(Alkylthio)alkynes as Addends in the Co(0) Catalyzed Intramolecular Pauson–Khand Reaction. Substituent Driven Enhancements of Annulation Efficiency and Stereoselectivity

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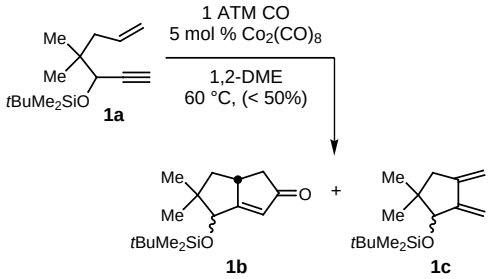
Abstract: Compared to terminal alkynes, (methylthio)alkynes are generally superior substrates for the thermally promoted, $Co_2(CO)_8$ catalyzed Pauson–Khand reaction of enynes and allenynes, providing enones in higher yields and with enhanced diastereoselectivity. Improvements in yield dependent upon the use of 2,2,2-trifluoroethanol as co-solvent and an apparent preference for *endo* selectivity with (ethoxy)alkynes are also disclosed.

Key words: annulations, carbonylations, catalysis, diastereoselectivity, sulfides

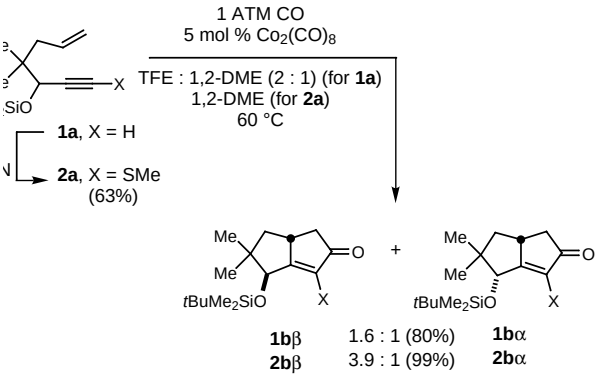
The Pauson–Khand Reaction (PKR) has come to be regarded as one of the most convergent and useful methods for effecting cyclopentenone annulations.[5] In 1996, we disclosed that high-intensity visible light can promote Co(0) catalyzed Pauson–Khand reactions at 50–55 °C and 1 atmosphere of CO pressure.[6] Our observations that temperatures of at least 50 °C are necessary for the photopromoted PKR suggested that the thermal dependency of the cobalt catalyzed process had been poorly appreciated. Upon close examination it was ascertained that a particularly narrow thermal window exists for the realization of the corresponding non-photo assisted process, but that these annulations can be readily executed using 5–10 mol% of high purity $Co_2(CO)_8$ at 60 °C under one atmosphere of CO.[7a] Although similar catalytic transformations have been recently achieved using titanium,[8] ruthenium[9] and rhodium[10] derived catalysts, the Co(0) catalyzed process would appear preferable in terms of its generality, experimental simplicity and independence from chemically labile catalysts.[7b]

Close examination of the results obtained from the assorted metal mediated intramolecular PKR variants reveals considerable disparity in substrate tolerance and cyclization efficiency. In addition, it has previously been recognized that electronic and conformational modification of the enyne substrate could lead to notable alterations in the annulative efficiency and stereoselectivity of the classical, stoichiometric PKR.[5b] For example, in pioneering investigations on the PKR, Magnus showed that annulation of (trimethylsilyl)alkynes displayed improved diastereoselectivity over their terminal alkyne counterparts.[11] Additionally, we have previously reported that (methylthio)alkynes are excellent substrates in $(Cp)_2Zr(II)$ mediated coupling reactions.[12] Curiously, enynes bearing (alkylthio)alkyne substitution had not been previously examined as substrates in $Co_2(CO)_8$ promoted [2+2+1] cycloadditions.[13,14] In this contribution we show that substrate modification of terminal alkynes via sulfenylation can lead to noteworthy enhancements of both reaction efficiency and stereoselectivity of the intramolecular Co(0) catalyzed PKR.

We began our investigation with enyne **1a**, a substrate that we had previously found to undergo the thermal Co(0)-catalyzed PKR [5 mol% $Co_2(CO)_8$, CO (1 atmosphere), 1,2-DME, 60 °C] with only poor efficiency, affording the expected enones **1b** (<50%) along with the diene **1c**[15] (Scheme 1). Interestingly, an analogous cyclization of **1a** in the mixed solvent system CF_3CH_2OH (TFE)/1,2-DME (2:1) furnished the desired enones **1bβ** and **1bα** (**1bβ**/**1bα** = 1.6) in 80% yield to the exclusion of **1c**.[16] By way of contrast, the carbonylative cyclization of the (methylthio)enyne **2a**[17] in 1,2-DME alone (vide supra) gave enones **2bβ** and **2bα** with improved diastereoselectivity (**2bβ**/**2bα** = 3.9) in 99% isolated yield (Scheme 2).

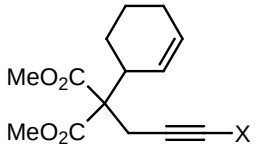
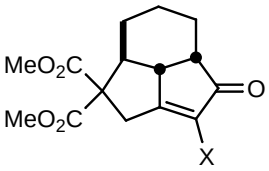
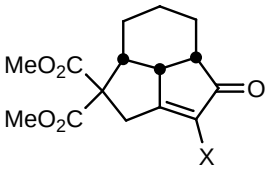
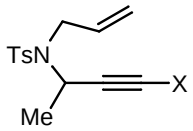
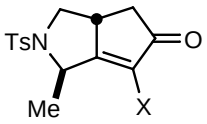
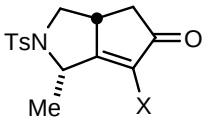
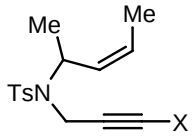
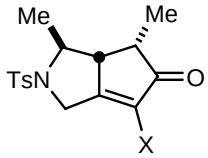
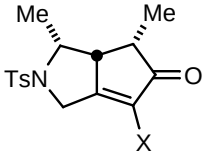


Scheme 1



Scheme 2

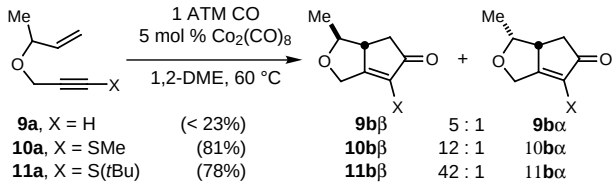
Table 1 Thermal Pauson-Khand Reaction of Stereogenic (Methylthio)-enynes with Catalytic $Co_2(CO)_8$

Entry	Substrate	Products		Yield (%)	
					
1	**3a**, X = H	**3bβ**	1 : 6.0	**3bα**	39[a]
2	**4a**, X = SMe	**4bβ**	1 : 12.3	**4bα**	75[a]
					
3	**5a**, X = H	**5bβ**	1.5 : 1	**5bα**	92[b]
4	**6a**, X = SMe	**6bβ**	2.7 : 1	**6bα**	93[b]
					
5	**7a**, X = H	**7bβ**	11.9 : 1	**7bα**	79[a]
6	**8a**, X = SMe	**8bβ**	13.0 : 1	**8bα**	80[a]

[a] 10 mol% $Co_2(CO)_8$.
[b] 5 mol% $Co_2(CO)_8$.

Some comparative Co(0) catalyzed cyclizations involving representative enynes and their terminal (methylthio)alkynyl counterparts are illustrated in the Table. As is evident from these results, the incorporation of a (methylthio)alkynyl ether as a modifying cycloaddition component usually, but not always, leads to an enhancement of cyclization efficiency and/or diastereoselectivity. Note in entries 5 and 6 that the stereochemistry of the *cis*-olefin is transferred to the product without isomerization. The ability of the Co(0) catalyzed PKR to cleanly translate alkene geometry into product stereochemistry contrasts sharply with the behavior of Ti(II) based catalyst systems.[8] Furthermore, no products were detected that may have resulted from isomerization prior to cyclization of precycles **7a** or **8a** to the corresponding terminal olefin.

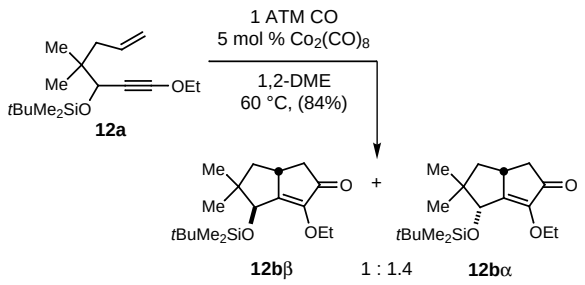
We next turned our attention to the effects caused by steric modification of the thioalkyl substituent. To this end, enyne **9a** was subjected to the usual cyclization protocol [5 mol% $Co_2(CO)_8$, CO (1 atmosphere), 1,2-DME, 60 °C] to provide enones **9bβ** and **9bα** with moderate diastereoselectivity (**9bβ**/**9bα** = 5) albeit in poor (<23%) overall yield. For the (methylthio)alkyne bearing substrate **10a**, a noteworthy improvement in both diastereoselectivity (**10bβ**/**10bα** = 12) and yield (81%) was observed. Importantly, for the corresponding (*t*-butylthio)alkyne **11a**[17] the expected enones **11bβ** and **11bα** were produced with outstanding stereoselectivity (**11bβ**/**11bα** = 42) and good (78%) yield. These results, summarized in Scheme 3, clearly indicate that the stereoselectivity of cyclization can be correlated with the size of the alkylthio substituent and point to further synthetic advantages intrinsic to this type of substrate modification.



Scheme 3

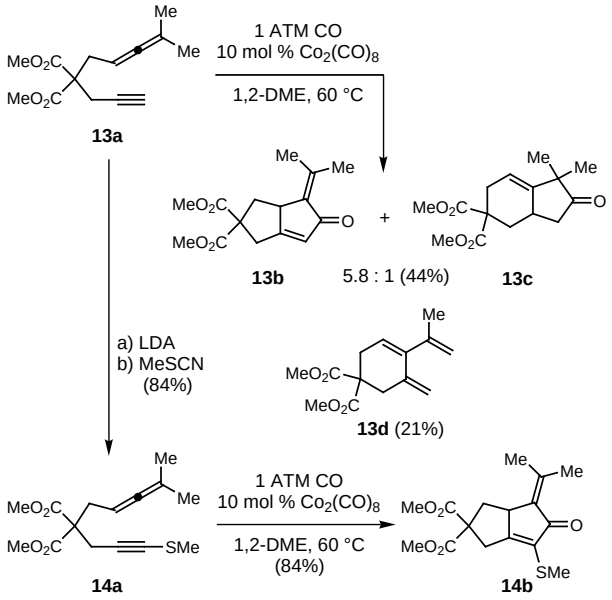
It is widely accepted that thioethers can serve as very effective ligands for transition metals.[18] In a control experiment, the ethoxyalkyne **12a** was subjected to the Co(0) catalyzed PKR (Scheme 4). Although the cyclization efficiency remained gratifyingly high (84% yield) compared to the terminal acetylene (<50%, Scheme 1), in this case the normal stereoselectivity was reversed, and anomalous preferential formation of the *endo*-product was observed (**12bβ**/**12bα** = 0.71).

