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# Phase-transfer-catalysed asymmetric synthesis of tetrasubstituted allenes

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**Allenes are molecules based on three carbons connected by two cumulated carbon–carbon double bonds. Given their axially chiral nature and unique reactivity, substituted allenes have a variety of applications in organic chemistry as key synthetic intermediates and directly as part of biologically active compounds. Although the demands for these motivated many endeavours to make axially chiral, substituted allenes by exercising asymmetric catalysis, the catalytic asymmetric synthesis of fully substituted ones (tetrasubstituted allenes) remained largely an unsolved issue. The fundamental obstacle to solving this conundrum is the lack of a simple synthetic transformation that provides tetrasubstituted allenes in the action of catalysis. We report herein a strategy to overcome this issue by the use of a phase-transfer-catalysed asymmetric functionalization of 1-alkylallene-1,3-dicarboxylates with *N*-arylsulfonyl imines and benzylic and allylic bromides.**

The creation of enantioenriched materials with the help of asymmetric catalysis has been one of the most significant challenges in organic chemistry for more than half a century, and uncountable efforts have now culminated in many industrial applications of asymmetric catalysis[1]. Naturally, given its prevalence in pharmaceuticals and agrochemicals, the focus of these efforts was on the stereoselective construction of central chirality (Fig. 1a, left) based on one carbon atom.

In modern organic chemistry, the demand for enantioenriched allenes with axial chirality based on three carbons (Fig. 1a, right) is also increasing for synthetic intermediates, molecular materials and even chiral ligands[2–4]. Although these strong demands have motivated much research to make these molecules efficiently, centre-to-axis chirality transfer from the corresponding enantioenriched propargyl alcohol derivatives is the prevailing method in the synthetic community[5,6]. However, the direct catalytic asymmetric synthesis of allenes is still in its infancy and only the preparation of di- and trisubstituted allenes has emerged as an achievable objective[7–10]. As for tetrasubstituted allenes (Fig. 1a, right, $a \neq b$, $c \neq d$, $a$–$d \neq$ H), there are no general solutions, but there are a few limited examples[11,12]. This situation contrasts sharply with the fact that catalytic asymmetric synthesis of a tetrasubstituted carbon centre (Fig. 1a, left, $a \neq b \neq c \neq d$, $a$–$d \neq$ H), which had been considered one of the most challenging issues in the first decade of the twenty-first century, now provides a broad array of solutions for use in constructing chiral tertiary alcohols, tertiary amines and all-carbon quaternary centres[13–15].

To open up a novel and robust strategy with which to access tetrasubstituted allenes in a catalytic manner, we report herein the first use of cumulenolate as a prochiral nucleophilic template in concert with a chiral phase-transfer catalyst. Cumulenolate is an anionic nucleophile that can be generated in the presence of a base from the corresponding allenoate, and its reaction with an electrophile results in the formation of a functionalized allene (Fig. 1b)[16]. It is rather surprising that the viability of cumulenolates as a prochiral template in asymmetric synthesis had remained completely unexplored, in sharp contrast to the ubiquity of enolates in this regard.

As a suitable substrate for this purpose, we opted for the use of 1-alkylallene-1,3-dicarboxylate **1** (Fig. 1c) because of its electron-deficient nature, which is necessary for the facile generation of cumulenolate under phase-transfer conditions[17,18]. We found that this substrate can be obtained easily in quantity by extending the

