JOC The Journal of Organic Chemistry

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Ruthenium-Catalyzed Asymmetric [2 + 2] Cycloadditions between Chiral Acyl Camphorsultam-Substituted Alkynes and Bicyclic Alkenes

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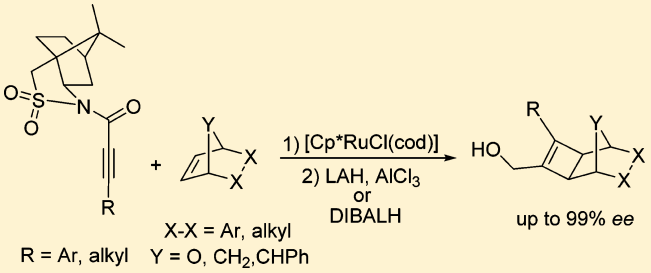
Supporting Information

ABSTRACT: Ruthenium-catalyzed asymmetric [2 + 2] cycloadditions between chiral acyl camphorsultam-functionalized alkynes and bicyclic alkenes were examined, providing adducts with complete *exo* stereoselectivity in good overall yield and enantioselectivity (up to 99% and 166:1, respectively), as well as appreciable diastereoselectivity (up to 163:1). The diastereoselectivity showed dependence on the solvent and temperature, as well as on the substitution pattern of the reacting alkyne and bicyclic alkene components. In general, higher diastereoselectivities were observed for reactions conducted in ethereal solvents and at lower temperatures between *N*-propynoyl camphorsultams and bicyclic alkenes.

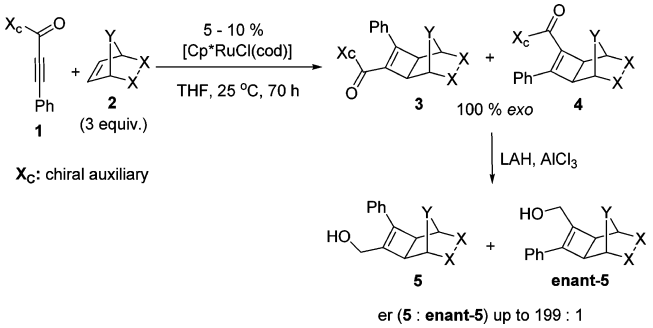


INTRODUCTION

Transition-metal-catalyzed cycloaddition reactions allow for facile and highly selective adduct formation between unactivated alkynes, alkenes, or dienes which would otherwise require high pressure, temperature or photochemical treatment to be cyclized.[1,2] This enhanced reactivity arises from complexation of the metal to the reacting ene and yne components, which transiently polarizes and activates them toward cycloaddition.[1] In particular, [2 + 2] cycloaddition reactions between bicyclic alkenes and alkynes have been found to proceed effectively with a large variety of transition-metal catalysts, including ruthenium,[3,4] rhodium,[5] nickel,[6,7] cobalt,[8,9] and rhenium,[10] demonstrating overall low catalyst loading and broad functional group compatibility, allowing for asymmetric transformations to be practiced.[11] We and others have studied various aspects of the transition-metal-catalyzed [2 + 2] cycloaddition between bicyclic alkenes and alkynes, such as the development of novel catalysts,[12,13] studies on the reactivity between different reacting partners,[14−18] on regioselectivity using unsymmetrical substrates,[15,19−21] and on asymmetric syntheses employing both chiral catalysts[5] and chiral substrates.[11,22] In particular, we have reported the first asymmetric induction study of ruthenium-catalyzed [2 + 2] cycloaddition between chiral alkynes **1** and bicyclic alkenes **2** to afford fully *exo* stereoselective chiral cyclobutenes **3**/**4** that were subsequently reduced to **5** and its enantiomer in good yield and excellent enantioselectivity (Scheme 1).[11]

Since our report in 2004, there have been few examples of asymmetric [2 + 2] cycloaddition reactions involving other bicycloalkene derivatives: In 2006, Shibata and co-workers demonstrated an enantioselective and high-yielding [2 + 2] cycloaddition between benzonorbornadiene or norbornene and selected alkynyl esters in the presence of a chiral cationic

Scheme 1. Ruthenium-Catalyzed [2 + 2] Cycloadditions between Chiral Alkynes 1 and Bicycloalkenes 2[a]



[a]For structures of X_c, see Table 2.

rhodium catalyst, [(Rh(cod)(H_8-binap)]BF_4.[5] However, the ability of rhodium to form stable [Rh(nbd)L_n]X complexes with norbornadiene[23−25] has largely detracted from the broader applications of this method. For instance, when we tried to perform a rhodium-catalyzed [2 + 2] cycloaddition reaction between alkyne **6a** and norbornadiene **2a** under conditions similar to those of Shibata's work (Scheme 2), the reaction did not proceed. We attributed this reactivity difference to the localized π-electron density in norbornadiene which allows for its coordination yielding complex **7**, whereas in benzonorbornadiene electronic delocalization of the aromatic ring prevents coordination, thus allowing for cycloaddition to take place.

For the present investigation, we selected the [Cp*RuCl(cod)] catalyst, since its reactivity with both alkyne and

Received: July 16, 2014
Published: October 10, 2014

   dx.doi.org/10.1021/jo501594g | J. Org. Chem. 2014, 79, 10002−10012

Scheme 2. Formation of a [Rh(η^4-norbornadiene)(binap)]BF_4 Complex That Inhibits [2 + 2] Cycloaddition

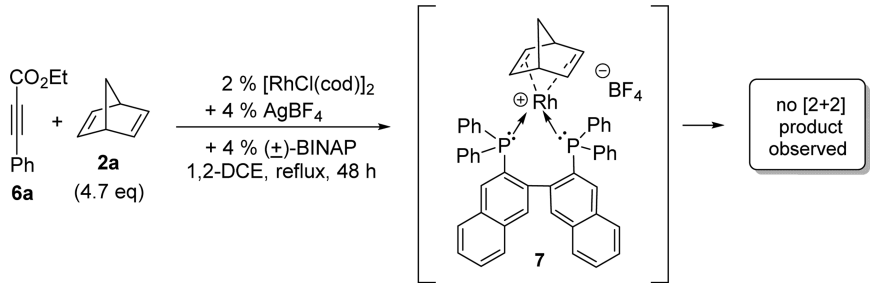
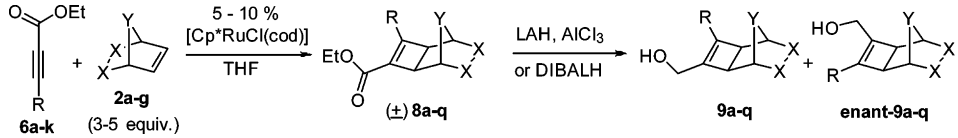
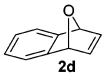
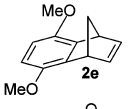
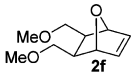


Table 1. Synthesis of Racemic Cycloadducts[a,b,c]



Entry	R	Alkyne	Alkene	Temp (°C)	Time (h)	Yield 8 (%)[a]
1	Ph	**6a**	 **2a**	65	48	90
2[b]	Ph	**6a**	 **2b**	80	48	92
3	Ph	**6a**	 **2c**	25	48	93
4	Ph	**6a**	 **2d**	65	72	71
5[c]	Ph	**6a**	 **2e**	85	48	88
6	Ph	**6a**	 **2f**	65	24	74
7	Ph	**6a**	 **2g**	65	48	89
8	3-F-C_6H_4	**6b**	**2g**	60	21	86
9	3-Cl-C_6H_4	**6c**	**2g**	60	42	67
10	3,5-CF_3-C_6H_4	**6d**	**2g**	60	48	52
11	2-Me-C_6H_4	**6e**	**2g**	60	240	62
12	2-OMe-C_6H_4	**6f**	**2g**	60	21	87
13	4-Me-C_6H_4	**6g**	**2g**	60	48	83
14	4-MeO-C_6H_4	**6h**	**2g**	60	66	63
15[c]	3-thienyl	**6i**	**2g**	60	72	93
16	2-pyridyl	**6j**	**2g**	60	66	95
17	CH_2OH	**6k**	**2g**	25	29	88

[a]Isolated yield after column chromatography. [b]Reaction was performed in Et_3N. [c]The methyl ester analogue was used.

bicycloalkene components is well understood,[16,18] and it serves as an effective catalyst under mild conditions with good functional group compatibility.[3,4] For the cycloaddition partners, we chose to react a variety of bicycloalkenes **2** with alkynes bearing the chiral acyl camphorsultam auxiliary **1c** (Scheme 1), which was highly successful in our previous work and was also employed by Moyano and Pericàs, showing high levels of regioselectivity in the cobalt-mediated Pauson−Khand [2 + 2 + 1] cycloaddition with norbornadiene.[26] As addressed in their work, we show that the diastereoselectivity of the cycloaddition is influenced by multiple factors, including temperature, solvent, and substitutent effects of both cyclo-

dx.doi.org/10.1021/jo501594g | J. Org. Chem. 2014, 79, 10002−10012

addition partners. In addition, we have extended the scope of the [2 + 2] cycloaddition reaction to encompass a broad class of chiral alkynes bearing various aryl and alkyl acetylenic substituents.

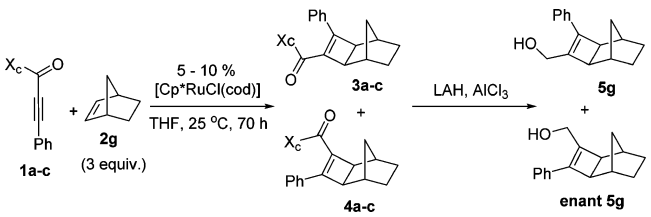
RESULTS AND DISCUSSION

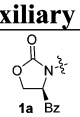
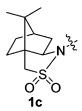
To begin this study, we prepared a series of racemic cycloadducts to which we could compare the outcomes of our later trials using novel chiral auxiliaries. The racemic ester cycloadducts **8a−q** were prepared via ruthenium-catalyzed [2 + 2] cycloaddition between alkynyl esters **6a−k** and bicyclic alkenes **2a−g**, and were further reduced to adducts **9a−q** (Table 1). Cycloaddition between the phenyl-substituted alkynyl ester and bicyclic alkenes generally gave high yields of the racemic cycloadduct (entries 1−7), whereas cycloadditions of aryl-substituted alkynyl esters with norbornene resulted in lower yields overall (entries 7−16).

With electron-donating methyl and methoxy aryl substituents of the alkyne, the methoxy derivative produced noticeably (≥20%) higher yields of **8** when substituents were present in the 2-position (entries 11 and 12), whereas the exact opposite was observed for the identical substituents at the 4-position (entries 13 and 14). Heterocyclic aromatic alkynyl esters gave excellent yields of cycloadducts (entries 15 and 16), and finally cycloaddition of a propargylic alcohol with **2g** occurred readily at room temperature (entry 17).

Studies of the chiral alkyne component in asymmetric [2 + 2] cycloadditions with norbornene **2g** showed that, albeit **1a** and **1b** provided low levels of asymmetric induction in the cycloadditions (entries 1 and 2), the analogous reaction using **1c** was highly diastereoselective, producing diastereomers **3c** and **4c** in a 131:1 ratio (Table 2).[11] Upon removal of the recoverable chiral auxiliary, compound **5g** was obtained as the major enantiomer in a ratio of 199:1.

Table 2. Ruthenium-Catalyzed [2 + 2] Cycloadditions between Norbornene 2g and Alkynes Bearing Various Chiral Auxiliaries[a,b,c,d]

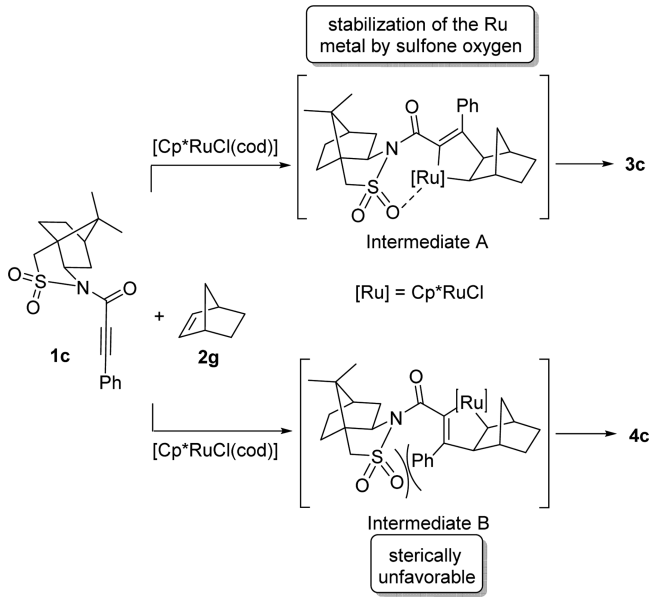


Entry	chiral auxiliary X_c	yield[a] (%)	dr 3 : 4	er 5 : enant-5
1	 1a Bz	97	1.3 : 1 [b]	-
2	 1b Ph	80	1.3 : 1 [b]	-
3	 1c	95	131 :1[c]	132 : 1[d]

[a]Isolated yield after column chromatography. [b]Determined by ^{1}H NMR. [c]Determined by HPLC. [d]Determined by HPLC on a chiral phase (OJ-H) column.

