Tetrahedron 68 (2012) 5492–5497

Contents lists available at SciVerse ScienceDirect

Tetrahedron

journal homepage: www.elsevier.com/locate/tet

Allenyl ester precursors for 1*H*-inden-1-ol carboxylates: comparisons with their propargylic equivalents having terminal alkyne functions

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ARTICLE INFO

Article history:
Received 17 February 2012
Received in revised form 9 April 2012
Accepted 23 April 2012
Available online 30 April 2012

Keywords:
Allene
Alkyne
Gold
Cycloisomerization
Reaction mechanism

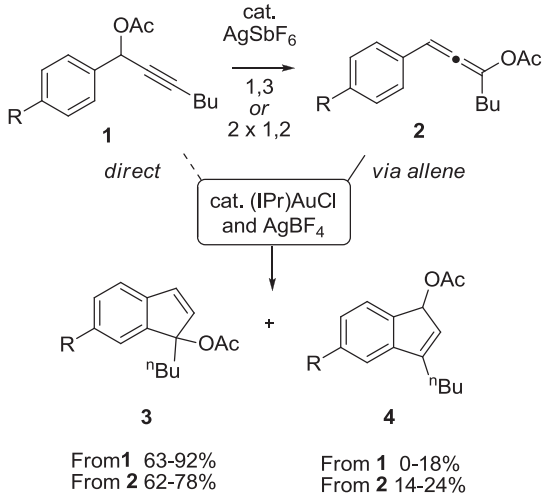
ABSTRACT

The reactivity of allenyl carboxylates, Ar(R^1)CCCH(O_2CR^2) and their isomeric equivalents the terminal propargylic carboxylates, ArC(R^1)(O_2CR^2)CCH, in gold-catalyzed carbocyclization to indenes provides information on 1,3 and 1,2-carboxylate shifts associated with their interconversion. Allenyl carboxylates transform specifically to 1*H*-inden-1-yl carboxylates in high yields, under Au^I-catalysis. Their equivalent propargylic carboxylates give complex mixtures of indene isomers and elimination products. Mechanistic tests indicate that interconversion of the terminal propargylic carbonate to its allene is at best slow in this case.

1. Introduction

Aryl propargylic carboxylates, ArC(R^1)(O_2CR^2)C≡CR^3 are easily attained, highly versatile, starting materials for gold-catalyzed transformations.[1] They have been used in the synthesis of indene derivatives,[2] Au-catalyzed nucleophilic substitutions,[3] isomerizations to dienes,[4] Meyer–Schuster rearrangements[5] and in the synthesis of various bicyclic compounds.[6] Their isomeric allenyl carboxylates Ar(R^1)CCCR^3(O_2CR^2) are attained by a formal 1,3 shift of the carboxylate in propargylic precursors and such shifts are frequently promoted by the coinage metals. The reactivity of such allenyl and propargylic carboxylates has been compared in DFT computational studies[7] and often the allenyl carboxylate is the true reactive intermediate in the reactions performed with equivalent propargylic starting materials.[1,2,4b,6b,7] While internal propargylic carboxylates (R^3=alkyl) can often be treated as 'allene equivalents' the situation is more complicated for terminal propargylic systems (R^3=H). Typically, such systems favour 1,2-carboxylate shifts and in cases where apparent 1,3-shifts occur it is not always clear if this arises from two successive 1,2-shifts or by a direct 1,3-process. To attempt to shed some light on this for the terminal propargylic analogues of the chemistry of Nolan[2] we have investigated these and their 'allene equivalents'.

In 2006 Nolan published a synthesis of 1*H*-indene derivatives[2a] starting from either the propargylic acetates **1** with internal alkynes or the corresponding allenyl acetates **2** (Scheme 1). As the two compounds gave very similar product pattern to indenes **3** and **4**, it was concluded that the allenyl acetate **2** acted as an intermediate via double gold-catalyzed 1,2 or single 1,3 shift of the propargylic acetate **1** (Scheme 1).[7]



Scheme 1. Nolan's route[2] to substituted 1*H*-indenes; see Table 1 for the structure of IPr.

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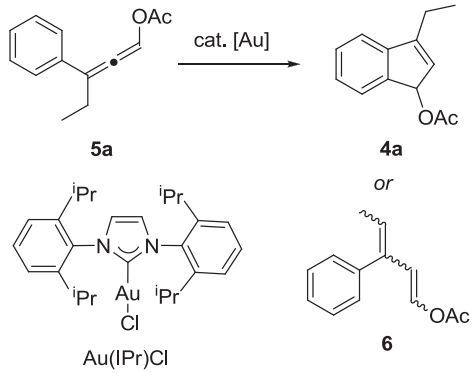
doi:10.1016/j.tet.2012.04.086

Later Nolan reported that the 1*H*-indenes **3**, if left for 14 h in the presence of the gold catalyst, can further rearrange to the 1*H*-indenes **4**[2b] and this causes the selectivity problem in the reaction. Clearly, it would be desirable to develop a mild gold-catalyzed synthesis of indenes, that is, selective towards one of these 1*H*-indenol carboxylate products rather than a mixture and this may be tied to mechanistic understanding.

2. Results and discussion

We have published a synthesis of the allenyl acetates **5** via S_N2' displacement of propargylic diacetates by organocuprates.[8] Such species **5**, the putative '1,3 shift products' of ArCR(OAc)CCH, have not been isolated or detected in the Au-promoted reactivity of ArCR(OAc)CCH before but could still be an important (undetected) intermediate. It is important to confirm allenes **5** are able to carry out gold-catalysed cyclisation to 1*H*-indene derivatives in order to find out if the poor reactivity of ArCR(OAc)CCH is associated with its initial conversion to **5** or due to intrinsic behaviour of **5** itself. Trial reactions of **5a** with $AuCl_3$ and $AuCl(PPh_3)$ (Table 1, entries 1–2) indicated the formation of complex reaction mixtures, but Nolan's gold–carbene complex Au(IPr)Cl, with a AgOTf co-catalyst, immediately gave very high yields of a single 1*H*-indene isomer **4a** (entry 3). In a control experiment AgOTf alone yielded the diene **6**, as a mixture of isomers, as only isolable product (entry 4), while no conversion was evident with just Au(IPr)Cl.