Allenynes have recently emerged as viable substrates for stoichiometric Pauson–Khand[19a] and related[19b] cycliza-

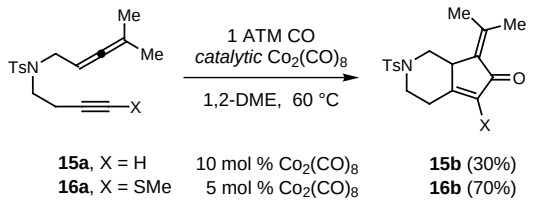


Scheme 4

tions. In an experiment to determine whether allenynes would be satisfactory substrates for the Co(0) catalyzed PKR, **13a** was found to afford the two possible dienones **13b** and **13c** in only 44% combined yield (**13b**/**13c** = 5.8) along with the cross conjugated triene **13d** (21%). In stark contrast, analogous cyclization of **14a** delivered **14b** as the exclusive dienone in 84% isolated yield (Scheme 5). As further illustration of the cyclization efficiency enhancement for allenynes, carbonylative cycloaddition of tosamide **15a** provided dienone **15b** in only 30% yield whereas the cyclization of the corresponding methyl sulfide **16a** secured **16b** in 70% isolated yield.



Scheme 5



Scheme 6

In conclusion, we have shown that the efficiencies and selectivities of the Co(0) catalyzed PKR can be improved, and many times markedly so, by substrate modification via the simple expedient of alkyne sulfenylation. Applications of this strategy to problems of synthetic interest will be described in future accounts from these laboratories.

For general experimental procedures, see reference 20.

Representative Catalytic Pauson−Khand Reaction with $Co_2(CO)_8$
Procedure A

To a solution of dicobalt octacarbonyl (8.5 mg, 0.025 mmol, 5 mol%) in degassed 1,2-DME (5 mL) under a CO atm (balloon) was added the enyne or dienyne (0.50 mmol) via a gas-tight syringe. After 15−30 min, the resulting solution was heated to 60 °C in a constant temperature bath until consumption of starting substrate was observed by TLC. After cooling to r.t., brine and EtOAc were added (1 mL each) and the biphasic mixture was stirred open to the atmosphere for 30 min. Workup with EtOAc/brine (50:25 mL) and drying (Na_2SO_4) followed by evaporation of solvent and subsequent purification by flash chromatography afforded the product. In some instances, further purification was required and was accomplished by passing a CH_2Cl_2 solution of substrate through a plug of neutral Al_2O_3.

Representative Catalytic Pauson−Khand Reaction with alkyne-$Co_2(CO)_6$
Procedure B

To a solution of 2-methyl-3-butyn-2-ol hexacarbonyldicobalt (9.2 mg, 0.025 mmol, 5 mol%) in degassed 1,2-DME (5 mL) under a CO atm (balloon) was sequentially added Et_3SiH (50 μL of a 0.5 M solution in *p*-xylene, 0.025 mmol) and cyclohexylamine (9 μL, 0.075 mmol). The resulting solution was heated at 65 °C for 15 min at which time the enyne or dienyne (0.50 mmol) was added via a gas-tight syringe. The resulting solution was maintained at 65 °C for 6 h, subsequently cooled to r.t. and processed as described in Procedure A.

4,4-Dimethyl-5-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-7-methylthiohept-1-en-6-yne (2a)

To a solution of alkyne **1a** (315 mg, 1.2 mmol) in THF (3 mL) was added a −20 °C, a solution of LDA•THF (2.04 mL, 0.67 M solution in methylcyclohexane, 1.1 equiv). After stirring for 30 min, CH_3SCN (97 μL, 1.15 equiv) was added neat and the resulting solution was allowed to warm to r.t. and was stirred overnight. The solution was subsequently treated with half-sat. $NaHCO_3$ (10 mL) and the resulting mixture was extracted with Et_2O (3 × 10 mL). The combined organic phases were washed with H_2O (5 mL), brine (5 mL), dried ($MgSO_4$), filtered and concentrated in vacuo. The residue was subjected to flash chromatography on silica gel (hexane) to afford 234 mg (63%) of the title compound as an air-sensitive yellow oil.

IR (thin film): ν = 3075, 2186, 1639, 1091, 837 cm^{-1}.

^1H NMR ($CDCl_3$): δ = 5.86−5.73 (m, 1H), 5.03−4.98 (m, 2H), 4.08 (s, 1H), 2.35 (s, 3H), 2.14−2.00 (m, 2H), 0.88 (s with fine structure, 15H), 0.12 (s, 3H), 0.07 (s, 3H).

^{13}C NMR ($CDCl_3$): δ = 135.2 (CH), 117.1 (CH_2), 93.4 (C), 71.4 (CH), 42.7 (CH_2), 39.4 (C), 25.8 (CH_3), 22.8 (CH_3), 22.7 (CH_3), 19.0 (CH_3), 18.2 (C), −4.2 (CH_3), −5.1 (CH_3).

HRMS: *m/z* calcd for $C_6H_{30}O_2SiS$ (M^+) 326.1736. Found: 326.1733.

***trans*-5,5-Dimethyl-4-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-3-methylthio-4,5,6,6a-tetrahydro-2(1*H*)-pentalenone (2bβ)**
Enyne **2a** (75 mg, 0.25 mmol) was cyclized according to general Procedure A except that 10 mol% $Co_2(CO)_8$ was employed to afford 80 mg (98%) of a 3.9:1 diastereomeric mixture of bicyclopentenones **2bβ** and **2bα** as determined by GC analysis of the crude reaction mixture.

2bβ: R_f = 0.45 (10% EtOAc/hexanes).

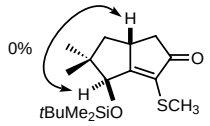
IR (thin film): ν = cm^{-1}.

^1H NMR ($CDCl_3$): δ = 4.19 (s, 1H), 3.11−3.21 (m, 1H), 2.72 (dd, *J* = 17.9, 6.8 Hz, 1H), 2.33 (s, 3H), 2.08−2.01 (m, 2H), 1.10 (s, 3H), 1.06 (dd, *J* = 13.0, 6.6 Hz, 1H), 0.85 (s, 9H), 0.81 (s, 3H), 0.11 (s, 3H), 0.02 (s, 3H).

^{13}C NMR ($CDCl_3$): δ = 207.2 (C), 183.8 (C), 130.6 (C), 76.9 (CH), 45.0 (C), 44.7 (CH_2), 42.9 (CH_2), 39.8 (CH), 28.9 (CH_3), 25.7 (CH_3), 23.8 (CH_3), 18.1 (C), 14.4 (CH_3), −4.5 (CH_3), −4.9 (CH_3).

HRMS: *m/z* for $C_{17}H_{30}O_2SiS$ (M^+) 326.1736. Found: 326.1736.

The assigned stereochemistry is consistent with the following observed NOE data.



***cis*-5,5-Dimethyl-4-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-3-methylthio-4,5,6,6a-tetrahydro-2(1*H*)-pentalenone (2bα)**
R_f = 0.23 (10% EtOAc/hexanes).

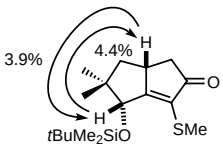
IR (thin film): ν = 1711, 1620, 1249, 1132, 838 cm^{-1}.

^1H NMR ($CDCl_3$): δ = 4.58 (s, 1H), 2.92−2.83 (m, 1H), 2.70 (dd, *J* = 17.1, 7.0 Hz,1 H), 2.32 (s, 3H), 2.08 (dd, *J* = 17.7, 3.5 Hz,1 H), 1.94 (dd, *J* = 13.1, 10.0 Hz, 1H), 1.28 (dd, *J* = 13.1, 8.2 Hz,1 H), 1.14 (s, 3H), 0.95 (s, 9H), 0.85 (s, 3H), 0.19 (s, 3H), 0.10 (s, 3H).

^{13}C NMR ($CDCl_3$): δ = 206.6 (C), 183.8 (C), 130.5 (C), 80.3 (CH), 44.1 (CH_2), 43.6 (CH_2), 36.3 (CH), 29.6 (C), 28.7 (CH_3), 26.1 (CH_3), 24.6 (CH_3), 18.2 (C), 15.0 (CH_3), −4.1 (CH_3), −4.3 (CH_3).

HRMS: *m/z* calcd for $C_{17}H_{30}O_2SSi$ (M^+) 326.1736. Found: 326.1730.

The assigned stereochemistry is consistent with the following observed NOE data.



Dimethyl 2-(2-Propynyl)-2-(2-cyclohexenyl)propan-1,3-dioate (3a)
A solution of dimethyl 2-(2-cyclohexenyl)propan-1,3-dioate (1.06 g, 5.0 mmol) in DMF (10 mL) was added dropwise to a cooled (0 °C) suspension of sodium hydride (300 mg, 7.5 mmol, 1.5 equiv, 60% disp.) in DMF (5 mL) via cannula. The yellow suspension was then stirred at r.t. for 1 h, recooled to 0 °C, and propargyl bromide (565 μL, 7.5 mmol, 1.5 equiv) was added. The mixture was allowed to attain r.t. and stirred overnight. The suspension was poured into H_2O (30 mL), and extracted with EtOAc (3 × 30 mL). The combined organic layers were washed with sat. $NaHCO_3$ (20 mL), brine (3 × 30 mL), dried ($MgSO_4$), filtered and concentrated in vacuo. Bulb to bulb distillation (190 °C/14 mmHg) followed by column chromatography on silica (0−2% EtOAc in hexanes) gave the enyne as a clear colorless oil (0.94 g, 75%).

IR (NaCl, film): ν = 3287, 3056, 2952, 2840, 2122, 1732, 1435 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 5.76 (d with fine structure, *J* = 10.6 Hz, 1H), 5.69 (d with fine structure, *J* = 10.6 Hz, 1H), 3.75 (s, 3 H), 3.71 (s, 3H), 3.14−3.04 (m, 1H), 2.88 (dd, *J* = 2.7, 17.2 Hz, 1H), 2.80 (dd, *J* = 2.7, 17.2 Hz, 1H), 2.00 (t, *J* = 2.7 Hz, 1H), 1.98−1.91 (m, 2H), 1.8−1.73 (m, 2H), 1.64−1.47 (m, 1H), 1.42−1.27 (m, 1H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 170.17 (C), 169.98 (C), 129.1 (CH), 127.2 (CH), 79.4 (C), 71.2 (CH), 60.3 (C), 52.43 (CH_3), 52.24 (CH_3), 38.9 (CH), 24.75 (CH_2), 24.18 (CH_2), 22.39 (CH_2), 22.16 (CH_2).

HRMS: *m/z* calcd for $C_{14}H_{18}O_4$ (M^+) 250.1205. Found: 250.1211.