We suggest that the exceptionally high level of asymmetric induction observed in the [2 + 2] cycloaddition between **1c** and **2g** is a result of coordination of the sulfone oxygen with ruthenium,[27] which could preferentially stabilize one of the two possible transition states during formation of the high energy ruthenacyclopentene intermediate postulated by Mitsudo et al. (Scheme 3).[3,4] Intermediate A shows how coordination of a sulfone oxygen of the sultam may stabilize the metal center, which leads to the preferential formation of major diastereomer **3c**. Intermediate B, in contrast, demonstrates how this stabilization is not geometrically feasible as the sulfone oxygen is too distant from the ruthenium center, and the acetylenic substituent would also impede their interaction. Moreover, there are unfavorable steric constraints between the sultam ring and the acetylenic substituent that could explain why diastereomer **4c** is formed as the minor isomer. The structure of the major diastereomer **3c** was confirmed by X-ray crystallography.[28]

Scheme 3. Possible Intermediates in the Mechanism of the Ruthenium-Catalyzed [2 + 2] Cycloaddition between Chiral Alkyne 1c and Norbornene 2g

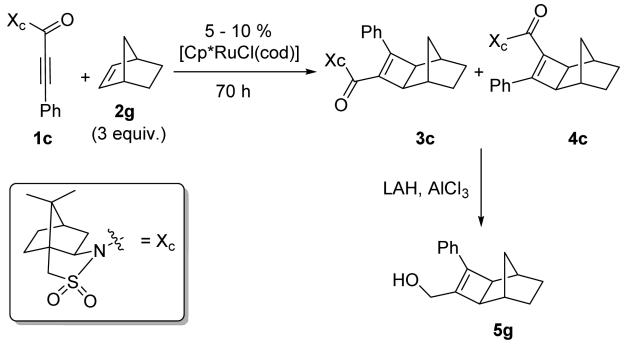


We then studied the temperature and solvent dependence on the regioselectivity in the ruthenium-catalyzed [2 + 2] cycloaddition between chiral alkyne **1c** and **2g** (Table 3).[11] When the cycloadditions were performed in tetrahydrofuran (THF), an increase in temperature from 25 to 50 °C led to a substantial decrease in diastereoselectivity (entries 1 and 2), although no additional loss of diastereoselectivity was noted upon further increasing the temperature to 80 °C (entry 3). Overall, ethereal solvents (THF, 1,2-dimethoxyethane (DME), and diglyme) gave the best yields of cycloadducts and optimal levels of asymmetric induction, whereas other solvents, such as dimethyl sulfoxide (DMSO), dimethylformamide (DMF), toluene, hexanes, and 1,2-dichloroethane (DCE), resulted in low yields (<20%).

With the optimal conditions established, trials focusing on the alkene component were carried out. Various bicycloalkenes, including derivatives of norbornadiene (**2a**, **2b**, **2c**), benzonorbornadiene (**2d**, **2e**), and norbornene (**2f**, **2g**), were investigated for their degree of asymmetric induction toward

dx.doi.org/10.1021/jo501594g | J. Org. Chem. 2014, 79, 10002−10012

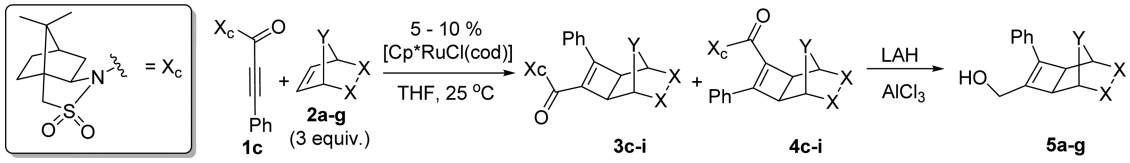
Table 3. Effect of Temperature and Solvent on the Ruthenium-Catalyzed [2 + 2] Cycloaddition of Chiral Alkyne 1c and Norbornene 2g



entry	solvent	temp (°C)	yield[a] (%)	dr[b] 3c:4c	er[c] 5:enant-5
1	THF	25	95	131:1	132:1
2	THF	50	95	64:1	
3	THF	80	99	64:1	
4	THF/Et_3N (1:1)	25	95	114:1	99:1
5	DME	25	76	132:1	
6	diglyme	25	90	126:1	

[a]Isolated yield after column chromatography. [b]Determined by HPLC. [c]Determined by HPLC on a chiral phase (OJ-H) column.

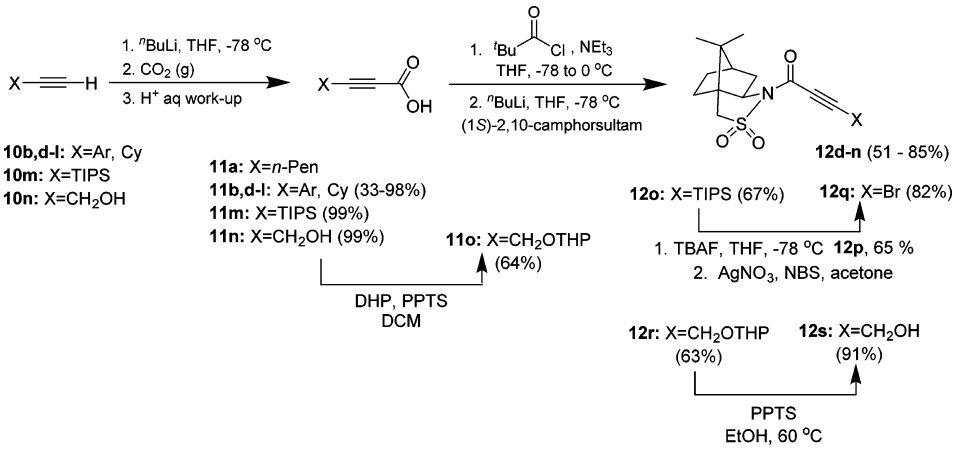
Table 4. Ruthenium-Catalyzed [2 + 2] Cycloadditions of Chiral Alkyne 1c and Bicyclic Alkenes 2a−g



entry	alkene	time (h)	yield[a] (%)	dr[b] 3:4	er[c] 5:enant-5
1	**2g**	70	95	131:1	132:1
2	**2f**	168	73	35:1	39:1
3	**2a**	168	27[d]	8:1	7:1
4[e]	**2a**	168	89	5:1	5:1
5	**2b**	168	44[d]	24:1	19:1
6	**2c**	70	85	10:1	11:1
7	**2d**	70	78	33:1	32:1
8	**2e**	70	98	163:1	166:1

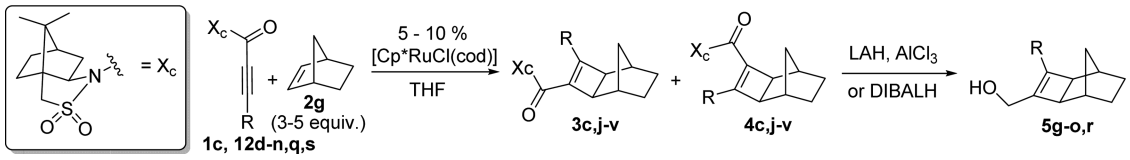
[a]Isolated yield after column chromatography. [b]Determined by HPLC, ^1H NMR, or indirectly from the *ee* value of the product obtained upon removal of the chiral auxiliary. [c]Determined by HPLC on a chiral phase (OJ-H) column. [d]Starting material was recovered. [e]Reaction was performed at 65 °C.

Scheme 4. Synthesis of Alkynyl Acids 11b,d−l, Chiral *N*-Propynoyl Camphorsultams 12d−n, Chiral Alkynyl Bromide 12q, and Chiral Propargylic Alcohol 12s



dx.doi.org/10.1021/jo501594g | J. Org. Chem. 2014, 79, 10002−10012

Table 5. Ruthenium-Catalyzed [2 + 2] Cycloadditions of Chiral Alkynes and 2g



entry	R	alkyne	temp (°C)	time (h)	yield 3 + 4 (%)[a]	dr 3:4[b]	er 5:enant-5[c]
1	Ph	**1c**	25	70	95	131:1	132:1
2	3-F-C_6H_4	**12d**	25	24	88	38:1	39:1
3	3-Cl-C_6H_4	**12e**	60	120	81	30:1	30:1
4	3,5-CF_3-C_6H_3	**12f**	25	12	99	4:1	4:1
5	2-Me-C_6H_4	**12g**	60	144	97	8:1	8:1
6	2-OMe-C_6H_4	**12h**	25	19	95	58:1	58:1
7	4-Me-C_6H_4	**12i**	25	17	73	104:1	99:1
8	4-OMe-C_6H_4	**12j**	25	24	72	31:1	32:1
9	3-thienyl	**12k**	25	18	98	20:1	19:1
10[d]	2-pyridinyl	**12l**	25	18	67	5:1	5:1
11	^{n}Pen	**12m**	60	72	92	9:1	
12	^{c}Hex	**12n**	60	120	99	4:1	
13	Br	**12q**	60	68	41	2.4:1	
14	CH_2OH	**12s**	25	22	32(39)[e]	49:1	49:1[f]

[a]Isolated yield after column chromatography (**3**/**4** are inseparable due to identical R_f). [b]Determined by HPLC, ^{1}H NMR, or from the *ee* of the product obtained upon removal of the chiral auxiliary. [c]Determined by HPLC on a chiral phase (OJ-H) column. [d]Product obtained was cyclobutane **13** (see Scheme 6). [e]Yield of chiral auxiliary recovered. [f]Measured indirectly by protecting the alcohol as a *p*-methoxyphenyl ether before removal of the chiral auxiliary.

cycloaddition with chiral alkyne **1c** (Table 4).[11] All alkenes were readily transformed to the corresponding cycloadduct with full *exo* stereoselectivity. For the norbornene series, the reaction of **1c** with **2g** proceeded with high yield and high diastereoselectivity at room temperature (entry 1), whereas, under similar conditions, the electron-poor oxanorbornene **2f** showed moderate yield and reduced diastereoselectivity (entry 2). The norbornadiene derivatives on average were both less effective and less selective in the cycloaddition compared to norbornenes (entries 3−6), and as was noted previously (Table 3), increasing the temperature of the reaction showed improved yields, although at the cost of reduced diastereoselectivity (entries 3 and 4). While cycloaddition of 7-phenylnorbornadiene **2b** (entry 5) was less efficient than 2,3-dibromonorbornadiene **2c** (entry 6), a noticeably higher diastereoselectivity was observed for the reaction of **2b**. Moreover, cycloaddition involving **2c** was completely regioselective with adduct formation only occurring on the less substituted π-bond. For the oxabicycloalkenes, oxabenzonorbornadiene **2d** showed similar reactivity to that of the oxanorbornene **2f**, giving comparable yields and levels of asymmetric induction (entries 2 and 7). Remarkably, benzonorbornadiene **2e** showed excellent yield and diastereoselectivity (entry 8), and upon removal of the chiral auxiliary, cyclobutene **5e** was obtained as the major enantiomer in 199:1 er.