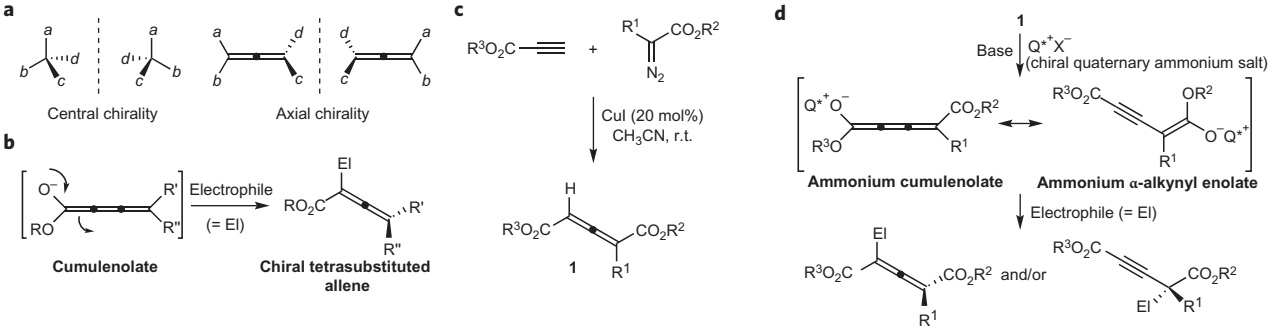


**Figure 1 | Strategy for the catalytic asymmetric synthesis of tetrasubstituted allenes. a**, Central chirality ($a \neq b \neq c \neq d$) and axial chirality ($a \neq b$, $c \neq d$) are shown using a mirror plane. **b**, Use of a cumulenolate as an intermediate can be considered as a direct way to form tetrasubstituted allenes. **c**, 1-Alkylallene-1,3-dicarboxylates can be prepared by the copper-catalysed coupling of alkyl propiolates and α-alkyl diazoesters. **d**, Phase-transfer-catalysed reaction of 1-alkylallene-1,3-dicarboxylate forms ammonium cumulenolate, which has an ammonium α-alkynyl enolate at the other end of the localized structure. This poses the issue of regioselectivity in the reaction with an electrophile. The *E*/*Z* stereochemistry is drawn arbitrarily. r.t. = room temperature.

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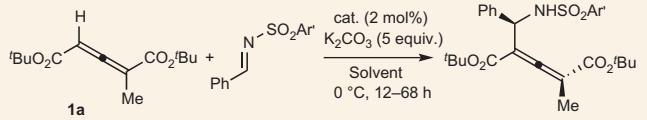
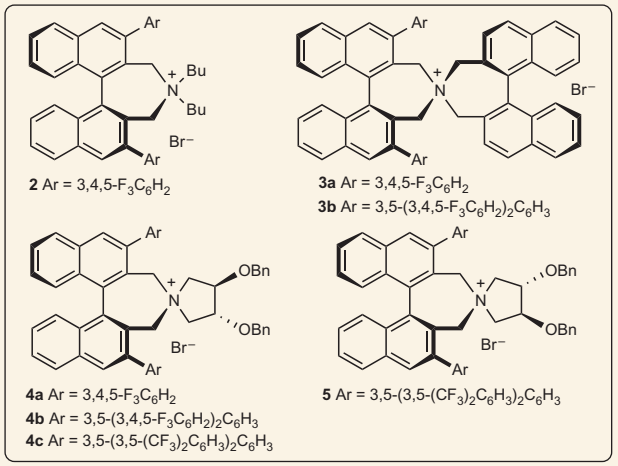
**Table 1 | Optimization of the alleno-Mannich-type reaction.**




| Entry | Catalyst | Ar′ | Solvent | Yield (%)* | d.r.† | e.e. (%)‡ |
|---|---|---|---|---|---|---|
| 1§ | $Bu_4NBr$ | 4-tolyl | Toluene | 9 | 56:44 | −/− |
| 2 | **2** | 4-tolyl | Toluene | 52 | 66:34 | 59/20 |
| 3 | **3a** | 4-tolyl | Toluene | 44 | 46:54 | 51/33 |
| 4 | **4a** | 4-tolyl | Toluene | 93 | 84:16 | 70/51 |
| 5 | **4b** | 4-tolyl | Toluene | 31 | 82:18 | 86/46 |
| 6 | **4c** | 4-tolyl | Toluene | 53 | 90:10 | 90/11 |
| 7 | **5** | 4-tolyl | Toluene | 30 | 80:20 | 23/29 |
| 8 | **4c** | Ph | Toluene | 86 | 91:9 | 93/16 |
| 9 | **4c** | 4-$ClC_6H_4$ | Toluene | 24 | 86:14 | 88/26 |
| 10 | **4c** | 4-$MeOC_6H_4$ | Toluene | 85 | 93:7 | 94/20 |
| 11 | **4c** | 4-$MeOC_6H_4$ | CPME | 90 | 92:8 | 94/3 |
| 12‖ | **4c** | 4-$MeOC_6H_4$ | CPME | 86 | 94:6 | 95/ND |

