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Abnormal Behaviour of Allenylsulfones under Lu's Reaction Conditions: Synthesis of Enantiopure Polyfunctionalised Cyclopentenes

Alberto Núñez, Jr., M. Rosario Martín,* Alberto Fraile, and José L. García Ruano*[a]

Dedicated to Professor Saverio Florio on the occasion of his 70th birthday

Abstract: Formal [3+2] cycloadditions of 5-alkoxyfuran-2(5*H*)-ones **1** and **2** with allenylsulfones **3**–**5**, promoted by different nucleophiles, afford 3-alkoxy-5-arylsulfonyl-3,3a,6,6a-tetrahydro-1*H*-cyclopenta[*c*]furan-1-ones in good yields with complete control of both regio- and π-facial selectivity. The incorporation of a sulfinyl group on the furanone ring enhances the reactivity of the furanones and allows the synthesis of optically pure, bicyclic adducts in good yields. Allenylsulfones evolve through a different mechanism to that proposed for allenoates (Lu's reaction) and afford bicyclic adducts in which the sulfonyl group is joined to C-5. This has advantages on the stereochemical control of further reactions leading to enantiomerically pure polyfunctionalised cyclopentenes and cyclopentanes.

Keywords: asymmetric synthesis · cycloaddition · lactones · polycycles

Introduction

Cyclopentanes are common substructures present in a wide array of natural and non-natural products.[1] One of the most direct methods for obtaining five-membered cycles is the [3+2] cycloaddition of olefins with 1,3-dipoles generated by the conjugate addition of nucleophiles to allenes. In 1995, Lu reported the first [3+2] cycloaddition of electron-deficient olefins with the 1,3-dipoles generated from phosphines and 2-butynoates or 2,3-butadienoates[2] to afford cyclopentenes. Since this disclosure, cycloadditions of allenes to a wide range of polarised C=X bonds (X = N,[3] O,[4] and C[5–7]) have been reported. Intramolecular processes work in a highly regio- and stereoselective manner,[8] whereas the efficiency of intermolecular processes is usually lower and clearly dependent on the structure of the dipolarophile. Despite reports of the asymmetric version of Lu's intermolecular reaction,[9] these reactions have not been widely exploited in the synthesis of optically pure cyclopentanes because of their rather modest stereoselectivity.

We have previously showed that the endocyclic character of dipolarophilic double bonds significantly improves both the reactivity and regioselectivity of 1,3-dipolar cycloadditions,[10] therefore, furan-2(5*H*)-ones exhibit much better behaviour than acyclic unsaturated esters. Moreover, the incorporation of a sulfinyl group at C-3 of the furanone ring reinforces these tendencies and also improves the *endo*/*exo* selectivity.[11] All of these facts allowed the synthesis of enantiomerically pure, functionalised cyclopentenes by treating 3-*p*-tolylsulfinyl-5-ethoxyfuran-2(5*H*)-ones with the 1,3-dipole generated by conjugate addition of phosphines to 2,3-buta- and 2,3-pentadienoates. Adducts obtained in these reactions bear an alkoxy carbonyl group at the C-4 position.[12] The mechanistic proposal is that usually accepted for Lu's reaction, depicted in Scheme 1[13] (in our reactions: X = H, SOTol (Tol = tolyl)).

This excellent behaviour of the sulfinylfuranones in [3+2] cycloadditions, in general and more specifically with allenoates under Lu's reaction conditions, prompted us to study their reactions with other electron-deficient allenes[14,15] to widen the scope of these cycloadditions. We chose allenylsulfones for these studies because of the presumably excellent features of the resulting cyclopentenylsulfones as chiral synthons in Michael additions[16] and cycloadditions.[11c,17] Additionally, desulfonylation made us consider them as synthetic equivalents of the allenes devoid of other functional

[a] A. Núñez, Jr., Dr. M. R. Martín, Dr. A. Fraile, Prof. Dr. J. L. García Ruano
Departamento de Química Orgánica
Universidad Autónoma de Madrid
Cantoblanco, 28049 Madrid (Spain)
Fax: (+34) 914973966
E-mail: joseluis.garcia.ruano@uam.es