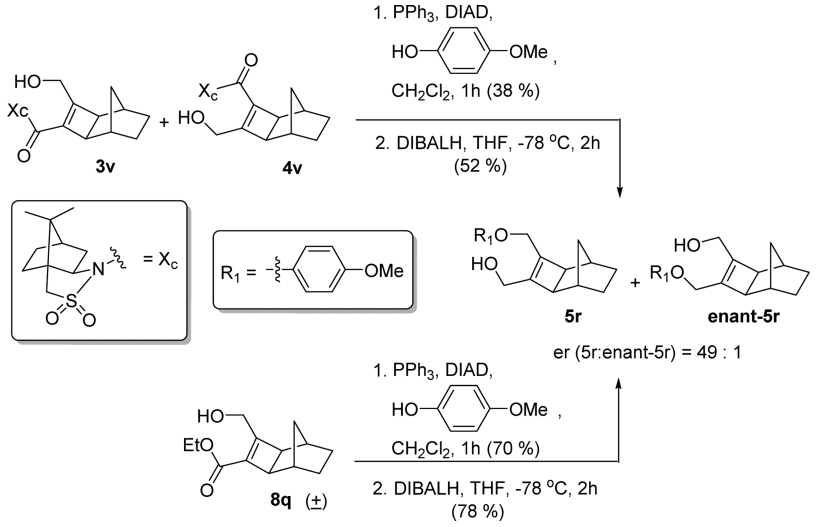
Finally, with focus on the alkyne component, a large number of aryl- and alkyl-substituted chiral alkynes were prepared from the corresponding alkynyl acids (Scheme 4). Because of the nature of the R group, the chiral acyl camphorsultam-substituted alkynes with the alkynyl bromide and propargylic alcohol functionalities were prepared by alternative methods: Alkynyl bromide **12q** was prepared from the corresponding chiral TIPS alkyne **12o**, which was deprotected to the chiral terminal alkyne **12p** using TBAF. The bromine was installed under mild conditions by treatment of **12p** with NBS in the presence of a catalytic amount of silver nitrate.[29] The chiral propargylic alcohol **12s** was instead prepared via THP protection of the hydroxyl group on the alkynyl acid **11n** to give **11o**, followed by incorporation of the chiral auxiliary to give the chiral THP-protected alkyne **12r**, which was subsequently deprotected.

The chiral alkynes **12** were then each reacted with norbornene **2g** to probe the effects of acetylenic substitution on asymmetric induction in the ruthenium-catalyzed [2 + 2] cycloaddition reaction (Table 5). As with our initial racemic trials (Table 1), the phenyl substituted alkyne underwent cycloaddition, affording a slightly higher yield of cycloadducts **3**/**4** than the alkynes bearing electron-poor 3-fluoro and 3-chloro acetylenic aromatic substituents, all of which showed high levels of asymmetric induction (entries 1−3). Although further trials with various acetylenic phenyl derivatives did not display obvious substituent effects, all cycloadditions were high-yielding and showed good to excellent asymmetric induction (entries 4−8). In addition, cycloaddition proceeded reasonably well with alkynes bearing heteroaromatic acetylenic substituents (entries 9 and 10).

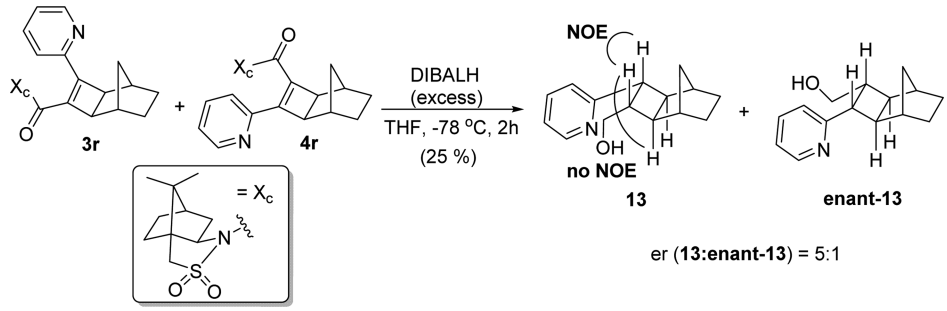
In contrast, both primary and secondary alkyl-based alkynes were far less reactive and required heating for efficient conversion to take place, although this afforded excellent yields of **3**/**4** with moderate diastereoselectivity (entries 11 and 12). Subjection of an alkynyl bromide to cycloaddition similarly showed reduced reactivity for this species, resulting in a low yield and poor diastereoselectivity even upon heating (entry 13). Finally, when a propargylic alcohol derivative was reacted, cycloaddition took place smoothly at room temperature (entry 14), although much of the unreacted auxiliary was also recovered. Through control experiments, we found that, in the absence of norbornene **2g**, the chiral propargylic alcohol was in fact decomposed by the ruthenium catalyst. In addition, as the diastereomeric ratio of the cycloadducts **3**/**4v** from reaction of the propargylic alcohol could not be discerned by ^{1}H NMR, we chose to derivatize **3**/**4v** and measure the ratio by

dx.doi.org/10.1021/jo501594g | J. Org. Chem. 2014, 79, 10002−10012

Scheme 5. Protection of Alcohol via Mitsunobu-type Reaction



Scheme 6. Formation and Analysis of the *cis*−*trans*−*cis* Cyclobutane 13



HPLC. Of the protecting groups *p*-chlorophenyl ether,[30] benzyl ether,[31] and *p*-methoxyphenyl ether,[32] we found *p*-methoxyphenyl ether to be the most successful, and following a Mitsunobu-type protection of **3**/**4v** and cleavage of the chiral auxiliary, the enantiomers **5r** and **enant-5r** were obtained in a ratio of 49:1 (Scheme 5). The identical protection-reduction sequence was applied to the racemic ester adduct **8q**, producing the same alcohol. The high level of asymmetric induction observed in this instance could arise from a stabilizing intramolecular hydrogen-bonding interaction between the alcohol oxygen of alkyne **12s** and the chloride of the Cp*RuCl(cod) catalyst, which has been investigated in cycloaddition studies involving propargylic alcohols.[33,34]

Although removal of the chiral auxiliary was typically achieved under reductive conditions with LAH/$AlCl_3$, several cycloadducts (**3**/**4**; Table 5 entries 2−4, 10) showed multiple degradation products by TLC upon use of LAH/$AlCl_3$, and thus a milder reducing agent, DIBALH, was chosen for auxiliary removal in these species. When we used an excess of DIBALH to reduce the 2-pyridinyl cycloadducts **3**/**4r** (entry 10) in THF at −78 °C, we did not obtain the expected cyclobutene product, but instead attained the enantiomeric pair of *cis*−*trans*−*cis* cyclobutanes **13** and **enant-13** in a ratio of 5:1. The structure of the major adduct **13** was confirmed by NOE experiments (Scheme 6). Reduction of the corresponding racemic ester cycloadduct **8q** under similar conditions also yielded this cyclobutane, which demonstrates a broader potential of the ruthenium-catalyzed [2 + 2] cycloaddition in the preparation of bicycle-fused cyclobutanes, in addition to cyclobutene derivatives.[35]

■ CONCLUSION

In conclusion, we have demonstrated asymmetric induction in ruthenium-catalyzed [2 + 2] cycloadditions using the acyl camphorsultam-substituted alkynes and bicycloalkenes, examining solvent and temperature effects, as well as effects of the individual ene and yne components on the reaction. The cycloadditions were found to be highly stereo- and regioselective, exhibiting excellent levels of asymmetric induction (up to er 166:1 after removal of the chiral auxiliary). The present work demonstrates the versatility of ruthenium catalysis in the [2 + 2] cycloaddition reaction, as this catalyst shows compatibility with a broader class of bicyclic substrates, including norbornadienes, which were not tolerated under rhodium catalysis. We have shown that the four-membered ring systems including both cyclobutenes and cyclobutanes can be constructed via a mild and simple procedure using the chiral *N*-propynoyl camphorsultam, which gives high to excellent yields of cycloadduction products with an overall excellent degree of asymmetric induction.

■ EXPERIMENTAL SECTION

General Experimental Methods. All reactions were carried out in flame-dried glassware under dry nitrogen at ambient temperature. Column chromatography was performed on 230−400 mesh silica gel using flash column chromatography techniques.[36] Analytical thin-layer chromatography was performed on precoated silica gel 60 F_{254} plates. ^1H and ^{13}C NMR spectra were recorded on 300, 400, and 600 MHz

dx.doi.org/10.1021/jo501594g | J. Org. Chem. 2014, 79, 10002−10012

spectrometers. Chemical shifts for NMR spectra are reported in parts per million (ppm) from tetramethylsilane, with the solvent resonance as the internal standard (deuterochloroform, ^{1}H: δ 7.26 ppm; ^{13}C: δ 77.0 ppm). HRMS samples were ionized by chemical ionization (CI), electron impact (EI) or electrospray ionization (ESI) as specified, and detection of the ions was performed by time-of-flight (TOF). Commercial reagents were used without purification. Solvents were purified by distillation under dry nitrogen: 1,2-dichloroethane, hexanes, DMF, and Et_3N from from CaH_2, toluene from sodium, and THF from potassium/benzophenone. Alkyne **6a**,[37] chiral alkynes **1a−c**,[11] **12d−o**,[26] 7-substituted norbornadiene **2b**,[38] 2,3-disubstituted norbornadiene **2c**,[39] 7-oxanorbornene **2f**,[40] and Cp*RuCl(COD)[41] were prepared according to literature procedures. Bicyclic alkene **2e** was prepared from the commercially available 1,4-dihydro-1,4-methanonaphthalene-5,8-diol diacetate via reduction with $LiAlH_4$, followed by methylation using methyl iodide. For experimental procedures and characterization data for cycloadducts **3**/**4c−i**, **5a−g** (or **9a−g**; Table 1, entries 1−7, and Table 4), see the Supporting Information section of our previous publication.[11] Diastereomeric ratios of **3**/**4j−r,v** were measured indirectly from the *ee* value of the product obtained upon removal of the chiral auxiliary, and ratios of **3**/**4s−u** were determined by ^{1}H NMR. Alkynyl esters **6b−k** were prepared by deprotonation of the corresponding terminal alkyne and trapping with the appropriate alkyl chloroformate.[42]

General Procedure for the Ruthenium-Catalyzed [2 + 2] Cycloadditions of Chiral Alkyne 1 with Bicycloalkene 2 and Subsequent Reduction of the Cycloadduct. A mixture of **2g** (17.5 mg, 0.186 mmol), **1c** (20.3 mg, 0.059 mmol), and THF (0.4 mL) in an oven-dried vial was added via cannula to an oven-dried screw-cap vial containing [Cp*RuCl(cod)] (weighed in a drybox, 4.4 mg, 0.012 mmol) under nitrogen. The residue in the first vial was transferred to the reaction mixture with rinses of THF (0.1 mL). The reaction was stirred in the dark at 25 °C for 70 h. The crude product was purified by column chromatography (ethyl acetate/hexanes mixture) to give an inseparable mixture of the cycloadducts **3c**/**4c** (24.5 mg, 0.056 mmol, 95%).

Reduction by LAH/AlCl$_3$. A solution of **3c**/**4c** (20.0 mg, 0.0457 mmol) in THF (0.7 mL) was transferred via cannula to an oven-dried vial containing a suspension of LAH (2.5 mg, 0.065 mmol) and $AlCl_3$ (1.8 mg, 0.014 mmol) in THF (0.3 mL) under nitrogen at 0 °C. The reaction was stirred for 45 min and then quenched slowly with water. Ethyl acetate was added and the layers were separated. The aqueous phase was extracted twice with ethyl acetate, and the combined organic layers were washed with brine, dried over $MgSO_4$, and concentrated to dryness.

Reduction by DIBALH. A solution of **3j**/**4j** (22.7 mg, 0.0498 mmol) in THF (0.5 mL) was stirred in an oven-dried vial under nitrogen and cooled to −78 °C. DIBALH (1.0 M in hexanes; 0.35 mL, 0.350 mmol) was added dropwise over 5 min. The solution was left to stir at −78 °C for 2 h, warmed to room temperature, and quenched gradually with water. The crude product was extracted as described above.

***rac*-(1*S*,2*R*,5*S*,6*R*)-Ethyl 4-(*m*-Fluorophenyl)tricyclo-[4.2.1.0^{2,5}]non-3-ene-3-methanoate, 8h (Table 1, entry 8).** 86% (91.3 mg); Brown oil. R_f 0.57 (1:9 EtOAc:hexanes); IR (CH_2Cl_2): 3072 (w), 2955 (s), 2871 (s), 1699 (s), 1608 (s), 1480 (s), 1580 (s), 1235 (s), 1206 (s), 1135 (s) 781 (s) cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz): δ 7.85−7.77 (m, 1H), 7.72 (d, 1H, J = 7.8 Hz), 7.37−7.27 (m, 1H), 7.01 (td, 1H, J = 8.3 Hz, J = 2.3 Hz), 4.23 (q, 2H, J = 7.1 Hz), 2.76 (d, 1H, J = 3.4 Hz), 2.68 (d, 1H, J = 3.4 Hz), 2.25 (br s, 1H), 2.21 (br s, 1H), 1.69−1.56 (m, 2H), 1.38−1.29 (m, 4H), 1.23−1.13 (m, 2H), 1.03 (d, 1H, J = 10.4 Hz); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 162.8, 162.7 (d, $^1J_{C-F}$ = 245.7 Hz), 154.0, 134.6 (d, $^3J_{C-F}$ = 7.9 Hz), 130.1, 129.7 (d, $^3J_{C-F}$ = 8.4 Hz), 124.4 (d, $^4J_{C-F}$ = 2.2 Hz), 116.6 (d, $^2J_{C-F}$ = 21.3 Hz), 115.5 (d, $^2J_{C-F}$ = 22.0 Hz), 60.1, 46.6, 46.1, 34.6, 34.2, 30.5, 28.3, 28.2, 14.3. HRMS (CI) calcd for $C_{18}H_{19}FO_2$ [M + H]$^+$: 287.1447; found: 287.1445.