Experiments were performed with **1a** (0.05 mmol), imine (0.06 mmol), catalyst (0.001 mmol) and powdered $K_2CO_3$ (0.25 mmol) in the solvent (0.5 ml). *Combined yield of the diastereomers determined by $^1$H NMR spectroscopy using mesitylene as an internal standard. †Determined by $^1$H NMR analysis of the crude material. ‡Determined by chiral high-performance liquid chromatography (HPLC) analysis. §Performed with 20 mol% catalyst. ‖Performed at −20 °C. cat. = catalyst. ND = not determined.

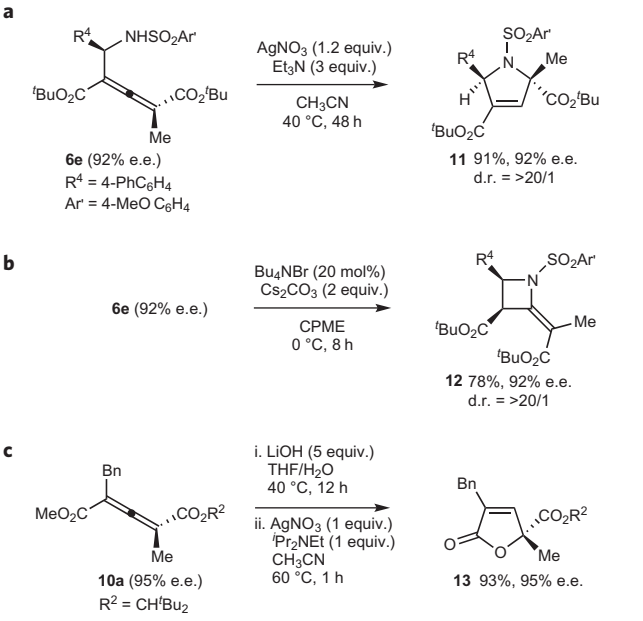



**Figure 2 | Derivatizations of the tetrasubstituted allenes. a**, Silver-mediated cyclization of the chiral tetrasubstituted allene proceeds via the axis-to-centre chirality transfer. **b**, Intramolecular nucleophilic addition of the sulfonamide moiety to the electron-deficient central carbon of the allene gives *cis*-azetidine. **c**, Hydrolysis and cyclization of the alkylation product gives furanone with a tetrasubstituted carbon centre.

copper-catalysed coupling of alkynes and diazoacetates developed by Fu and co-workers[19] to the combination of alkyl propiolates and α-alkyl diazoesters (see the Supplementary Information)[19–21]. Deprotonation of this substrate at its γ-position under phase-transfer conditions is expected to form the delocalized ammonium cumulenolate, with the α-alkynyl enolate as the other end of the localized structure (Fig. 1d). Although this delocalization helps to enhance the acidity of the substrate, it poses the possibility of nucleophilic addition proceeding at the C1-position of 1,3-dicarboxylate to give an alkyne with a tetrasubstituted carbon centre[22–24].

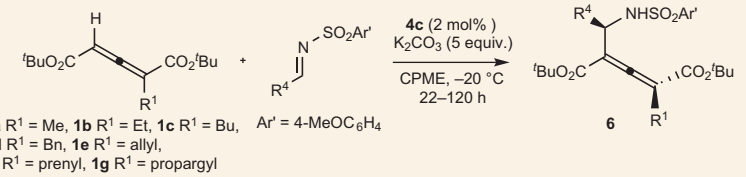
## Results and discussion

**Diastereo- and enantioselective alleno-Mannich-type reaction.** As a primary goal of this study, we set out to investigate the reaction, using imines as the electrophiles, by which tetrasubstituted allenes with an additional vicinal secondary amine stereocentre can be generated (Table 1). In consideration of the similarity to Mannich-type reactions using enolates and imines[25], we termed the reaction an 'alleno-Mannich-type' reaction. In the inaugural experiment, the reaction of di-*tert*-butyl 1-methylallene-1,3-dicarboxylate (**1a**) and benzaldehyde-derived *N*-tosyl imine was implemented in the presence of a catalytic amount of tetrabutylammonium bromide and an excess of $K_2CO_3$ (Table 1, entry 1). The reaction gave the desired tetrasubstituted allene in a regiospecific manner, albeit in low yield and diastereoselectivity. The low yield resulted from the slow reaction rate and the partial overreaction, which produced an azetidine (see Fig. 2b). From this result, we started to search for a catalyst that simultaneously controls the diastereo- and enantioselectivity with high productivity.

