $CDCl_3$) δ 6.13 (d, 1 H, *J* = 16.2 Hz), 3.41 (d, 1 H, *J* = 16.2 Hz), 3.41 (m, 1 H, overlapping with 3.41 d), 2.59 (m, 2 H), 2.01 (m, 2 H), 1.19 (d, 3 H, *J* = 6.6 Hz), 1.09 (s, 3 H), 0.94 (s, 3 H); ^{13}C nmr (75 MHz, $CDCl_3$) δ 175.6, 166.9, 137.6, 127.2, 65.4, 53.2, 51.9, 48.2, 47.7, 44.7, 38.7, 38.5, 37.7, 33.0, 26.5, 20.8, 19.9, 17.3; ir (neat) 2953, 1726, 1684, 1632, 1460, 1393, 1331, 1271, 1229, 1154, 1136, 1061, 978 cm^{-1}; HRms calcd for $C_{18}H_{27}NO_5S$ (M^+), 369.1610, found 369.1610.

4-((2*R*)-2-methyl-1-oxopent-4-enyl)-(7R)-10,10-dimethyl-5-thia-4-azatricyclo[5.2.1.0]-decane-5,5-dioxide (6a). To a solution of diisopropylamine (62 mg, 0.55 mmol) in THF (20 ml) at 0°C was slowly added BuLi (1.43 M, 0.305 ml, 0.44 mmol). After 10 min, the solution was cooled to –78°C, and a solution of **7** (109 mg, 0.37 mmol) was slowly added *via* syringe. After 1 h, methyl iodide (260 mg, 1.83 mmol) was added, and the solution was gradually warmed to ambient temperature. Ether workup and column chromatographic purification with 10/1 hexane/ethyl acetate afforded **6a** mixed with **5a** (93 mg, 1/12, 81% yield). ^{1}H Nmr (300 MHz, $CDCl_3$) δ 5.79 (m, 1 H), 5.05 (m, 2 H), 3.87 (t, 1 H, *J* = 6.4 Hz), 3.50 (d, 1 H, *J* = 16.2 Hz), 3.42 (d, 1 H, *J* = 16.2 Hz), 3.15 (sextet, 1 H, *J* = 7.0 Hz), 2.52 (m, 1 H), 2.09 (m, 3 H), 1.87 (m, 3 H), 1.39 (m, 2 H), 1.21 (d, 3 H, *J* = 17.0 Hz), 1.15 (s, 3 H), 0.96 (s, 3 H); ^{13}C nmr (75 MHz, $CDCl_3$) δ 176.6, 135.5, 116.9, 65.1, 53.2, 48.3, 47.8, 44.7, 39.8, 28.5, 36.6, 32.8,. 28.5, 20.8, 19.9, 18.4; ir (neat) 2957, 2942, 1682, 1458, 1395, 1329, 1283, 1275, 1242, 1217, 1167, 1136, 1121, 1063 cm^{-1}; HRms calcd for $C_{16}H_{25}NO_3S$ (M^+), 311.1555; found, 311.1555.

4-(2-Iodo-1-oxopropyl)-(7*S*)-10,10-dimethyl-8,8-dimethoxyl-5-thia-4-azatricyclo-[5.2.1.0]decane-5,5-dioxide (8). Acylation and iodination were conducted following the procedures for **2** and **3** (71%). The iodide was a 10/1 mixture of diastereomers: ^{1}H Nmr (300 MHz, $CDCl_3$) δ 5.25 (q, 1 H, *J* = 6.6 Hz), 3.85 (s, 1 H), 3.45 (s, 3 H), 3.44 (d, 1 H, *J* = 13.5 Hz), 3.36 (d, 1 H, *J* = 13.5 Hz), 3.22 (s, 3 H), 2.18 (d, 1 H, *J* = 4.5 Hz), 2.10-2.00 (m, 1 H), 1.95 (d, 3 H, *J* = 6.7 Hz), 1.94-1.47 (m, 3 H), 1.45 (s, 3 H),

0.96 (s, 3 H); ^{13}C nmr (75 MHz, $CDCl_3$) δ 172.7, 109.0, 69.6, 52.3, 51.0, 49.8, 49.7, 47.6, 32.0, 22.6, 21.5, 21.0, 20.9, 14.7.

4-((2*S*)-2-methyl-1-oxopent-4-enyl)-(7*S*)-8,8-dimethoxy-10,10-dimethyl-5-thia-4-azatricyclo[5.2.1.0]decane-5,5-dioxide (9a). This was prepared by procedure **B**: ^{1}H Nmr (300 MHz, $CDCl_3$) δ 5.85-5.71 (m, 1 H), 5.13-5.10 (m, 2 H), 3.56 (s, 1 H), 3.47 (s, 3 H), 3.47 (s, 3 H), 3.42 (d, 1 H, *J* = 14.0 Hz), 3.34 (d, 1 H, *J* = 14.0 Hz), 3.30-3.16 (m, 1 H), 3.16 (s, 3 H), 2.57-1.42 (m, 7 H), 1.40 (s, 3 H), 1.10, (d, *J* = 7.0 Hz, 3 H), 0.94 (s, 3 H); ^{13}C nmr (75 MHz, $CDCl_3$) δ 177.5, 135.1, 117.2, 108.4, 69.9, 52.4, 51.1, 50.3, 49.8, 49.5, 47.3, 40.7, 39.2, 32.2, 21.4, 21.3, 20.9, 14.9; ms (*m/z*) 356, 340, 307, 292, 274, 260, 244, 219, 194, 129, 101; HRms cald for $C_{17}H_{26}NO_4$ ($M^+ - OCH_3$), 340.1582, found, 340.1567; isomer **10a** exhibited a similar ^{1}H nmr spectra, but with a characteristic resonance at δ 1.25 (d, 3 H, *J* = 7.0 Hz).