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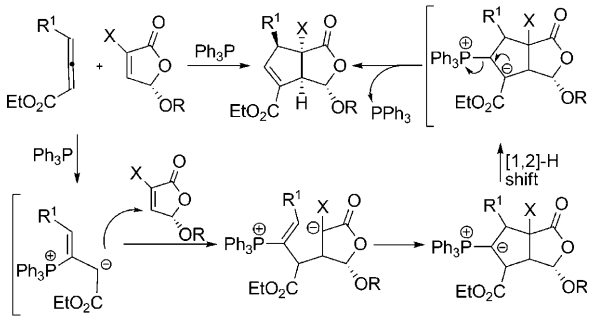
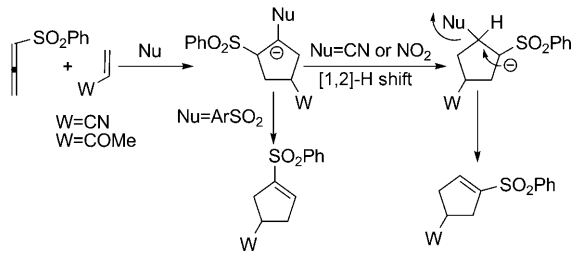


Scheme 1. Mechanism of Lu's reaction applied to furan-2(5*H*)-ones and allenoates.

groups, which are not susceptible to attack by the nucleophile generating the dipole and thus, unreactive. We also decided to explore the role of nucleophiles other than PPh_3 for activation of the allene. In this sense, we have used $NaSO_2Ar$ mainly because the arylsulfinate acts as a leaving group in the last step of Lu's reaction.

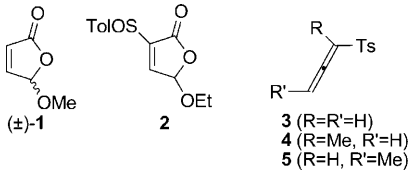
Allenylsulfones have been successfully used as dienophiles[18] and dipolarophiles,[19] as well as in Pauson–Kahnd reactions.[20] However, their behaviour as precursors of 1,3-dipoles has scarcely been exploited. The first report on the use of allenylsulfones as precursors of 1,3-dipoles was described by Padwa et al.[21] Reactions with acrylonitrile or methyl vinyl ketone, catalysed by ionic species (KCN, $NaNO_2$ or $NaSO_2Ph$) in polar solvent (THF), were studied. These reaction conditions are different to the standard ones reported several years later for Lu's reactions (phosphines as catalysts and benzene or toluene as solvent). The mechanistic proposal suggested by Padwa et al.[21] (Scheme 2) is



Scheme 2. Mechanistic proposal suggested by Padwa.[21]

similar to that postulated some years later for explaining the course of Lu's reaction. Therefore, these processes must be considered as the first reactions of allenyl sulfones with electron-deficient alkenes, catalysed by nucleophiles, affording cyclopentenyl sulfones.

Herein, we report the results obtained from the highly stereoselective reactions of furan-2(5*H*)-ones (±)-**1** and **2** with allenylsulfones **3–5** in the presence different nucleophilic catalysts, which yield the 5-sulfonyl-substituted adducts instead of the 4-derivatives expected from Lu's reaction mechanism (Scheme 1). Experiments aimed at clarifying the mechanistic evolution of the allenylsulfones and the transformation of the resulting adducts into polysubstituted cyclopentanes are also reported.

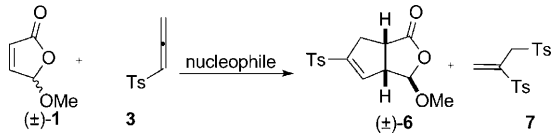


(±)-**1** **2** **3** (R=R'=H) **4** (R=Me, R'=H) **5** (R=H, R'=Me)

Results and Discussion

Cycloaddition reactions: Initially we explored the reaction of racemic furanone (±)-**1** with *p*-tolylsulfonylallene (**3**) under the best conditions reported for Lu's reaction of furanones with allenoates (catalytic amount of PPh_3, benzene as the solvent and room temperature).[12] A mixture of (±)-**6** and **7**[22] and other unidentified products, presumably polymers derived from **3**, were obtained. Compounds (±)-**6** and **7** were isolated and purified by column chromatography, with low isolated yield for compound (±)-**6** (Table 1, entry 1). Better results were obtained under the conditions of entry 2, compound (±)-**6** was isolated in 40% yield after 5 h, which could be slightly improved to 50% by the use 2.5 equiv of allene and an increase in the reaction time to 24 h (Table 1, entry 3). Complete transformation of the furanone was never achieved under these conditions, but unaltered (±)-**1** could be recovered in all of the experiments. The ^1H NMR signals corresponding to allene **3** could not be detected in the crude reaction spectra, despite the fact that **3** was used in excess, which suggests that **3** intervenes in reactions not involving the furanone (see below).

Table 1. Reactions of furanone (±)-**1** with sulfonyl allene **3**.