Table 1
Optimisation of gold-catalysed cyclisation of **5a**[a]

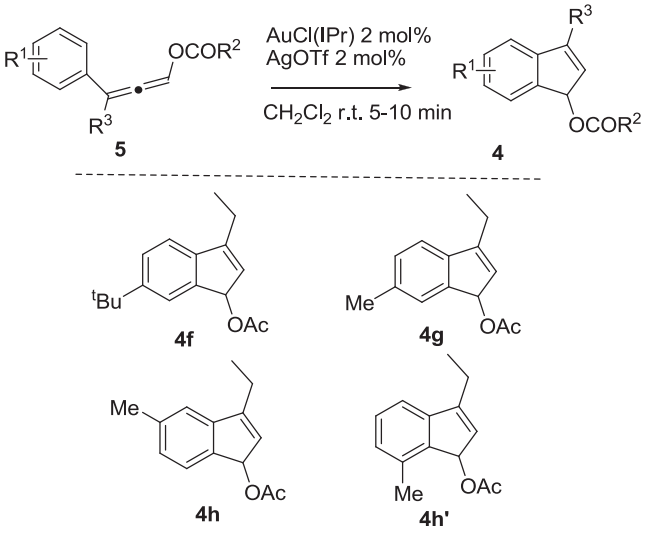


Run	Catalyst	Time/min	Yield (**4** or **6**)/%
1	$AuCl_3$ (2 mol %)	20	12 (**4a**)
2	$(PPh_3)AuCl/AgOTf$ (2/2 mol %)	20	50 (**4a**)
3	(IPr)AuCl/AgOTf (2/2 mol %)	<5	>99 (**4a**)
4	AgOTf (5 mol %)	30	37[b] (**6**)
5	(IPr)AuCl (2 mol %)	45	<2[c]

[a] Reactions preformed in CH_2Cl_2 as 0.1 mmol/mL solution of allene **5**; yields by NMR versus standard.
[b] Isolated yield, only tractable product.
[c] Starting material **5** recovered intact.

The scope of the reaction proved general providing high to quantitative yields of indene derivatives **4**, as no byproducts arise with the Au(IPr)Cl/AgOTf catalyst system (Table 2). Pivalate and benzoate carboxylates are tolerated providing high yields (entries 4–5). When the reaction was scaled up (>0.5 g scale), only 1 mol % of the catalyst was needed to provide quantitative isolated yield of **4a**. The cycloisomerisation was tested with one non-aromatic allene (entry 9), but this gave no desired bicyclic product, suggesting an S_EAr cyclisation mechanism is involved. The reaction of allenyl acetates **5** with $Au(IPr)^+$ catalyst is both rapid and highly selective. The reaction is complete as soon as we can monitor it by TLC; 5 min

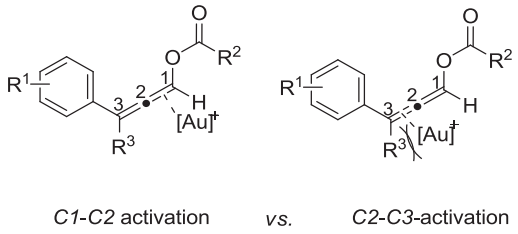
Table 2
Generalised gold-catalysed cyclisation of **5**[a]



Run	R^1	R^2	R^3	Yield (**4**)/%
1	H	Me	Et	>99 (**4a**)
2	H	Me	Me	64 (**4b**)
3	H	Me	Bu	92 (**4c**)
4	H	Ph	Et	82 (**4d**)
5	H	*t*-Bu	Et	96 (**4e**)
6	4-*t*-BuPh	Me	Et	97 (**4f**)
7	4-Me	Me	Et	70 (**4g**)
8	3-Me	Me	Et	92 (**4h**/**h**′)
9	1-Cyclohexene[b]	Me	Et	0

[a] Isolated yields. Run 1 performed with a 1 mol % catalyst system.
[b] A 1-cyclohexenyl substituent was used in place of the phenyl group.

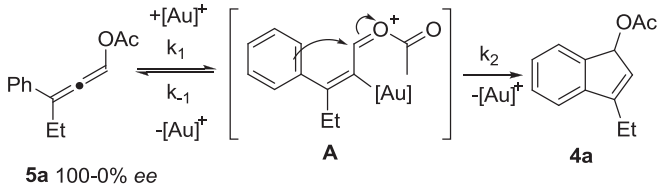
represents an upper limit at room temperature. The selectivity of the reaction is likely due to the unhindered *C1–H* α to the acetate group. As the gold catalyst favours this unhindered *C1–C2* bond there is no competition between the two allenyl bonds to be activated towards in the subsequent carbocyclisation (Scheme 2).



Scheme 2. Assumed steric factors in the cyclisation of **5**.