4a-*syn*-7a-*syn*-4,4-Bis(methoxycarbonyl)-3,4,4a,5,6,7,7a,7b-octahydrocyclopenta[*c,d*]inden-1-one (3bα)
Enyne **3a** (125 mg, 0.50 mmol) was cyclised according to procedure A, affording 54 mg (39%) of a 6.0:1 mixture of enones after 12 h.

IR (thin film): ν = 2963, 2850, 1728, 1699, 1627, 1435, 1398, 1252, 1234 cm^{-1}.

^1H NMR ($CDCl_3$): δ = 5.81 (m, 1H), 3.75 (s, 6H), 3.60 (d with fine structure, *J* = 20.6 Hz, 1H), 3.33 (m, 1H), 3.20 (d, *J* = 20.6 Hz, 1H), 2.94 (m, 1H), 2.60 (dt, *J* = 18.7, 9.4 Hz, 1H), 2.01 (m, 1H), 1.63 (m, 1H), 1.40 (m, 1H), 1.10 (m, 1H), 0.90 (m, 1H), 0.60 (m, 1H).

^{13}C NMR ($CDCl_3$): δ = 213.5 (C), 183.4 (C), 172.3 (C), 169.8 (C), 123.5 (C), 66.2 (C), 53.5 (CH_3), 53.2 (CH_3), 49.8 (CH), 46.6 (CH), 42.3 (CH), 34.5 (CH_2), 25.5 (CH_2), 23.6 (CH_2), 23.2 (CH_2).

HRMS: *m/z* calcd for $C_{15}H_{18}O_5$ (M^+) 278.1154. Found: 278.1158.

4a-*syn*-7a-*syn*-4,4-Bis(methoxycarbonyl)-2-methylthio-3,4,4a,5,6,7,7a,7b-octahydrocyclopenta[*c,d*]inden-1-one (4bα)
Enyne **4a** (148 mg, 0.50 mmol) was cyclized according to procedure A, affording 122 mg (75%) of a 12.3:1 mixture of enones after 12 h.

IR (thin film): ν = 2932, 1762, 1718, 1589, 1478, 1291, 1154 cm^{-1}.

^1H NMR ($CDCl_3$): δ = 3.75 (s, 3H), 3.74 (s, 3H), 3.60 (dd, *J* = 20.9, 2.6 Hz, 1H), 3.29 (br m, 1H), 3.10 (d, *J* = 20.9 Hz, 1H), 2.93 (m, 1H), 2.70 (m, 1H), 2.37 (s, 3H), 2.05 (m, 1H), 1.60 (m, 1H), 1.30 (m, 1H), 1.10 (m, 1H), 0.90 (m, 1H), 0.60 (m, 1H).

^{13}C NMR ($CDCl_3$): δ = 209.1 (C), 178.5 (C), 172.2 (C), 169.7 (C), 129.9 (C), 66.0 (C), 53.6 (CH_3), 53.2 (CH_3), 48.3 (CH), 46.1 (CH), 42.3 (CH), 34.5 (CH_2), 25.4 (CH_2), 23.5 (CH_2), 23.2 (CH_2), 14.5 (CH_3).

HRMS: *m/z* calcd for $C_{16}H_{20}O_5S$ (M^+) 324.1031. Found: 324.1029.

1-Methyl-2-[(4-methylbenzene)sulfonyl]-2,3,3a,4-tetrahydro-1*H*-cyclopenta[*c*]pyrrol-5-one (5b)
The title compound was prepared from **5a**[21] as a mixture of diastereomers (2.1:1) in 92% yield using Procedure A (12 h). The title compound was prepared as a mixture of diastereomers (1.9:1) in 77% yield using Procedure B (12 h). Purification by flash chromatography (SiO_2, 15% EtOAc in hexanes to 40% EtOAc gradient for elution) afforded the title compound as a colorless, viscous oil.

IR (thin film): ν = 3409 (m), 2978 (m), 2930 (m), 1716 (br s), 1652 (s), 1343 (br s), 1163 (br s), 1093 (s), 819 (s), 667 (s) cm^{-1}.

1H NMR (300 MHz, $CDCl_3$): δ = 7.68 (d, *J* = 7.7 Hz, 2H), 7.61 (d, *J* = 7.7 Hz, 2H), 7.25 (approx. d, *J* = 7.7 Hz, 4H), 5.88 (s, 1H), 5.76 (s, 1H), 4.46 (q, *J* = 6.7 Hz, 1H), 4.22 (q, *J* = 6.7 Hz, 1H), 3.94 (approx. t, *J* = 10.2 Hz, 1H), 3.87 (approx. t, *J* = 8.4 Hz, 1H), 3.32 (m, 1H), 2.87 (approx. t, *J* = 11.6 Hz, 1H), 2.51 (dd, *J* = 17.9, 6.5 Hz, 1H), 2.42−2.38 (m, 2H), 2.34 (br s, 6H), 1.96 (m, 1H), 1.95 (m, 2H), 1.52 (d, *J* = 6.7 Hz, 3H), 1.48 (d, *J* = 6.7 Hz, 3H).

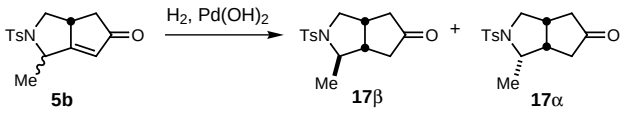
^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 207.4 (2 × C), 185.5 (C), 182.8 (C), 143.94 (C), 143.81 (C), 135.3 (C), 132.7 (C), 129.90 (2 × CH), 129.73 (2 × CH), 127.4 (2 × CH), 126.9 (2 × CH), 125.5 (CH), 124.1 (CH), 55.3 (CH), 55.2 (CH), 53.2 (CH_2), 51.7 (CH_2), 42.9 (CH), 41.1 (CH), 40.0 (CH_2), 39.5 (CH_2), 22.0 (CH_3), 21.3 (2 × CH_3), 20.3 (CH_3).

Major diastereomer: HRMS (EI): *m/z* calcd for $C_{15}H_{17}NO_3S$ (291.0930). Found: 291.0929.

Minor diastereomer: HRMS (EI): *m/z* calcd for $C_{15}H_{17}NO_3S$ (M^+) 291.0933. Found: 291.0929.

ex*o*-1-Methyl-2-[(4-methylbenzene)sulfonyl]hexahydro-1*H*-cyclopenta[*c*]pyrrol-5-one (17β) and *endo*-1-Methyl-2-[(4-methylbenzene)sulfonyl]hexahydro-1*H*-cyclopenta[*c*]pyrrol-5-one (17α)

A solution of *endo*- and *exo*-1-methyl-2-[(4-methylbenzene)sulfonyl]-2,3,3a,4-tetrahydro-1*H*-cyclopenta[*c*]pyrrol-5-one (**5b**) (0.129 g, 0.443 mmol, 1.00 equiv, 1.5:1 mixture of diastereomers) and $Pd(OH)_2$ (13 mg of 20% $Pd(OH)_2$ on C) in EtOAc (1.5 mL) under an atmosphere of H_2 was allowed to stir 2 h. Filtration of the suspension through Celite and concentration afforded 0.126 g of the title compounds. Analysis of the crude residue by ^{1}H NMR revealed a 1.5:1 mixture of diastereomers. Purification by flash chromatography (basic Al_2O_3, 13 × 2 cm, 5% EtOAc in hexanes to 25% EtOAc in hexanes gradient for elution) afforded **17β** and **17α**.



ex*o*-1-Methyl-2-[(4-methylbenzene)sulfonyl]-2,3,3a,4-tetrahydro-1*H*-cyclopenta[*c*]pyrrol-5-one (17β)

Major diastereomer, less polar

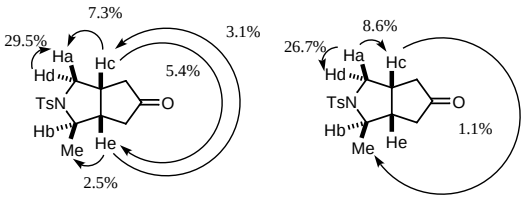
^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.68 (d, *J* = 8.2 Hz, 2H), 7.29 (d, *J* = 8.2 Hz, 2H), 3.76 (dd, *J* = 10.0, 7.2 Hz, 1H), 3.50 (dq, *J* = 6.4, 3.4 Hz, 1H), 3.00 (m, 1H), 2.90 (dd, *J* = 10.0, 7.2 Hz, 1H), 2.47 (m, 1H), 2.41 (s, 3H), 2.28 (approx. d, *J* = 8.5 Hz, 1H), 2.21 (approx. d, *J* = 8.5 Hz, 1H), 1.79 (dd, *J* = 19.1, 3.4 Hz, 1H), 1.40−1.23 (obscured peak, 1H), 1.39 (d, *J* = 6.4 Hz, 3H).

^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 216.5 (C), 143.8 (C), 134.2 (C), 129.8 (2 × CH), 127.3 (2 × CH), 61.3 (CH), 52.9 (CH_2), 47.6 (CH), 41.5 (CH_2), 41.1 (CH_2), 37.6 (CH), 22.3 (CH_3), 21.6 (CH_3).

IR (NaCl, thin film): ν = 2966 (w), 2928 (w), 2851 (w), 1742 (s), 1341 (m), 1091 (s) cm^{-1}.

HRMS (EI): *m/z* calcd for $C_{14}H_{16}NO_3S$ $(M-CH_3)^+$ 278.1086. Found: 278.1084.

The stereochemical assignment was based on the following NOE data determined at 500 MHz ($CDCl_3$).



ex*o*-1-Methyl-2-[(4-methylbenzene)sulfonyl]-2,3,3a,4-tetrahydro-1*H*-cyclopenta[*c*]pyrrol-5-one (17β)

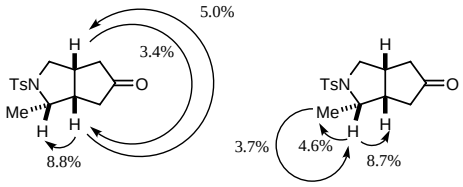
IR (NaCl, thin film): ν = 2929 (w), 1742 (s), 1338 (s), 1161 (s), 1090 (m) cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.70 (d, *J* = 8.1 Hz, 2H), 7.32 (d, *J* = 8.1 Hz, 2H), 3.67 (q, *J* = 6.6 Hz, 1H), 3.58 (dd, *J* = 11.4, 8.7 Hz, 1H), 3.16 (dd, *J* = 11.4, 8.7 Hz, 1H), 2.74 (m, 1H), 2.52 (m, 1H), 2.42 (s, 3H), 2.31−2.23 (m, 2H), 2.14 (dd, *J* = 19.0, 3.4 Hz, 1H), 1.41−1.35 (obscured peak, 1H), 1.34 (d, *J* = 6.6 Hz, 3H).

^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 216.0 (C), 143.7 (C), 134.2 (C), 129.8 (2 × CH), 127.5 (2 × CH), 58.3 (CH_2), 53.6 (CH_2), 45.0 (CH), 42.0 (CH_2), 38.3 (CH_2), 37.5 (CH), 21.5 (CH_3), 18.4 (CH_3).

HRMS (EI): *m/z* calcd for $C_{14}H_{16}NO_3S$ $(M-CH_3)^+$ 293.1086. Found: 293.1084.

