Bulky Thioureas as New Ligands for Gold(I)-Catalyzed Cyclization of Acetylenic 1,3-Dicarbonyl Compounds

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Abstract: We illustrate the first use of bulky N,N′-disubstituted cyclic thioureas as ligands for gold(I) catalysis. X-ray crystal structures of the thiourea–gold(I) complexes presented important information about the nature of the complexation. These complexes were found to be active catalysts for the cyclization of 1,3-dicarbonyl compounds with alkynes (Conia-ene reaction). Various acetylenic 1,3-dicarbonyl compounds underwent cycloisomerization to give mono- and bicyclic olefinic cyclopentanes in the presence of one mol% of a thiourea–gold(I) chloride complex and silver triflate.

Key words: alkynes, catalysis, cyclizations, 1,3-dicarbonyl compounds, ligands

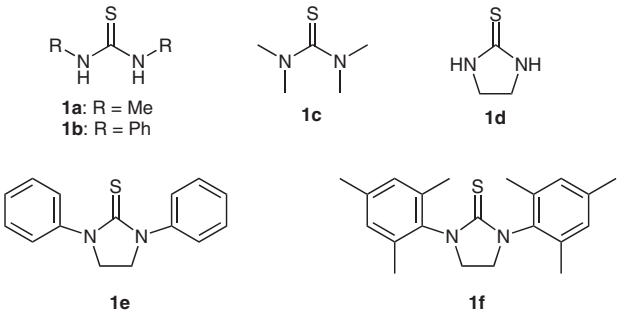
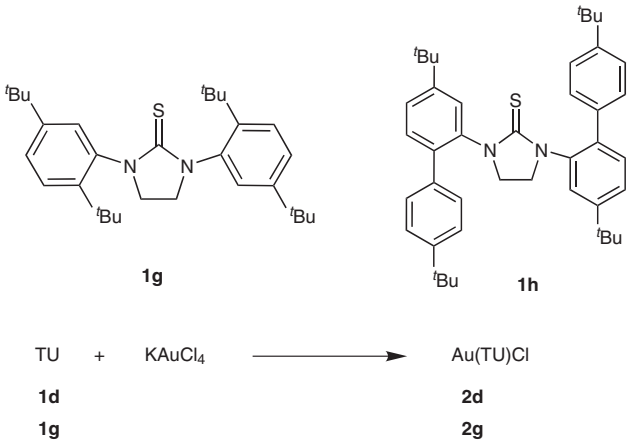


Figure 1 Structures of thiourea ligands

The use of phosphine ligands for transition metals in organometallic chemistry and catalysis is widespread. However, the air- and moisture-sensitivity of many phosphine ligands place significant limits on their synthetic applications. New types of phosphine-free ligands have become a popular challenge for chemists. Thioureas have attracted considerable attention as a new type of possible alternative to the widely used phosphine ligands in ruthenium-, palladium-, and cobalt-catalyzed reactions.[1–3] Therefore, transition-metal-catalyzed reactions using thiourea ligands are worthy of further investigation.

Gold was considered to be a metal with low catalytic activity until, in 1972, Hüttel et al. found that gold(III) chloride or gold(I) cyanide catalyzed the ring-opening reaction of bicyclo[1.1.0]butane, a symmetric strained compound.[4] It is now recognized that gold has unique properties as a catalyst for many reactions.[5] Gold(I) catalysts have been found to activate alkynes for nucleophilic attack and have been widely investigated since the first report in 1985 by Hutchings et al.[6] Recently, Toste and coworkers[7] applied phosphine–gold(I) complexes in the carbocyclization of β-keto esters with alkynes (also called the Conia-ene reaction) under mild and neutral conditions. In the presence of a low catalyst loading (1 mol%) of cationic gold complexes generated from [AuCl(PPh$_3$)] and silver triflate, a series of alkynic β-keto esters gave the cycloisomerization products in high yield. However, the chemistry of gold(I) catalysts has been mainly focused on the use of phosphine ligands. Here we report that bulky N,N′-disubstituted cyclic thiourea ligands can be applied in gold(I) catalysis, in particular in the cycloisomerization of 1,3-dicarbonyl compounds with alkynes.