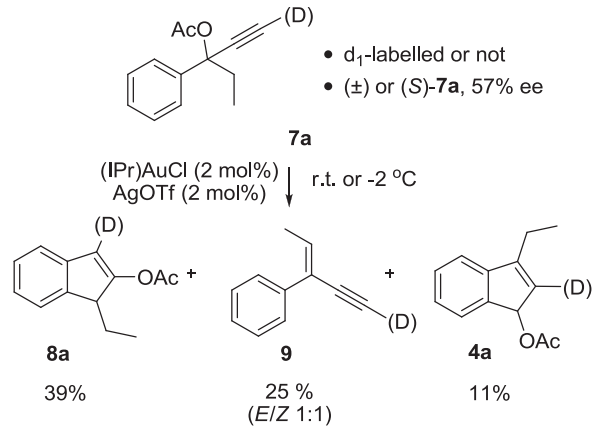
In our earlier report we also described the synthesis of the enantiomerically enriched allenyl acetate (*S*)-(+)-**5a** by lipase-catalyzed kinetic resolution.[8] Gold-catalyzed cycloisomerization of **5a** is too fast to monitor easily at room temperature, but if the reaction mixture is cooled down to −2 °C the conversion slows enough that aliquots can be taken over 40 min (below this temperature the catalyst starts to precipitate). Following the reaction by chiral GC reveals that the allene (+)-**5a** is racemised (zero order dependence) during the course of the reaction; after 20 min reaction only racemic allene **5a** is left. This behaviour was fitted to the kinetic model given in Scheme 3 and values of k_1, k_{-1} and k_2 could be determined by standard methods.[9] The data, although reproducible, has quite a high error bar due to issues of fast quenching of aliquots from such a reactive mixture. Nevertheless, we are unaware of any previous kinetic determination. We could

derive the equilibrium constant K_{eq}=0.16 (±0.08) for formation of the unseen planar intermediate **A**. Aside from unlikely racemisation of the ultimate product, only this achiral species can explain the formation of racemic **4a** when k_2 is greater than k_{-1}. Intermediate **A** can thus cyclize via electrophilic aromatic substitution (S_EAr) chemistry or return indene **5a** in racemic form. On no occasion was any trace (>1%) of **7a** detected in these reactions by GC.



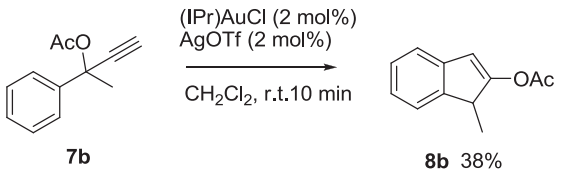
Scheme 3. Racemisation of **5** versus cyclisation.

To provide comparative data on the potential involvement of allenes of type **5** in gold-catalysed rearrangement of propargylic alcohols with terminal alkyne units the catalytic reaction of **7a** was studied in some detail (Scheme 4).



Scheme 4. Mechanistic studies of propargylic alcohol **7a** as a potential precursor to **5a**.

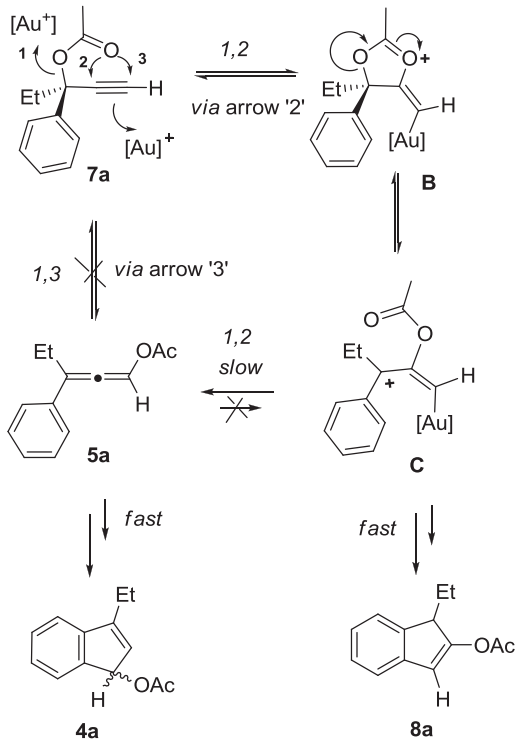
Several points arise from the reactions of Scheme 4: (i) The reaction is unclean—compounds **4a** and **8**–**9** account for only 75% of the reaction mass, but no other long-lived organic species could be detected in the reaction mixture. (ii) Deuterium labelled **7a** results in complete retention of the label at the expected positions. (iii) Monitoring quenched aliquots of the reaction at −2 °C using enantiomerically enriched (*S*)-**7a** does reveal the formation of small amounts of *racemic* **5a** within the first 90 s (appreciable amounts of (*S*)-**7a** remain along with generated **9**) in the reaction. Subsequent smooth formation of *racemic* **4a** and **8** follows thereafter. A 1,3-acetate shift via [3,3]-sigmatropic rearrangement of **7a** to **5a** is not consistent with such observations. Such processes are expected to proceed with high chirality transfer, even when gold-promoted.[10] Under the −2 °C conditions of Scheme 4, racemisation of **5a** would be slow enough that if a stereoselective 1,3-acetate shift had occurred it would have been detected. When the chemistry of Scheme 4 was repeated with the methyl analogue (±)-**7b** only racemic **8b** was isolated in low yield (38%) (Scheme 5). Because of the low mass balance of the reaction enantiomerically enriched **7b** and subsequent reaction monitoring were not carried out.



Scheme 5. Conversion of **7b** into **8b**.