The stereochemical assignment was based on the following NOE data determined at 500 MHz ($CDCl_3$).



N-(1-Methyl-3-(methylthio)prop-2-ynyl)-*N*-(2-propenyl)-4-methylbenzenesulfonamide (6a)

To a solution of *N*-(1-methylprop-2-ynyl)-*N*-(2-propenyl)-4-methylbenzenesulfonamide (**5a**) (0.631 g, 2.40 mmol, 1.00 equiv) in THF (6 mL) at −78 °C was added *n*-BuLi (1.6 mL of a 1.6 M solution in hexanes, 2.52 mmol, 1.05 equiv) over 5 min. The resulting solution stirred for 5 min at −78 °C at which time MeSCN (189 μL, 2.76 mmol, 1.15 equiv) was added dropwise. The resulting suspension was stirred for 1 h at −78 °C and then was quenched by the addition of sat. NH_4Cl (3 mL) and allowed to warm to r.t. The reaction mixture was poured into EtOAc and H_2O (30:25 mL). The organic phase was washed with H_2O (25 mL), brine (25 mL), and dried ($MgSO_4$). Evaporation of solvent and purification by flash chromatography (SiO_2, hexanes to 10% EtOAc in hexanes gradient for elution) afforded 1.0 g (85%) of the title compound as a pale yellow semi-solid.

IR (NaCl, thin film): ν = 3081 (w), 2985 (m), 2930 (m), 2870 (w), 2173 (m), 1344 (s), 1167 (s), 1008 (br m), 668 (s), 566 (s) cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.64 (d, *J* = 8.2 Hz, 2H), 7.22 (d, *J* = 8.2 Hz, 2H), 5.84 (m, 1H), 5.41 (approx. dt, *J* = 17.1, 1.4 Hz, 1H), 5.04 (approx. dt, *J* = 10.2, 1.4 Hz, 1H), 4.87 (approx. q, *J* = 7.1 Hz, 1H), 3.84 (m, 1H), 3.62 (m, 1H), 2.33 (s, 3H), 2.05 (s with fine structure, 3H), 1.33 (d with fine structure, *J* = 7.1 Hz, 3H).

^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 143.1 (C), 135.95 (CH), 135.68 (C), 129.2 (2 × CH), 127.4 (2 × CH), 116.7 (CH_2), 89.6 (C), 76.6 (C), 47.17 (CH), 47.14 (CH_2), 22.3 (CH_3), 21.2 (CH_3), 18.5 (CH_3).

HRMS (EI): *m/z* calcd for $C_{15}H_{19}NO_2S_2$ (M^+) 309.0855. Found: 309.0857.

1-Methyl-2-[(4-methylbenzene)sulfonyl]-7-methylthio-2,3,3a,4-tetrahydro-1*H*-cyclopenta[*c*]pyrrol-5-one (6b)

The title compound was prepared as a mixture of diastereomers (2.7:1) in 93% yield using Procedure A (12 h). The title compound was prepared as a mixture of diastereomers (2.6/1) in 90% yield using Procedure B (12 h). Purification by flash chromatography (SiO_2, 15% EtOAc in hexanes to 40% EtOAc gradient for elution) afforded the title compound as a colorless, viscous oil. Further purification by flash chromatography (SiO_2, 5% EtOAc to 25% EtOAc in hexanes gradient for elution) afforded **6bβ**, (major diastereomer, less polar).

IR (NaCl, thin film): ν = 2977 (w), 2927 (w), 1714 (br m), 1343 (br m), 1162 (s) cm^{-1}.

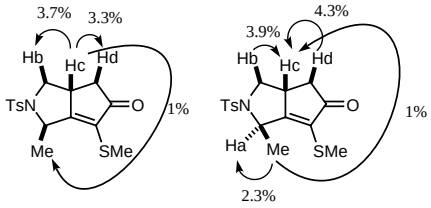
^1H NMR (300 MHz, $CDCl_3$): δ = 7.70 (d, *J* = 8.1 Hz, 2H), 7.32 (d, *J* = 8.1 Hz, 2H), 4.38 (q, *J* = 6.5 Hz, 1H), 3.90 (approx. t, *J* = 8.2 Hz, 1H), 3.28 (m, 1H), 2.65 (dd, *J* = 17.8, 6.5 Hz, 1H), 2.46−2.38 (obscured peak, 1H), 2.42 (s, 3H), 2.30 (s, 3H), 2.04 (dd, *J* = 17.8, 3.4 Hz, 1H), 1.56 (d, *J* = 6.5 Hz, 3H).

^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 203.9 (C), 176.0 (C), 144.1 (C), 133.2 (C), 130.9 (C), 129.9 (2 × CH), 127.7 (2 × CH), 55.5 (CH_2), 53.3 (CH_2), 39.76 (CH), 39.70 (CH), 21.6 (2 × CH_3), 13.8 (CH_3).

HRMS (EI): *m/z* calcd for $C_{16}H_{19}NO_3S_2$ (337.0800). Found: 337.0806.

Minor diastereomer: HRMS (EI): *m/z* calcd for $C_{16}H_{19}NO_3S_2$ (M^+) 337.0803. Found: 337.0806.

The stereochemical assignment of the major diastereomer was based on the following GOESY data (mixing time = 800 msec) determined at 250 MHz ($CDCl_3$).



***N*-2-(But-3-ynyl)-*N*-(2-methyl-2-propyloxycarbonyl)-4-methylbenzenesulfonamide**

Diisopropylazodicarboxylate (11.8 mL, 60 mmol, 1.2 equiv) was added dropwise via addition funnel, over 50 min, to a solution of *N*-*t*-butoxycarbonyl-*p*-toluenesulfonamide (13.57 g, 50 mmol), Ph_3P (15.7 g, 60 mmol, 1.2 equiv) and 2-but-3-ynol (4.70 mL, 60 mmol, 1.2 equiv) in THF (130 mL) at 0 °C under Ar. The mixture was stirred at 0 °C for a further 10 min and then allowed to warm rapidly to ambient temperature. After 30 min at r.t., the mixture was concentrated in vacuo to a brown red oil. The mixture was placed under high vacuum (100 μ) for 4 h. Et_2O (200 mL) was added and the mixture was stirred for 30 min, before addition of hexane (200 mL). The resultant suspension was filtered, the filter cake washed with Et_2O/hexane (1:1, 200 mL), and the filtrate concentrated to a light brown-orange pasty solid. Column chromatography on silica (0−5% EtOAc in hexanes) gave a pale yellow oil. Recrystallisation from Et_2O/hexane afforded the title compound as white prisms (14.76 g, 91%); mp 70.4−73.2 °C.

IR (KBr disc): ν = 3277, 2982, 2940, 2121 (w), 1738, 1733, 1598, 1360, 1152 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 7.85 (d, *J* = 8.2 Hz, 2H), 7.30 (d, *J* = 8.2 Hz, 2H), 5.47 (dq, *J* = 2.5, 7.0 Hz, 1H), 2.43 (s, 3H), 2.37 (d, *J* = 2.5 Hz, 1H), 1.74 (d, *J* = 7.0 Hz, 3H), 1.35 (s, 9H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 149.8 (*C*), 144.1 (*C*), 137.1 (*C*), 129.1 (*C*H), 127.6 (*C*H), 84.7 (*C*), 82.2 (*C*), 71.3 (*C*H), 44.9 (*C*H), 27.7 (CH_3), 21.77 (CH_3), 21.44 (CH_3).

EIMS (CI/NH_3): *m/z* = 341 ($M+NH_4^+$, 5%), 324 ($M+H^+$, 1%), 285 (100%).

HRMS (PCI/NH_3): *m/z* calcd for $C_{16}H_{21}NO_4S$ ($M+H^+$) 324.1270. Found: 324.1258.

***N*-2-(Pent-3-ynyl)-4-methylbenzenesulfonamide**

Butyllithium (8.14 mL, 21.0 mmol, 2.58 M in hexanes, 1.05 equiv) was added to a solution of *N*-2-(but-3-ynyl)-*N*-(2-methyl-2-propyloxycarbonyl)-4-methylbenzenesulfonamide (6.47 g, 20.0 mmol) in THF (40 mL) at −78 °C over 5 min. After 30 min at −78 °C, methyl iodide (1.49 mL, 24 mmol, 1.2 equiv) was added dropwise, followed by HMPA (6.96 mL, 40 mmol, 2 equiv) dropwise. The solution was stirred at -78 °C for 1 h and then allowed to attain r.t. The mixture was poured into H_2O (50 mL), extracted with EtOAc (3 × 50 mL), and the combined organic layers were washed with sat. $CuSO_4$ (30 mL), brine (30 mL), dried ($MgSO_4$), filtered and concentrated to a yellow oil. Column chromatography on silica (0−5% EtOAc in hexanes) gave a pale yellow oil (6.46 g). A portion of this oil (3.10 g, 9.19 mmol) in DMSO (50 mL) was heated to reflux for 20 min. The cooled solution was poured into H_2O (50 mL) and the mixture extracted with EtOAc (3 × 40 mL). The combined organic layers were washed with H_2O (50 mL), sat. $NaHCO_3$ (30 mL), brine (50 mL), dried ($MgSO_4$), filtered and concentrated. The residue was purified by chromatography on silica gel (0−12.5% EtOAc in hexanes) to afford the title compound as an off-white solid. Recrystallisation from CH_2Cl_2/hexane (10:30 mL) gave fine white needles (2.04 g, 90% over 2 steps); mp 128.7−129.8 °C.

^1H NMR (300 MHz, $CDCl_3$): δ = 7.78 (d, *J* = 8.2 Hz, 2H), 7.29 (d, *J* = 8.2 Hz, 2H), 4.70 (d, *J* = 8.5 Hz, 1H), 4.18−4.04 (m, 1H), 2.41 (s, 3H), 1.51 (d, *J* = 2.2 Hz, 3H), 1.35 (d, *J* = 6.9 Hz, 3H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 143.1 (C), 137.4 (C), 129.2 (CH), 127.3 (CH), 79.7 (C), 78.1 (C), 41.4 (CH), 23.3 (CH_3), 21.3 (CH_3), 3.0 (CH_3).

EIGCMS: *m/z* = 237 (M^+, 0.4%), 222 (M^+−Me, 100%).

HRMS: *m/z* calcd for $C_{12}H_{15}NO_2S$ (M^+) 237.0824. Found: 237.0817.

***N*-2-(*cis*-Pent-3-enyl)-4-methylbenzenesulfonamide**

$NaBH_4$ (130 μL, 0.13 mmol, 1M in 95:5 EtOH/2M NaOH, 0.03 equiv) was added dropwise to a degassed solution of $Ni(OAc)_2.4H_2O$ in EtOH (10 mL) to give a black suspension. Ethylene diamine (28 μL, 0.42 mmol, 0.04 equiv) was added followed by a solution of *N*-2-(pent-3-ynyl)-4-methylbenzenesulfonamide (997 mg, 4.20 mmol) in EtOH (40 mL), quantitatively transferred with further EtOH (10 mL). The flask was purged with H_2 and the mixture stirred under an atm of H_2 for 4.5 h. The mixture was filtered through a pad of Celite layered over silica, the filter cake washed with EtOAc, and the filtrate concentrated in vacuo. Column chromatography on silica (0−15% EtOAc in hexanes) and 10% $AgNO_3/SiO_2$ (0−10% EtOAc in hexanes) gave the title compound as a pale yellow solid (718 mg, 76%); mp 55.3−57.1 °C (needles from Et_2O/hexanes, 1:10).