We synthesized cyclic thioureas **1e**–**h** (Figure 1) according to our previous reports,[3] as well as thiourea–gold(I) complexes **2d** and **2g** (Scheme 1). We chose the Conia-ene reaction to examine the catalytic efficiency of various thiourea ligand–gold(I) complexes (Table 1). Only 1 mol% of thiourea–gold(I) chloride species and silver triflate was employed to catalyze the reaction at room temperature from alkynic β-keto ester **3a** to the desired cyclopentane derivative **4a**. Based on the results shown in Table 1, the following observations were made: (a) The preformed gold(I)–thiourea complexes (Table 1, entries 1 and 2) exhibited higher activity than those generated in situ (entries 3–9), even though the latter is more convenient to use in practice. (b) Gold(I) catalysts complexed



Scheme 1 Synthesis of thiourea–gold(I) complexes. *Reagents and conditions*: thiourea (TU) (1 equiv), S(CH$_2$CH$_2$CO$_2$H)$_2$, CH$_2$Cl$_2$–H$_2$O, 0 °C to r.t., 2 h.

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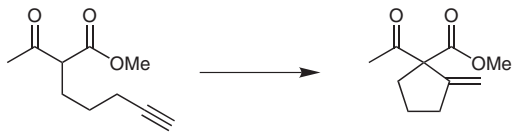
Table 1 Screening of Thiourea Ligands for the Gold(I)-Catalyzed Conia-Ene Reaction[a]



3a **4a**

Entry	Thiourea	Time	Yield[b] (%)
1[c]	**1d**	16 h	88
2[c]	**1g**	2.5 h	96
3[d]	**1a**	3 d	57
4[d]	**1b**	3 d	63
5[d]	**1c**	1 d	70
6[d]	**1e**	8 h	90
7[d]	**1f**	6 h	94
8[d]	**1g**	4.5 h	93
9[d]	**1h**	12 h	90

[a] Reaction conditions: **3a** (0.3 mmol), Au catalyst (1 mol%), AgOTf (1 mol%), CH_2Cl_2 (1 mL), air, r.t.
[b] Isolated yield.
[c] Au catalyst: Au(TU)Cl (1 mol%).
[d] Au catalyst: AuCl (1 mol%), TU (1 mol%).

with tetrasubstituted thioureas **1c** and **1e**–**h** (Table 1, entries 2 and 5–9) gave higher yields of the cyclization product in shorter reaction times than with complexes with disubstituted thioureas **1a**, **1b**, and **1d** (entries 1, 3 and 4). (c) High yields were obtained when cyclic thioureas **1e**–**h** were employed. The most bulky cyclic thiourea **1g** provided the highest yield and rate of the cyclization reaction (Table 1, entries 2 and 8).

X-ray crystal structures of complex **2g** and ligand **1g** gave us important information on the nature of *N*,*N*′-diaryl cyclic thiourea–gold(I) complexes (Figure 2 and Table 2). Upon coordination to the gold(I) ion, the S(1)–C(1) bond became longer, whereas the N(1)–C(1) bond was shortened; this indicates that the interaction of the sulfur atom with gold(I) mainly involves the lone-pair electrons in the sp^2 orbital of the sulfur atom. Distinct from that of [AuCl(PPh$_3$)],[8] the X-ray crystal structure of complex **2g** revealed that the gold ion lay in the plane of the thiourea functional group, yet above one of the two phenyl rings bearing two *tert*-butyl groups. Interestingly, the S–Au–Cl bond angle is 171° instead of 180°, as expected, with the Au–Cl bond slightly bent away from the phenyl ring, and with a distance between Au(1) and the nearest carbon C(18) of 3.1019 Å, a little longer than that of the calculated gold–phenyl coordination bond [Au(C_6H_6)$^+$, 2.19 Å; Au(C_6H_6)$_2^+$, 2.30 Å; Au(C_6H_6), 2.77 Å].[9] It is possible that the weak interaction between gold(I) and the phenyl ring may contribute to the high activity of complex **2g**.