3. Conclusions

It has been proposed, on the basis of DFT calculations, that allenes of type **5** freely interconvert with propargylic acetates **7** through a 'carousel' of intermediates, that is, characterized by low energy (typically 3–9 kcal mol^{-1}) interconversion barriers.[7a] For at least **5a** this cannot be the case—it must be isolated from the 'carousel' by significant energy barriers as it provides a different product distribution to its nominal interconversion partner **7a**. Pure **5a** does not retroisomerise to **7a** by either 1,2 or 1,3-acetate shifts in the presence of (IPr)Au$^+$ cations under our conditions. While forward isomerisation of **7a** to **5** is viable this appears to take place by two successive 1,2 acetate shifts. The lack of clean reactivity for **7a** can be traced to its solvolysis to the implied carbocation [PhCEt(CCH)]$^+$OAc$^-$ (Scheme 6, mechanistic arrow '1'), decomposition of which provides the E1 product **9** (25%) and uncharacterized polymeric products (25%)—as the major reaction pathways. All evidence (studies on isolated **5a** and the absence of chirality transfer from (*S*)-**7a** at low temperature and short reaction times) indicate that a 1,3 carboxylate shift does not occur (mechanistic arrow '3' and its reverse). The expected 1,2 shift (mechanistic arrow '2') from **7a** is facile affording unseen **B** and subsequently **C**. However, only a minority of **C** can 'leak back' to **5a** (the ultimate source of **4a**) and the reverse 1,2 shift from **5a** to **C** must be of higher (non viable) energy as no **8a** is isolated from **5a** alone in the presence of (IPr)Au$^+$.



Scheme 6. Mechanistic behaviour of **5a** and **7a**; **C** can also be drawn in its cationic carbene resonance form.

It can be concluded that an ability to prepare **5** via an alternative precursor to **7** is useful as this allows access to an otherwise poorly populated intermediate **A**.

4. Experimental

4.1. General

All reactions involving air sensitive materials were carried out under argon atmosphere using standard Schlenk techniques. Reagents and catalysts were purchased reagent grade and used without further purification. Dichloromethane was distilled from CaH_2. Flash column chromatography: silica gel 35–70 u, 60 A; petroleum ether used in column chromatography had boiling range 40–60 °C. ^1H and ^{13}C NMR spectra were recorded on Bruker (DPX400 or AV400) spectrometers using $CDCl_3$ as standard (7.26 ppm for ^1H spectra and 77.0 ppm for ^{13}C spectra); *J* values are given in Hertz. Infrared spectra were recorded using a Bruker Tensor 27 spectrometer. Mass spectra were obtained on Bruker Daltonics micro TOF (ESI), Bruker Daltonics APEX 4 ECR FTMS (EI) and VG Autospec (EI). Gas Chromatography on a Varian 420 machine with a *octakis*(2,6-di-*O*-methyl-3-*O*-pentyl)-γ-cyclodextrin column was used. The allenes **5**[8] were prepared as previously described and used immediately. Racemic **7a**–**b** are available through acylation of the known alcohols[11] only the enantiomerically enriched and labelled compounds are described here for brevity. Supported lipase A from *Candida antarctica* was purchased from Sigma–Aldrich.

4.2. 3-Ethyl-1*H*-inden-1-yl acetate: general procedure towards the gold-catalyzed cyclization of allenic acetates (4a)

To a solution of 3-phenylpenta-1,2-dienyl acetate **5a** (140 mg, 0.64 mmol) in CH_2Cl_2 (10 mL) was added Au(IPr)Cl (9.2 mg, 0.013 mmol, 2.0 mol %) and AgOTf (2.8 mg, 0.013 mmol, 2.0 mol %) at room temperature under air. After 10 min the reaction mixture was filtrated through a pad of silica gel with a CH_2Cl_2 wash and the product, 3-ethyl-1*H*-inden-1-yl acetate **4a**, was obtained as yellow oil (140 mg, 0.64 mmol, 99%). The product did not need purifying but it could be subjected to flash column chromatography (30:1 pentane/Et_2O); R_f=0.64 (9:1 petroleum ether/Et_2O); ^1H NMR (400 MHz, $CDCl_3$) δ_H 7.44–7.43 (m, 1H), 7.34–7.30 (m, 1H), 7.25–7.19 (m, 2H), 6.20–6.18 (m, 1H), 6.06–6.05 (m, 1H), 2.54–2.47 (m, 2H), 2.15 (s, 3H), 1.27 (t, 3H, *J*=7.6 Hz); ^{13}C NMR (67.9 MHz, $CDCl_3$) δ_C 171.6, 149.8, 144.0, 142.7, 128.7, 126.3, 125.8, 124.1, 119.3, 77.2, 21.2, 20.7, 11.6; IR (cm^{-1}) ν_{max} 2973, 1732, 1372, 1241; MS *m*/*z* (ESI) for $C_{13}H_{14}NaO_2$ $[M+Na]^+$ calcd 225.0886, found 225.0884, error 1.10 ppm. Chiral GC analysis with an *octakis*(2,6-di-*O*-methyl-3-*O*-pentyl)-γ-cyclodextrin column and a temperature gradient program 60–150 °C 2 °C/min gave retention times for the enantiomers of (50.9/51.0 min).

4.3. 3-Methyl-1*H*-inden-1-yl acetate (4b)

3-Phenylbuta-1,2-dienyl acetate **5b** (80 mg, 0.42 mmol) gave the title compound as a yellow oil (51.0 mg, 0.27 mmol, 64%); R_f=0.69 (9:1 petroleum ether/Et_2O); ^1H NMR (400 MHz, $CDCl_3$) δ_H 7.43–7.41 (m, 1H), 7.33–7.31 (m, 1H), 7.24–7.22 (m, 2H), 6.19–6.18 (m, 1H), 6.07–6.05 (m, 1H), 2.14 (s, 3H), 2.12 (d, 3H, *J*=1.6 Hz); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ_C 171.5, 133.5, 143.8, 142.5, 128.8, 127.9, 126.2, 124.0, 119.3, 76.7, 21.2, 13.0; IR (cm^{-1}) ν_{max} 3011, 1732, 1626, 1372, 1244; MS *m*/*z* (EI) for $C_{12}H_{12}NaO_2$ $[M+Na]^+$ calcd 211.0730, found 211.0723, error 3.10 ppm. The compound had identical properties to that formed by an alternative route.[12]