(±)-**1** **3** (±)-**6** **7**

Entry	Conditions[a]	Allene [equiv]	Nu [equiv]	*t* [h]	Ratio of **1/6/7**	Yield of **6** [%]
1	A	2.0	0.3	1	54:27:19	30
2	A	2.0	0.2	5	45:38:17	40
3	A	2.5	0.2	24	34:53:13	50
4	B	1.5	0.4	14	65:20:15	15
5	C	1.5	0.7	1	26:69:5	64
6	C	1.5	0.3	3	25:71:4	63

[a] A: PPh_3, benzene; B: *p*-$TolSO_2Na$, THF; C: *p*-$TolSO_2Na$, [18]crown-6, benzene.

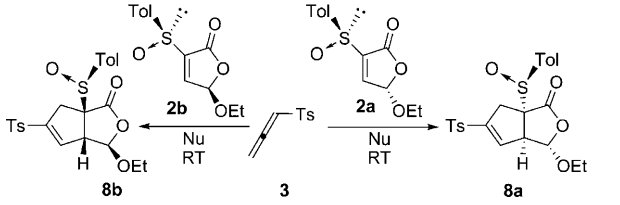
Only one cycloadduct, (±)-**6**, was detected by ^{1}H NMR spectroscopy, which indicates that (±)-**1** evolves with complete control of the regio- and facial selectivity. The *anti* arrangement between the cyclopentene ring and the OMe group suggests that the orientation of the latter is responsible for the stereocontrol. After a detailed NMR study, we concluded that compound (±)-**6** has the sulfonyl group at C-5 of the expected bicyclic system. Therefore, the obtained adduct is an isomer of the expected product (the 4-sulfonyl-substitututed analogue), predicted in accordance with the mechanism depicted in Scheme 1. This evidenced abnormal behaviour of the allenyl sulfone under the conditions of Lu. Padwa et al. had proposed a similar mechanism to that of Lu's reaction (see Scheme 2) after studying reactions of **3** with methyl vinyl ketone and acrylonitrile, under different conditions to those used by Lu (THF as the solvent and $NaSO_2Ar$ as the catalyst versus toluene or benzene as solvent and PPh_3 as the catalyst). We investigated the reaction of (±)-**1** with **3** under Padwa's conditions. Compound (±)-**6** was the only adduct, although it was obtained in poor yield (15%). To carry out the reaction in a non-polar solvent such as benzene, the addition of [18]crown-6 was required to increase the solubility of *p*-$TolSO_2Na$ (Table 1, entries 5 and 6). Under these conditions, we observed that both conversion of the dipolarophile (73%) and the yield of (±)-**6** (64%) were substantially improved, even when the amount of the allene **3** was reduced to 1.5 equiv and a sub-stoichiometric amount of *p*-$TolSO_2Na$ (0.3 or 0.7 equiv) was used.

We next studied the reactions of **3** with sulfinylfuranones **2a** and **2b** in the presence of PPh_3. Reactions with **2a** were complete at room temperature in short periods of time (Table 2, entries 1–3) and thus, indicate a substantial increase in the reactivity of the furanone as a consequence of the presence of the sulfinyl group. Consequently, the amount of disulfone **7** formed in these reactions was smaller than that obtained from reaction with **1** (Table 1). Adduct **8a** was isolated as the only diastereoisomer in yields higher than 65%. Reaction times were longer when the amount of PPh_3 was reduced (Table 2, entries 1 and 2) and the yield was slightly improved when the amount of allene **3** was increased (Table 2, entry 3). When *p*-$TolSO_2Na$ was used as the catalyst, the reactions in THF were improved by the addition of [18]crown-6 (Table 2, entries 4 and 5). However, the best results were observed in benzene/[18]crown-6 (Table 2, entries 6 and 7), with yields of **8a** up to 90%. This behaviour was similar to that observed for (±)-**1**. The use of $NaNO_2$ as a nucleophilic catalyst produced similar results to those obtained with PPh_3 (Table 2, entries 8 and 9), but worse than those obtained with *p*-$TolSO_2Na$. As in previous cases, the addition of [18]crown-6 slightly improved the results.

Reaction of allene **3** with sulfinylfuranone **2b**, catalysed by PPh_3, afforded the cycloadduct **8b** only, which was easily isolated by column chromatography in moderate yield (42%), lower than that obtained for **8a** (Table 2, entries 10 and 1).[23] Slightly higher yields of **8b** were obtained by using tolylsulfinate as the nucleophile in THF (Table 2, entry 11) but, unexpectedly, worse results were obtained when [18]crown-6 was added (Table 2, entry 12).