4-((2-Bromo-1-oxopropyl)-(7*S*)-8,8-dichloro-10,10-dimethyl-5-thia-4-azatricyclo[5.2.1.0]-decane-5,5-dioxide (11). Acylation was conducted by the procedure for 2 with 2-bromopropionyl chloride. The product was a 2/1 mixture of stereoisomeric bromides: ^{1}H Nmr (300 MHz, $CDCl_3$) δ 5.18-5.00 (m, 1 H), 4.47 (s, 1 H), 3.58 (d, 1 H, *J* = 13.4 Hz), 3.48 (d, 1 H, *J* = 13.4 Hz), 2.60-2.40 (m, 2 H), 2.13-1.60 (m, 3 H), 1.90 (d, 3 H, *J* = 6.6 Hz), 1.52 (s, 3 H), 1.10 (s, 3 H), ^{13}C nmr (75 MHz, $CDCl_3$) δ 170.5, 170.2, 93.5, 93.2, 78.5, 78.2, 62.2, 62.1, 52.5, 52.4, 50.8, 50.7, 49.7, 49.5, 42.2 (2 C), 39.2 (2 C), 31.5, 31.4, 25.3, 24.1, 23.8, 22.8, 20.4.

4-(2*S*)-2-methyl-1-oxopent-4-enyl)-(7*S*)-8,8-dichloro-10,10-dimethyl-5-thia-4-azatricyclo-[5.2.1.0]decane-5,5-dioxide (12a). This was prepared by procedure **A**. ^{1}H Nmr (300 MH, $CHCl_3$) δ 5.86-5.69 (m, 1 H), 5.17-5.02 (m, 2 H), 4.41 (s, 1 H), 3.53 (d, 1 H, *J* = 13.8 Hz), 3.47 (d, 1 H, *J* = 13.8 Hz), 3.28 -3.13 (m, 1 H), 2.64-2.50 (m, 2 H), 2.49 -1.49 (m, 5 H), 1.45 (s, 3 H), 1.16, (d, 3 H, *J* = 6.5 Hz), 1.07 (s, 3 H); ^{13}C nmr δ 177.1, 134.9, 117.9, 93.6, 78.5, 62.1, 52.6, 50.4, 49.5, 40.5, 39.4, 31.6, 25.4, 24.0, 22.6, 15.0; Isomer **13a** exhibited very similar ^{1}H nmr spectra, but with characteristic resonances of δ 4.47 (s, 1 H), and 1.34 (d, 3 H, *J* = 6.5 Hz).

Tandem Addition with Methyl Acrylate. To an nmr tube was added cyclohexyl iodide (105 mg, 0.5 mmol), methyl acrylate (43.0 mg, 0.5 mmol), allyltributylstannane (827 mg, 2.5 mmol), AIBN (10 mg), and benzene-d_6 (1 ml). After the mixture was heated at 80°C for 6 h, it was diluted with wet ether (10 ml), followed by addition of DBU (5 drops). After 10 min, the mixture was filtered through a plug of silica gel, and the residue from the evaporation of the filtrate was purified by column chromatography (10/1 hexane/ethyl acetate) to afford (in order of elution) **14** (60.8 mg, 58%), and **15** (20.1 mg, 19%).

Methyl 1-Cyclohexylpent-4-enyl-2-carboxylate (14): ^{1}H Nmr (300 MHz, $CDCl_3$ δ 5.75 (m, 1 H), 5.02 (m, 2 H), 3.66 (s, 3 H), 2.56 (m, 1 H), 2.32 (m, 1 H), 2.19 (m 1 H), 1.81-1.50 (m, 6 H), 1.36-1.06 (m, 5 H), 0.86 (m, 2 H); ^{13}C nmr (75 MHz, $CDCl_3$) δ 176.5, 135.6, 116.7, 51.43, 51.37, 42.8, 39.7, 37.1, 35.6, 33.6, 32.9, 26.5, 26.3; ir (neat) 2824, 1740, 1641, 1449, 1266, 1192, 1165, 916 cm^{-1}; HRms calcd for $C_{13}H_{22}O_2$ (M^+) 210.1620, found 210. 1620.

Dimethyl 1-Cyclohexylhept-6-enyl-2,4-dicarboxylate (15). Less polar isomer: ^{1}H Nmr (300 MHz, $CDCl_3$) δ 5.64 (m, 1 H), 5.02 (m, 2 H), 3.64 (s, 6 H), 2.51-2.14 (m, 5 H), 1.78-1.58 (m, 7 H), 1.50 (m, 1 H), 1.30-1.03 (m, 5 H), 0.83 (m, 2 H); ^{13}C nmr ($CDCl_3$) δ 176.56, 175.41, 134.75, 117.05, 51.44, 43.23, 40.73 (2 C), 37.17, 35.29, 34.30, 33.13, 32.94, 26.40, 26.08 (2 C); ir (neat) 2924, 2852, 1737, 1448, 1162, cm^{-1}; ms (*m/z*) 297 ($M^+ + 1$), 265, 232; HRms calcd for $C_{16}H_{24}O_3$ ($M^+ - 32$) 264.1725, found 264.1697. More polar isomer: ^{1}H Nmr (300 MHz, $CDCl_3$) δ 5.69 (m, 1 H), 5.15-4.87 (m, 2 H), 3.64 (m, 6 H), 2.49 (m, 2 H), 2.29 (m, 2 H), 1.95 (m, 1 H), 1.80-1.47 (m, 7 H), 1.33-1.07 (m, 5 H), 0.85 (m, 2 H); ^{13}C nmr ($CDCl_3$) δ 176.31, 175.25, 134.81, 117.14, 51.47, (2 C), 43.10, 40.65, 39.36, 36.10, 35.46, 34.20, 33.58, 32.65, 26.42, 26.10 (2 C); ir (neat) 2920, 2850, 1740, 1450, 1165, cm^{-1}; ms (*m/z*) 265, 232; HRms calcd for $C_{16}H_{24}O_3$ ($M^+ - 32$) 264.1725, found 264.1690.