^1H NMR (300 MHz, $CDCl_3$): δ = 7.74 (d, *J* = 8.3 Hz, 2H), 7.27 (d, *J* = 8.3 Hz, 2H), 5.32 (ddq, *J* = 0.9, 10.8, 6.9 Hz, 1H), 5.11 (approx. tq, *J* = 9.1, 1.7 Hz, 1H), 4.55 (br s, 1H), 4.25−4.08 (m, 1H), 2.41 (s, 3H, 1.44 (dd, *J* = 1.7, 6.9 Hz, 3H), 1.16 (d, *J* = 6.6 Hz, 3H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 143.0 (*C*), 138.0 (*C*), 131.5 (*C*H), 129.3 (*C*H), 127.1 (*C*H), 125.3 (*C*H), 46.6 (*C*H), 22.2 (CH_3), 21.4 (CH_3), 12.7 (CH_3);

HRMS: *m/z* calcd for $C_{12}H_{17}NO_2S$ (M^+) 239.0980. Found: 239.0976.

***N*-2-(*cis*-Pent-3-enyl)-*N*-2-propynyl-4-methylbenzenesulfonamide (7a)**

A 25 mL flask was charged with *N*-2-(*cis*-pent-3-enyl)-4-methylbenzenesulfonamide (700 mg, 2.93 mmol), anhyd K_2CO_3 (1.21 g, 8.78 mmol, 3 equiv) and DMF (10 mL). Propargyl bromide (660 μL, 8.78 mmol, 3 equiv) was added to the stirred suspension. After 3.5 h, the mixture was poured into H_2O (40 mL), and extracted with EtOAc (3 × 20 mL). The organic layers were washed with brine (3 × 30 mL), dried ($MgSO_4$), filtered and concentrated to an orange oil. Column chromatography on silicagel (0−5% EtOAc in hexanes) gave the title compound as a pale yellow oil (789 mg, 97%).

IR (KBr disc): ν = 3278, 3022, 2978, 2931, 2876, 2121, 1655, 1598, 1333, 1153 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 7.78 (approx. dt, *J* = 8.2, 1.9 Hz, 2H), 7.26, (d, *J* = 8.2 Hz, 2H), 5.57−5.41 (m, 2H), 4.83 (approx. pentet, *J* = 7.1 Hz, 1H), 4.14 (dd, *J* = 2.5, 18.6 Hz, 1H), 4.07 (dd, *J* = 2.5, 18.6 Hz, 1H), 2.41 (s, 3H), 2.15 (t, *J* = 2.5 Hz, 1H), 1.57 (d with fine structure, *J* = 5.2 Hz, 3H), 1.26 (d, *J* = 6.9 Hz, 3H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 143.0 (C), 137.7 (C), 129.1 (CH), 128.8 (CH), 127.3 (CH), 127.3 (CH), 79.9 (C), 72.4 (CH), 50.2 (CH), 32.5 (CH_2), 21.3 (CH_3), 19.9 (CH_3), 12.8 (CH_3).

MS (EI): *m/z* = 277 (M^+, 2%), 262 (M^+−Me, 94%), 91 (100%).

HRMS: *m/z* calcd for $C_{15}H_{19}NO_2S$ (M^+) 277.1137. Found: 277.1139.

2,3,3a,4-Tetrahydro-2-((4-methylphenyl)sulfonyl)-3-*exo*-,4-*endo*-dimethylcyclopenta[c]pyrrol-5(1*H*)-one (7bβ)

The title compound was prepared from **7a** (139 mg, 0.50 mmol) to afford the enones 121 mg (79%) as a mixture of diastereomers (13.0:1) using Procedure A (12 h) except that 10 mol% $Co_2(CO)_8$ was used. Recrystallisation from Et_2O/hexane gave the major diastereomer as a white solid; mp 97.0−98.2 ºC.

IR (thin film): ν = 2969, 2932, 1709, 1651, 1344, 1163, 1090, 1040, 684, 664 cm^{-1}.

^1H NMR ($CDCl_3$): δ =7.67 (d, *J* = 8.2 Hz, 2H), 7.67 (d, *J* = 8.2 Hz, 2H), 5.76 (br s, 1H), 4.37 (d, *J* = 16.9 Hz, 1H), 4.19 (d, *J* = 16.9 Hz, 1H), 3.16 (m, 1H), 3.02 (m, 1H), 2.57 (m, 1H), 2.41 (s, 3H), 1.58 (d, *J* = 5.9 Hz, 3H), 0.88 (d, *J* = 7.7 Hz, 3H).

^{13}C NMR ($CDCl_3$): δ = 211.0 (C), 175.4 (C), 144.0 (C), 133.6 (C), 129.8 (2 × CH), 127.3 (2 × CH), 122.8 (CH), 56.8 (CH), 55.5 (CH), 49.8 (CH_2), 42.5 (CH), 21.5 (CH_3), 21.4 (CH_3), 12.8 (CH_3).

HRMS: *m/z* calcd for $C_{16}H_{19}NO_3S$ (M^+) 305.1079. Found: 305.1086

***N*-2-(*cis*-Pent-3-enyl)-N-(3-methylthioprop-2-ynyl)-4-methylbenzenesulfonamide (8a)**

BuLi (312 μL, 0.81 mmol, 2.58 M in hexanes, 1.15 equiv) was added to a solution of *N*-2-(*cis*-pent-3-enyl)-*N*-2-propynyl-4-methylbenzenesulfonamide (194 mg, 0.70 mmol) in THF (3 mL) at −78 °C. After 45 min at −78 °C, methyl thiocyanate (62 μL, 0.91 mmol, 1.3 equiv) was added dropwise to the orange solution. The color faded instantly to yellow, the turbid solution was stirred at −78 °C for 1 h and then allowed to warm to -20 °C. Sat. NH_4Cl (3 mL) was added and the solution allowed to attain r.t. The aqueous layer was extracted with EtOAc (3 × 15 mL), and the combined organic layers dried ($MgSO_4$), filtered and concentrated to a yellow oil. Column chromatography on silica (0−3.5% EtOAc in hexanes) gave the title compound as a pale yellow oil, which solidified on standing to an off-white solid (190 mg, 84%).

IR (KBr disc): ν = 2980, 2928, 2178, 1652, 1595, 1341, 1161 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 7.77 (d, *J* = 8.3 Hz, 2H), 7.27 (d, *J* = 8.3 Hz, 2H), 5.57−5.40 (m, 2H), 4.84 (approx. pentet, *J* = 7.1 Hz, 1H), 4.25 (d, *J* = 18.9 Hz, 1H), 4.17 (d, *J* = 18.9 Hz, 1H), 2.41 (s, 3H), 2.24 (s, 3H), 1.58 (d, *J* = 5.6 Hz, 3H), 1.23 (d, *J* = 6.9 Hz, 3H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 142.8 (C), 137.8 (C), 129.0 (CH), 128.95 (CH), 127.33 (CH), 127.21 (CH), 88.8 (C), 75.8 (C), 50.0 (CH), 33.8 (CH_2), 21.3 (CH_3), 19.9 (CH_3), 18.4 (CH_3), 12.8 (CH_3).

MS (EI): *m/z* = 323 (M^+, 7%), 293 (100%).

HRMS: *m/z* calcd for $C_{16}H_{21}NO_2S_2$ (M^+) 323.1014. Found: 323.1005.

3-Methyl-4-methyl-2-[(4-methylbenzene)sulfonyl]-6-methylthio-2,3,3a,4-tetrahydro-1*H*-cyclopenta[*c*]pyrrol-5-one (8bβ)

The title compound was prepared from **8a** (81 mg, 0.25 mmol) to afford the enones 70 mg (80%) as a mixture of diastereomers (13.0:1) using Procedure A (12 h) except that 10 mol% $Co_2(CO)_8$ was used.

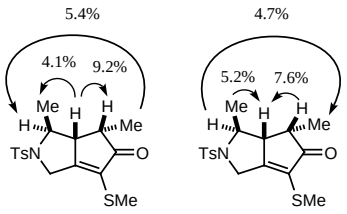
IR (NaCl, thin film): ν = 2968 (m), 2928 (m), 1711 (s), 1643 (m), 1597 (m), 1454 (m), 1346 (s), 1160 (br s), 1090 (s), 1040 (m), 817 (m), 716 (m), 655 (s) cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 7.68 (d, *J* = 8.1 Hz, 2H), 7.30 (d, *J* = 8.1 Hz, 2H), 4.35−4.21 (m, 2H), 3.10 (m, 1H), 2.93 (m, 1H), 2.62 (dq, *J* = 14.6, 7.6 Hz, 1H), 2.39 (s, 3H), 2.24 (s, 3H), 1.53 (d, *J* = 6.0 Hz, 3H), 0.84 (d, *J* = 7.6 Hz, 3H).

^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 207.1 (C), 167.8 (C), 144.0 (C), 133.8 (C), 129.8 (2 × CH), 127.48 (2 × CH), 127.42 (C), 56.7 (CH), 54.1 (CH), 49.7 (CH_2), 42.2 (CH), 21.5 (2 × CH_3), 14.2 (CH_3), 13.0 (CH_3).

HRMS (EI): *m/z* calcd for $C_{17}H_{21}NO_3S_2$ (M^+) 351.0963. Found: 351.0963.

The indicated stereochemistry is consistent with the following NOE data.



3-Methyl-3-(3-methylthio-2-propynloxy)-1-propene (10a)

The title compound was prepared from 220 mg (2.0 mmol) of enyne **9a** as described for the preparation of **16a** to afford 96 mg (31%) of **10a** as a slightly yellow oil; R_f = 0.41 (5% EtOAc/Hexanes).

IR (thin film): ν = 3078, 2180, 1642, 1081 cm^{-1}.

^1H NMR ($CDCl_3$): δ = 5.65 (ddd, *J* = 17.7, 10.2, 7.7 Hz, 1H), 5.23−5.12 (m, 2H), 4.22 (d, 1H), 4.08 (d, *J* = 16.2 Hz, 1H), 4.04−4.16 (m, 1H), 2.35 (s, 3H), 1.23 (d, *J* = 6.3 Hz, 3H).

^{13}C NMR ($CDCl_3$): δ = 139.2 (CH), 117.0 (CH_2), 89.5 (C), 77.7 (C), 75.6 (CH), 56.1 (CH_2), 21.1 (CH_3), 19.0 (CH_3).

HRMS: *m/z* calcd for $C_8H_{13}OS$ ($M+H)^+$) 157.0687. Found: 157.0691.