***rac*-(1*S*,2*R*,5*S*,6*R*)-Ethyl 4-(*m*-Chlorophenyl)tricyclo-[4.2.1.0^{2,5}]non-3-ene-3-methanoate, 8i (Table 1, entry 9).** 67% (219.8 mg); Brown oil. R_f 0.68 (5:95 EtOAc:hexanes); IR (CH_2Cl_2): 3065 (w), 2956 (s), 2871 (m), 1745 (m), 1703 (s), 1617 (m), 1562 (m), 1471 (m), 1265 (s), 1219 (s), 1204 (s), 1133 (m), 1110 (m), 1030 (m), 746 (m) cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz): δ 7.85−7.77 (m, 1H), 7.72 (d, 1H, J = 7.8 Hz), 7.36−7.27 (m, 1H), 7.03 (td, 1H, J = 8.3 Hz, J = 2.1 Hz), 4.23 (q, 2H, J = 7.2 Hz), 2.76 (d, 1H, J = 3.4 Hz), 2.68 (d, 1H, J = 3.4 Hz), 2.36 (br s, 1H), 2.21 (br s, 1H), 1.69−1.55 (m, 2H), 1.38−1.29 (m, 4H), 1.22−1.14 (m, 2H), 1.03 (d, 1H, J = 10.5 Hz); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 162.7, 153.7, 134.3 (2C), 130.3, 129.6, 129.5, 128.7, 126.8, 60.1, 46.6, 46.1, 34.6, 34.1, 30.5, 28.2 (2C), 14.3. HRMS (CI) calcd for $C_{18}H_{19}ClO_2$ [M + H]$^+$: 303.1152; found: 303.1156.

***rac*-(1*S*,2*R*,5*S*,6*R*)-Ethyl 4-(3,5-Bis(trifluoromethyl)phenyl)-tricyclo[4.2.1.0^{2,5}]non-3-ene-3-methanoate, 8j (Table 1, entry 10).** 52% (61.9 mg); Orange-brown solid, mp: 48−51 °C. R_f 0.48 (5:95 EtOAc:hexanes); IR (KBr): 3081 (w), 2959 (m), 2876 (m), 1702 (m), 1383 (m), 1288 (s), 1278 (s), 1135 (s), 897 (m) cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.44 (s, 2H), 7.81 (s, 1H), 4.26 (q, 2H, J = 7.2 Hz), 2.84−2.80 (m, 1H), 2.75 (d, 1H, J = 3.1 Hz), 2.29 (br s, 1H), 2.21 (br s, 1H), 1.69−1.62 (m, 2H), 1.36−1.29 (m, 4H), 1.26−1.19 (m, 2H), 1.08 (d, 1H, J = 10.5 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 162.4, 151.2, 134.3, 132.9, 131.8 (q, $^2J_{C-F}$ = 33.5 Hz), 128.6, 123.2 (q, $^1J_{C-F}$ = 272.7 Hz), 122.7, 60.6, 46.6 (2C), 34.4, 34.1, 30.6, 28.2 (2C), 14.2. HRMS (CI) calcd for $C_{20}H_{18}F_6O_2$ [M + H]$^+$: 405.1289; found: 405.1295.

***rac*-(1*S*,2*R*,5*S*,6*R*)-Ethyl 4-(*o*-Tolyl)tricyclo[4.2.1.0^{2,5}]non-3-ene-3-methanoate, 8k (Table 1, entry 11).** 62% (78.7 mg); Brown wax. R_f 0.54 (5:95 EtOAc:hexanes); IR (CH_2Cl_2): 3066 (w), 2953 (s), 2870 (s), 1709 (s), 1633 (m), 1459 (m), 1450 (s), 1128 (m), 1203 (s), 1125 (s), 1045 (m), 1023 (m), 747 (m), 720 (m) cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz): δ 7.46 (d, 1H, J = 7.4 Hz), 7.23−7.00 (m, 3H), 4.20−4.08 (q, 2H, J = 7.2 Hz), 2.88 (d, 1H, J = 3.4 Hz), 2.71 (d, 1H, J = 3.4 Hz), 2.37 (s, 3H), 2.31 (br s, 1H), 2.05 (br s, 1H), 1.65−1.53 (m, 2H), 1.49 (d, 1H, J = 10.4 Hz), 1.21 (t, 3H, J = 7.1 Hz), 1.18−1.08 (m, 2H), 1.04 (d, 1H, J = 10.4 Hz); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 162.9, 157.1, 136.6, 133.2, 131.6, 130.4, 129.2, 128.6, 125.2, 59.8, 50.4, 46.6, 35.0, 33.8, 30.7, 28.2, 28.1, 20.7, 14.2. HRMS (CI) calcd for $C_{19}H_{22}O_2$ [M + H]$^+$: 283.1698; found: 283.1702.

***rac*-(1*S*,2*R*,5*S*,6*R*)-Ethyl 4-(*o*-Methoxyphenyl)tricyclo-[4.2.1.0^{2,5}]non-3-ene-3-methanoate, 8l (Table 1, entry 12).** 87% (65.1 mg); Brown oil. R_f 0.46 (1:9 EtOAc:hexanes); IR (CH_2Cl_2): 3076 (w), 2954 (s), 2873 (m), 1699 (s), 1595 (s), 1485 (m), 1251 (s), 1214 (s), 1199 (s), 1164 (s), 1135 (s), 1114 (s), 1046 (s), 1028 (s), 750 (s) cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz): δ 8.02 (dd, 1H, J = 7.7 Hz, J = 1.6 Hz), 7.32−7.21 (m, 1H), 6.92 (t, 1H, J = 7.3 Hz), 6.85 (d, 1H, J = 8.3 Hz), 4.18 (q, 2H, J = 7.1 Hz), 3.79 (s, 3H), 2.95 (d, 1H, J = 3.4 Hz), 2.66 (d, 1H, J = 3.3 Hz), 2.25 (br s, 1H), 2.10 (br s, 1H), 1.65−1.50 (m, 2H), 1.44 (d, 1H, J = 10.3 Hz), 1.26 (t, 3H, J = 7.1 Hz), 1.20−1.07 (m, 2H), 0.96 (d, 1H, J = 10.4 Hz); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 163.3, 158.2, 153.3, 131.2, 130.6, 130.2, 121.9, 120.1, 110.8, 59.7, 55.1, 50.0, 47.2, 35.0, 34.3, 30.5, 28.2, 28.1, 14.3. HRMS (CI) calcd for $C_{19}H_{22}O_3$ [M + H]$^+$: 299.1647; found: 299.1651.

***rac*-(1*S*,2*R*,5*S*,6*R*)-Ethyl 4-(*p*-Tolyl)tricyclo[4.2.1.0^{2,5}]non-3-ene-3-methanoate, 8m (Table 1, entry 13).** 83% (81.2 mg); Brown solid, mp: 50−52 °C. R_f 0.41 (1:9 EtOAc:hexanes); IR (KBr): 2955 (s), 2936 (s), 2905 (m), 2863 (m), 1704 (s), 1613 (s), 1562 (m), 1470 (m), 1223 (s), 1201 (s), 1179 (s), 1135 (s), 1135 (s), 1106 (s), 1062 (s), 821 (s), 783 (s) cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz): δ 7.92 (d, 2H, J = 8.1 Hz), 7.17 (d, 2H, J = 8.0 Hz), 4.22 (q, 2H, J = 7.1 Hz), 2.76 (d, 1H, J = 3.3 Hz), 2.66 (d, 1H, J = 3.2 Hz), 2.35 (s, 3H), 2.24 (br s, 1H), 2.21 (br s, 1H), 1.68−1.52 (m, 2H), 1.41−1.27 (m, 4H), 1.22−1.12 (m, 2H), 1.00 (d, 1H, J = 10.4 Hz); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 163.2, 155.7, 140.1, 130.1, 129.0, 128.9, 127.6, 59.8, 46.5, 45.9, 34.8, 34.3, 30.6, 28.3 (2C), 21.5, 14.4. HRMS (CI) calcd for $C_{19}H_{22}O_2$ [M + H]$^+$: 283.1698; found: 283.1689.

***rac*-(1*S*,2*R*,5*S*,6*R*)-Ethyl 4-(*p*-Methoxyphenyl)tricyclo-[4.2.1.0^{2,5}]non-3-ene-3-methanoate, 8n (Table 1, entry 14).** 63% (131.8 mg); Light brown solid, mp: 43−45 °C. R_f 0.47 (1:9 EtOAc:hexanes); IR (KBr): 3066 (w), 2954 (s), 2933 (s), 2866 (m), 1694 (s), 1603 (s), 1457 (w), 1509 (s), 1260 (m), 1220 (s), 1202 (s), 1174 (s), 1138 (m) cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz): δ 8.00 (d,

2H, J = 8.8 Hz), 6.89 (d, 2H, J = 8.8 Hz), 4.21 (q, 2H, J = 7.1 Hz), 3.81 (s, 3H), 2.73 (d, 1H, J = 3.5 Hz), 2.65 (d, 1H, J = 3.5 Hz), 2.23 (br s, 1H), 2.19 (br s, 1H), 1.67−1.51 (m, 2H), 1.37 (d, 1H, J = 10.6 Hz), 1.31 (t, 3H, J = 7.1 Hz), 1.22−1.11 (m, 2H), 1.00 (d, 1H, J = 10.4 Hz); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 163.3, 160.8, 155.6, 130.8, 126.0, 125.9, 113.7, 59.8, 55.3, 46.5, 45.8, 34.8, 34.4, 30.6, 28.4 (2C), 14.4. HRMS (CI) calcd for $C_{19}H_{22}O_3$ $[M + H]^+$: 299.1647; found: 299.1653.

***rac*-(1*S*,2*R*,5*S*,6*R*)-Methyl 4-(3-Thienyl)tricyclo[4.2.1.0^{2,5}]non-3-ene-3-methanoate, 8o (Table 1, entry 15).** 93% (87.2 mg); Light brown oil. R_f 0.69 (1:9 EtOAc:hexanes); IR (CH_2Cl_2): 3108 (w), 2949 (s), 2869 (s), 1701 (s), 1617 (s), 1304 (m), 1283 (m), 1232 (s), 1203 (s), 1131 (s), 1065 (s), 864 (m), 779 (s) cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz): δ 8.00 (d, 1H, J = 2.3 Hz), 7.66 (dd, 1H, J = 5.0 Hz, J = 0.6 Hz), 7.26 (dd, 1H, J = 5.0 Hz, J = 3.0 Hz), 3.76 (s, 3H), 2.72 (d, 1H, J = 3.4 Hz), 2.68 (d, 1H, J = 3.4 Hz), 2.24 (br s, 1H), 2.20 (br s, 1H), 1.66−1.54 (m, 2H), 1.37 (d, 1H, J = 10.5 Hz), 1.22−1.09 (m, 2H), 1.02 (d, 1H, J = 10.5 Hz); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 163.4, 150.4, 135.2, 133.0, 128.4, 128.0, 125.3, 51.0, 47.2, 46.4, 34.6, 34.3, 32.2, 30.6, 28.2. HRMS (CI) calcd for $C_{15}H_{16}O_2S$ $[M]^+$: 260.0871; found: 260.0876.

***rac*-(1*S*,2*R*,5*S*,6*R*)-Ethyl 4-(2-Pyridyl)tricyclo[4.2.1.0^{2,5}]non-3-ene-3-methanoate, 8p (Table 1, entry 16).** 95% (86.0 mg); Light brown solid. mp: 35−36 °C. R_f 0.51 (2:8 EtOAc:hexanes); IR (CH_2Cl_2): 3047 (m), 2955 (s), 2870 (s), 1704 (s), 1618 (s), 1462 (s), 1580 (s), 1291 (s), 1256 (s), 1223 (s), 1201 (s), 1133 (s), 1098 (s), 1050 (s), 1030 (s), 779 (s), 743 (m) cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz): δ 8.62 (d, 1H, J = 4.7 Hz), 8.58 (d, 1H, J = 8.0 Hz), 7.68 (td, 1H, J = 7.8 Hz, J = 1.6 Hz), 7.22−7.14 (m, 1H), 4.22 (q, 2H, J = 7.1 Hz), 2.94 (d, 1H, J = 3.3 Hz), 2.68 (d, 1H, J = 3.3 Hz), 2.36 (br s, 1H), 2.24 (br s, 1H), 1.66−1.52 (m, 2H), 1.37−1.27 (m, 4H), 1.24−1.15 (m, 2H), 1.00 (d, 1H, J = 10.4 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 162.8, 155.6, 150.9, 149.4, 136.1, 132.0, 125.4, 123.6, 60.1, 47.0, 46.3, 34.5, 34.2, 30.5, 28.2 (2C), 14.2. HRMS (CI) calcd for $C_{17}H_{19}NO_2$ $[M]^+$: 269.1416; found: 269.1399.