However, extensive screening of the established chiral catalysts failed to give any promising selectivities, as exemplified in entries 2 and 3 of Table 1, whereas the reaction yields were improved considerably. Accordingly, we decided to find a new catalyst that fits into this challenging transformation. This exploration led to the advent of catalysts **4a**–**4c**, which incorporated (3*R*,4*R*)-3,4-bis(benzyloxy)pyrrolidine as a right-hand building block (Table 1, entries 4–6). Of these catalysts, which bear different aromatic groups at the 3,3′-positions of the binaphthyl unit, catalyst **4c** was especially effective as it gave the tetrasubstituted allene with 90:10 diastereomeric ratio (d.r.) and 90% enantiomeric excess (e.e.) for the major isomer (Table 1, entry 6). The proper setting of the stereocentres in this catalyst is important because its diastereomer (**5**) furnished the allene with only 23% e.e. (Table 1, entry 7). With this catalyst set as optimal, we further screened other reaction parameters to maximize the efficiency of the reaction (Table 1, entries 8–12). This study led to the use of *N*-4-methoxyphenylsulfonyl imine as the electrophile and cyclopentyl methyl ether (CPME) as the solvent at −20 °C to give the allene in 86% yield with 94:6 d.r. and 95% e.e. after 30 hours of stirring (Table 1, entry 12).

With the optimized conditions in hand, we turned our attention to the investigation of the substrate scope on a 0.1 mmol scale (Table 2). As shown in entries 2–5, aromatic imines that bear methyl or phenyl groups on the aromatic ring were converted into the desired allenes, regardless of the position of the substituent. Also, the 2-naphthaldehyde-derived imine could be used in the reaction with comparable stereoselectivity (Table 2, entry 6). Electron-poor and electron-rich aromatic rings were installed in the resulting allenes with an excellent level of diastereo- and enantioselectivities (Table 2, entries 7, 8, 10 and 11). The nitro group was the only inapplicable functionality,

**Table 2 | Substrate scope of the alleno-Mannich-type reaction.**



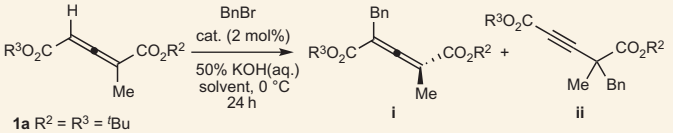

**1a** $R^1$ = Me, **1b** $R^1$ = Et, **1c** $R^1$ = Bu, **1d** $R^1$ = Bn, **1e** $R^1$ = allyl, **1f** $R^1$ = prenyl, **1g** $R^1$ = propargyl