We then examined the application of bulky thiourea–gold(I) complex **2g** in catalyzing the cycloisomerization

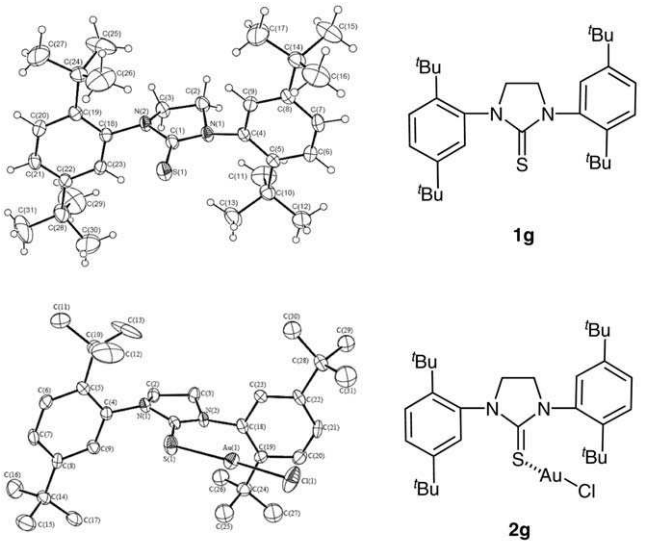


Figure 2

Table 2 Selected Data from the X-ray Crystal Structures of **1g** and **2g**

		1g	**2g**	[AuCl(PPh$_3$)][a]
Bond lengths (Å)	Au–S(or P)		2.2541	2.235
	Au–Cl		2.2718	2.279
	S(1)–C(1)	1.657	1.69	
	N(1)–C(1)	1.37	1.346	
Bond angles (°)	Cl–Au–S(or P)		171.07	179.63
	Au(1)–S(1)–C(1)		111.70	

[a] Data from ref. 8.

of a wide range of α-alkynic β-keto ester substrates (Table 3). With increasing steric size of either the ester (Table 3, entry 2) or the ketone moiety (entries 3 and 4), slightly longer reaction times are needed. For substrates containing both olefinic and alkynic groups, only the alkyne group participates in the cyclization (Table 3, entries 5 and 6). The cyclization is applicable not only to β-keto esters, but also 1,3-diketones and N-monosubstituted β-keto amides (Table 3, entries 7 and 8).

The cyclization catalyzed by the bulky thiourea–gold(I) complex **2g** was further applied to the synthesis of bicyclic compounds. Conia-ene reactions of cyclopentanone- and cyclohexanone-bearing substrates afforded the corresponding *cis*-fused 6,5- and 5,5-bicylic products in high yields (Table 3, entries 9 and 10). Notably, for starting materials **3k** and **3l** with a lactone and a lactam ring, respectively, heterobicyclic products were prepared in excellent yield (Table 3, entries 11 and 12). Even α-3′-alkynyl β-keto ester **3m** underwent 5-*endo*-*dig* cyclization and produced the corresponding cyclopentene product **4m** in 93% yield (Table 3, entry 13).

Table 3 Conia-Ene Reactions Catalyzed by Gold(I)–Thiourea Complex **2g** with Silver Triflate[a]