***rac*-(1*S*,2*R*,5*S*,6*R*)-Ethyl 4-(Hydroxymethyl)tricyclo[4.2.1.0^{2,5}]-non-3-ene-3-methanoate, 8q (Table 1, entry 17).** 88% (80.3 mg); Yellow oil. R_f 0.32 (2:8 EtOAc:hexanes); IR (CH_2Cl_2): 3416 (br), 2954 (s), 2871 (m), 1712 (s), 1681 (s), 1303 (s), 1285 (s), 1217 (s), 779 (w) cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz): δ 7.43 (t, 1H, J = 5.2 Hz), 4.29−4.23 (m, 2H), 4.16 (q, 2H, J = 7.1 Hz), 2.58−2.51 (m, 1H), 2.40−2.35 (m, 1H), 2.16−2.10 (m, 1H), 2.03−1.97 (m, 1H), 1.62−1.46 (m, 2H), 1.36−1.23 (m, 1H), 1.26 (t, 3H, J = 7.1 Hz), 1.11−0.96 (m, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 164.4, 164.2, 130.2, 60.9, 60.7, 47.1, 46.1, 33.9, 33.5, 30.4, 28.0, 27.7, 14.1. HRMS (ESI) calcd for $C_{13}H_{18}O_3$ $[M + H]^+$: 223.1334; found: 223.1340.

3-((1*S*,5*R*,7*R*)-10,10-Dimethyl-3,3-dioxo-3-thia-4-azatricyclo-[5.2.1.0^{1,5}]decane-4-carbonyl)-(1*S*,2*R*,5*S*,6*R*)-4-(*m*-fluorophenyl)tricyclo[4.2.1.0^{2,5}]non-3-ene, 3/4j (Table 5, entry 2). 88% (60.6 mg); Yellow-brown solid. mp: 174−176 °C. R_f 0.60 (3:7 EtOAc:hexanes); IR (KBr): 3085 (w), 3005 (m), 2948 (s), 2871 (s), 1650 (s), 1578 (s), 1343 (s), 1284 (s), 1238 (s), 1212 (s), 1056 (m), 998 (m) cm^{-1}; dr 38:1 for **3j**/**4j**; ^{1}H NMR ($CDCl_3$, 300 MHz): δ 7.63−7.50 (m, 2H), 7.33−7.24 (m, 1H), 7.00 (td, 1H, J = 8.1 Hz, J = 2.1 Hz), 4.09 (dd, 1H, J = 7.4 Hz, J = 5.0 Hz), 3.58 (d, 1H, J = 13.7 Hz), 3.41 (d, 1H, J = 13.6 Hz), 3.27 (d, 1H, J = 3.4 Hz), 2.81 (d, 1H, J = 3.5 Hz), 2.24 (br s, 1H), 2.16 (br s, 1H), 2.10 (dd, 1H, J = 13.7 Hz, J = 7.7 Hz), 2.05−1.80 (m, 4H), 1.64−1.55 (m, 2H), 1.42−1.30 (m, 3H), 1.24 (s, 3H), 1.22−1.11 (m, 2H), 1.02 (d, 1H, J = 10.8 Hz), 0.98 (s, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 162.5 (d, $^1J_{C-F}$ = 245.8 Hz), 162.7, 155.1, 134.6 (d, $^3J_{C-F}$ = 7.9 Hz), 131.3, 129.6 (d, $^3J_{C-F}$ = 8.0 Hz), 124.1 (d, $^4J_{C-F}$ = 2.4 Hz), 116.7 (d, $^2J_{C-F}$ = 21.4 Hz), 115.2 (d, $^2J_{C-F}$ = 22.0 Hz), 65.7, 53.7, 48.24, 48.20, 47.7, 47.0, 45.1, 38.7, 35.4, 34.3, 33.3, 30.7, 28.1, 28.0, 26.4, 21.3, 19.9. HRMS (CI) calcd for $C_{26}H_{30}FNO_3S$ $[M + H]^+$: 456.2009; found: 456.2003.

(1*S*,2*R*,5*S*,6*R*)-3-Hydroxymethyl-4-(*m*-fluorophenyl)tricyclo-[4.2.1.0^{2,5}]non-3-ene, 5h (Table 5, entry 2). 86% (10.4 mg); Yellow oil. R_f 0.40 (2:8 EtOAc:hexanes). $[\alpha]_D^{26}$ −34.2 (*c* 0.81, $CHCl_3$, 95% *ee*, er 39:1 for **5h**/**enant-5h**); HPLC (OJ-H column, 0.4 mL/min, 1% ^{i}PrOH/99% hexanes, 254 nm), t_R (major enantiomer): 33.31 min, t_R (minor enantiomer): 31.50 min; IR (CH_2Cl_2): 3352 (br), 2950 (s), 2870 (s), 1610 (s), 1485 (m), 1445 (s), 1581 (s), 1267 (s), 1172 (s), 1155 (s), 1034 (s), 1005 (s), 870 (s), 783 (s), 686 (s) cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.30−7.20 (m, 1H), 7.09 (d, 1H, J = 7.6 Hz), 7.04−6.98 (m, 1H), 7.01 (td, 1H, J = 8.6 Hz, J = 2.5 Hz), 4.44 (d, 1H, J = 14.3 Hz), 4.37 (d, 1H, J = 14.3 Hz), 2.68 (s, 1H), 2.57 (d, 1H, J = 3.3 Hz), 2.17 (br s, 1H), 2.12 (br s, 1H), 1.67−1.52 (m, 2H), 1.44 (br s, 1H), 1.39 (d, 1H, J = 10.2 Hz), 1.21−1.04 (m, 2H), 1.01 (d, 1H, J = 10.2 Hz); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 163.0 (d, $^1J_{C-F}$ = 244.7 Hz), 142.2, 139.0 (d, $^4J_{C-F}$ = 2.2 Hz), 136.5 (d, $^3J_{C-F}$ = 7.5 Hz), 129.9 (d, $^3J_{C-F}$ = 8.0 Hz), 122.9 (d, $^4J_{C-F}$ = 2.1 Hz), 114.0 (d, $^2J_{C-F}$ = 21.7 Hz), 113.3 (d, $^2J_{C-F}$ = 21.4 Hz), 58.9, 46.6, 46.4, 34.5, 34.2, 30.7, 28.5, 28.2. HRMS (EI) calcd for $C_{16}H_{17}FO$ $[M]^+$: 244.1263; found: 244.1269.

3-((1*S*,5*R*,7*R*)-10,10-Dimethyl-3,3-dioxo-3-thia-4-azatricyclo-[5.2.1.0^{1,5}]decane-4-carbonyl)-(1*S*,2*R*,5*S*,6*R*)-4-(*m*-chlorophenyl)tricyclo[4.2.1.0^{2,5}]non-3-ene, 3/4k (Table 5, entry 3). 81% (73.6 mg); Beige solid. mp: 160−161 °C. R_f 0.51 (3:7 EtOAc:hexanes); IR (KBr): 3012 (w), 2949 (m), 1636 (s), 1585 (m), 1560 (m), 1338 (s), 1314 (m), 1068 (m), 788 (m) cm^{-1}; dr 30:1 for **3k**/**4k**; ^{1}H NMR ($CDCl_3$, 300 MHz): δ 7.79−7.76 (m, 1H), 7.71 (td, 1H, J = 6.8 Hz, J = 1.9 Hz), 7.30−7.25 (m, 2H), 4.12−4.05 (m, 1H), 3.48 (d, 1H, J = 13.6 Hz), 3.41 (d, 1H, J = 13.6 Hz), 3.27 (d, 1H, J = 3.7 Hz), 2.80 (d, 1H, J = 3.7 Hz), 2.24 (br s, 1H), 2.16 (br s, 1H), 2.10 (dd, 1H, J = 13.6 Hz, J = 7.6 Hz), 2.06−1.96 (m, 1H), 1.96−1.80 (m, 3H), 1.60 (m, 2H), 1.46−1.34 (m, 3H), 1.22−1.12 (m, 5H), 1.02 (d, 1H, J = 10.6 Hz), 0.98 (s, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 162.7, 154.8, 134.3, 134.1, 131.5, 129.7, 129.4, 128.2, 126.6, 65.7, 53.7, 48.2, 47.7 (2C), 46.9, 45.1, 38.7, 35.4, 34.3, 33.2, 30.7, 28.1, 28.0, 26.3, 21.3, 19.9. HRMS (CI) calcd for $C_{26}H_{30}ClNO_3S$ $[M + H]^+$: 472.1713; found: 472.1717.

(1*S*,2*R*,5*S*,6*R*)-3-Hydroxymethyl-4-(*m*-chlorophenyl)tricyclo-[4.2.1.0^{2,5}]non-3-ene, 5i (Table 5, entry 3). 91% (14.1 mg); Yellow oil. R_f 0.41 (2:8 EtOAc:hexanes); $[\alpha]_D^{26}$ −30.6 (*c* 0.46, $CHCl_3$, 93.5% *ee*, er 30:1 for **5i**/**enant-5i**); HPLC (OJ-H column, 0.4 mL/min, 1% ^{i}PrOH/99% hexanes, 254 nm), t_R (major enantiomer): 28.70 min, t_R (minor enantiomer): 32.39 min; IR (CH_2Cl_2): 3423 (br), 2958 (s), 2933 (s), 2871 (s), 1592 (m), 1453 (m), 1299 (m), 690 (s) cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.30−7.27 (m, 1H), 7.26−7.14 (m, 3H), 4.43 (d, 1H, J = 14.3 Hz), 4.36 (d, 1H, J = 14.4 Hz), 2.67 (s, 1H), 2.56 (d, 1H, J = 3.3 Hz), 2.17 (br s, 1H), 2.12 (br s, 1H), 1.65−1.56 (m, 2H), 1.53 (br s, 1H), 1.38 (d, 1H, J = 10.2 Hz), 1.18−1.08 (m, 2H), 1.01 (d, 1H, J = 10.2 Hz); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 142.5, 138.7, 136.1, 134.4, 129.7, 127.1, 126.5, 124.7, 58.9, 46.7, 46.3, 34.5, 34.2, 30.6, 28.5, 28.2. HRMS (CI) calcd for $C_{16}H_{17}ClO$ $[M - H]^-$: 259.0890; found: 259.0893.

3-((1*S*,5*R*,7*R*)-10,10-Dimethyl-3,3-dioxo-3-thia-4-azatricyclo-[5.2.1.0^{1,5}]decane-4-carbonyl)-(1*S*,2*R*,5*S*,6*R*)-4-(3,5-bis-(trifluoromethyl)phenyl)tricyclo[4.2.1.0^{2,5}]non-3-ene, 3/4l (Table 5, entry 4). 99% (78.0 mg); Dark brown wax. R_f 0.54 (3:7 EtOAc:hexanes); IR (KBr): 3090 (w), 2959 (s), 2876 (m), 1652 (s), 1379 (s), 1349 (s), 1279 (s), 1223 (s), 1174 (s), 1135 (s), 900 (m), 761 (m), 739 (m), 701 (m), 681 (m) cm^{-1}; dr 4:1 for **3l**/**4l**; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.52 (s, 2H), 7.79 (s, 1H), 4.09 (dd, 1H, J = 7.4 Hz, 4.4 Hz), 3.50 (d, 1H, J = 13.6 Hz), 3.42 (d, 1H, J = 13.6 Hz), 3.33 (d, 1H, J = 3.5 Hz), 2.87 (d, 1H, J = 3.5 Hz), 2.23 (br s, 1H), 2.20 (br s, 1H), 2.11 (dd, 1H, J = 13.6 Hz, 7.8 Hz), 2.04−1.78 (m, 4H), 1.58−1.45 (m, 2H), 1.38−1.21 (m, 3H), 1.12 (s, 3H), 1.17−1.04 (m, 2H), 0.94 (d, 1H, J = 10.7 Hz), 0.88 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 162.3, 152.5, 134.4, 134.1, 131.6 (q, $^2J_{C-F}$ = 33.3 Hz), 128.3, 123.2 (q, $^1J_{C-F}$ = 272.8 Hz), 122.8, 65.8, 53.7, 48.7, 48.3, 47.7, 46.8, 45.2, 38.6, 35.2, 34.2, 33.3, 30.7, 28.1, 28.0, 26.3, 21.3, 19.9. HRMS (CI) calcd. for $C_{28}H_{29}F_6NO_3S$ $[M + H]^+$: 574.1851; found: 574.1849.