Ar' = 4-$MeOC_6H_4$

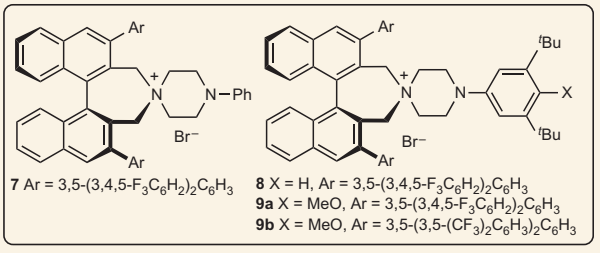
| Entry | $R^1$ | $R^4$ | Yield (%)* | d.r.† | e.e. (%)‡ |
|---|---|---|---|---|---|
| 1 | Me | Ph | 79 (**6a**) | 94:6 | 94 |
| 2§ | Me | 2-tolyl | 87 (**6b**) | 97:3 | 92 |
| 3 | Me | 3-tolyl | 80 (**6c**) | 93:7 | 94 |
| 4 | Me | 4-tolyl | 92 (**6d**) | 95:5 | 95 |
| 5 | Me | 4-$PhC_6H_4$ | 90 (**6e**) | 91:9 | 92 |
| 6‖ | Me | 2-naphthyl | 84 (**6f**) | 86:14 | 92 |
| 7¶ | Me | 4-$BrC_6H_4$ | 73 (**6g**) | 88:12 | 91 |
| 8¶ | Me | 4-$ClC_6H_4$ | 88 (**6h**) | 89:11 | 91 |
| 9 | Me | 4-$NO_2C_6H_4$ | ND (**6i**) | - | - |
| 10 | Me | 3-$MeOC_6H_4$ | 86 (**6j**) | 94:6 | 92 |
| 11 | Me | 4-$MeOC_6H_4$ | 93 (**6k**) | 96:4 | 96 |
| 12# | Me | $^t$Bu | 73 (**6l**) | 92:8 | 90 |
| 13‖ | Et | Ph | 74 (**6m**) | 76:24 | 85 |
| 14** | Bu | Ph | 92‡‡(**6n**) | 76:24 | 86 |
| 15** | Bn | Ph | 86‡‡(**6o**) | 77:23 | 85 |
| 16** | $H_2C{=}CHCH_2$ | Ph | 92‡‡(**6p**) | 72:28 | 89 |
| 17** | $(CH_3)_2C{=}CHCH_2$ | Ph | 98‡‡(**6q**) | 68:32 | 91 |
| 18** | $HC{\equiv}CCH_2$ | Ph | 80‡‡(**6r**) | 88:12 | 91 |
| 19†† | Me | Ph | 89 (**6a**) | 94:6 | 96 |

Experiments were performed with **1** (0.1 mmol) and imine (0.12 mmol), **4c** (0.02 mmol) and $K_2CO_3$ (0.5 mmol) in the solvent (1 ml). *Isolated yield of the major diastereomer. †Determined by $^1$H NMR analysis of the crude material. ‡e.e. of the major diastereomer determined by chiral HPLC analysis. §$K_2CO_3$ (0.25 mmol). ‖**4c** (0.04 mmol) and $K_2CO_3$ (0.25 mmol). ¶**4c** (0.04 mmol) at −30 °C. #**4c** (0.04 mmol) and $Cs_2CO_3$ (0.5 mmol) at −40 °C. **4c (0.04 mmol). ††Performed on a 1.0 mmol scale. ‡‡Combined yield of two diastereomers.

**Table 3 | Optimization of the alkylation.**




**1a** $R^2$ = $R^3$ = $^t$Bu
**1h** $R^2$ = $CH^tBu_2$, $R^3$ = $^t$Bu
**1i** $R^2$ = $CH^tBu_2$, $R^3$ = Et
**1j** $R^2$ = $CH^tBu_2$, $R^3$ = Me




**7** Ar = 3,5-(3,4,5-$F_3C_6H_2$)$_2C_6H_3$

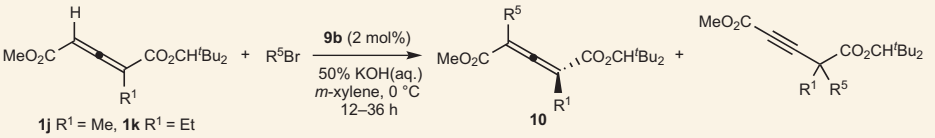
**8** X = H, Ar = 3,5-(3,4,5-$F_3C_6H_2$)$_2C_6H_3$
**9a** X = MeO, Ar = 3,5-(3,4,5-$F_3C_6H_2$)$_2C_6H_3$
**9b** X = MeO, Ar = 3,5-(3,5-$(CF_3)_2C_6H_3$)$_2C_6H_3$