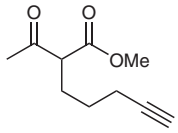
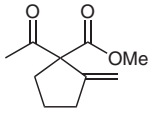
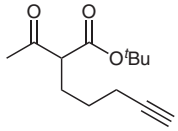
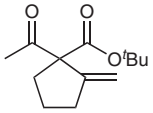
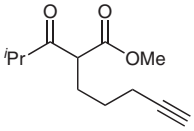
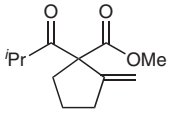
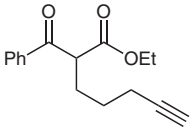
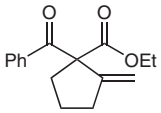
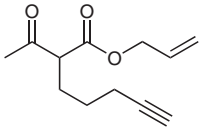
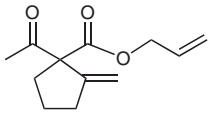
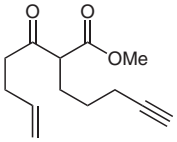
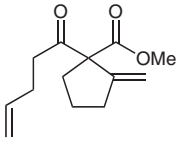
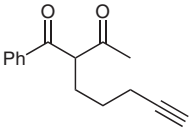
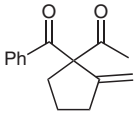
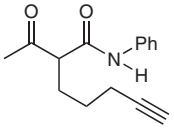
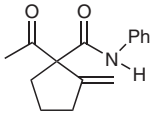
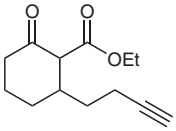
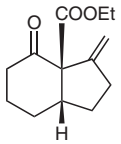
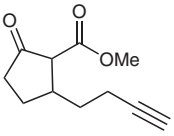
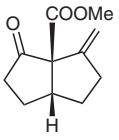
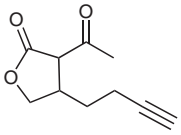
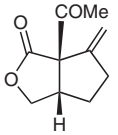
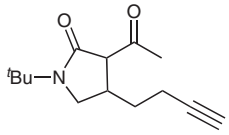
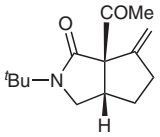
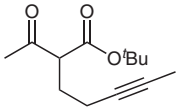
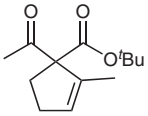
Entry	Starting material		Time (h)	Product		Yield[b] (%)
1		**3a**	2.5		**4a**	96
2		**3b**	3.5		**4b**	91
3		**3c**	4		**4c**	88
4		**3d**	6		**4d**	85
5		**3e**	3.5		**4e**	94
6		**3f**	4		**4f**	89
7		**3g**	3		**4g**	90
8		**3h**	4.5		**4h**	93
9		**3i**	3.5		**4i**	90
10		**3j**	3		**4j**	91
11		**3k**	4		**4k**	87

Table 3 Conia-Ene Reactions Catalyzed by Gold(I)–Thiourea Complex **2g** with Silver Triflate[a] (continued)

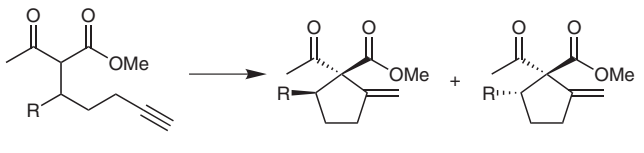
Entry	Starting material		Time (h)	Product		Yield[b] (%)
12		**3l**	6		**4l**	83
13		**3m**	2		**4m**	93

[a] Reaction conditions: **3** (0.3 mmol), **2g** (1 mol%), AgOTf (1 mol%), CH_2Cl_2 (1 mL), air, r.t.
[b] Isolated yield.

We next chose to study the carbocyclization of ε-acetylenic β′-substituted β-keto esters to examine the stereocontrol over two contiguous stereogenic centers.[10] The β-keto ester moiety, through its enol tautomer, should be the reactive intermediate in the cyclization reaction and the presence of β′-substituents could control the transformation of the keto–enol prochiral group into a new stereogenic center. Under the standard conditions of the Conia-ene cyclization, **3n–q** were converted into cycloadducts **4n–q** and **5n–q** with a high level of diastereoselectivity (Table 4). Products **4n–q** were favored with increasing size of the β′-substituents. β′-Alkyl-substituted compounds gave the cyclization products in higher diastereomeric ratios (Table 4, entries 1–3), whereas the compound with a β′-phenyl group gave a lower diastereomeric ratio (entry 4). *tert*-Butyl-substituted substrate **3n** gave the highest diastereoselectivity (Table 4, entry 1).