4-((2*R*)-2-Cyclohexylmethyl-1-oxopent-4-enyl)-(7*R*)-10,10-dimethyl-5-thia-4-azatricyclo[5.2.1.p]decane-5,5-dioxide (16). Procedure A was used to run the radical reaction. The crude product was purified by column chromatography, (10/1 hex/ethyl acetate) to give **16** (81%): ^{1}H Nmr (300 MHz, $CDCl_3$ δ 5.78 (m, 1 H), 5.01 (dd, 2 H, *J* = 10.3, 20.6 Hz), 3.89 (dt, 1 H, *J* = 1.7, 6.3 Hz), 3.49 (d, 1 H, *J* = 16.2 Hz), 3.41 (d, 1 H, *J* = 16.2 Hz), 3.22 (quintet, 1 H, *J* = 6.6 Hz), 2.34 (m, 2 H), 2.02 (m, 2 H), 1.78-1.93 (m, 4 H), 1.58-1.71 (m, 4 H), 1.40 (m, 1 H), 1.33 (m, 1 H), 1.08-1.28 (m, 5 H), 1.15 (s, 3 H), 0.96 (s, 3 H), 0.86 (m, 3 H); ^{13}C nmr (75 MHz, $CDCl_3$) δ 175.3, 135.2, 117.3, 65.4, 65.3, 53.3, 48.2, 47.8, 44.6, 42.4, 38.6, 38.3, 38.2, 35.4, 33.5, 32.9, 26.6, 26.5, 26.3, 26.2, 20.9, 20.0; ir (neat) 2928, 2851, 1680, 1645, 1449, 1329, 1273, 1252, 1217, 1121, 909 cm^{-1}; HRms calcd for $C_{22}H_{35}NO_3S$ (M^+) 393.2338, found 393.2328.

5-Iodopentanoic acid. A solution of 5-chloropentanoic acid (10.0 g, 73.2 mmol), NaI (16.5 g, 110 mmol), and methyl ethyl ketone (100 ml) was refluxed for 20 h. The reaction mixture was concentrated under reduced pressure and partitioned between ether (200 ml) and 5% aqueous sodium thiosulfate (200 ml). The organic phase was then washed with H_2O and brine, and dried over $MgSO_4$. The solvent was removed under reduced pressure and the yellow solid residue was recrystallized from hexane/EtOAc to afford white crystals (12.0 g, 72%), mp 55°C: ^{1}H Nmr ($CDCl_3$) δ 3.20 (t, 2 H, J = 6.7 Hz), 2.40 (t, 2 H, J = 7.3 Hz), 1.90 (m, 2 H), 1.75 (m, 2 H).

7-(Trimethylsilyl)heptanoic acid. To a solution of trimethylsilylacetylene (7.0 ml, 49.6 mmol at 0°C) in THF (200 ml) was added a 1.6 M solution of *n*-BuLi in hexane (34.1 ml, 54.5 mmol). After 20 min, a solution of 5-iodopentanoic acid (7.64 g, 25 mmol) and HMPA (100 ml) in THF (100 ml) was added by a syringe. After stirring 2 h at 0°C, the reaction mixture was extracted with H_2O (3 x 150 ml). The aqueous layer was then acidified with saturated NH_4Cl and 5% HCl to pH 2, and extracted with ether (3 x 150 ml). The combined organic layer was washed with H_2O and brine, then dried over $MgSO_4$. Evaporation of the solvent under reduced pressure furnished compound the acid as a light brown oil (3.90 g, 79%). ^{1}H Nmr ($CDCl_3$) 2.39 (t, 2 H, J = 7.4 Hz), 2.25 (t, 2 H, J = 7.1 Hz), 1.75 (m, 2 H), 1.58 (m, 2 H), 0.14 (9 H, s); ir (thin film) 2955, 2174, 1707, 1416, 1289, 1250, 1148, 1048, 1030, 986, 941, 843, 760, 698 cm^{-1}; ms (*m/z*) 83 (M – Me), 165, 137, 127, 109, 93, 75, 61; HRms calcd for $C_9H_{15}O_2Si$, 183.0841; found, 183.0841.

7-(Trimethyl)silylheptanoyl Chloride. A solution of the above acid (0.89 g, 4.49 mmol) and thionyl chloride (0.49 ml, 6.7 mmol) in benzene (50 ml) was refluxed for 2.5 h. The solvent and excess thionyl chloride were removed under reduced pressure to give the crude acid chloride (0.97 g, 100%) as an oil. ^{1}H Nmr ($CDCl_3$) δ 2.94 (t, 2 H, J = 7.2 Hz), 2.26 (t, 2 H, J = 6.9 Hz), 1.83 (m, 2 H), 1.58 (m, 2 H), 0.14 (s, 9 H).

4-(7-Trimethylsilyl-1-oxohept-6-ynyl)-(7*R*)-10,10-dimethyl-5-thia-4-azatricyclo[5.2.1.0^{3,7}]decane-5,5-dioxide. To a suspension of 60% NaH (103 mg, 2.56 mmol) and benzene (30 ml) was added L-2,10-camphor sultam (0.46 g, 2.14 mmol). After 1 h at 25°C the above acid chloride (0.57 g, 2.6 mmol) in benzene (10 ml) was slowly added. After 6 h, the reaction mixture was quenched with H_2O (30 ml) and extracted with ether (3 x 30 ml). The combined ethereal solution was washed with H_2O and brine, and dried over $MgSO_4$. Evaporation of the solvent under reduced pressure and purification by chromatography with 9/1 hexane/EtOAc afforded a clear oil (0.69 g, 82%): ^{1}H Nmr ($CDCl_3$) δ 3.84 (dd, 1 H, J = 7.1, 5.5 Hz), 3.46 (d, 1 H, J = 13.8 Hz), 3.40 (d, 1 H, J = 13.8 Hz), 2.73 (dt, 2 H, J = 7.1, 1.5 Hz), 2.26 (t, 2 H, J = 7.1 Hz), 2.07 (m, 2 H), 1.88 (m, 3 H), 1.75 (m, 2 H), 1.54 (m, 2 H), 1.36 (m, 2 H), 1.13 (s, 3 H), 0.95 (s, 3 H), 0.11 (s, 9 H); ^{13}C nmr ($CDCl_3$) δ 171.6, 106.9, 84.7, 69.0, 65.3, 65.2, 53.1, 53.0, 52.9, 48.4, 47.8, 44.7, 38.6, 35.0, 32.9, 31.7, 27.9, 26.5, 23.6, 20.9, 19.9, 19.7, 0.2; ir (thin film) 2957, 1686, 1387, 1313, 1271, 1250, 1237, 1165, 1116, 762 cm^{-1}; ms (*m/z*) 395 (M$^+$), 380, 330, 316, 302, 288, 280, 262, 250, 181, 165, 150, 135, 125, 107, 93, 73, 59; HRms calcd for $C_{20}H_{33}NO_3SSi$, 395.1950; found, 395.1950.