| Entry | Catalyst | $R^2$ | $R^3$ | Solvent | Yield (%)* | r.r.† | e.e. (%)‡ |
|---|---|---|---|---|---|---|---|
| 1§ | $Bu_4NBr$ | $^t$Bu | $^t$Bu | CPME | 85 | 15:85 | - |
| 2 | **2** | $^t$Bu | $^t$Bu | CPME | 48 | 59:41 | 33 |
| 3 | **3b** | $^t$Bu | $^t$Bu | CPME | 63 | 27:73 | 87 |
| 4 | **2** | $CH^tBu_2$ | $^t$Bu | CPME | 79 | 89:11 | 21 |
| 5 | **4c** | $CH^tBu_2$ | $^t$Bu | CPME | 65 | 43:57 | 46 |
| 6 | **7** | $CH^tBu_2$ | $^t$Bu | CPME | 34 | 62:38 | 82 |
| 7 | **8** | $CH^tBu_2$ | $^t$Bu | CPME | 52 | 76:24 | 67 |
| 8‖ | **8** | $CH^tBu_2$ | Et | CPME | 56 | 77:23 | 79 |
| 9‖ | **8** | $CH^tBu_2$ | Et | *m*-xylene | 66 | 74:26 | 84 |
| 10‖ | **9a** | $CH^tBu_2$ | Et | *m*-xylene | 67 | 77:23 | 86 |
| 11‖ | **9b** | $CH^tBu_2$ | Et | *m*-xylene | 76 | 83:17 | 94 |
| 12¶ | **9b** | $CH^tBu_2$ | Me | *m*-xylene | 78 | 86:14 | 95 |

Experiments performed with **1** (0.05 mmol), benzyl bromide (0.06 mmol), catalyst (0.001 mmol), 50% KOH(aq.) (0.1 ml) in the solvent (0.25 ml). *Combined yield of the regioisomers determined by $^1$H NMR using mesitylene as an internal standard. †Determined by $^1$H NMR of the crude mixture. ‡e.e. of the allene determined by chiral HPLC. §Performed with 20 mol% catalyst. ‖Performed with benzyl bromide (0.1 mmol). ¶Performed with benzyl bromide (0.25 mmol).

with a rapid degradation of the imine (Table 2, entry 9). Use of aliphatic imines was found to be difficult, presumably because of the competitive isomerization of the imine to the enamide under basic conditions. In line with this assumption, we found that a pivalaldehyde-derived aliphatic imine that lacked an α-hydrogen could be utilized to give the allene with 92:8 d.r. and 90% e.e. (Table 2, entry 12). Then the focus was switched to the 1-alkyl substituent of allene-1,3-dicarboxylate. It turned out that the longer alkyl chains, such as ethyl and butyl groups, were applicable in this reaction (Table 2, entries 13 and 14). In addition, benzyl-, allyl-, prenyl- and propargyl-substituted allene-1,3-dicarboxylates (**1d**–**1g**) could be used without difficulty (Table 2, entries 15–18). Finally, to demonstrate scalability, the reaction was performed on a 1.0 mmol scale to give **6a** in 89% yield with 96% e.e. (Table 2, entry 19). The relative and absolute configuration of **6e** was determined unambiguously by X-ray crystallographic analysis (see the Supplementary Information).

**Table 4 | Substrate scope of the alkylation.**




**1j** $R^1$ = Me, **1k** $R^1$ = Et
**1l** $R^1$ = Bn, **1m** $R^1$ = allyl

| Entry | $R^1$ | $R^5$ | Yield (%)* | r.r.† | e.e. (%)‡ |
|---|---|---|---|---|---|
| 1 | Me | Bn | 75 (**10a**) | 88:12 | 95 |
| 2 | Me | 4-$MeC_6H_4CH_2$ | 83 (**10b**) | 79:21 | 94 |
| 3 | Me | 3-$MeC_6H_4CH_2$ | 72 (**10c**) | 82:18 | 95 |
| 4 | Me | 3-$MeOC_6H_4CH_2$ | 72 (**10d**) | 79:21 | 93 |
| 5 | Me | 2-$ClC_6H_4CH_2$ | 88 (**10e**) | 93:7 | 93 |
| 6 | Me | 4-$BrC_6H_4CH_2$ | 82 (**10f**)§ | 88:12 | 95 |
| 7 | Me | 2-$BrC_6H_4CH_2$ | 84 (**10g**) | >95:5 | 94 |
| 8 | Me | 2-$NpCH_2$ | 85 (**10h**) | 83:17 | 94 |
| 9 | Me | $H_2C{=}CHCH_2$ | 50 (**10i**) | 74:26 | 91 |
| 10 | Me | $H_2C{=}C(CH_3)CH_2$ | 68 (**10j**) | 90:10 | 94 |
| 11 | Me | $PhCH{=}CHCH_2$ | 89 (**10k**) | 71:29 | 92 |
| 12 | Me | $HC{\equiv}CCH_2$ | 65 (**10l**) | 91:9 | 96 |
| 13 | Et | Bn | 97 (**10m**) | 94:6 | 95 |
| 14 | Et | $H_2C{=}CHCH_2$ | 86 (**10n**) | 87:13 | 90 |
| 15 | Et | $HC{\equiv}CCH_2$ | 85 (**10o**) | 90:10 | 94 |
| 16 | Bn | Bn | 87 (**10p**) | >95:5 | 93 |
| 17 | $H_2C{=}CHCH_2$ | Bn | 86 (**10q**) | 93:7 | 96 |