If it is assumed that the cycloisomerization catalyzed by the thiourea–gold(I) complex follows a mechanism similar to that of [Au(OTf)(PPh_3)], the diastereoselectivities observed in our study could be explained reasonably by conformational control. There are two transition states **A** and **B**, leading to the formation of products **4** and **5**, respectively (Figure 3). The β′-substituent is equatorial in transition state **A**, whereas it is axial in transition state **B**. The strong allylic 1,3-strain encountered in transition state **B** disfavors the formation of products **5**, especially those with large β′-substituents such as the *tert*-butyl group.

Table 4 Diastereoselectivity of the Cycloisomerization of Compounds **3n–q**[a]



3n–q **4n–q** **5n–q**

Entry	Starting material	Yield (%)	dr[b]
1	**3n** (R = *t*-Bu)	96	24.4:1
2	**3o** (R = *n*-Bu)	97	16.2:1
3	**3p** (R = Me)	96	16.5:1
4	**3q** (R = Ph)	88	5.0:1

[a] Reaction conditions: **3** (0.3 mmol), **2g** (1 mol%), AgOTf (1 mol%), CH_2Cl_2 (1 mL), air, r.t.
[b] The dr was determined by use of the ^{1}H NMR integration of the methyl ester groups.

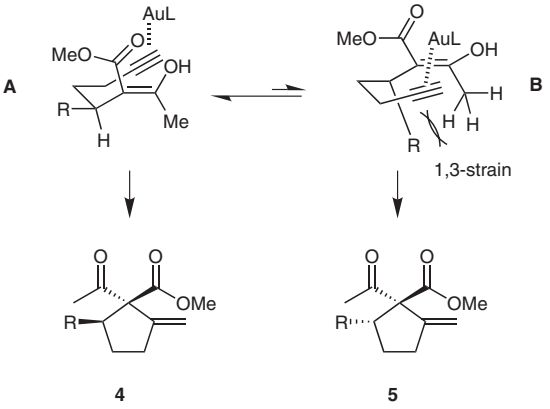


Figure 3

In conclusion, we have demonstrated the first use of bulky N,N′-disubstituted cyclic thioureas as ligands for gold(I) catalysis. Some important information about the complexation has been obtained from the X-ray crystal structure of **2g**. The combination of **2g** with silver triflate has been found to be an excellent catalyst for the Conia-ene cyclization of 1,3-dicarbonyl compounds with alkynes. The reactions can be readily conducted in high yield under mild and neutral conditions with a low catalytic loading in an 'open flask' system, and holds high promise in natural product synthesis.

All reagents and solvents for reactions were used as received. Flash column chromatography was performed using the indicated solvents on E. Merck silica gel 60 (230–400 mesh ASTM). NMR spectra were recorded in $CDCl_3$ with TMS as an internal standard at ambient temperature on a Bruker Avance DPX 300 Fourier Transform Spectrometer operating at 300 MHz for ^{1}H and 75.47 MHz for ^{13}C, or a Bruker Avance DPX 400 Fourier Transform Spectrometer operating at 400 MHz for ^{1}H and 100 MHz for ^{13}C. Mass spectra were recorded on a Finnigan MAT 95 mass spectrometer for both low-resolution and high-resolution mass spectra. IR absorption

spectra were recorded as a solution in CH_2Cl_2 on a Bio-Rad FTS 165 Fourier Transform Spectrophotometer. X-ray crystallographic data collection was performed on an Enraf-Nonius CAD4 single crystal diffractometer or a Rigaku AFC 7R rotating anode X-ray single crystal diffractometer.

Thiourea–Gold(I) Chloride Complex 2g; Typical Procedure

$S(CH_2CH_2CO_2H)_2$ (53 mg, 0.3 mmol) was added slowly to a soln of $KAuCl_4$ (37.8 mg, 0.1 mmol) in H_2O (2 mL) at 0 °C. After the mixture had stirred for 10 min, a soln of thiourea ligand **1g** (48 mg, 0.1 mmol) in CH_2Cl_2 (3 mL) was added dropwise over 20 min while stirring of the mixture continued. After stirring had continued at r.t. for 1.5 h, the organic layer was separated and washed with brine (2 mL). The organic layer was dried (Na_2SO_4) and concentrated. The residue was purified by recrystallization (CH_2Cl_2–MeOH); this afforded complex **2g**.