4-(2-Iodo-7-trimethylsilyl-1-oxohept-6-ynyl)-(7R)-10,10-dimethyl-5-thia-4-azatricyclo[5.2.1.0^{3,7}]decane-5,5-dioxide (18a). To a 0°C solution of diisopropylamine (127 µl, 0.91 mmol) and THF (5 ml) was added a 1.6 M solution of nBuLi in hexane (0.57 ml, 0.91 mmol). The solution was allowed to stir at 0°C for 20 min and then a solution of the above sultam (0.30 g, 0.76 mmol) in THF (4 ml) was added. After 3 h at –78°C, the resulting enolate solution was slowly added to a solution of iodine (0.27 g, 1.06 mmol) in THF (1 ml) at –78°C. The reaction mixture was stirred for another 1 h. It was then poured into ether (75 ml), and washed with 5% aqueous sodium thiosulfate solution and brine. The resulting ethereal solution was dried over $MgSO_4$. Evaporation of the solvent and purification of the crude product by chromatography with 12/1 hexane/EtOAc afforded the desired diastereomeric iodo compounds(**18a**)(9/1, 0.27 g, 68%). ^{1}H Nmr ($CDCl_3$) of the major isomer: δ 4.97 (t, 1 H, J = 7.3 Hz), 3.97 (dd, 1 H, J = 7.3, 5.3 Hz), 3.50 (dd, 2 H, J = 13.7, 9.5 Hz), 2.30-2.20 (m, 6 H), 2.20-1.80 (m, 3 H), 1.75-1.46 (m, 2 H), 1.45-1.30 (m, 2 H), 1.20 (s, 3 H), 0.97 (s, 3 H), 0.13 (s, 9 H); ir (thin film) 2996, 2894, 2172, 1679, 1455, 1384, 1361, 1314, 1289, 1247, 1231, 1172, 1116, 1064, 844, 767, 760 cm^{-1}; ms (*m/z*) 506 (M – Me), 394, 380, 366, 330, 288, 224, 185, 165, 151, 135, 107, 93, 73, 59; HRms calcd for $C_{19}H_{29}NO_3ISSi$, 506.0682; found, 506.0682.

4-1-((1*R*)-2-Methylenecyclopentyl)-1-oxomethyl)-(7*R*)-10,10-dimethyl-5-thia-4-azatricyclo[5.2.1.0^{3,7}]decane-5,5-dioxide (19 and 20). A solution of iodide(**18a**)(23.0 mg, 0.044 mmol), hexamethylditin (3.3 µl, 0.007 mmol), and benzene-d_6 (0.5 ml) in a nmr tube was irradiated for 15 min with a 275 W sunlamp. To the reaction mixture was then added Bu_3SnH (15.4 µl, 0.05 mmol) and a catalytic amount of AIBN. The resulting solution was heated at 80°C for 3 h. The solution was then transferred to a flask, and concentrated HI (3 drops) was added. After stirring at room temperature for 0.5 h, the solution was extracted with ether (3 x 10 ml). The combined organic layer was washed with H_2O, saturated aqueous sodium thiosulfate

solution and brine, and then dried over $MgSO_4$. Evaporation of the solvent afforded the crude products. Both gc and ^1H nmr analyses showed a ratio of 9/1 in favor of **19** over **20**, and no 6-*endo* cyclized product **21** was detected. Purification by flash chromatography with 12/1 hexane/EtOAc gave a white solid (7.2 mg, 51%), mp 152-154°C: $[\alpha]^D = +76°$ (c = 2.0, $CHCl_3$). ^1H Nmr (C_6D_6) of **19** δ 5.48 (d, 1 H, *J* = 1.9 Hz), 5.08 (d, 1 H, *J* = 1.9 Hz), 4.43 (m, 1 H), 3.65 (dd, 1 H, *J* = 7.6, 5.8 Hz), 2.80 (d, 1 H, *J* = 13.8 Hz), 2.76 (d, 1 H, *J* = 13.8 Hz), 2.36 (m, 2 H), 2.17 (m, 1 H), 2.05-1.80 (m, 4 H), 1.56 (m, 1 H), 1.40-1.20 (m, 3 H), 0.73 (m, 1 H), 0.57 (m, 1 H), 1.09 (s, 3 H), 0.41 (s, 3 H); ir (thin film) 3005, 2957, 1686, 1651, 1460, 1402, 1361, 1313, 1236, 1217, 1134, 873 cm^{-1}; ms (*m/z*) 323 (M^+), 135, 108, 81; HRms calcd for $C_{17}H_{25}NO_3S$, 323.1555; found, 323.1555.

4-(1-Oxohept-6-ynyl)-(7*R*)-10,10-dimethyl-5-thia-4-azatricyclo[5.2.1.0]decane-5,5-dioxide (18b). To solution of **18a** (22.0 mg, 0.042 mmol) in THF (2 ml) was added 1M Bu_4NF in THF (46 µl, 0.046 mmol) slowly at 0°C over 20 min. After stirring for another 15 min, H_2O (5 ml) was poured into the solution. The mixture was extracted with ether (3 x 10 ml), and the combined organic phases were washed with H_2O and brine. Evaporation of the solvent and purification by chromatography with 12/1 hexane/EtOAc afforded **18b** as a mixture of diastereomers in a ratio of 5/1 (14.3 mg, 70%). ^1H Nmr (C_6D_6) of **18b**: δ 5.29 (dd, 1 H, *J* = 8.4, 6.4 Hz), 3.61 (m, 1 H), 2.82 (dt, 1 H, *J* = 7.3, 3.0 Hz), 2.76 (d, 1 H, 13.8 Hz), 2.69 (d, 1 H, *J* = 13.8 Hz), 2.10-23.0 (m, 1 H), 2.10-1.77 (m, 1 H); 1.65-1.20 (m, 4 H), 0.85-0.55 (m, 2 H), 1.11 (s, 3 H), 0.39 (s, 3 H); ir (thin film) 3290, 2958, 2888, 1691, 1457, 1383, 1330, 1282, 1248, 1237, 1133, 1116, 1083, 1036 cm^{-1}; ms (*m/z*) 449 (M^+), 340, 322, 257, 234, 207, 152, 135, 107, 93, 79, 68; HRms calcd for $C_{17}H_{24}NO_3IS$, 449.0522; found, 449.0522.