(1*S*,2*R*,5*S*,6*R*)-3-Hydroxymethyl-4-(3,5-bis(trifluoromethyl)-phenyl)tricyclo[4.2.1.0^{2,5}]non-3-ene, 5j (Table 5, entry 4). 89% (25.9 mg); Yellow oil. R_f 0.45 (2:8 EtOAc:hexanes); $[\alpha]_D^{26}$ −17.4 (*c* 1.4, $CHCl_3$, 59.6% *ee*, er 4:1 for **5j**/**enant-5j**); HPLC (OD-H column, 0.2 mL/min, 2% ^{i}PrOH/98% hexanes, 254 nm), t_R (major enantiomer): 35.76 min, t_R (minor enantiomer): 34.67 min; IR (CH_2Cl_2): 3330 (br), 2953 (s), 2874 (s), 1467 (m), 1452 (m), 1383 (s), 1277 (s), 1175 (s), 1130 (s), 1044 (s), 894 (s), 702 (s), 682 (s)

cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz): δ 7.77 (m, 2H), 7.68 (s, 1H), 4.56−4.40 (m, 2H), 2.75 (s, 1H), 2.59 (d, 1H, J = 3.0 Hz), 2.18 (br s, 1H), 2.14 (br s, 1H), 1.67−1.58 (m, 2H), 1.56 (br s, 1H), 1.38 (d, 1H, J = 10.4 Hz), 1.22−1.10 (m, 2H), 1.05 (d, 1H, J = 10.4 Hz); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 145.3, 137.1, 136.1, 131.7 (q, $^2J_{C-F}$ = 33.4 Hz), 128.5, 123.3 (q, $^1J_{C-F}$ = 273.0 Hz), 120.3, 59.1, 46.8, 46.2, 34.6, 34.1, 30.6, 28.4, 28.1. HRMS (CI) calcd for $C_{18}H_{16}F_6O$ $[M]^+$: 362.1105; found: 362.1101.

3-((1*S*,5*R*,7*R*)-10,10-Dimethyl-3,3-dioxo-3-thia-4-azatricyclo-[5.2.1.0^{1,5}]decane-4-carbonyl)-(1*S*,2*R*,5*S*,6*R*)-4-(*o*-tolyl)tricyclo-[4.2.1.0^{2,5}]non-3-ene, 3/4m (Table 5, entry 5). 97% (107.9 mg); Dark brown oil. R_f 0.50 (3:7 EtOAc:hexanes); IR (CH_2Cl_2): 3065 (w), 2955 (s), 2873 (s), 2255 (w), 1652 (s), 1617 (m), 1485 (m), 1456 (m), 1335 (s), 1286 (s), 1236 (s), 1167 (s), 1128 (s), 1060 (s), 992 (s), 914 (s), 734 (s) cm^{-1}; dr 8:1 for **3m**/**4m**; ^1H NMR ($CDCl_3$, 300 MHz): δ 7.37 (d, 1H, J = 7.0 Hz), 7.20−7.00 (m, 3H), 3.99−3.92 (m, 1H), 3.46 (d, 1H, J = 13.7 Hz), 3.31 (d, 1H, J = 13.7 Hz), 3.25−3.21 (m, 1H), 2.79 (d, 1H, J = 3.0 Hz), 2.34−2.27 (m, 4H), 2.22 (br s, 1H), 2.04−1.96 (m, 2H), 1.93−1.75 (m, 3H), 1.70−1.50 (m, 3H), 1.40−1.27 (m, 2H), 1.20- 1.15 (m, 4H), 1.15−1.04 (m, 2H), 0.95 (s, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 162.3, 157.3, 136.4, 134.2, 133.3, 130.3, 128.3, 128.2, 125.2, 65.4, 53.5, 50.8, 48.8, 48.2, 47.6, 45.0, 38.6, 35.4, 34.8, 33.1, 30.7, 28.0 (2C), 26.3, 21.1, 20.7, 19.8. HRMS (CI) calcd for $C_{27}H_{33}NO_3S$ $[M + H]^+$: 452.2259; found: 452.2250.

(1*S*,2*R*,5*S*,6*R*)-3-Hydroxymethyl-4-(*o*-tolyl)tricyclo[4.2.1.0^{2,5}]-non-3-ene, 5k (Table 5, entry 5). 77% (25.6 mg); White solid. mp: 41−43 °C. R_f 0.42 (2:8 EtOAc:hexanes); $[\alpha]_D^{24}$ −113.5 (c 1.2, $CHCl_3$, 77.9% *ee*, er 8:1 for **5k**/**enant-5k**); HPLC (OJ-H column, 0.4 mL/min, 5% ^{i}PrOH/95% hexanes, 210 nm), t_R (major enantiomer): 17.86 min, t_R (minor enantiomer): 30.28 min; IR (KBr): 3298 (br), 3202 (m), 3054 (m), 3019 (m), 2952 (s), 2868 (m), 1486 (m), 1458 (m), 1448 (m), 1021 (m), 995 (m) cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz): δ 7.16−7.10 (m, 4H), 4.26 (d, 1H, J = 13.7 Hz), 4.19 (dd, 1H, J = 13.7 Hz, J = 2.4 Hz), 2.85−2.81 (m, 1H), 2.61−2.57 (d, 1H, J = 3.3 Hz), 2.36 (s, 3H), 2.18−2.13 (m, 1H), 2.04−2.00 (m, 1H), 1.61−1.55 (m, 2H), 1.55−1.49 (m, 1H), 1.31−1.25 (br m, 1H), 1.16−1.04 (m, 2H), 1.01 (d, 1H, J = 10.1 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 142.3, 141.8, 135.9, 134.0, 130.5, 128.9, 127.3, 125.5, 58.9, 49.9, 46.7, 34.8, 34.3, 30.7, 28.4, 28.1, 20.7. HRMS (EI) calcd for $C_{17}H_{20}O$ $[M]^+$: 240.1514; found: 240.1521.

3-((1*S*,5*R*,7*R*)-10,10-Dimethyl-3,3-dioxo-3-thia-4-azatricyclo-[5.2.1.0^{1,5}]decane-4-carbonyl)-(1*S*,2*R*,5*S*,6*R*)-4-(*o*-methoxyphenyl)tricyclo[4.2.1.0^{2,5}]non-3-ene, 3/4n (Table 5, entry 6). 95% (50.0 mg); Gold-brown solid. mp: 135−136 °C. R_f 0.41 (3:7 EtOAc:hexanes); IR (KBr): 2952 (s), 2869 (m), 1685 (m), 1654 (m), 1623 (m), 1493 (m), 1457 (m), 1336 (s), 752 (m) cm^{-1}; dr 58:1 for **3n**/**4n**; ^1H NMR ($CDCl_3$, 300 MHz): δ 7.42 (d, 1H, J = 7.5 Hz), 7.27−7.18 (m, 1H), 6.88 (t, 1H, J = 7.5 Hz), 6.82 (d, 1H, J = 8.2 Hz), 3.90 (dd, 1H, J = 6.9 Hz, J = 5.3 Hz), 3.77 (s, 3H), 3.40 (d, 1H, J = 13.6 Hz), 3.34 (d, 1H, J = 13.8 Hz), 2.98 (d, 1H, J = 2.1 Hz), 2.82 (d, 1H, J = 2.2 Hz), 2.29 (br s, 1H), 2.13−2.10 (m, 2H), 2.04−1.78 (m, 4H), 1.66 (d, 1H, J = 10.5 Hz), 1.58 (d, 2H, J = 9.2 Hz), 1.45−1.25 (m, 2H), 1.17 (s, 3H), 1.14 (d, 2H, J = 9.0 Hz), 1.02 (d, 1H, J = 10.5 Hz), 0.94 (s, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 163.4, 158.1, 132.4, 130.2, 128.9, 122.0, 120.0, 110.7, 64.7, 54.7, 52.9, 49.1, 48.8, 48.3, 47.7, 44.9, 38.4, 35.6, 34.5, 33.0, 30.9, 28.2, 28.1, 26.4, 20.7, 19.9. HRMS (CI) calcd for $C_{27}H_{33}NO_4S$ $[M + H]^+$: 468.2209; found: 468.2215.

(1*S*,2*R*,5*S*,6*R*)-3-Hydroxymethyl-4-(*o*-methoxyphenyl)-tricyclo[4.2.1.0^{2,5}]non-3-ene, 5l (Table 5, entry 6). 78% (7.3 mg); Yellow oil. R_f 0.29 (2:8 EtOAc:hexanes); $[\alpha]_D^{24}$ −53.4 (c 0.46, $CHCl_3$, 96.6% *ee*, er 58:1 for **5l**/**enant-5l**); HPLC (OJ-H column, 0.4 mL/min, 5% ^{i}PrOH/95% hexanes, 254 nm), t_R (major enantiomer): 21.93 min, t_R (minor enantiomer): 31.73 min; IR (CH_2Cl_2): 3438 (br), 3072 (w), 2950 (s), 2869 (m), 1643 (m), 1464 (s), 1599 (s), 1246 (s), 1180 (m), 1163 (m), 1053 (m), 1026 (s), 752 (s) cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz): δ 7.30−7.10 (m, 2H), 7.00−6.75 (m, 2H), 4.33−4.16 (m, 2H), 3.84 (s, 3H), 2.71 (br s, 1H), 2.52 (br s, 1H), 2.12 (br s, 2H), 1.98 (br s, 1H), 1.65−1.54 (m, 2H), 1.49 (d, 1H, J = 10.2 Hz), 1.19−1.05 (m, 2H), 0.97 (d, 1H, J = 10.2 Hz); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 156.2, 142.6, 136.0, 128.8, 128.6, 123.8, 120.8, 110.9, 60.1, 55.3, 47.4, 46.8, 34.8, 34.3, 30.6, 28.6, 28.3. HRMS (CI) calcd for $C_{17}H_{20}O_2$ $[M]^+$: 256.1463; found: 256.1470.

3-((1*S*,5*R*,7*R*)-10,10-Dimethyl-3,3-dioxo-3-thia-4-azatricyclo-[5.2.1.0^{1,5}]decane-4-carbonyl)-(1*S*,2*R*,5*S*,6*R*)-4-(*p*-tolyl)tricyclo-[4.2.1.0^{2,5}]non-3-ene, 3/4o (Table 5, entry 7). 73% (58.9 mg); White solid. mp: 186−189 °C. R_f 0.69 (3:7 EtOAc:hexanes); IR (KBr): 3082 (w), 3006 (m), 2954 (s), 2867 (m), 1644 (s), 1586 (s), 1454 (m), 1505 (s), 1329 (s), 1286 (s), 1220 (s), 1108 (s), 1058 (s), 992 (m), 764 (m), 570 (m), 548 (m) cm^{-1}; dr 104:1 for **3o**/**4o**; ^1H NMR ($CDCl_3$, 300 MHz): δ 7.75 (d, 2H, J = 8.1 Hz), 7.12 (d, 2H, J = 8.0 Hz), 4.09 (dd, 1H, J = 7.3 Hz, 5.1 Hz), 3.48 (d, 1H, J = 13.6 Hz), 3.41 (d, 1H, J = 13.6 Hz), 3.27 (d, 1H, J = 3.5 Hz), 2.80 (d, 1H, J = 3.5 Hz), 2.32 (s, 3H), 2.23 (br s, 1H), 2.16 (br s, 1H), 2.09 (dd, 1H, J = 13.7 Hz, J = 7.9 Hz), 2.05−1.80 (m, 4H), 1.57 (m, 2H), 1.46−1.32 (m, 3H), 1.24 (s, 3H), 1.23−1.11 (m, 2H), 1.02−0.95 (m, 4H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 162.8, 157.5, 140.3, 130.0, 128.8, 128.7, 128.6, 65.7, 53.6, 48.1, 47.8, 47.6, 46.8, 45.1, 38.8, 35.5, 34.5, 33.2, 30.7, 28.2, 28.1, 26.4, 21.5, 21.3, 19.9. HRMS (CI) calcd for $C_{27}H_{33}NO_3S$ $[M + H]^+$: 452.2259; found: 452.2264.