Experiments performed with **1** (0.1 mmol), alkyl bromide (0.5 mmol), **9b** (0.02 mmol) and 50% KOH(aq.) (0.2 ml) in *m*-xylene (0.5 ml). *Combined yield of the regioisomers. †Determined by $^1$H NMR of the crude mixture. ‡e.e. of the allene determined by chiral HPLC. §Isolated yield of the allene.

**Regio- and enantioselective alkylation.** With the success of the phase-transfer-catalysed alleno-Mannich-type reaction as a means to provide chiral tetrasubstituted allenes with an amino functionality, we decided to move forwards to the use of alkyl halides as electrophiles best suited for phase-transfer catalysis (Table 3)[17,18]. It became immediately obvious that the alkylation of 1-alkylallene-1,3-dicarboxylates by phase-transfer catalysis raised the issue of regioselectivity (see Fig. 1d). Namely, the alkylation of **1a** with benzyl bromide catalysed by achiral tetrabutylammonium bromide gave a mixture of the tetrasubstituted allene **i** and the alkyne **ii** with a central chirality that problematically prefers the formation of the alkyne with a 15:85 regioisomeric ratio (r.r.), (Table 3, entry 1). When the chiral quaternary ammonium salt **2** was used, the regioisomeric ratio could be shifted to the favourable formation of the allene, but the enantioselectivity was disappointingly low (Table 3, entry 2). However, use of catalyst **3b** led to the formation of the allene with a promising 87% e.e., albeit a poor 27:73 r.r. (Table 3, entry 3). That the alkyne **ii** was obtained with 91% e.e. in this reaction offers a procedure to form selectively alkynes with a quaternary carbon centre. These two experiments clearly indicated the possibility of controlling not only the enantioselectivity, but also the regioselectivity by elaborating a catalyst. However, before we pursued this solution, we decided to examine a substrate-controlled strategy as a facile way to bias the regioselectivity of the alkylation, assuming that replacement of one *tert*-butyl ester at C1 of the substrate allene with a bulkier ester would prevent alkylation from occurring at its α-position. As anticipated, the reaction of di-(*tert*-butyl)methyl ester **1h** using catalyst **2** provided the allene with an improved regioselectivity of 89:11 r.r., albeit with low enantioselectivity (Table 3, entry 4). Encouraged by this result, next we screened extensively a variety of catalysts using substrate **1h** to find a highly enantioselective process. However, it was difficult to identify a catalyst that both attained a satisfactory enantioselectivity and retained the regioselectivity. For example, the use of catalyst **4c**, which was optimal in the above-described alleno-Mannich-type reaction, was completely inefficient as it resulted in 43:57 r.r. and 46% e.e. (Table 3, entry 5). Only when catalyst **7**, which contained *N*-phenylpiperazine, was employed did the enantioselectivity of the allene reach a promising level of 82% e.e., thus compensating for a drop in the regioisomeric ratio to 62:38 (Table 3, entry 6). We decided to make this the lead catalyst structure and modify the *N*-aryl group of the piperazine in anticipation of improving the regioselectivity. This study led to the identification of catalyst **8** with a 3,5-di-*tert*-butylphenyl group as an *N*-substituent, with which the regioisomeric ratio could be improved to 76:24 with some loss of the enantioselectivity (Table 3, entry 7). In the additional experiments, the replacement of the *tert*-butyl ester at C3 of the substrate allene with ethyl ester (**1i**) and the solvent with *m*-xylene resulted in a substantial increase in the enantioselectivity (Table 3, entries 8 and 9). At the last stage of the optimization, the catalyst structure was fine tuned to identify catalyst **9b** as optimal (Table 3, entries 10 and 11) and, finally, by use of this catalyst and with methyl ester **1j** as substrate, the allene could be obtained with 86:14 r.r. and 95% e.e. (Table 3, entry 12). The use of five equivalents of benzyl bromide was required under these optimized conditions because of the competitive degradation of the substrate under the basic reaction conditions.