4.4. 3-Butyl-1*H*-inden-1-yl acetate (4c)

3-Phenylhepta-1,2-dienyl acetate **5c** (0.36 g, 1.56 mmol) gave the title compound as a clear oil (0.33 g, 1.43 mmol, 92%). R_f=0.68 (4:1 petroleum ether/Et_2O); ^1H NMR (400 MHz, $CDCl_3$) δ_H 7.44–7.19 (m, 4H), 6.18–6.17 (m, 1H), 6.05–6.04 (m, 1H), 2.50–2.46 (m, 2H), 2.14 (s, 3H), 1.69–1.62 (m, 2H), 1.46–1.61 (m, 2H), 0.96 (t, 3H, *J*=7.2 Hz); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ_C 171.6, 148.3, 144.1, 142.7, 128.7, 126.6, 126.2, 124.1, 119.4, 76.7, 29.5, 27.2, 22.6, 21.2, 13.9; IR (cm^{-1}) ν_{max} 3012, 2960, 2361, 1732. 1372, 1243; MS *m*/*z* (ESI), for $C_{15}H_{18}NaO_2$ $[M+Na]^+$ calcd 253.1199, found 253.1198, error 0.50 ppm.

4.5. 3-Ethyl-1*H*-inden-1-yl benzoate (4d)

3-Phenylpenta-1,2-dienyl benzoate **5d** (92.0 mg, 0.35 mmol) gave the title compound as a yellow oil (68.7 mg, 0.26 mmol, 82%); R_f=0.68 (9:1 petroleum ether/Et_2O); ^1H NMR (400 MHz, $CDCl_3$) δ_H 8.09–8.07 (m, 2H), 7.58–7.50 (m, 2H), 7.45–7.41 (m, 1H), 7.37–3.21 (m, 4H), 6.44–6.42 (m, 1H), 6.19–6.17 (m, 1H), 2.58–2.51 (m, 2H), 1.30 (t, 3H, *J*=7.4 Hz); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ_C 167.1, 149.8, 144.1, 142.9, 133.0, 130.1, 129.8, 128.7, 128.3, 126.2, 126.1, 124.2, 119.3, 77.1, 20.7, 11.7; IR (cm^{-1}) ν_{max} 2973, 1713, 1452, 1268; MS *m*/*z* (ESI) for $C_{18}H_{16}NaO_2$ $[M+Na]^+$ calcd 287.1043, found 287.1038, error 1.50 ppm.

4.6. 3-Ethyl-1*H*-inden-1-yl pivalate (4e)

3-Phenylpenta-1,2-dienyl pivalate **5e** (0.150 g, 0.61 mmol) gave the title compound as a clear oil (0.140 g, 0.59 mmol, 96%); R_f=0.87 (9:1 petroleum ether/Et_2O); ^1H NMR (400 MHz, $CDCl_3$) δ_H 7.38–7.18 (m, 4H), 6.19–6.17 (m, 1H), 6.04–6.03 (m, 1H), 2.54–2.50 (m, 2H), 1.28 (t, 3H, *J*=7.2 Hz), 1.24 (s, 9H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ_C 179.1, 149.4, 144.0, 143.2, 128.5, 126.3 (2*C*), 123.8, 119.3, 76.5, 39.0, 27.2, 20.7, 11.7; IR (cm^{-1}) ν_{max} 2973, 2934, 2254, 1719, 1159; MS *m*/*z* (ESI), for $C_{16}H_{20}NaO_2$ $[M+Na]^+$ calcd 267.1356, found 267.1344, error 4.20 ppm.

4.7. 6-*tert*-Butyl-3-ethyl-1*H*-inden-1-yl acetate (4f)

3-(4-*tert*-Butylphenyl)penta-1,2-dienyl acetate **5f** (0.180 g, 0.68 mmol) gave the title compound as a clear oil (0.170 g, 0.65 mmol, 97%); R_f=0.77 (4:1 petroleum ether/Et_2O); ^1H NMR (400 MHz, $CDCl_3$) δ_H 7.48–7.47 (m, 1H), 7.37–7.34 (m, 1H), 7.18–7.16 (m, 1H), 6.19–6.18 (m, 1H), 6.02–6.00 (m, 1H), 2.52–2.46 (m, 2H), 2.16 (s, 3H), 1.33 (s, 9H), 1.26 (t, 3H, *J*=7.6 Hz); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ_C 171.6, 149.7, 142.6, 141.4, 125.5 (2*C*), 125.3, 121.4, 118.8, 76.7, 34.8, 31.5, 21.3, 20.7, 11.7; IR (cm^{-1}) ν_{max} 3011, 2970, 1731, 1602, 1243; MS *m*/*z* (ESI), for $C_{17}H_{22}NaO_2$ $[M+Na]^+$ calcd 281.1512, found 281.1501, error 4.00 ppm.

4.8. 3-Ethyl-6-methyl-1*H*-inden-1-yl acetate (4g)

3-*p*-Tolylpenta-1,2-dienyl acetate **5g** (0.170 g, 0.79 mmol) gave the title compound as clear oil (0.120 g, 0.55 mmol, 70%); R_f=0.49 (9:1 petroleum ether/Et_2O); ^1H NMR (400 MHz, $CDCl_3$) δ_H 7.26–7.25 (m, 1H), 7.13–7.12 (m, 2H), 6.17–6.16 (m, 1H), 6.00–5.97 (m, 1H), 2.50–2.47 (m, 2H), 2.36 (s, 3H), 2.14 (s, 3H), 1.26 (t, 3H, *J*=7.2 Hz); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ_C 171.6, 149.8, 143.0, 141.3, 136.2, 129.2, 125.2, 124.9, 119.1, 76.7, 21.4, 21.2, 20.7, 11.7; IR (cm^{-1}) ν_{max} 3011, 2972, 1732, 1372, 1243; MS *m*/*z* (ESI), for $C_{14}H_{16}NaO_2$ $[M+Na]^+$ calcd 239.1043, found 239.1042, error 0.30 ppm.