***trans*-3-Methyl-6-methylthio-3a,4-dihydro-1*H*,3*H*-cyclopenta[*c*]furan-5-one (10bβ)**

Enyne **10a** (65 mg, 0.42 mmol) was cyclized according to general procedure A to afford 63 mg (81%) of a 11.9:1 diastereomeric mixture of bicyclopentenones **10bβ** and **10bα** as determined by GC analysis of the crude reaction mixture.

10bβ: R_f = 0.45 (50% EtOAc/hexanes); white crystals, mp 67−78 °C.

IR (thin film): ν = 1709, 1629, 1442, 1067 cm^{-1}.

^1H NMR ($CDCl_3$): δ = 4.71 (dd, *J* = 16.3, 1.5 Hz, 1H), 4.55 (dt, *J* = 16.3, 1.43 Hz, 1H), 3.49−3.40 (m, 1H), 2.76−2.68 (m, 1H), 2.64 (dd, *J* = 6.4, 17.1 Hz, 1H), 2.36 (s, 3H), 2.11 (dd, *J* = 17.4, 2.9 Hz, 1H), 1.36 (d, *J* = 6.0 Hz, 3H).

^{13}C NMR ($CDCl_3$): δ = 205.1 (C), 176.1 (C), 132.9 (C), 79.9 (CH), 66.6 (CH_2), 51.3 (CH), 38.8 (CH_2), 19.4 (CH_3), 14.6 (CH_3).

HRMS: *m/z* calcd for $C_9H_{12}O_2S$ (M^+) 184.0558. Found: 184.0556.

cis-3-Methyl-6-methylthio-3a,4-dihydro-1*H*,3*H*-cyclopenta[*c*]furan-5-one (10bα)

Waxy tan-colored semi-solid; R_f = 0.32 (50% EtOAc/hexanes).

^1H NMR ($CDCl_3$): δ = 4.59 (s with fine structure, 2H), 4.54−4.43 (m, 1H), 3.42−3.34 (m, 1H), 2.63 (dd, *J* = 18.0, 6.6 Hz), 2.40 (s, 3H), 2.17 (dd, *J* = 16.7, 3.5 Hz, 1H), 0.94 (d, *J* = 6.6 Hz, 3H)

HRMS: *m/z* calcd for $C_9H_{12}O_2S$ (M^+) 184.0558. Found: 184.0553.

3-Methyl-3-(3-[(1,1-dimethylethyl)thio]-2-propynloxy)prop-1-ene (11a)

To a solution of enyne **9a** 146 mg (1.3 mmol) and $[(Me_2)N]_3P(O)$ (271 μL,1.5 mmol,1.2 equiv) in THF (2 mL) cooled to −78 °C was added a solution of *n*-BuLi (0.65 mL, 2.20 M in heptane, 1.4 mmol, 1.1 equiv) dropwise over 2 min. After 5 min, a solution of 4-(*t*-butylthio)tosylate (381 mg, 1.5 mmol, 1.2 equiv) in THF (4 mL) cooled to −78 °C was added via cannula and the resulting solution was allowed to warm to r.t., and was stirred overnight. After 8 h, the solution was treated with half-sat. NH_4Cl (10 mL) and the aqueous phase was separated. The aqueous phase was extracted with Et_2O (3 × 15 mL) and the combined organic fractions were washed with H_2O (3 × 5 mL), brine (20 mL), dried ($MgSO_4$), filtered and concentrated in vacuo. The residue was purified by silica gel chromatography (hexane) and afforded 183 mg (71%) of the title compound as a slightly yellow oil; R_f = 0.31 (5% EtOAc/hexanes).

IR (thin film): ν = 3079, 2175, 1643, 1366, 1083 cm^{-1}.

^1H NMR ($CDCl_3$): δ = 5.65 (ddd, *J* = 17.5, 10.2, 7.6 Hz, 1H), 5.21−5.10 (m, 2H), 4.28 (d, 16.4 Hz, 1H), 4.15 (d, *J* = 16.4 Hz, 1H), 4.10−3.99 (m, 1H), 1.36 (s, 9H), 1.23 (s, 3H), 1.20 (s, 3H).

^{13}C NMR ($CDCl_3$): δ = 139.4 (CH), 117.0 (CH_2), 93.9 (C), 75.7 (C), 75.4 (CH), 56.3 (CH_2), 47.7 (C), 30.3 (CH_3), 21.2 (CH_3).

HRMS: *m/z* calcd for $C_{11}H_{18}OS$ (M^+) 198.1078. Found: 198.1071.

trans-6-*tert*-Butylthio-3-methyl-3a,4-dihydro-1*H*,3*H*-cyclopenta[*c*]furan-5-one (11bβ)

Enyne **11a** (40 mg, 0.20 mmol) was cyclized according to general procedure A except that gradient flash chromatography was performed with 5−10% EtOAc/hexanes to afford 35 mg (78%) of a 41.6:1 diastereomeric mixture of bicyclopentenones **11bβ** and **11bα** as determined by GC analysis of the crude reaction mixture.

11bβ: Colorless needles; mp 70−71 °C.

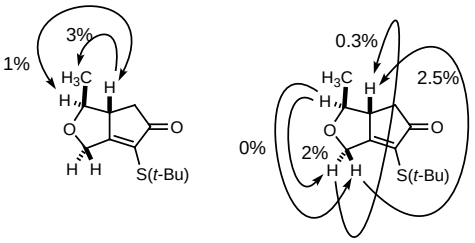
IR (thin film): ν = 1713, 1633, 1365 cm^{-1}.

^1H NMR ($CDCl_3$): δ = 4.76 (dd, *J* = 17.0, 1.0 Hz, 1H), 4.61 (dt, *J* = 17.0, 1.2 Hz, 1H), 3.56−3.47 (m, 1H), 2.89−2.82 (m, 1H), 2.73 (dd, *J* = 17.6, 6.6 Hz, 1H), 2.15 (dd, *J* = 17.1, 3.6 Hz, 1H), 1.40 (d, *J* = 6.0 Hz, 3H), 1.27 (s, 9H).

^{13}C NMR ($CDCl_3$): δ = 206.4 (C), 191.2 (C), 129.4 (C), 79.9 (CH), 67.0 (CH_2), 50.7 (CH), 48.4 (C), 38.4 (CH_2), 31.7 (CH_3), 19.2 (CH_3).

HRMS: *m/z* calcd for $C_{12}H_{18}O_2S$ (M^+) 226.1028. Found: 225.1021.

The structural assignment is consistent with the following NOE data.



cis-6-*tert*-Butylthio-3-methyl-3a,4-dihydro-1*H*,3*H*-cyclopenta[*c*]furan-5-one (11bα)

^1H NMR ($CDCl_3$): δ = 4.67 (s with fine structure, 2H), 4.64 (m, 1H), 3.54−3.95 (m, 1H), 2.71 (dd, *J* = 17.9, 6.7 Hz, 1H), 2.22 (dd, *J* = 17.9, 4.0 Hz, 1H) 1.2 (s, 9H), 0.95 (d, *J* = 6.6 Hz, 3H).

HRMS: *m/z* calcd for $C_{12}H_{18}O_2S$ (M^+) 226.1028. Found: 225.1034.

4,4-Dimethyl-1-ethoxyhept-7-en-1-yn-3-ol

To a solution of ethoxy acetylene (0.84 g of a 50% solution in hexane, 6.0 mmol, 1.2 equiv) in THF (10 mL) cooled to −78 °C was added a solution of *n*-BuLi (2.37 mL, 2.32 M in heptane, 5.5 mmol, 1.1 equiv) dropwise over 5 min and the reaction mixture was stirred for an additional 5 min. Next, 2,2-dimethylpent-4-en-1-al (0.56 g, 5.0 mmol, 1.0 equiv) was added, neat. The dry-ice acetone bath was removed and the reaction mixture was allowed to warm to r.t. while being vigorously stirred. After stirring for 10 min at 26 °C, the reaction mixture was treated with sat. $NaHCO_3$ (5 mL) and diluted with Et_2O (15 mL). The organic layer was separated and the aqueous layer was extracted with Et_2O (2 × 15 mL) and the combined organic fractions were washed with H_2O (5 mL), brine (10 mL) and concentrated in vacuo. The residue was purified by gradient flash chromatography on silica gel (2−10% EtOAc/hexane for elution with approx. 0.1% TEA added) to afford 0.847 g (93%) of the title compound as a colorless oil.

IR (thin film): ν = 3440 (br), 3075, 2263, 1640, 1234, 1007, 912 cm^{-1}.

^1H NMR ($CDCl_3$): δ = 5.89−5.75 (m, 1H), 5.07−4.99 (m, 2H), 4.07 (q, *J* = 7.1 Hz, 2H), 4.06 (s, 1H), 2.15−2.04 (m, 2H), 1.70 (br s, 1H), 1.35 (t, *J* = 7.1 Hz, 3H), 0.91 (s, 3H), 0.90 (s, 3H).

^{13}C NMR ($CDCl_3$): δ = 135.7 (CH), 117.7 (CH_2), 95.0 (C), 74.9 (CH_2), 70.6 (CH), 43.3 (CH_2), 39.3 (C), 38.2 (C), 23.1 (CH_3), 23.0 (CH_3), 14.8 (CH_3).

4,4-Dimethyl-5-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-7-ethoxyhept-1-en-6-yne (12a)

A solution of *t*-$BuMe_2SiCl$ (178 mg, 1.18 mmol, 1.05 equiv) and imidazole (191 mg, 2.80 mmol, 2.5 equiv) in DMF (1 mL) was stirred for 10 min at r.t. and subsequently treated with a solution of 4,4-dimethyl-1-ethoxyhept-7-en-1-yn-3-ol (205 mg, 1.12 mmol) in DMF (0.25 mL). The resulting solution was stirred for 96 h and then diluted with hexane/Et_2O, 6:1 (20 mL) and sat. K_2CO_3 (20 mL). The organic layer was separated and the aqueous layer was washed with hexane/Et_2O, 6:1 (2 × 15 mL). The aqueous layers were combined and washed with H_2O (25 mL portion), brine (25 mL), dried ($MgSO_4$), filtered and concentrated in vacuo. The residual material was purified by flash chromatography on silica gel (hexane) to afford 248 mg (76%) of the title compound as a colorless oil.

IR (thin film): ν = 3076, 2264, 1640, 1250, 1067, 1005, 837 cm^{-1}.

^1H NMR ($CDCl_3$): δ = 5.87−5.73 (m, 1H), 5.02−4.97 (m, 2H), 4.05 (q, *J* = 7.1 Hz, 2H), 4.06 (s, 1H), 2.14−2.01 (m, 2H), 1.35 (t, *J* = 7.1

Hz, 3H), 0.89 (s, 9H), 0.88 (s, 3H), 0.87 (s, 3H), 0.12 (s, 3H), 0.06 (s, 3H).

^{13}C NMR ($CDCl_3$): δ = 136.1 (CH), 117.2 (CH_2), 94.4 (C), 74.5 (CH_2), 70.9 (CH), 43.1 (CH_2), 39.8 (C), 38.8 (C), 26.2 (CH_3), 23.2 (CH_3), 23.1 (CH_3), 18.6 (C), 14.8 (CH_3), −3.7 (CH_3), −4.8 (CH_3).