(1*S*,2*R*,5*S*,6*R*)-3-Hydroxymethyl-4-(*p*-tolyl)tricyclo[4.2.1.0^{2,5}]-non-3-ene, 5m (Table 5, entry 7). 83% (8.4 mg); Yellow oil. R_f 0.50 (2:8 EtOAc:hexanes); $[\alpha]_D^{24}$ −40.2 (c 0.26, $CHCl_3$, 98% *ee*, er 99:1 for **5m**/**enant-5m**); HPLC (OJ-H column, 0.4 mL/min, 5% ^{i}PrOH/95% hexanes, 254 nm), t_R (major enantiomer): 21.81 min, t_R (minor enantiomer): 32.83 min; IR (CH_2Cl_2): 3435 (br), 3026 (m), 2952 (s), 2870 (s), 1608 (s), 1451 (s), 1510 (s), 1297 (s), 1265 (s), 1183 (s), 1039 (s), 993 (s), 820 (s), 737 (s) cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz): δ 7.23 (d, 2H, J = 8.0 Hz), 7.12 (d, 2H, J = 7.9 Hz), 4.44 (dd, 1H, J = 13.9 Hz, J = 4.0 Hz), 4.36 (dd, 1H, J = 13.8 Hz, J = 5.0 Hz), 2.72−2.66 (m, 1H), 2.56 (d, 1H, J = 3.1 Hz), 2.32 (s, 3H), 2.17 (br s, 1H), 2.11 (br s, 1H), 1.65−1.51 (m, 2H), 1.41 (d, 1H, J = 10.2 Hz), 1.36 (br t, 1H, J = 5.4 Hz), 1.18−1.08 (m, 2H), 0.99 (d, 1H, J = 10.2 Hz); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 140.2, 139.5, 137.1, 131.6, 129.1, 126.5, 59.0, 46.5, 46.3, 34.6, 34.3, 30.7, 28.6, 28.2, 21.3. HRMS (CI) calcd for $C_{17}H_{20}O$ $[M + H]^+$: 241.1592; found: 241.1598.

3-((1*S*,5*R*,7*R*)-10,10-Dimethyl-3,3-dioxo-3-thia-4-azatricyclo-[5.2.1.0^{1,5}]decane-4-carbonyl)-(1*S*,2*R*,5*S*,6*R*)-4-(*p*-methoxyphenyl)tricyclo[4.2.1.0^{2,5}]non-3-ene, 3/4p (Table 5, entry 8). 72% (96.0 mg); Light brown solid. mp: 170−172 °C. R_f 0.51 (3:7 EtOAc:hexanes); IR (KBr): 2951 (s), 1650 (m), 1603 (m), 1506 (s), 1332 (s), 1223 (s), 994 (m), 836 (m) cm^{-1}; dr 31:1 for **3p**/**4p**; ^1H NMR ($CDCl_3$, 400 MHz): δ 7.88 (d, 2H, J = 8.9 Hz), 6.84 (d, 2H, J = 8.9 Hz), 4.14−4.06 (m, 1H), 3.80 (s, 3H), 3.48 (d, 1H, J = 13.6 Hz), 3.41 (d, 1H, J = 13.6 Hz), 3.26 (d, 1H, J = 3.5 Hz), 2.79 (d, 1H, J = 3.5 Hz), 2.21 (br s, 1H), 2.18 (br s, 1H), 2.09 (dd, 1H, J = 13.6 Hz, J = 7.8 Hz), 2.02−1.80 (m, 4H), 1.65−1.56 (m, 2H), 1.44−1.37 (m, 2H), 1.35 (d, 1H, J = 9.8 Hz), 1.25 (s, 3H), 1.21−1.12 (m, 2H), 1.04−0.96 (m, 4H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 162.8, 161.0, 158.0, 130.7, 127.0, 125.8, 113.5, 65.9, 55.2, 53.8, 48.1, 47.7, 47.6, 46.8, 45.3, 38.9, 35.7, 34.6, 33.3, 30.7, 28.19, 28.16, 26.4, 21.4, 19.9. HRMS (CI) calcd for $C_{27}H_{33}NO_4S$ $[M + H]^+$: 468.2209; found: 468.2217.

(1*S*,2*R*,5*S*,6*R*)-3-Hydroxymethyl-4-(*p*-methoxyphenyl)-tricyclo[4.2.1.0^{2,5}]non-3-ene, 5n (Table 5, entry 8). 55% (8.7 mg); Yellow solid. mp: 41−43 °C. R_f 0.29 (2:8 EtOAc:hexanes); $[\alpha]_D^{24}$ −30.6 (c 0.71, $CHCl_3$, 94% *ee*, er 32:1 for **5n**/**enant-5n**); HPLC (OJ-H column, 0.4 mL/min, 5% ^{i}PrOH/95% hexanes, 254 nm), t_R (major enantiomer): 50.93 min, t_R (minor enantiomer): 65.50 min; IR(KBr): 3398 (br), 2949 (s), 2868 (m), 1606 (m), 1509 (s), 1249 (s), 1174 (m), 1033 (m), 834 (s) cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz): δ 7.28 (d, 2H, J = 8.8 Hz), 6.85 (d, 2H, J = 8.7 Hz), 4.41 (dd, 1H, J = 13.9 Hz, J = 5.4 Hz), 4.33 (dd, 1H, J = 13.7 Hz, J = 5.7 Hz), 3.79 (s, 3H), 2.67 (s, 1H), 2.54 (d, 1H, J = 3.0 Hz), 2.15 (br s, 1H), 2.10 (br s, 1H), 1.64−1.54 (m, 2H), 1.41 (d, 1H, J = 10.1 Hz), 1.29 (t, 1H, J = 5.7 Hz), 1.17−1.07 (m, 2H), 0.99 (d, 1H, J = 10.2 Hz); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 158.8, 139.7, 138.1, 127.9, 127.4, 113.9, 58.9, 55.2, 46.4, 46.3, 34.5, 34.3, 30.6, 28.5, 28.2. HRMS (CI) calcd. for $C_{17}H_{20}O_2$ $[M + H]^+$: 257.1542; found: 257.1551.

3-((1*S*,5*R*,7*R*)-10,10-Dimethyl-3,3-dioxo-3-thia-4-azatricyclo-[5.2.1.0^{1,5}]decane-4-carbonyl)-(1*S*,2*R*,5*S*,6*R*)-4-(3-thienyl)-tricyclo[4.2.1.0^{2,5}]non-3-ene, 3/4q (Table 5, entry 9). 98% (65.0 mg); Brown solid, mp: 199−201 °C dec R_f 0.61 (3:7 EtOAc:hexanes);

IR (KBr): 3126 (w), 2963 (s), 2870 (m), 1633 (s), 1583 (s), 1326 (s), 1300 (s), 1222 (s), 1117 (s), 1056 (s), 998 (m), 913 (m), 808 (m), 742 (m) cm^{-1}; dr 20:1 for **3q**/**4q**; ^1H NMR ($CDCl_3$, 300 MHz): δ 8.08 (dd, 1H, J = 2.9 Hz, J = 0.9 Hz), 7.56 (dd, 1H, J = 5.0 Hz, J = 1.0 Hz), 7.22 (dd, 1H, J = 5.1 Hz, J = 3.0 Hz), 4.09 (dd, 1H, J = 7.2 Hz, J = 5.2 Hz), 3.48 (d, 1H, J = 13.6 Hz), 3.41 (d, 1H, J = 13.5 Hz), 3.29 (d, 1H, J = 3.6 Hz), 2.76 (d, 1H, J = 3.6 Hz), 2.22 (br s, 1H), 2.20 (br s, 1H), 2.09 (dd, 1H, J = 13.4 Hz, J = 7.6 Hz), 2.04−1.80 (m, 4H), 1.62−1.55 (m, 2H), 1.45−1.30 (m, 3H), 1.25 (s, 3H), 1.23−1.10 (m, 2H), 1.10−0.94 (m, 4H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 162.1, 153.4, 135.3, 129.3, 128.2, 126.7, 125.0, 66.0, 53.8, 48.3, 48.1, 47.6, 47.3, 45.3, 38.9, 35.3, 34.7, 33.4, 30.8, 28.2, 28.0, 26.4, 21.4, 19.9. HRMS (CI) calcd for $C_{24}H_{29}NO_3S_2$ $[M]^+$: 443.1589; found: 443.1604.

(1*S*,2*R*,5*S*,6*R*)-3-Hydroxymethyl-4-(3-thienyl)tricyclo-[4.2.1.0^{2,5}]non-3-ene, 5o (Table 5, enty 9). 95% (10.0 mg); Orange liquid. R_f 0.40 (3:7 EtOAc:hexanes); $[\alpha]_D^{24}$ +13.1 (*c* 0.46, $CHCl_3$, 90.3% *ee*, er 19:1 for **5o**/**enant-5o**); HPLC (OJ-H column, 0.4 mL/min, 5% ^{i}PrOH/95% hexanes, 254 nm), t_R (major enantiomer): 26.64 min, t_R (minor enantiomer): 34.85 min; IR(neat): 3371 (br), 3103 (m), 2946 (s), 2868 (s), 1470 (m), 1448 (m), 1296 (s), 1079 (s), 1031 (s), 1003 (s), 910 (s), 853 (s), 779 (s), 733 (s), 648 (s) cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz): δ 7.28−7.21 (dd, 1H, J = 5.0 Hz, J = 3.0 Hz), 7.21−7.17 (m, 1H), 7.15 (dd, 1H, J = 4.9 Hz, J = 1.0 Hz), 4.36 (d, 1H, J = 14.0 Hz), 4.29 (d, 1H, J = 14.0 Hz), 2.64 (s, 1H), 2.55 (d, 1H, J = 3.1 Hz), 2.16 (br s, 1H), 2.10 (br s, 1H), 1.65−1.53 (m, 2H), 1.42 (d, 1H, J = 10.2 Hz), 1.32 (br s, 1H), 1.17−1.07 (m, 2H), 1.00 (d, 1H, J = 10.3 Hz); ^{13}C NMR (APT, $CDCl_3$, 75 MHz): δ 138.2, 136.3, 135.7, 126.4, 125.7, 121.9, 59.0, 47.0, 46.9, 34.4, 34.2, 30.7, 28.4, 28.2. HRMS (CI) calcd. for $C_{14}H_{16}OS$ $[M + H]^+$: 233.1000; found: 233.1009.

3-((1*S*,5*R*,7*R*)-10,10-Dimethyl-3,3-dioxo-3-thia-4-azatricyclo-[5.2.1.0^{1,5}]decane-4-carbonyl)-(1*S*,2*R*,5*S*,6*R*)-4-(2-pyridinyl)-tricyclo[4.2.1.0^{2,5}]non-3-ene, 3/4r (Table 5, entry 10). 67% (44.3 mg); Brown solid, mp: 190−191 °C dec R_f 0.37 (4:6 EtOAc:hexanes); IR (KBr): 3002 (m), 2955 (s), 1656 (s), 1459 (s), 1336 (s), 1292 (s), 1269 (s), 1223 (s) cm^{-1}; dr 5:1 for **3r**/**4r**; ^1H NMR ($CDCl_3$, 400 MHz): δ 8.58 (d, 1H, J = 4.2 Hz), 8.05 (d, 1H, J = 7.9 Hz), 7.60 (dt, 1H, J = 7.7 Hz, J = 1.8 Hz), 7.17−7.11 (m, 1H), 4.07−4.00 (m, 1H), 3.46 (d, 1H, J = 13.7 Hz), 3.39 (d, 1H, J = 13.7 Hz), 3.22 (d, 1H, J = 3.4 Hz), 2.95 (d, 1H, J = 3.4 Hz), 2.38 (br s, 1H), 2.16 (br s, 1H), 2.06 (d, 2H, J = 6.3 Hz), 1.95−1.78 (m, 3H), 1.62−1.52 (m, 2H), 1.47 (d, 1H, J = 10.5 Hz), 1.43−1.27 (m, 2H), 1.22 (s, 3H), 1.22−1.16 (m, 2H), 1.01 (d, 1H, J = 10.5 Hz), 0.96 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 163.0, 155.0, 150.9, 149.4, 135.9, 133.5, 124.1, 123.5, 65.5, 53.5, 48.5, 48.3, 47.7, 47.2, 45.1, 38.6, 35.3, 34.4, 33.2, 30.8, 28.08, 28.06, 26.4, 21.2, 19.9. HRMS (CI) calcd for $C_{25}H_{30}N_2O_3S$ $[M + H]^+$: 439.2055; found: 439.2052.