4.9. 3-Ethyl-5-methyl-1*H*-inden-1-yl acetate and 3-ethyl-7-methyl-1*H*-inden-1-yl acetate (4h/h′)

3-*m*-Tolylpenta-1,2-dienyl acetate **5h** (0.240 g, 1.11 mmol) gave the title compounds as a clear oil and inseparable mixture of isomers (0.220 g, 1.02 mmol, 92%); R_f=0.50 (9:1 petroleum ether/Et_2O); The individual isomers could not be differentiated in the mixture so they are named as A and B (A/B 2:1) ^1H NMR (400 MHz, $CDCl_3$) δ_H 7.31 (d, 1H, *J*=7.6 Hz, A), 7.23 (d, 1H, *J*=8.0 Hz, B),

7.09–7.01 (m, 2+2H, A+B), 6.25–6.23 (m, 1H, B), 6.16–6.15 (m, 1H, A), 6.08–6.06 (m, 1H, B), 6.04–6.03 (m, 1H, A), 2.52–2.46 (m, 2+2H, A+B), 2.38 (s, 3H, A), 2.31 (s, 3H, B), 2.14 (s, 3H, B), 2.13 (s, 3H, A), 1.27 (t, 3H, J=7.2 Hz, A), 1.25 (t, 3H, J=7.6 Hz, B); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ_C 171.6 (A), 171.3 (B), 149.8 (2*C*), 144.2, 144.1, 140.0, 139.8, 138.7, 134.2, 129.0, 128.1, 126.8, 126.1, 125.6, 123.9, 120.3, 117.1, 76.5 (A), 76.3 (B), 21.6, 21.2, 21.0, 20.7, 20.6, 17.9, 11.7 (2*C*); IR (cm^{-1}) ν_{max} 3011, 2972, 1732, 1372, 1243; MS *m*/*z* (ESI), for $C_{14}H_{16}NaO_2$ $[M+Na]^+$ calcd 239.1043, found 239.1042, error 0.10 ppm.

4.10. (1*E*/*Z*, 3*E*/*Z*)-3-Phenylpenta-1,3-dienyl acetate (6)

3-Phenylpenta-1,2-dienyl acetate **5a** (0.100 g, 0.49 mmol) was dissolved in CH_2Cl_2 (5 mL) and AgOTf (6.3 mg, 0.024 mmol, 5 mol %) added. The reaction was stirred for 30 min at room temperature, then filtered through a pad of silica with a CH_2Cl_2 wash and concentrated in vacuo. The crude product was purified with flash column chromatography (9:1 petroleum ether/Et_2O) to give the product as a mixture of two isomers as a yellow oil. As the two C=C isomers could not be distinguished from the four possible cases, they are marked in the NMR data as A and B. Compound **6** (37.0 mg, 0.18 mmol, 37%); R_f=0.54 (9:1 petroleum ether/Et_2O); ^{1}H NMR (400 MHz, $CDCl_3$) δ_H 7.38–7.17 (m, 10H, A+B), 7.13 (d, 1H, J=12.4 Hz, A), 6.82 (d, 1H, J=12.8 Hz, B), 6.52 (d, 1H, J=12.4 Hz, A), 6.25 (d, 1H, J=12.8 Hz, B), 5.75 (q, 1H, J=6.8 Hz, B), 5.58 (q, 1H, J=6.8 Hz, A), 2.13 (s, 3H, A), 2.08 (s, 3H, B), 1.86 (d, 3H, J=6.8 Hz, A), 1.56 (d, 3H, J=6.8 Hz, B); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ_C 167.9, 167.8, 141.5, 139.2, 137.7, 137.4, 137.0, 136.3, 129.2, 128.8, 128.5, 128.2, 127.3, 127.1, 127.0, 126.6, 120.2, 112.6, 30.9, 20.7, 14.8, 14.1; IR (cm^{-1}) ν_{max} 3156, 2903, 2254, 1794, 1752, 1466, 1373, 1103, 919; MS *m*/*z* (ESI), for $C_{13}H_{14}NaO_2$ $[M+Na]^+$ calcd 225.0886, found 225.0884, error 0.80 ppm.

4.11. Kinetic study of the conversion of (+)-(*S*)-5a to (±)-4a

To a mixture of (IPr)AuCl (3.7 mg, 5.9 μmol, 2.4 mol %) and AgOTf (1.7 mg, 6.6 μmol, 2.6 mol %) in CH_2Cl_2 (10 mL) at −2 °C was added (+)-(*S*)-**5a**[8] (50.1 mg, 0.25 mmol, 71% ee) in CH_2Cl_2 (1.8 mL) to afford the following initial concentrations: $[\mathbf{5}]_0$=21.2 mM, $[(IPr)Au^+]$= 0.5 mM. Small aliquots (ca. 0.5 mL) were withdrawn at 1–10 min intervals and immediately filtered through Celite, which removed the catalyst and quenched the system. The samples were analysed by chiral GC on a (*octakis*(2,6-di-*O*-methyl-3-*O*-pentyl)-γ-cyclodextrin) column with a temperature programme of 40–150 °C at 1 °C min^{-1}. Enantiomer retention times: (*S*)-**5a** 85.1 min, (*R*)-**5a** 85.6 min; enantiomers of **4a** 80.9/81.4 min. The [**4a**] product data was fitted to the model of Scheme 3 assuming: (i) as [**4a**] >> $[(IPr)Au^+]$ pseudo first order analysis is valid; (ii) the mass balance of the reaction involves only **4a** and **5a**. Using the non-linear regression (solver) approach of Billo to solving Espenson's model for Scheme 3 [9] provided the following best fit values: k_1=1.2×10^{-2} s^{-1}; k_{-1}=7.5×10^{-2} s^{-1}; k_2=1.2×10^{-2} s^{-1} with an error of ±0.3×10^{-2} s^{-1} and $K_{eq}=k_1/k_{-1}$=0.16 (±0.08) for the formation of **A** under these conditions. A plot of $[\mathbf{4a}]_t$ and ee($\mathbf{5a}$)$_t$ is shown in Fig. 1. The study was conducted in duplicate, similar results were attained in acetone as a solvent.