HRMS (CI/NH_3): *m/z* calcd for $C_{17}H_{33}O_2Si$ $(M+H)^+$ 297.2250. Found: 297.2244.

trans-5,5-Dimethyl-4-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-3-[(ethyl)oxy]-4,5,6,6a-tetrahydro-2(1*H*)-pentalenone (12bβ)

Enyne **12a** (74 mg, 0.25 mmol) was cyclized according to general procedure A to afford 68 mg (84%) of a 0.72:1 diastereomeric mixture of bicyclopentenones **12bβ** and **12bα** as determined by GC analysis of the crude reaction mixture.

12bβ: R_f = 0.22 (5% EtOAc/hexane).

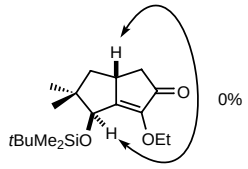
IR (thin film): ν = 1712, 1663, 1472, 1257, 1127, 838 cm^{-1}.

^{1}H NMR ($CDCl_3$): δ = 4.28 (s, 1H), 4.24−4.13 (m, 2H), 3.17−3.10 (m, 1H), 2.65 (dd, *J* = 18.2, 6.4 Hz, 1H), 2.02−1.91 (m, 2H), 1.29 (t, *J* = 7.0 Hz, 3H), 1.08 (s, 3H), 1.03 (dd, *J* = 12.8, 7.6 Hz, 1H), 0.87 (s, 3H), 0.86 (s, 3H), 0.08 (s, 3H), 0.02 (s, 3H).

^{13}C NMR ($CDCl_3$): δ = 205.6 (C), 158.5 (C), 148.0 (C), 76.6 (CH), 66.2 (CH_2), 46.5 (C), 44.2 (CH_2), 43.2 (CH_2), 36.6 (CH), 29.8 (CH_3), 26.2 (CH_3), 24.3 (CH_3), 18.6 (C), 15.9 (CH_3), −4.1 (CH_3), −4.5 (CH_3).

HRMS (CI/NH_3): *m/z* calcd for $C_{18}H_{33}O_3Si$ $(M+1)^+$ 325.2199. Found: 324.2192.

The indicated stereochemistry is consistent with the following NOE data.



cis-5,5-Dimethyl-4-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-3-[(ethyl)oxy]-4,5,6,6a-tetrahydro-2(1*H*)-pentalenone (12bα)

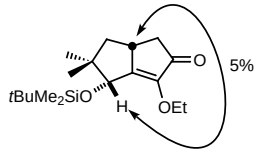
IR (thin film): ν = cm^{-1}.

^{1}H NMR ($CDCl_3$): δ = 4.42 (s, 1H), 4.24−4.13 (m, 2H), 2.76−2.68 (m, 1H), 2.56 (dd, *J* = 17.7, 6.4 Hz, 1H), 1.97 (dd, *J* = 17.7, 2.8 Hz, 1H), 1.84 (dd, *J* = 12.9, 9.2 Hz, 1H), 1.24 (t, *J* = 7.0 Hz, overlapping with CH*H*, 4H), 1.10 (s, 3H), 0.91 (s, 9H), 0.90 (s, 3H), 0.12 (s, 3H), 0.09 (s, 3H).

^{13}C NMR ($CDCl_3$): δ = 205.6 (C), 163.9 (C), 149.0 (C), 79.7 (CH), 66.3 (CH_2), 45.0 (C), 44.7 (CH_2), 42.8 (CH_2), 33.4 (CH), 29.0 (CH_3), 26.3 (CH_3), 25.4 (CH_3), 18.7 (C), 16.0 (CH_3), −4.4 (CH_3).

HRMS (CI/NH_3): *m/z* calcd for $C_{18}H_{33}O_3Si$ (M^+) 324.2199. Found: 324.2195.

The indicated stereochemistry is consistent with the following NOE data.



2-(4-Methyl-2,3-pentadienyl)-2-(2-propynyl)malonic Acid Dimethyl Ester (13a)

To a suspension of NaH [0.187 g (deoiled), 7.80 mmol, 1.10 equiv] in DMF/THF (7:3 mL) at 0 °C was added 2-(4-methylpenta-2,3-dienyl)malonic acid dimethyl ester (1.50 g, 7.07 mmol, 1.00 equiv) dropwise. The reaction mixture was allowed to stir at r.t. for 1 h, then the reaction vessel was cooled to 0 °C and propargyl bromide (0.70 mL, 8.5 mmol, 1.2 equiv) was added dropwise. The resulting suspension was allowed to warm to r.t. and was stirred overnight. The reaction mixture was quenched with the addition of sat. NH_4Cl (5 mL) and then poured into EtOAc/H_2O (50:25 mL). The organic phase was washed with H_2O (20 mL), brine (20 mL), and dried (Na_2SO_4). Evaporation of solvent and purification by flash chromatography (SiO_2, 5% EtOAc in hexanes) afforded 1.65 g (92%) of 2-(4-methylpenta-2,3-dienyl)-2-(2-propynyl)malonic acid dimethyl ester (**13a**) as a slightly yellow oil.

IR (NaCl, thin film): ν = 3292 (br s), 2981 (s), 2954 (s), 2910 (s), 2854 (s), 2123 (m), 1969 (m), 1735 (br s), 1438 (s), 1210 (s br) cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 4.74 (m, 1H), 3.71 (s, 6H), 2.95 (s, 2H), 2.68 (d, *J* = 7.6 Hz, 2H), 2.30 (s, 1H), 1.63 (s, 6H).

^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 203.7 (C), 169.8 (2 × C), 95.2 (C), 82.0 (CH), 78.5 (C), 71.1 (CH), 56.9 (C), 52.5 (2 × CH_3), 32.2 (CH_2), 22.2 (CH_2), 20.2 (2 × CH_3).

HRMS (EI): *m/z* calcd for $C_{14}H_{18}O_4$ (M^+) 250.1205. Found: 250.1203.

1-Isopropylidene-2-oxo-4,5,6,6a-tetrahydro-1*H*-pentalene-5,5-dicarboxylic Acid Dimethyl Ester (13b) and 5,5-Dimethyl-2-oxo-1,2,4,6-tetrahydroindene-5,5-dicarboxylic Acid Dimethyl Ester (13c)

The title compounds were prepared as a mixture of isomers (5.8:1) in 47% yield using Procedure A except that 10 mol% $Co_2(CO)_8$ was used (12 h). Purification by flash chromatography (SiO_2, 15% EtOAc in hexanes to 30% EtOAc in hexanes gradient for elution) afforded 33 mg (47%) of 1-isopropylidene-2-oxo-4,5,6,6a-tetrahydro-1*H*-pentalene-5,5-dicarboxylic acid dimethyl ester (**13b**) and 5,5-dimethyl-2-oxo-1,2,4,6-tetrahydroindene-5,5-dicarboxylic acid dimethyl ester (**13c**) as a slightly yellow oil. Ester **13b** was found identical in all respects to an authentic sample prepared according to a literature procedure.[19c]

1-Isopropylidene-2-oxo-4,5,6,6a-tetrahydro-1*H*-pentalene-5,5-dicarboxylic Acid Dimethyl Ester (13b)

Major isomer; mp 80−81 °C.

IR (NaCl, thin film): ν = 2993 (m), 2955 (m), 2848 (m), 1734 (br s), 1690 (s), 1651 (s), 1632 (s), 1435 (s), 1264 (br s) cm^{-1}.

^{1}H NMR (300 MHz, C_6D_6): δ = 5.88 (br s, 1H), 3.36−3.25 (obscured peak, 1H), 3.33 (s, 3H), 3.29 (s, 3H), 3.11 (m, 1H), 2.98 (m, 1H), 2.90 (dd, *J* = 12.6, 7.8 Hz, 1H), 2.27 (s, 3H), 1.53 (approx. t, *J* = 12.6 Hz, 1H), 1.46 (s, 3H).

^{13}C NMR (75.5 MHz, C_6D_6): δ = 196.2 (C), 174.2 (C), 172.0 (C), 171.0 (C), 145.1 (C), 133.3 (C), 128.7 (CH), 61.2 (C), 52.66 (CH_3), 52.48 (CH_3), 48.9 (CH), 38.0 (CH_2), 34.4 (CH_2), 24.1 (CH_3), 19.5 (CH_3).

HRMS (EI): *m/z* calculated for $C_{15}H_{18}O_5$ (M^+) 278.1156. Found: 278.1154.

5,5-Dimethyl-2-oxo-1,2,4,6-tetrahydroindene-5,5-dicarboxylic Acid Dimethyl Ester (13c)

HRMS (EI): *m/z* calcd for $C_{15}H_{20}O_5$ (M^+) 280.1166. Found: 280.1154.

5-Methylene-4-(propen-2-yl)-cyclohex-3-ene-1,1-dicarboxylic Acid Dimethyl Ester (13d)

The title compound was isolated from a $Co_2(CO)_8$-catalyzed carbonylative cyclization reaction of 2-(4-methylpenta-2,3-dienyl)-2-(2-propynyl)malonic acid dimethyl ester (**13a**) using Procedure A. Purification by flash chromatography (SiO_2, 15% EtOAc in hexanes to 30% EtOAc in hexanes gradient for elution) afforded crude triene **13d**. Further purification by flash chromatography (neutral Al_2O_3, 5% EtOAc in hexanes to 15% EtOAc in hexanes gradient for elution) afforded 13 mg (21%) of the title compound as a colorless oil.

IR (NaCl, thin film): ν = 3091 (w), 2955 (m), 2918 (m), 2849 (m), 1735 (s) 1436 (m) cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 5.59 (dt, *J* = 4.1, 1.0 Hz, 1H), 4.99−4.93 (m, 3H), 4.81 (m, 1H), 3.69 (s, 6H), 2.86 (s, 2H), 2.70 (d, *J* = 4.1 Hz, 2H), 1.82 (d, *J* = 1.0 Hz, 3H).

^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 171.3 (2 × C), 144.1 (C), 141.7 (C), 137.8 (C), 123.0 (CH), 114.5 (CH_2), 114.0 (CH_2), 54.3 (2 × C), 52.7 (CH_3), 37.4 (CH_2), 31.5 (CH_2), 22.9 (CH_3).

HRMS (EI): *m/z* calcd for $C_{14}H_{18}O_4$ (M^+) 250.1205. Found: 250.1202.

2-(4-Methyl-2,3-pentadienyl)-2-(3-methylthio-2-propynyl)malonic Acid Dimethyl Ester (14a)

To a suspension of NaH (98 mg (60% dispersion in oil), 2.44 mol, 1.08 equiv) in DMF/THF (2:1 mL) at 0 °C was added 2-(4-methylpenta-2,3-dienyl) malonic acid dimethyl ester (**13a**) (0.479 g, 2.26 mmol, 1.00 equiv). The resulting mixture was allowed to stir for 30 min at which time 1-chloro-3-thiomethylpropyne (341 mg, 2.83 mmol, 1.25 equiv) was added dropwise. The resulting solution was stirred for 4 h at r.t., and then quenched with the addition of sat. NH_4Cl (1 mL). The suspension was partitioned between Et_2O/H_2O (25:10 mL). The organic phase was washed with H_2O (10 mL) and dried ($MgSO_4$). Evaporation of solvent and purification by flash chromatography (SiO_2, hexanes to 5% EtOAc in hexanes gradient for elution) afforded 400 mg (60%) of 2-(4-methylpenta-2,3-dienyl)-2-(3-methylthio-2-propynyl)malonic acid dimethyl ester (**14a**) as a yellow oil.