General Procedure for Ditin Mediated Annulation. A solution of the acyl sultam (70.0 mg, 0.26 mmol), iodobutyne(**22b**)(140.5 mg, 0.781 mmol), and hexamethylditin (19.7 µl, 0.039 mmol) in benzene (2.6 ml) was irradiated with light from a 275 W sunlamp for 1 h. The solution was filtered through Celite™, and the filtrate was concentrated under vacuum to afford an oily residue. The resulting residue was dissolved in benzene (2.6 ml), and to the solution was added *n*Bu_3SnH (90.9 µl, 0.33 mmol) and a catalytic amount of AIBN. The reaction mixture was refluxed for 2 h. Purification by chromatography with 12/1 hexane/EtOAc afforded a white solid of all three isomers(**19-21**)(37.8 mg, 51%).

General Procedure For Hexamethylditin Cyclizations of Alkenes 23a-c: The precursor was dissolved in benzene to give a 0.09 M solution and hexamethylditin (0.08-0.12 equiv 0.52 M in benzene) was added. The solution was placed in 20-30 cm front of a GE-275 W sunlamp angled at 30-40° above the solution. The mixture was irradiated at 80-85°C oil bath for 30-60 min. Appearance of characteristic iodine color indicated that the ditin was consumed. After evaporation of the solvent, the residue was either purified by MPLC or was treated with tin hydride, and then purified.

General Procedure For Tributyltin Hydride Reductions: The crude iodide product was redissolved to form a 0.08 M benzene solution and tributyltin hydride (1.2 equiv) and a small amount of AIBN were added to the solution. The mixture was refluxed for 3 h and was diluted with reagent grade (wet) ether (5-10 ml). Workup was conducted by the DBU method, as described above.

4-(2-Iodo-1-oxohept-6-enyl)-(7*R*)-10,10-dimethyl-5-thia-4-azatricyclo[5.2.1.$0^{3,7}$]decane-5,5-dioxide (23a). The iodination procedure for **3a** was used. The product was purified by MPLC with 12/1 hexane/EtOAc to afford a less polar, solid isomer (344.3 mg 52%) and a more polar, liquid isomer (59.1 mg 9%). Major (less polar): ^1H Nmr (300 MHz, $CDCl_3$) δ 5.82-5.69 (m, 1 H), 5.04-4.95 (m, 3 H), 3.97 (dd, 1 H, *J* = 7.1 Hz, 5.2 Hz), 3.51 (d, 1 H, *J* = 13.7 Hz), 3.43 (d, 1 H, *J* = 13.7 Hz), 2.17-1.96 (m, 6 H), 1.90-1.86 (m, 3 H), 1.53-1.35 (m, 4 H), 1.20 (s, 3 H), 0.98 (s, 3 H); ^{13}C nmr (75 MHz, $CDCl_3$) δ 170.1, 137.8, 115.3, 64.9, 53.1, 48.8, 47.9, 44.4, 37.1, 34.8, 32.9, 32.8, 28.5, 26.6, 21.7, 20.7, 20.0; ir (neat) 3074, 2959, 1678, 1639, 1456, 1387, 1325, 1284, 1238, 1136 cm^{-1}; ms (*m/z*) 452 (M^+ + 1), 436, 410, 387, 372, 358, 324, 260, 237, 209, 152, 135, 126, 107, 93, 81, 67, 55; HRms calcd for $C_{16}H_{23}NO_3IS$, 436.0443; found 436.0443. Minor (more polar): ^1H Nmr (300 MHz, $CDCl_3$) δ 5.78-5.69 (m, 1 H), 5.03-4.87 (m, 3 H), 3.87 (t, 1 H, *J* = 6.7 Hz), 3.52 (d, 1 H, *J* = 13.9 Hz), 3.47 (d, 1 H, *J* = 13.9 Hz), 2.17-1.98 (m, 6 H), 1.92-1.88 (m, 3 H), 1.53-1.32 (m, 4 H), 1.13 (s, 3 H), 0.97 (s, 3 H); ^{13}C nmr (75 MHz, $CDCl_3$) δ 169.2, 137.7, 115.4, 66.0, 52.8, 48.7, 47.9, 44.7, 38.5, 37.4, 33.0, 28.4, 26.4, 21.4, 20.9, 20.0; ir (neat) 3080, 2959, 2880, 1689, 1639, 1456, 1414, 1383, 1331, 1280, 1238, 1217, 1134 cm^{-1}.

4-(2-Iodo-*Z*-1-oxooct-6-enyl)-(7*R*)-10,10-dimethyl-5-thia-4-azatricyclo[5.2.1.$0^{3,7}$]decane-5,5-dioxide (23b). The iodination procedure for **3a** was used. Evaporation of the solvent and purification of crude product by MPLC with 12/1 hexane/EtOAc gave the less polar solid isomer 126.1 mg (25%), the more

polar, solid isomer 32.4 mg (6%), and recovered starting material, 39.1 mg (10.5 %). Major (less polar): ^{1}H Nmr (300 MHz, $CDCl_3$) δ 5.49-5.43 (m, 1 H), 5.37-5.31 (m, 1 H), 4.98 (t, 1 H, *J* = 7.4 Hz), 3.96 (dd, 1 H,*J* = 7.3 Hz, 5.3 Hz), 3.51 (d, 1 H, *J* = 13.7 Hz), 3.43 (d, 1 H, *J* = 13.7 Hz), 2.13-2.0 (m, 6 H), 1.97-1.90 (m, 3 H), 1.59 (d, 3 H, *J* = 6.4 Hz) 1.49-1.33 (m, 4 H), 1.25 (s, 3 H), 0.98 (s, 3 H); ^{13}C nmr (75 MHz, $CDCl_3$) δ 170.2, 129.5, 124.8, 64.9, 53.1, 48.8, 47.9, 44.4, 37.1, 35.0, 32.8, 29.1, 26.6, 26.1, 21.9, 20.7, 20.0, 12.9; ir (neat) 3035, 2957, 2900, 1693, 1383, 1331, 1269, 1238, 1217, 1165, 1113; ms (*m/z*) 466 (M^+), 388, 276, 257, 135 cm^{-1}. Minor (more polar): ^{1}H Nmr (300 MHz, $CDCl_3$) δ 5.49-5.40 (m, 1 H), 5.34-5.26 (m, 1 H), 4.89 (t, 1 H, *J* = 7.5 Hz), 3.87 (t, 1 H, *J* = 6.6 Hz), 3.52 (d, 1 H, *J* = 13.8 Hz), 3.47 (d, 1 H, *J* = 13.8 Hz), 2.21-1.97 (m, 6 H), 1.92-1.87 (m, 3 H), 1.58 (d, 3 H, *J* = 6 Hz), 1.51-1.41 (m, 3 H), 1.13 (s, 3 H), 0.97 (s, 3 H); ^{13}C nmr (75 MHz, $CDCl_3$) δ 169.2, 129.3, 124.9, 65.9, 52.7, 48.7, 47.9,44.7, 38.5, 37.6, 33.0, 29.1, 26.4, 25.9, 21.6, 20.9, 20.0, 12.9; ir (neat) 2993, 2941, 1678, 1452, 1385, 1333, 1282, 1242, 1138, 1117 cm^{-1}; ms (*m/z*) 466 (M^+), 388, 276, 135, 95.