4.12. 1-d-3-Phenylpent-1-yn-3-yl acetate (d-7a)

The reagent was prepared in two stages.

(a) *Deuteration of 3-phenylpent-1-yn-3-ol* The parent alcohol (1.00 g, 6.24 mmol) was dissolved in dry THF (50 mL) and *n*-BuLi (1.6 M in hexanes, 8.0 mL, 12.8 mmol) was added slowly at −60 °C. After 30 min the reaction was taken out of the cold bath and D_2O (1 mL) was added while the reaction was kept under an argon atmosphere. The reaction mixture was diluted with Et_2O and washed

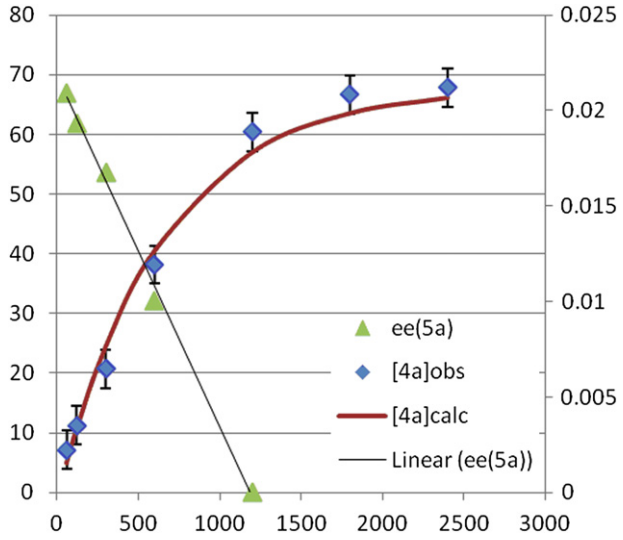


Fig. 1. Simulation of $[\mathbf{4a}]_t$ (◆ in mol dm^{-3}, RHS *y* axis) and ee($\mathbf{5a}$)$_t$ (▲ in %, LHS *y* axis), *x* axis time in s. The simulated fit is shown as a solid line.

once with brine. The organic layer was dried ($MgSO_4$) and concentrated in vacuo. The product (0.99 g, 6.16 mmol, 99%) was obtained as a clear oil, which did not need further purification and was ~99% isotopically pure based on ^{1}H NMR spectroscopy; R_f=0.65 (4:1 petroleum ether/EtOAc); ^{1}H NMR (400 MHz, $CDCl_3$) δ_H 7.64–7.61 (m, 2H), 7.39–7.28 (m, 3H), 2.69 (s, 0.01H, 99% d_1), 2.36 (s, 1H, *OH*), 2.06–1.83 (m, 2H), 0.97 (t, 3H, J=7.2 Hz); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ_C 143.9, 128.2, 127.8, 125.4, 85.6, 73.8, 38.2, 8.9, *CD* not apparent; IR (cm^{-1}) ν_{max} 3590, 3011, 2595, 1978, 1492, 1449, 1327; MS *m*/*z* (EI), for $C_{11}H_{11}DO$ $[M]^+$ calcd 161.0951, found 161.0955, error 2.50 ppm.

(b) *Acetylation. 1-d-3-Phenylpent-1-yn-3-ol* (0.90 g, 5.58 mmol) was dissolved in CH_2Cl_2 (45 mL) and dimethylaminopyridine (345 mg, 2.85 mmol) and triethylamine (1.60 mL, 11.4 mmol) were added. Acetic anhydride (108 μL, 11.4 mmol) was added slowly and the reaction was left to stir overnight. The mixture was concentrated in vacuo to give an oil. Purification of the product with flash column chromatography (9:1 petroleum ether/Et_2O) gave the title compound as a clear oil with 81% isotopic purity; R_f=0.72 (4:1 petroleum ether/EtOAc); ^{1}H NMR (400 MHz, $CDCl_3$) δ_H 7.53–7.51 (m, 2H), 7.37–7.28 (m, 3H), 2.82 (s, 0.19H, 81% d_1), 2.21–2.14 (m, 1H), 2.08 (s, 3H), 2.02–1.95 (m, 1H), 0.94 (t, 3H, J=7.2 Hz); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ_C 168.6, 140.9, 128.2, 127.8, 125.2, 79.3, 76.4, 37.4, 21.7, 8.5, *CD* not apparent; IR (cm^{-1}) ν_{max} 3306, 3010, 2596, 1984, 1743, 1493, 1369, 1242; MS *m*/*z* (ESI), for $C_{13}H_{13}DNaO_2$ $[M+Na]^+$ calcd 226.0949, found 226.0942, error 3.00 ppm.