With the optimized reaction conditions in hand, the substrate scope was examined on a 0.1 mmol scale. As shown in Table 4, benzylic bromides that bear a variety of functionalities at an arbitrary position could be used to give the corresponding tetrasubstituted allenes in good yields with high enantioselectivities that ranged from 93% to 95% (Table 4, entries 1–8). There was an apparent tendency for the regioselectivity to be improved substantially when a sterically encumbered benzylic bromide, such as 2-chlorobenzyl bromide, was utilized (Table 4, entries 5 and 7). In addition to benzylic bromides, allylic bromides (such as allyl bromide, methallyl bromide and cinnamyl bromide) were utilized (Table 4, entries 9–11). Use of propargyl bromide resulted in a higher regioselectivity compared to the selectivity using allyl bromide (Table 4, entry 12). Finally, the alkylation was conducted with other 1-alkylallene-1,3-dicarboxylates (**1k**–**1m**) to give the corresponding tetrasubstituted allenes regioselectively in good yields and enantioselectivities (Table 4, entries 13–17). The absolute configuration of **10f** was determined unambiguously by X-ray crystallographic analysis after the derivatization (see the Supplementary Information).

As a conventional transformation of the thus-obtained tetrasubstituted allenes, we implemented the *endo*-cyclization of the amino functionality to give the densely functionalized dihydropyrrole **11** via an axis-to-centre chirality transfer (Fig. 2a)[26,27]. This cyclization was facilitated in a stereospecific manner by the use of silver nitrate as the catalyst, which transferred the chirality of the allene in the tertiary amine moiety of the dihydropyrrole. In an additional study, we exploited the electron-deficient nature of the central carbon of the allene in the base-mediated intramolecular cyclization using the sulfonamide moiety (Fig. 2b). Although the chirality of the allene was destroyed in this reaction, a new stereogenic centre was generated diastereoselectively to give azetidine **12** with two vicinal stereocentres as an essentially single *cis*-isomer.

As for the tetrasubstituted allene **10a** synthesized by the alkylation, the methyl ester moiety was hydrolysed selectively, building on the steric bias of two ester moieties (Fig. 2c). The revealed carboxylic acid was then used as a linchpin to cyclize internally via the axis-to-centre chirality transfer to give furanone **13** with a tetrasubstituted carbon centre in 93% yield without a loss in enantioselectivity.

## Conclusion

Whereas a vast majority of chiral compounds are now within the reach of synthetic chemists by exercising asymmetric catalysis, chiral tetrasubstituted allenes have remained an elusive objective in this regard. To conquer this frontier, we introduced the concept of asymmetric functionalization of cumulenolates under phase-transfer catalysis. The two reactions examined, the alleno-Mannich-type reaction and the alkylation, raised the issues of either diastereoselectivity or regioselectivity, respectively. By elaborating new catalysts for each purpose, we succeeded in controlling these factors rigorously, in addition to controlling the enantioselectivities. Given the similarity of cumulenolate chemistry to the well-established enolate chemistry, it is envisaged that a variety of catalysts and electrophiles could be used in combination with cumulenolates to give chiral allenes.

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## Author contributions

T.H. conceived the study and wrote the manuscript. K.S. principally performed the experiments. F.T. and M.J.D. performed experiments on alkylation. K.M. organized the research. All authors contributed to designing the experiments, analysing data and editing the manuscript.

## Additional information

Supplementary information and chemical compound information are available in the online version of the paper. Reprints and permission information is available online at http://www.nature.com/reprints. Correspondence and requests for materials should be addressed to K.M.

## Competing financial interests

The authors declare no competing financial interests.