4-(4-Iodo-Z-7-trimethylsilyl-1-oxohept-6-enyl)-(7*R*)-10,10-dimethyl-5-thia-4-azatricyclo[5.2.1.0]decane-5,5-dioxide (23c). The iodination procedure for **3a** was used. Evaporation of the solvent and purification of crude iodo product by MPLC with 12/1 hexane/EtOAc afforded the less polar isomer (450 mg, 60%) and the more polar isomer (63.3 mg, 8.7%). Major (less polar): ^{1}H Nmr (300 MHz, $CDCl_3$) δ 6.23 (dt, 1 H, *J* = 14.3, 7.3 Hz), 5.49 (d, 1 H, *J* = 14.3 Hz), 4.96 (t, 1 H, *J* = 7.2 Hz), 3.96 (t, 1 H, *J* = 5.8 Hz), 3.51 (d, 1 H, *J* = 13.7 Hz), 3.43 (d, 1 H, *J* = 13.7 Hz), 2.18-1.99 (m, 5 H), 1.94-1.90 (m, 3 H), 1.57-1.28 (m, 5 H), 1.20 (s, 3 H), 0.98 (s, 3 H), 0.10 (s, 9 H); ^{13}C nmr (75 MHz, $CDCl_3$) δ 170.1, 147.7, 130.0, 64.9, 53.1, 48.8, 47.9, 44.4, 37.1, 35.1, 32.7 (2 C's), 29.2, 26.5, 21.9, 20.9, 19.9, 0.3; ir (neat) 2953, 1686, 1605, 1458, 1379, 1331, 1244, 1134, 1057, 837 cm^{-1}; ms (*m/z*) 509 (M^+), 397, 383, 327, 289, 225, 185, 135, 107, 93, 73, 53; HRms calcdd for $C_{19}H_{32}NO_3ISSi$, 509.0917; found, 509.0917. Minor (more polar): ^{1}H Nmr (300 MHz, $CDCl_3$) δ 6.20 (dt, 1 H, *J* = 14.0, 7.0 Hz); .5.50 (d, 1 H, *J* = 14.0 Hz), 4.89 (t, 1 H, *J* = 7.3 Hz), 3.88 (t, 1 H, *J* = 6.4 Hz), 3.51 (d, 1 H, *J* = 13.5 Hz), 3.48 (d, 1 H, *J* = 13.5 Hz), 2.15-1.98 (m, 5 H), 1.94-1.84 (m, 3 H), 1.60-1.31 (m, 5 H), 1.12 (3 H,s), 0.94 (s, 3 H), 0.10 (s, 9 H); ^{13}C nmr (75 MHz, $CDCl_3$) δ 169.1, 147.4, 130.3, 65.9, 52.7, 48.7, 47.9, 44.7, 38.4, 37.6, 33.0, 32.5, 29.3, 26.4, 21.7, 20.9, 20.0, 0.3; ir (neat) 2993, 2955, 1676, 1605, 1458, 1412, 1391, 1331, 1246, 1138, 837, 767 cm^{-1};.ms (*m/z*) 509 (M^+),461, 397, 383, 327, 289, 271, 225, 185, 135, 107, 93, 73, 55; HRms calcdd for $C_{19}H_{32}NO_3ISSi$, 509.0917; found, 509.0917.

4-(1-(2-Iodomethylcyclopentanyl)-1-oxomethyl)-(7*R*)-10,10-dimethyl-5-thia-4-azatricyclo[5.2.1.0^{3,7}]decane-5,5-dioxide (24d, 25d, 26d) and **4-(1-(3-Iodocyclohexanyl)-1-oxomethyl)-(7*R*)-10,10-dimethyl-5-thia-4-azatricyclo[5.2.1.0]decane-5,5-dioxide (28d).** Compounds **(24d), (25d), (26d),** and **(28d)** were prepared by hexamethylditin cyclization method from compound **(23a)** (31 mg, 0.069 mmol). Purification by MPLC (hexane/EtOAc = 12.5/1) gave in order of increasing polarity **26d** (7%), **24d** (38%), **25d** (23%), and **28d** (10%). **24d** (solid) ^{1}H Nmr (300 MHz, $CDCl_3$) δ 3.88 (t, 1 H, *J* = 6.7 Hz), 3.54 (q, 1 H, *J* = 7.1 Hz), 3.52 (d, 1 H, *J* = 13.8 Hz), 3.43 (d, 1 H, *J* = 13.8 Hz), 3.31 (dd, 1 H, *J* = 9.4 Hz, 6.6 Hz), 3.09 (t, 1 H, *J* = 9.4 Hz), 2.74-2.60 (m, 1 H), 2.15-1.97 (m, 5 H), 1.94-1.84 (m, 4 H), 1.77-1.60 (m, 2 H), 1.43-1.31 (m, 2 H), 1.20 (s, 3 H), 0,97 (s, 3 H); ^{13}C nmr (75 MHz, $CDCl_3$) δ 173.6, 65.6, 53.3, 48.2, 47.8 (2 C's), 44.7, 38.9, 33.6, 33.0, 30.2, 26.6, 24.0, 21.0, 20.0, 7.1. **25d:** (solid) ^{1}H Nmr (300 MHz, $CDCl_3$) δ 3.89 (dd, 1 H, *J* = 5.3, 7.4 Hz), 3.52 (d, 1 H, *J* = 13.8 Hz), 3.43 (d, 1 H, *J* = 13.8 Hz), 3.30-3.15 (m, 2 H), 3.06 (q, 1 H, *J* = 7.8 Hz), 2.68-2.58 (m, 1 H), 2.24-2.01 (m, 4 H), 1.97-1.85 (m, 4 H), 1.82-1.70 (m, 2 H), 1.48-1.32 (m, 3 H), 1.19 (s, 3 H), 0.97 (s, 3 H); ^{13}C nmr (75 MHz, $CDCl_3$) δ 174.9, 65.6, 53.3, 51.1, 48.5, 48.3, 47.9, 44.7, 38.6, 34.3, 33.0, 32.1, 26.5, 24.7, 21.1, 20.0, 10.1; ir (neat) 2924, 1695, 1678, 1653, 1558, 1506, 1458, 1394, 1331, 1269, 1232, 1215 cm^{-1}. **26d** (solid): ^{1}H Nmr (300 MHz, $CDCl_3$) δ 3.89 (t, 1 H, *J* = 6.5 Hz), 3.55-3.40 (m, 4 H), 3.16 (t, 1 H, *J* = 9.7 Hz), 2.73-2.58 (m, 1 H), 2.15-2.03 (m, 3 H), 1.95-1.80 (m, 4 H), 1.72-1.58 (m, 2 H), 1.45-1.34 (m, 2 H), 1.30-1.20 (m, 2 H), 1.14 (s, 3 H), 0.97 (s, 3 H). **28d** (solid): ^{1}H Nmr (300 MHz, $CDCl_3$) δ 4.16 (tt, 1 H*J* = 12.2 4.1 Hz), 3.86 (t, 1 H, *J* = 6.6 Hz), 3,49 (d, 1 H, *J* = 13.7 Hz), 3.42 (d, 1 H, *J* = 13.7 Hz), 2.99 (tt, 1 H, *J* = 11.6, 3.4 Hz), 2.67-2.59 (m, 1 H), 2.46-2.39 (m, 1 H), 2.38-2.20 (m, 1 H), 2.14-1.20 (m, 12 H), 1.14 (s, 3 H), 0.97 (s, 3 H).