4.13. Kinetic resolution of 3-phenyl-1-yn-3-yl acetate to give (*S*)-(7a)

To racemic 3-phenyl-1-yn-3-yl acetate (±)-**7a** (0.50 g, 2.50 mmol) in phosphate buffer (pH 7.4, 20 mL) was added Lipase A from *C. antarctica* (1.00 g on solid support) with vigorous stirring at ambient temperature. After 18 h the products were extracted with Et_2O (5×20 mL) and the combined organics were concentrated in vacuo. Purification by flash chromatography (9:1 petroleum ether/EtOAc) gave (−)-(*S*)-**7a** (0.25 g, 48%) with 57% ee showing $[\alpha]_D$ −33.9 (*c* 0.86, $CHCl_3$) followed by (−)-(*R*)-3-phenylpent-1-yn-3-ol (0.13 g, 32%) with 90% ee showing $[\alpha]_D$ −33.9 (*c* 0.86, $CHCl_3$). The spectroscopic properties of the two components are given above. Their enantiomeric purities were determined by chiral GC (*octakis*(2,6-di-*O*-methyl-3-*O*-pentyl)-γ-cyclodextrin) and the temperature

programme 60–150 °C at 2 °C min^{-1}. Enantiomer retention times: (*S*)-**7a** 44.1 min, (*R*)-**7a** 44.3 min; (*R*)-alcohol 45.9, (*S*)-alcohol 46.5 min. The CIP assignments are tentatively based on comparisons against literature optical rotations.[13]

4.14. Products from gold-catalyzed transformation of (*S*)-3-phenylpent-1-yn-3-yl acetate (*S*)-7a

To 3-phenylpent-1-yn-3-yl acetate **7a** (130 mg, 0.65 mmol, racemic or 57% ee) in CH_2Cl_2 (15 mL) at room temperature were added Au(IPr)Cl (9.2 mg, 0.013 mmol, 2.0 mol %) and AgOTf (2.8 mg, 0.013 mmol, 2.0 mol %). After 10 min the reaction mixture was filtered through a pad of Celite with a CH_2Cl_2 wash and the solvents were evaporated on a rotary evaporator. Purification of the residue by column chromatography (30:1 pentane/Et_2O) gave 1-ethyl-1*H*-inden-2-yl acetate (**8a**, 51 mg, 0.25 mmol, 39%), 3-ethyl-1*H*-inden-1-yl acetate (**4a**, 14 mg, 0.07 mmol, 11%) and *Z*/*E*-pent-3-en-1-yn-3-ylbenzene (**9**, 23 mg, 0.16 mmol, 25%). By running the reaction at −2 °C the reaction could be monitored by chiral GC in a manner analogous to Section 4.10.

4.15. 1-Ethyl-1*H*-inden-2-yl acetate (8a)

The title compound was obtained as a clear oil. R_f=0.28 (30:1 petroleum ether/Et_2O); ^1H NMR (400 MHz, $CDCl_3$) δ_H 7.31–7.22 (m, 3H), 7.16–7.12 (m, 1H), 6.65–6.64 (m, 1H), 3.62–3.59 (m, 1H), 2.27 (s, 3H), 1.96–1.83 (m, 2H), 0.76 (t, 3H, *J*=7.2 Hz); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ_C 168.1, 158.0, 142.5, 141.0, 126.7, 124.3, 122.6, 121.0, 114.3, 49.0, 22.4, 21.3, 9.3; IR (cm^{-1}) ν_{max} 2969, 1761, 1601, 1463, 1192; MS *m*/*z* (ESI), for $C_{13}H_{14}NaO_2$ $[M+Na]^+$ calcd 225.0886, found 225.0890, error 1.70 ppm.

4.16. (*Z*)/(*E*)-Pent-3-en-1-yn-3-ylbenzene (9)

The title compound comprised a 1:1 mixture of *E*/*Z* isomers and was obtained as a yellow oil; R_f=0.75 (20:1 petroleum ether/Et_2O); ^1H NMR (400 MHz, $CDCl_3$) δ_H 7.61–7.58 (m, 2H), 7.36–7.24 (m, 3H), 6.56 (qd, 1H, *J*=6.8, 0.8 Hz), 3.37 (s, 1H, the 0.8 Hz coupling to the alkene was not resolved), 2.10 (d, 3H, *J*=6.8 Hz); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ_C 137.8, 134.8, 128.3, 127.5, 125.8, 123.6, 83.3, 80.8, 16.9; IR (cm^{-1}) ν_{max} 3306, 3009, 2914, 1711, 1598, 1495, 1440, 1363; MS *m*/*z* (EI), for $C_{11}H_{10}$ $[M]^+$ calcd 142.0783, found 142.0777, error 4.20 ppm.

4.17. 1-Methyl-1*H*-inden-2-yl acetate (8b)

Using the same method as described for the preparation of **8a**, 2-phenylbut-3-yn-2-yl acetate **7b** (94.0 mg, 0.50 mmol) gave **8b** as a clear oil (36.0 mg, 0.19 mmol, 38%). R_f=0.75 (9:1 petroleum ether/Et_2O); ^1H NMR (400 MHz, $CDCl_3$) δ_H 7.31–7.14 (m, 4H), 6.62 (d, 1H, *J*=1.2 Hz), 3.58–3.60 (m, 1H), 2.28 (s, 3H), 1.34 (d, 3H, *J*=7.6 Hz); ^{13}C NMR (67.9 MHz, $CDCl_3$) δ_C 168.0, 159.9, 141.7, 142.8, 126.8, 124.5, 122.3, 121.0, 113.1, 43.2, 21.3, 14.8; IR (cm^{-1}) ν_{max} 2971, 1764, 1600, 1463, 1370, 1199; MS *m*/*z* (ESI) for $C_{12}H_{12}NaO_2$ $[M+Na]^+$ calcd 211.0730, found 211.0742, error 5.80 ppm.

Acknowledgements

The financial support by the European Community (Marie Curie Early Stage Researcher Training), (MEST-CT-2005-019780) and the EPSRC (Grant EP/F033478/1) are gratefully acknowledged.

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