Yield: 66 mg (93%).

IR (CH_2Cl_2): 1422, 1254 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 7.55–7.46 (m, 4 H), 6.86 (s, 2 H), 4.26–4.23 (m, 2 H), 4.07–4.04 (m, 2 H), 1.53 (s, 18 H), 1.33 (s, 18 H).

^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 182.0, 151.5, 144.5, 136.8, 129.6, 127.2, 126.6, 54.3, 35.7, 34.3, 32.1, 31.0.

ESI-MS: *m*/*z* (%) = 1153 (100) $[L_2Au^+]$.

2d

Yield: 93%.

^1H NMR (300 MHz, CD_3OD): δ = 4.86 (s, 4 H), 3.32–3.30 (m, 1 H).

^{13}C NMR (75.5 MHz, CD_3OD): δ = 181.7, 44.5.

ESI-MS: *m*/*z* (%) = 401 (100) $[L_2Au^+]$.[10]

Compound 4a by a Conia-Ene Reaction Catalyzed by a Thiourea–Gold(I) Chloride Complex; Typical Procedure

To a small screw-cap sample vial equipped with a magnetic stir bar and charged with a soln of **3a** (91 mg, 0.5 mmol) in CH_2Cl_2 (1 mL) was added **2g** (1 mol%) followed by AgOTf (1 mol%). The cloudy white reaction mixture was then stirred at r.t. and monitored periodically by TLC. Upon completion, the solvent was removed and the residue was purified by flash column chromatography (*n*-hexane–EtOAc, 9:1); this gave **4a**.

Yield: 87 mg (96%).

^1H NMR (300 MHz, $CDCl_3$): δ = 5.30 (t, *J* = 2.0 Hz, 1 H), 5.23 (t, *J* = 2.0 Hz, 1 H), 3.75 (s, 3 H), 2.48–2.36 (m, 3 H), 2.22 (s, 3 H), 2.24–2.15 (m, 1 H), 1.76–1.64 (m, 2 H).

Compound 4b

Yield: 91%.

^1H NMR (400 MHz, $CDCl_3$): δ = 5.28 (t, *J* = 2.0 Hz, 1 H), 5.23 (t, *J* = 2.0 Hz, 1 H), 2.43–2.33 (m, 3 H), 2.21 (s, 3 H), 2.15–2.10 (m, 1 H), 1.73–1.59 (m, 2 H), 1.47 (s, 9 H).

Compound 4c

Yield: 88%.

^1H NMR (400 MHz, $CDCl_3$): δ = 5.30 (t, *J* = 2.0 Hz, 1 H), 5.23 (t, *J* = 2.0 Hz, 1 H), 3.74 (s, 3 H), 2.98 (sept, *J* = 6.7 Hz, 1 H), 2.48–2.42 (m, 2 H), 2.40–2.35 (m, 1 H), 2.30–2.23 (m, 1 H), 1.76–1.63 (m, 2 H), 1.10 (d, *J* = 6.6 Hz, 3 H), 1.07 (d, *J* = 6.6 Hz, 3 H).

Compound 4d

Yield: 85%.

^1H NMR (300 MHz, $CDCl_3$): δ = 7.84 (app d, *J* = 7.4 Hz, 2 H), 7.52 (td, *J* = 7.4, 1.2 Hz, 1 H), 7.42 (app t, *J* = 7.4 Hz, 2 H), 5.36 (t, *J* = 2.0 Hz, 1 H), 5.21 (t, *J* = 2.0 Hz, 1 H), 4.18–4.07 (m, 2 H), 2.85 (dt, *J* = 13.6, 7.0 Hz, 1 H), 2.51 (tt, *J* = 7.4, 2.0 Hz, 2 H), 2.18 (dt, *J* = 13.6, 7.0 Hz, 1 H), 1.92–1.81 (m, 1 H), 1.74–1.63 (m, 1 H), 1.05 (t, *J* = 7.1 Hz, 3 H).