4-(1-(2-Methylcyclopentanyl)-1-oxomethyl)-(7*R*)-10,10-dimethyl-5-thia-4-azatricyclo[5.2.1.0^{3,7}]decane-5,5-dioxide (24a, 25a, 26a) and **4-(1-(3-Iodocyclohexanyl)-1-oxomethyl)-(7*R*)-10,10-dimethyl-5-thia-4-azatricyclo[5.2.1.0^{3,7}]decane-5,5-dioxide (28a).** Compound **(25a)** was prepared from compound **(25d)** (14.2 mg, 99%) by tributyltin hydride reduction. Purification from MPLC (Hexane/ EtOAc = 13.5) gave solid **25a** (10.2 mg, 99%). ^{1}H Nmr (300 MHz, $CDCl_3$)

δ 3.87 (t, 1 H, *J* = 6.5 Hz), 3.51 (d, 1 H, *J* = 13.5 Hz), 3.42 (d, 1 H, *J* = 13.5 Hz), 2.92 (q, 1 H, *J* = 8.5 Hz), 2.29-2.20 (m, 1 H), 2.13-1.98 (m, 3 H), 1.95-1.80 (m, 4 H), 1.79-1.58 (m, 2 H), 1.44-1.15 (m, 4 H), 1.16 (s, 3 H), 1.05 (d, 3 H, *J* = 7.4 Hz), 0.97 (3 H,s); ^{13}C nmr (75 MHz, $CDCl_3$) δ 176.5, 65.5, 53.4, 52.7, 48.1, 47.8, 44.8, 42.3, 38.9, 34.8, 33.0, 30.5, 26.5, 25.2, 24.4, 21.0, 20.0, 18.7; ms (*m/z*) 325, 284, 269, 213, 177, 155, 135.

24a (80% yield) from **24d** (28.8 mg) (solid): ^{1}H Nmr (300 MHz, $CDCl_3$) δ 3.88 (t, 1 H, *J* = 6.7 Hz), 3.55-3.37 (m, 3 H), 2.55-2.38 (m, 1 H), 2.12-1.98 (m, 3 H), 1.95-1.65 (m, 6 H), 1.63-1.50 (m, 1 H), 1.48-1.30 (m, 3 H), 1.17 (s, 3 H), 0.98 (s, 3 H), 0.90 (d, 3 H, *J* = 7.7 Hz); ^{13}C nmr (75 MHz, $CDCl_3$) δ 174.7, 65.5, 53.3, 48.9, 48.0, 47.8, 44.7, 38.9, 38.5, 34.4, 33.0, 27.8, 26.6, 23.9, 20.8, 20.0, 16.4; ms (*m/z*) 325, 284, 270, 261, 152, 135, 111; HRms calcd for 325.1712; found, 325.1712.

26a (90% yield) from **26d** (5.8 mg) (solid): ^{1}H Nmr (300 MHz, $CDCl_3$) δ 3.83 (dd, 1 H, *J* = 5.4, 7.3 Hz), 3.51 (d, 1 H, *J* = 13.6 Hz), 3.43 (d, 1 H, *J* = 13.6 Hz), 3.39 (q, 1 H, *J* = 7.8 Hz), 2.45-2.32 (m, 1 H), 1.92-1.68 (m, 7 H), 1.52-1.27 (m, 4 H), 1.10 (s, 3 H), 0.91 (s, 3 H) 0.91 (d, 3 H, *J* = 7.0 Hz).

28a (85% yield) from **28d** (10.3 mg): (solid) ^{1}H Nmr (300 MHz, $CDCl_3$) δ 3.81 (t, 1 H, *J* = 6.4 Hz), 3.44 (d, 1 H, *J* = 13.8 Hz), 3.37 (d, 1 H, *J* =13.8 Hz), 2.83 (tt, 1 H, *J* = 11.6, 3.8 Hz), 1.99-1.91 (m, 3 H), 1.84-1.73 (m, 3 H), 1.78-1.56 (m, 3 H), 1.55-1.43 (m, 1 H), 1.38-1.14 (m, 7 H), 1.09 (s, 3 H), 0.91 (s, 3 H).