IR (NaCl, thin film): ν = 2980 (m), 2952 (s), 2930 (s), 2853 (m), 2194 (w), 1696 (m), 1234 (br s), 1436 (s), 1288 (s), 1208 (br s) cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 4.72 (m, 1H), 3.69 (s, 6H), 2.93 (s, 2H), 2.66 (d, *J* = 7.5 Hz, 2H), 2.28 (s, 3H), 1.62 (s, 3H), 1.61 (s, 3H).

^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 203.9 (C), 170.2 (2 × C), 95.3 (C), 87.4 (C), 82.3 (CH), 73.7 (C), 57.4 (C), 52.6 (2 × CH_3), 32.6 (CH_2), 24.1 (CH_2), 20.4 (2 × CH_3), 19.2 (CH_3).

HRMS (EI): *m/z* calcd for $C_{15}H_{20}O_4S$ (M^+) 296.1076. Found: 296.1082.

1-Isopropylidene-2-oxo-4,5,6,6a-tetrahydro-3-methylthio-1*H*-pentalene-5,5-dicarboxylic Acid Dimethyl Ester (14b)

The title compound was prepared in 84% yield using Procedure A. Purification by flash chromatography (SiO_2, 15% EtOAc in hexanes to 30% EtOAc in hexanes gradient for elution) afforded 69 mg (84%) of 1-isopropylidene-2-oxo-4,5,6,6a-tetrahydro-3-methylthio-1*H*-pentalene-5,5-dicarboxylic acid dimethyl ester (**14b**); mp 90−91 °C.

IR (NaCl, thin film): ν = 2995 (m), 2954 (m), 1733 (s), 1682 (s), 1651 (m), 1622 (m), 1435 (br m), 1260 (br m), 1063 (m) cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 3.80 (s, 3H), 3.73 (s, 3H), 3.51 (dd with fine structure, *J* = 12.5, 7.3 Hz, 1H), 3.33 (d, *J* = 19.4 Hz, 1H), 3.26 (d, *J* = 19.4 Hz, 1H), 2.91 (dd, *J* = 12.5, 7.3 Hz, 1H), 2.42 (s, 3H), 2.27 (s, 3H), 1.91 (s, 3H), 1.67 (approx. t, *J* = 12.5 Hz, 1H).

^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 193.3 (C), 172.0 (C), 171.1 (C), 168.6 (C), 147.7 (C), 135.0 (C), 131.5 (C), 61.1 (C), 53.3 (CH_3), 53.1 (CH_3), 47.9 (CH), 37.7 (CH_2), 34.3 (CH_2), 24.6 (CH_3), 19.9 (CH_3), 14.6 (CH_3).

HRMS (EI): *m/z* calcd for $C_{16}H_{20}O_5S$ (M^+) 324.1026. Found: 324.1031.

***N*-(But-3-ynyl)-*N*-(4-methylpenta-2,3-dienyl)-4-methylbenzenesulfonamide (15a)**

To solution of *N*-(but-3-ynyl)-4-methylbenzenesulfonamide (1.72 g, 6.74 mmol, 1.00 equiv), Ph_3P (2.73 g, 10.4 mmol, 1.35 equiv) and 4-methylpenta-2,3-dien-1-ol (0.985 g, 10.0 mmol, 1.30 equiv) in THF (23 mL) at 0 °C was added diisopropylazodicarboxylate (2.05 mL, 10.4 mmol, 1.35 equiv) over 10 min. The resulting solution was allowed to slowly warm to r.t. and stirred overnight (12 h). Evaporation of solvent and purification by flash chromatography (SiO_2, hexanes to 5% EtOAc in hexanes gradient for elution) afforded 2.05 g (91%) of *N*-(but-3-ynyl)-*N*-(4-methylpenta-2,3-dienyl)-4-methylbenzenesulfonamide (**15a**) as a colorless solid. Recrystallization from EtOAc/hexanes afforded colorless prisms; mp 67−68 °C.

IR (NaCl, thin film): ν = 3292 (br m), 2980 (m), 2912 (m), 2869 (m), 2120 (w), 1968 (w), 1598 (m), 1344 (br s) cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 7.64 (d, *J* = 8.2 Hz, 2H), 7.24 (d, *J* = 8.2 Hz, 2H), 4.70 (m, 1H), 3.73 (d, *J* = 7.1 Hz, 2H), 3.28 (approx. t, *J* = 7.6 Hz, 2H), 2.42 (dt, *J* = 7.6, 2.5 Hz, 2H), 2.36 (s, 3H), 1.93 (t, *J* = 2.5 Hz, 1H), 1.61 (s, 3H), 1.60 (s, 3H).

^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 203.4 (C), 143.2 (C), 136.7 (C), 129.6 (2 × CH), 126.9 (2 × CH), 96.9 (C), 84.1 (CH), 80.7 (C), 70.0 (CH), 48.2 (CH_2), 45.5 (CH_2), 21.3 (CH_3), 20.1 (2 × CH_3), 18.9 (CH_2).

HRMS (EI): *m/z* calcd for $C_{17}H_{21}NO_2S$ (M^+) 303.1292. Found: 303.1293.

2-[(4-Methylbenzene)sulfonyl]-5-isopropylidene-1,2,3,4,4a,5-hexahydro-[2]-pyridin-6-one (15b)

The title compound was prepared in 30% yield using Procedure A except that 10 mol% $Co_2(CO)_8$ was used.

IR (thin film, NaCl): ν = 2922 (m), 2850 (m), 1688 (s), 1645 (m), 1627 (s), 1361 (m), 1340 (m), 1163 (s), 1097 (m), 720 (m) cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 7.62 (d, *J* = 8.2 Hz, 2H), 7.29 (d, *J* = 8.2 Hz, 2H), 5.96 (s, 1H), 4.36 (ddd, *J* = 7.5, 5.6, 1.8 Hz, 1H), 4.10 (m, 1H), 3.36 (dd, *J* = 10.8, 5.6 Hz, 1H), 2.72−2.57 (m, 2H), 2.40 (s, 3H), 2.40−2.27 (m, 2H), 2.25 (s, 3H), 1.96 (s, 3H).

^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 195.4 (C), 168.4 (C), 148.7 (C), 143.9 (C), 134.1 (C), 130.8 (CH), 129.9 (2 × CH), 129.7 (C), 127.3 (2 × CH), 51.7 (CH_2), 46.8 (CH_2), 44.8 (CH), 29.89 (CH_2), 24.2 (CH_3), 21.5 (CH_3), 20.1 (CH_3).

HRMS (EI): *m/z* calcd for $C_{18}H_{21}NO_3S$ (M^+) 331.1798. Found: 331.1804.

***N*-(4-Methylthiobut-3-ynyl)-*N*-(4-methylpenta-2,3-dienyl)-4-methylbenzenesulfonamide (16a)**

To a solution of *N*-(but-3-ynyl)-*N*-(4-methylpenta-2,3-dienyl)-4-methylbenzenesulfonamide (**15a**) (1.57 g, 4.69 mmol, 1.00 equiv) in THF (16 mL) at −78 °C was added *n*-BuLi (3.4 mL of a 1.6 M solution in hexanes, 5.4 mmol, 1.2 equiv) dropwise. After stirring 15 min at −78 °C, MeSCN (0.40 mL, 5.9 mmol, 1.3 equiv) was added dropwise. The solution was stirred 30 min at −78 °C, and then placed in a 0 °C bath for 15 min, at which time H_2O (5 mL) was added. The mixture was partitioned between EtOAc/H_2O (50:50 mL), washed with H_2O (2 × 25 mL), brine (50 mL) and dried (Na_2SO_4). Evaporation of solvent and purification by flash chromatography

(SiO_2, 5 × 2 cm, 5% EtOAc in hexanes) afforded 2.05 g (91%) of the title compound as an orange-yellow oil.

IR (NaCl, thin film): ν = 2979 (w), 2927 (m), 1967 (w), 1598 (w), 1344 (m), 1160 (s) cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 7.64 (d, *J* = 8.2 Hz, 2H), 7.24 (d, *J* = 8.2 Hz, 2H), 4.70 (m, 1H), 3.72 (d, *J* = 7.1 Hz, 2H), 3.26 (approx. t with fine structure, *J* = 7.6 Hz, 2H), 2.52 (approx. t with fine structure, *J* = 7.6 Hz, 2H), 2.36 (s, 3H), 2.25 (s, 3H), 1.60 (s, 3H), 1.59 (s, 3H).

^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 203.4 (C), 143.1 (C), 136.8 (C), 129.6 (2 × CH), 126.9 (2 × CH), 96.9 (C), 89.3 (C), 84.1 (CH), 72.2 (C), 48.2 (CH_2), 45.6 (CH_2), 21.3 (CH_3), 20.5 (CH_2), 20.1 (2 × CH_3), 18.9 (CH_3).

HRMS (EI): *m/z* calcd for $C_{18}H_{23}NO_2S_2$ (M^+) 349.1167. Found: 349.1170.

2-[(4-Methylbenzene)sulfonyl]-5-isopropylidene-7-methylthio-1,2,3,4,4a,5-hexahydro-[2]-pyridin-6-one (16b)

The title compound was prepared in 70% yield using Procedure A.

IR (NaCl, thin film): ν = 2925 (w), 1685 (m), 1643 (m), 1607 (m), 1336 (m), 1165 (s), 1098 (m), 749 (m), 651 (m) cm^{-1}.

^1H NMR (300 MHz, C_6D_6): δ = 7.58 (d, *J* = 8.1 Hz, 2H), 6.78 (d, *J* = 8.1 Hz, 2H), 4.38 (ddd, *J* = 11.2, 5.5, 1.8 Hz, 1H), 3.89 (m, 1H), 2.96 (dd with fine structure, *J* = 11.2, 5.5 Hz, 1H), 2.77 (m, 1H), 2.28 (s, 3H), 2.19 (s, 3H), 2.16 (m, 1H), 1.90 (s, 3H), 1.84 (m, 1H), 1.61 (approx. t, *J* = 11.2 Hz, 1H), 1.48 (s, 3H).

^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 191.9 (C), 165.4 (C), 149.7 (C), 143.8 (C), 135.8 (C), 133.9 (C), 129.8 (2 × CH), 128.2 (C), 127.2 (2 × CH), 51.5 (CH_2), 46.4 (CH_2), 43.9 (CH), 28.3 (CH_2), 24.1 (CH_3), 21.4 (CH_3), 20.2 (CH_3), 15.0 (CH_3).

HRMS (EI): *m/z* calcd for $C_{19}H_{23}NO_3S_2$ (M^+) 377.1123. Found: 377.1119.

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