Compound 4e

Yield: 94%.

^1H NMR (300 MHz, $CDCl_3$): δ = 5.97–5.84 (m, 1 H), 5.36–5.22 (m, 2 H), 5.29 (t, *J* = 2.0 Hz, 1 H), 5.24 (t, *J* = 2.0 Hz, 1 H), 4.65 (t, *J* = 1.3 Hz, 1 H), 4.63 (t, *J* = 1.3 Hz, 1 H), 2.49–2.37 (m, 3 H), 2.22 (s, 3 H), 2.24–2.15 (m, 1 H), 1.80–1.65 (m, 2 H).

Compound 4f

Yield: 89%.

^1H NMR (300 MHz, $CDCl_3$): δ = 5.82–5.73 (m, 1 H), 5.29 (t, *J* = 2.0 Hz, 1 H), 5.22 (t, *J* = 2.0 Hz, 1 H), 5.06–4.95 (m, 2 H), 3.74 (s, 3 H), 2.74–2.51 (m, 2 H), 2.48–2.29 (m, 5 H), 2.31–2.15 (m, 1 H), 1.81–1.60 (m, 2 H).

Compound 4g

Yield: 90%.

^1H NMR (400 MHz, $CDCl_3$): δ = 7.78 (app d, *J* = 7.9 Hz, 2 H), 7.52 (app t, *J* = 8.0 Hz, 1 H), 7.41 (app t, *J* = 6.0 Hz, 2 H), 5.41 (t, *J* = 2.0 Hz, 1 H), 5.12 (t, *J* = 2.0 Hz, 1 H), 2.77–2.70 (m, 1 H), 2.59–2.45 (m, 2 H), 2.29–2.18 (m, 1 H), 2.24 (s, 3 H), 1.86–1.72 (m, 2 H).

Compound 4h

Yield: 93%.

^1H NMR (400 MHz, $CDCl_3$): δ = 8.50 (br s, 1 H), 7.52 (app d, *J* = 7.9 Hz, 2 H), 7.32 (app t, *J* = 8.0 Hz, 1 H), 7.12 (app t, *J* = 6.0 Hz, 2 H), 5.42 (t, *J* = 2.0 Hz, 1 H), 5.32 (t, *J* = 2.0 Hz, 1 H), 2.67–2.52 (m, 3 H), 2.50–2.37 (m, 1 H), 2.29 (s, 3 H), 1.87–1.75 (m, 2 H).

Compound 4i

Yield: 90%.

^1H NMR (400 MHz, $CDCl_3$): δ = 5.22 (t, *J* = 2.4 Hz, 1 H), 4.98 (t, *J* = 2.4 Hz, 1 H), 4.28–4.18 (m, 2 H), 3.04 (app quin, *J* = 7.2 Hz, 1 H), 2.51–2.46 (m, 2 H), 2.43–2.36 (m, 2 H), 1.97–1.84 (m, 3 H), 1.71–1.64 (m, 1 H), 1.58–1.50 (m, 2 H), 1.26 (t, *J* = 7.0 Hz, 3 H).

Compound 4j

Yield: 91%.

^1H NMR (400 MHz, $CDCl_3$): δ = 5.36 (t, *J* = 2.4 Hz, 1 H), 5.21 (t, *J* = 2.0 Hz, 1 H), 3.71 (s, 3 H), 3.25–3.18 (m, 1 H), 2.52–2.48 (m, 2 H), 2.45–2.40 (m, 2 H), 2.19–2.10 (m, 1 H), 2.06–1.97 (m, 1 H), 1.67–1.56 (m, 2 H).

Compound 4k

Yield: 87%.