4-1-(2-(Trimethylsilylmethyl)-cyclopentanyl)-1-oxomethyl}-(7*R*)-10,10-dimethyl-5-thia-4-azatricyclo[5.2.1.0^{3,7}]decane-5,5-dioxide (24c, 25c, 26c and **27c).** The title compounds were prepared from **23c** (62.6 mg, 0.120 mmol) by hexamethylditin cyclization and the crude products were treated with tributyltin hydride to obtain the mixtures of **24c, 25c, 26c** and **27c** (23.5 mg, 50% from **23c**). Purification by HPLC (Hexane/ EtOAc = 13.5/1) gave (in order of elution) **26c, 27c, 24c**, and **25c. 24c** (solid): ^{1}H Nmr (300 MHz, $CDCl_3$) δ 3.89 (t, 1 H, *J* = 6.2 Hz), 3.52-3.37 (m, 3 H), 2.48-2.34 (m, 1 H) 2.10-1.70 (m, 9 H), 1.60-1.50 (m, 1 H), 1.45-1.20 (m, 3 H), 1.17 (s, 3 H), 0.97 (s, 3 H), 0.71 (dd, 1 H, *J* = 14.0, 2.3 Hz), 0.42 (t, 1 H, *J* = 13.4 Hz), -0.03 (s, 9 H). **25c** (solid): ^{1}H Nmr (500 MHz, $CDCl_3$) δ 3.89 (dd, 1 H, *J* = 7.4, 4.5 Hz), 3.51 (d, 1 H, *J* = 13.8 Hz), 3.43 (d, 1 H, *J* = 13.8 Hz), 2.94 (q, 1 H, *J* = 8.4 Hz), 2.27-2.10 (m, 1 H), 2.10-1.20 (m, 13 H) 1.19 (s, 3 H), 0.97 (s, 3 H), 0.80 (dd, 1 H, *J* = 14.5 Hz, 2.8 Hz), 0.60 (dd, 1 H, *J* = 14.5 Hz, 11.9 Hz), -0.03 (s, 9 H); ^{13}C nmr (75 MHz, $CDCl_3$) δ 176.6, 65.4, 55.0, 53.4, 48.0, 47.7, 44.8, 44.3, 38.8, 34.4, 33.0, 29.8, 26.5, 24.5, 21.7, 20.9, 19.9, -0.9. **26c** (solid): ^{1}H Nmr (300 MHz, $CDCl_3$) δ 3.90 (dd, 1 H, *J* = 7.4, 5.3 Hz), 3.52-3.40 (m, 3 H), 2.40-2.30 (1 H, m), 2.13-2.04 (3 H,m), 2.00-1.80 (m, 7 H,), 1.56-1.33 (m, 3 H), 1.15 (s, 3 H), 0.96 (s, 3 H), 0.72 (dd, 1 H, *J* = 14.0, 3.2 Hz), 0.65 (dd, 1 H, *J* = 14.0, 12.0 Hz), -0.02 (s, 9 H). **27c** (solid): ^{1}H Nmr (300 MHz, $CDCl_3$) δ 3.90 (t, 1 H, *J* = 6.2 Hz), 3.51 (d, 1 H, *J* = 14.2 Hz), 3.43 (d, 1 H, *J* = 14.2 Hz), 2.95 (q, 1 H, *J* = 8.8 Hz), 2.30-2.10 (m, 1 H), 2.08-2.04 (m, 2 H), 2.00-1.83 (m, 4 H), 1.78-1.55 (m, 3 H), 1.45-1.17 (m, 4 H), 1.14 (s, 3 H), 0.96 (s, 3 H), 0.85 (dd, 1 H, *J* = 14.4 Hz, 3.2 Hz), 0.49 (dd, 1 H, *J* = 14.4, 11.3 Hz), -0.17 (s, 9 H).

4-(1-(2-Ethylcyclopentanyl)-1-oxomethyl)-(7*R*)-10,10-dimethyl-5-thia-4-azatricyclo-[5.2.1.0^{3,7}]decane-5,5-dioxide (24b, 25b, and **27b).** The title compounds were prepared from compound **23b** (62.2 mg, 0.133 mmol) by hexamethylditin cyclizations and the crude products were treated with tributyltin hydride to obtain the mixtures of **24b, 25b,** and **27b** (24.8 mg, 55% from **23b**). Purification by HPLC (Hexane/ EtOAc = 13.5/1) gave (in order of elution) **27b, 24b,** and **25b. 24b** (solid): ^{1}H Nmr (300 MHz, $CDCl_3$) δ 3.88 (t, 1 H, *J* = 6.3 Hz), 3.51 (d, 1 H, *J* = 13.8 Hz), 3.43 (d, 1 H, *J* = 13.8 Hz), 3.35 (m, 1 H), 2.72-2.65 (m, 1 H), 2.18-1.20 (m, 15 H), 1.16 (s, 3 H), 0.97 (s, 3 H), 0.90 (t, 3 H, *J* = 7.4 Hz). **25b** (solid): ^{1}H Nmr (300 MHz, $CDCl_3$) δ 3.89 (t, 1 H, *J* = 6.3 Hz), 3.51 (d, 1 H, *J* = 13.8 Hz), 3.42 (d, 1 H, *J* = 13.8 Hz), 2.94 (q, 1 H, *J* = 8.2 Hz), 2.21-2.03 (m, 4 H), 2.00-1.55 (m, 6 H), 1.52-1.20 (m, 6 H), 1.17 (s, 3 H), 0.97 (s, 3 H), 0.87 (t, 3 H, *J* = 7.5 Hz); ^{13}C nmr (75 MHz, $CDCl_3$) δ 176.8, 65.5, 53.4, 51.1, 48.7, 48.1, 47.8, 44.8, 38.8, 33.0, 32.3, 31.5, 27.3, 26.5, 24.8, 20.9, 20.0, 12.8; ms (*m/z*) 339, 310, 298, 270, 216, 125, 97; HRms calcd for 339.1868; found, 339.1868. **27b** (solid): ^{1}H Nmr (300 MHz, $CDCl_3$) δ 3.89 (t, 1 H, *J* = 6.4 Hz), 3.50 (d, 1 H, *J* = 13.7 Hz), 3.43 (d, 1 H, *J* = 13.7 Hz), 2.96 (q, 1 H, *J* = 8.2 Hz), 2.22-2.15 (m, 1 H), 2.08-2.02 (m, 2 H), 1.97-1.82 (m, 6 H), 1.75-1.55 (m, 3 H), 1.52-1.20 (m, 4 H), 1.14 (s, 3 H), 0.94 (s, 3 H), 0.88 (t, 3 H, *J* = 7.4 Hz).

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20. Full details of these studies will be presented in the projected Ph.D. thesis of C.-H. Lin.

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