(1*S*,2*R*,3*S*,4*R*,5*S*,6*R*)-3-Hydroxymethyl-4-(2-pyridinyl)tricyclo[4.2.1.0^{2,5}]nonane, 13 (Table 5 entry 10, Scheme 6). 25 % (2.0 mg); Clear oil. R_f 0.30 (4:6 EtOAc:hexanes); $[\alpha]_D^{26}$ +60.5 (*c* 0.15, $CHCl_3$, 68% *ee*, er 5:1 for **13**/**enant-13**); HPLC (OJ-H column, 0.4 mL/min, 5% ^{i}PrOH/95% hexanes, 254 nm), t_R (major enantiomer): 15.53 min, t_R (minor enantiomer): 22.91 min; IR (CH_2Cl_2): 3296 (br), 2948 (s), 2869 (m), 1594 (s), 1476 (m), 1430 (m), 1566 (m), 1034 (s), 1002 (m), 789 (m), 757 (m) cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz): δ 8.42−8.35 (m, 1H), 7.61 (td, 1H, J = 7.7 Hz, J = 1.9 Hz), 7.11−7.02 (m, 2H), 6.49 (br s, 1H), 4.25−4.10 (m, 2H), 3.44 (dd, 1H, J = 11.7 Hz, J = 4.9 Hz), 3.32−3.16 (m, 1H), 2.78−2.67 (m, 1H), 2.38−2.28 (m, 1H), 2.22−2.17 (m, 1H), 2.08 (d, 1H, J = 3.2 Hz), 1.51−1.35 (m, 2H), 1.35−1.27 (m, 1H), 1.11−1.00 (m, 2H), 1.00−1.91 (m, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 161.8, 147.6, 136.1, 123.0, 120.5, 58.6, 43.8, 43.0, 41.09, 41.06, 36.1, 35.9, 34.7, 29.3, 27.9. HRMS (ESI) calcd for $C_{15}H_{19}NO$ $[M + H]^+$: 230.1545; found: 230.1530.

3-((1*S*,5*R*,7*R*)-10,10-Dimethyl-3,3-dioxo-3-thia-4-azatricyclo-[5.2.1.0^{1,5}]decane-4-carbonyl)-(1*S*,2*R*,5*S*,6*R*)-4-pentyltricyclo-[4.2.1.0^{2,5}]non-3-ene, 3/4s (Table 5, entry 11). 92% (43.0 mg); White solid. mp: 106−107 °C. R_f 0.50 (2:8 EtOAc:hexanes); IR (CH_2Cl_2): 2952 (s), 2931 (s), 2866 (s), 1648 (s), 1337 (s) cm^{-1}; dr 10:1 for **3s**/**4s**; ^1H NMR ($CDCl_3$, 400 MHz) major isomer: δ 4.00 (dd, 1H, J = 7.4 Hz, J = 5.0 Hz), 3.45 (d, 1H, J = 13.6 Hz), 3.39 (d, 1H, J = 13.6 Hz), 3.03 (br s, 1H), 2.55−2.46 (m, 1H), 2.42 (d, 1H, J = 3.1 Hz), 2.38−2.31 (m, 1H), 2.17 (br s, 1H), 2.10−1.98 (m, 3H), 1.96−1.80 (m, 3H), 1.56−1.50 (m, 2H), 1.50−1.24 (m, 9H), 1.22 (s, 3H), 1.15−1.00 (m, 2H), 0.99−0.93 (m, 4H), 0.87 (t, 3H, J = 6.9 Hz); visible peaks for minor isomer: δ 3.96−3.80 (1H, m), δ 2.73 (br s, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 168.2, 162.2, 131.2, 65.7, 53.7, 48.5, 48.1, 48.0, 47.6, 45.1, 38.8, 34.6, 34.3, 33.2, 32.0, 30.7, 29.5, 28.1, 27.9, 26.4, 26.3, 22.4, 21.2, 19.9, 14.0. HRMS (CI) calcd for $C_{25}H_{37}NO_3S$ $[M + H]^+$: 432.2572; found: 432.2578.

3-((1*S*,5*R*,7*R*)-10,10-Dimethyl-3,3-dioxo-3-thia-4-azatricyclo-[5.2.1.0^{1,5}]decane-4-carbonyl)-(1*S*,2*R*,5*S*,6*R*)-4-cyclohexyl-tricyclo[4.2.1.0^{2,5}]non-3-ene, 3/4t (Table 5, entry 12). 99% (67.5 mg); Light brown oil. R_f 0.49 (2:8 EtOAc:hexanes); IR (CH_2Cl_2): 2927 (s), 2870 (s), 2852 (m), 1651 (s), 1617 (m), 1449 (m), 1335 (s), 1132 (s), 1282 (s), 1271 (s), 1236 (s), 1219 (s), 1193 (s), 1129 (s), 1113 (s), 993 (m), 769 (m), 734 (s) cm^{-1}; dr 4:1 for **3t**/**4t**; ^1H NMR ($CDCl_3$, 600 MHz) major isomer: δ 3.97 (dd, 1H, J = 7.4 Hz, J = 4.8 Hz), 3.44 (d, 1H, J = 13.6 Hz), 3.37 (d, 1H, J = 13.6 Hz), 2.98 (d, 1H, J = 3.4 Hz), 2.82−2.70 (m, 1H), 2.42 (d, 1H, J = 3.4 Hz), 2.10 (br s, 1H), 2.08 (br s, 1H), 2.03 (dd, 1H, J = 13.8 Hz, 7.8 Hz), 2.00−1.95 (m, 1H), 1.93−1.79 (m, 5H), 1.77−1.58 (m, 5H), 1.53−1.45 (m, 2H), 1.43−1.27 (m, 3H), 1.27−1.14 (m, 3H), 1.19 (s, 3H), 1.09−0.97 (m, 2H), 0.95 (s, 3H), 0.94−0.91 (m, 1H); visible peaks for minor isomer:δ 1.12 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) major isomer: δ 171.2, 162.1, 129.7, 65.5, 53.7, 48.1, 47.7, 47.6, 47.3, 45.1, 39.2, 38.8, 35.1, 34.4, 33.2, 30.6, 30.5, 30.1, 28.1, 27.9, 26.4, 26.0, 25.9, 25.8, 21.2, 19.9; visible peaks for minor isomer: δ 67.2, 53.8, 44.2, 38.85, 32.7, 26.6, 20.4. HRMS (CI) calcd. for $C_{26}H_{37}NO_3S$ $[M + H]^+$: 444.2572; found: 444.2558.

3-((1*S*,5*R*,7*R*)-10,10-Dimethyl-3,3-dioxo-3-thia-4-azatricyclo-[5.2.1.0^{1,5}]decane-4-carbonyl)-(1*S*,2*R*,5*S*,6*R*)-4-bromotricyclo-[4.2.1.0^{2,5}]non-3-ene, 3/4u (Table 5, entry 13). 41% (20.5 mg); Light brown wax. R_f 0.50 (3:7 EtOAc:hexanes); IR (CH_2Cl_2): 2958 (s), 2876 (m), 1679 (s), 1663 (s), 1335 (s), 1287 (s), 1172 (s) cm^{-1}; dr 2.4:1 for **3u**/**4u**; ^1H NMR ($CDCl_3$, 400 MHz) major isomer: δ 4.02 (dd, 1H, J = 7.5 Hz, J = 5.0 Hz), 3.59 (d, 1H, J = 13.5 Hz), 3.43 (d, 1H, J = 13.7 Hz), 3.30 (d, 1H, J = 3.4 Hz), 2.76 (d, 1H, J = 3.5 Hz), 2.28 (br s, 1H), 2.17 (br s, 1H), 2.13−2.00 (m, 2H), 2.00−1.82 (m, 3H), 1.65−1.52 (m, 2H), 1.48−1.30 (m, 3H), 1.21 (s, 3H), 1.19−1.10 (m, 3H), 0.99 (s, 3H); visible peaks for minor isomer: δ 3.95 (dd, J = 7.5 Hz, J = 5.0 Hz, 1H), 3.02 (d, 1H, J = 3.4 Hz), 2.81 (d, 1H, J = 3.3 Hz), 1.24 (s, 3H), 0.97 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) major isomer: δ 159.8, 137.6, 131.9, 65.6, 55.0, 53.8, 51.5, 48.4, 47.7, 45.1, 38.7, 34.8, 34.1, 33.3, 30.4, 27.4, 27.0, 26.4, 21.5, 19.9; visible peaks for minor isomer: 161.7, 139.5, 64.8, 55.5, 53.3, 52.1, 48.6, 47.8, 44.9, 38.4, 35.2, 34.4, 33.0, 30.5, 27.3, 27.2, 26.5, 21.0. HRMS (EI) calcd for $C_{20}H_{26}BrNO_3S$ $[M]^+$: 439.0817; found: 439.0811.

3-((1*S*,5*R*,7*R*)-10,10-Dimethyl-3,3-dioxo-3-thia-4-azatricyclo-[5.2.1.0^{1,5}]decane-4-carbonyl)-(1*S*,2*R*,5*S*,6*R*)-4-hydroxymethyl-tricyclo[4.2.1.0^{2,5}]non-3-ene, 3/4v (Table 5, entry 14). 32% (15.7 mg); White solid. mp: 175−176 °C. R_f 0.38 (1:1 EtOAc:hexanes); IR (KBr): 3432 (br), 2959 (s), 2870 (m), 1627 (m), 1614 (s), 1334 (s), 1134 (s), 1036 (m), 539 (s) cm^{-1}; dr 49:1 for **3v**/**4v**; ^1H NMR ($CDCl_3$, 600 MHz): δ 4.48 (t, 1H, J = 5.5 Hz), 4.28 (d, 2H, J = 4.2 Hz), 4.00 (dd, 1H, J = 7.5 Hz, J = 5.0 Hz), 3.48 (d, 1H, J = 13.6 Hz), 3.42 (d, 1H, J = 13.6 Hz), 2.43 (d, 1H, J = 2.7 Hz), 2.21 (br s, 1H), 2.06 (br s, 1H), 2.05 (dd, 1H, J = 13.9 Hz, J = 6.2 Hz), 2.02−1.81 (m, 5H), 1.59−1.48 (m, 2H), 1.41−1.29 (m, 3H), 1.20 (s, 3H), 1.07−0.94 (m, 3H), 0.97 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 167.3, 163.2, 131.6, 65.9, 60.9, 53.8, 48.4, 48.3, 47.7, 47.5, 45.1, 38.8, 34.5, 34.2, 33.3, 30.6, 27.9, 27.8, 26.3, 21.3, 19.9. (Note: both the ^1H and ^{13}C NMR spectra of **3**/**4v** contain residual camphorsultam that could not be separated by column chromatography). HRMS (ESI) calcd for $C_{21}H_{29}NO_4S$ $[M + Na]^+$: 414.1715; found: 414.1703.

(1*S*,2*R*,5*S*,6*R*)-3-Hydroxymethyl-4-(*p*-phenoxymethyl)tricyclo[4.2.1.0^{2,5}]non-3-ene, 5r (Scheme 5). 52% (21.3 mg); Yellow oil. R_f 0.30 (4:6 EtOAc:hexanes); $[\alpha]_D^{26}$ +12.3 (*c* 0.65, $CHCl_3$, 96.0% *ee*, er 49:1 for **5r**/**enant-5r**); HPLC (OD-H column, 1.0 mL/min, 1% ^{i}PrOH/99% hexanes, 210 nm), t_R (major enantiomer): 43.22 min, t_R

dx.doi.org/10.1021/jo501594g | J. Org. Chem. 2014, 79, 10002−10012

(minor enantiomer): 45.69 min; IR(CH_2Cl_2): 3416 (br), 2947 (s), 2868 (s), 2834 (m), 1507 (s), 1229 (s), 1181 (m), 1039 (s), 825 (s), 732 (m) cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz): δ 6.87−6.77 (m, 4H), 4.47 (d, 1H, J = 14.0 Hz), 4.43 (d, 1H, J = 14.0 Hz), 4.18−4.03 (m, 2H), 3.74 (s, 3H), 2.61 (br s, 1H), 2.39 (s, 2H), 1.99 (br s, 2H), 1.60−1.48 (m, 2H), 1.43 (d, 1H, J = 10.2 Hz), 1.10−0.99 (m, 2H), 0.97 (d, 1H, J = 10.2 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 154.1, 152.2, 143.1, 136.7, 115.5, 114.6, 64.8, 59.1, 55.6, 46.9, 46.6, 38.8, 33.7, 30.5, 28.1 (2C). HRMS (ESI) calcd for $C_{18}H_{22}O_3$ $[M + H]^+$: 287.1647; found: 287.1653.

■ ASSOCIATED CONTENT

Supporting Information

^1H and ^{13}C NMR spectra and HPLC chromatograms of novel cycloadducts. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

■ ACKNOWLEDGMENTS

This work was supported by the Natural Sciences and Engineering Research Council of Canada (NSERC).

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