^1H NMR (400 MHz, $CDCl_3$): δ = 5.58 (t, *J* = 2.0 Hz, 1 H), 5.33 (t, *J* = 1.9 Hz, 1 H), 4.37 (dd, *J* = 9.3, 7.9 Hz, 1 H), 3.98 (dd, *J* = 9.3, 4.9 Hz, 1 H), 3.53–3.49 (m, 1 H), 2.54–2.47 (m, 2 H), 2.44 (s, 3 H), 2.20–2.11 (m, 1 H), 1.67–1.58 (m, 1 H).

Compound 4l

Yield: 83%.

^1H NMR (300 MHz, $CDCl_3$): δ = 5.53 (t, *J* = 2.2 Hz, 1 H), 5.21 (t, *J* = 2.2 Hz, 1 H), 3.53 (dd, *J* = 8.3, 10.6 Hz, 1 H), 3.14–3.05 (m, 2 H), 2.44–2.31 (m, 2 H), 2.37 (s, 3 H), 2.12–2.01 (m, 1 H), 1.50–1.39 (m, 1 H), 1.37 (s, 9 H).

Compound 4m

Yield: 93%.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 5.66 (br s, 1 H), 2.58 (m, 1 H), 2.42–2.24 (m, 2 H), 2.16 (s, 3 H), 2.11 (m, 1 H), 1.81 (q, *J* = 2.4 Hz, 3 H), 1.47 (s, 9 H).

The complete spectroscopic and analytical data of known compounds **4a**–**m** have been published elsewhere.[7]

Compounds 4n and 5n
Yield: 96%.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 5.03 (t, *J* = 2.3 Hz, 1 H), 4.92 (t, *J* = 2.7 Hz, 1 H), 3.67 (s, 3 H), 2.64–2.60 (m, 1 H), 2.50–2.45 (m, 1 H), 2.39 (s, 3 H), 1.52–1.43 (m, 1 H), 1.30–1.25 (m, 2 H), 0.85 (s, 9 H).

Compounds 4o and 5o
Yield: 97%.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 5.23 (t, *J* = 2.2 Hz, 1 H), 5.17 (t, *J* = 2.8 Hz, 1 H), 3.71 (s, 3 H), 2.73–2.70 (m, 1 H), 2.48–2.46 (m, 1 H), 2.35–2.29 (m, 1 H), 2.25 (s, 3 H), 1.96–1.89 (m, 1 H), 1.52–1.41 (m, 1 H), 1.40–1.10 (m, 6 H), 0.86 (t, *J* = 6.6 Hz, 3 H).

Compounds 4p and 5p
Yield: 96%.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 5.27 (t, *J* = 1.6 Hz, 1 H), 5.24 (t, *J* = 2.2 Hz, 1 H), 3.71 (s, 3 H), 2.87–2.80 (m, 1 H), 2.58–2.50 (m, 1 H), 2.42–2.30 (m, 1 H), 2.22 (s, 3 H), 1.98–1.89 (m, 1 H), 1.49–1.40 (m, 1 H), 0.92 (d, *J* = 6.6 Hz, 3 H).

Compounds 4q and 5q
Yield: 88%.

Compound 4q
^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.29–7.23 (m, 5 H), 5.40 (dd, *J* = 2.7, 1.6 Hz, 1 H), 5.36 (dd, *J* = 2.7, 1.6 Hz, 1 H), 4.30 (dd, *J* = 9.3, 7.1 Hz, 1 H), 3.21 (s, 3 H), 2.57–2.40 (m, 2 H), 2.29 (s, 3 H), 2.19–2.11 (m, 2 H).

Compound 5q
^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.21–7.14 (m, 5 H), 5.26 (dd, *J* = 2.7, 1.6 Hz, 1 H), 5.18 (dd, *J* = 2.7, 1.6 Hz, 1 H), 4.20 (dd, *J* = 6.6, 5.5 Hz, 1 H), 3.81 (s, 3 H), 2.76–2.63 (m, 2 H), 2.10–2.02 (m, 2 H), 1.5 (s, 3 H).

The complete spectroscopic and analytical data of known compounds **4n**–**q** and **5n**–**q** have been published elsewhere.[11]

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