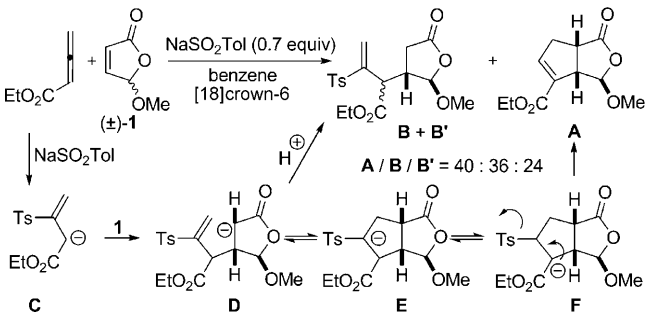
To check whether the use of $NaSO_2Ar$ as the catalyst (instead of PPh_3) also has advantages in normal Lu's reactions, we studied the reaction of ethyl allenoate with **1** in benzene, [18]crown-6 and *p*-$TolSO_2Na$. The expected Lu's product **A** is obtained as the only bicyclic compound (the yield is lower than that obtained with PPh_3) along with the monocyclic lactones **B** and **B′**. The formation of these products can be justified as depicted in Scheme 3. Protonation of **D** generates **B** and **B′**, whereas elimination of the sulfonyl group from **F** produces **A**. The higher stability of the α-sulfonylcarbanion **E** with respect to the ester enolates in equilibrium (**D** and **F** are both of similar stability) determines that the [1,2]-hydrogen migration was not particularly favoured, which decreases the yield of Lu's product. Therefore, it is noteworthy that

Table 2. Reactions of furanones **2a** and **2b** with allene **3**, catalysed by different nucleophiles.



Entry	Furanone	Allene [equiv]	Nu ([equiv])	*t* [h]	Product (yield [%])
1	**2a**	1.5	PPh_3 (0.3)[a]	1	**8a** (68)[d]
2	**2a**	1.5	PPh_3 (0.4)[a]	0.5	**8a** (65), **7** (15)
3	**2a**	2.0	PPh_3 (0.4)[a]	1.5	**8a** (71), **7** (21)
4	**2a**	1.5	$TolSO_2Na$ (0.4)[a]	7	**8a** (40)
5	**2a**	1.5	$TolSO_2Na$ (0.2)[b]	1	**8a** (64), **7** (12)
6	**2a**	1.5	$TolSO_2Na$ (0.4)[c]	0.5	**8a** (85)
7	**2a**	1.5	$TolSO_2Na$ (0.7)[c]	0.5	**8a** (90)
8	**2a**	1.5	$NaNO_2$ (1.5)[a]	2.5	**8a** (60)
9	**2a**	1.5	$NaNO_2$ (0.7)[b]	1	**8a** (75)
10	**2b**	1.5	PPh_3 (0.3)[a]	1	**8b** (42)
11	**2b**	1.5	$TolSO_2Na$ (0.4)[a]	2	**8b** (47)
12	**2b**	1.5	$TolSO_2Na$ (0.7)[c]	1	**8b** (31)

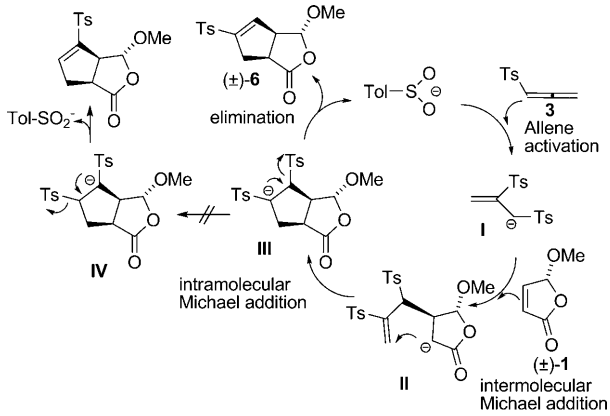
[a] THF used as solvent. [b] THF used as solvent and [18]crown-6. [c] Benzene used as solvent and [18]crown-6. [d] The crude reaction was an 87:13 mixture of **8a** and **7** (determined by ^{1}H NMR spectroscopy).



Scheme 3. Reaction of ethyl allenoate and (±)-**1** with $NaSO_2Tol$ as catalyst.

intermediate **D** evolved through two paths of similar significance (60:40), and in a different manner to that of intermediate **II** shown in Scheme 4.

Taking into account that disulfone **7** is obtained in variable amounts in many of these reactions, the formation of adducts (±)-**6** and **8** with *p*-TolSO$_2$Na as the catalyst could be explained as indicated in Scheme 4 for adduct (±)-**6**. The



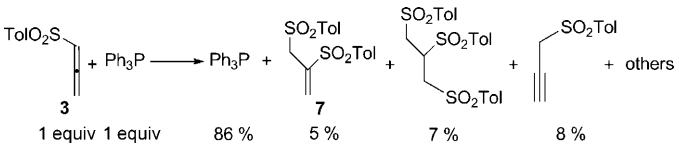
Scheme 4. Mechanistic proposal for reaction of allenylsulfones with furanones, catalysed by *p*-Tol-SO$_2$Na (Ts = tosyl).

addition of a sulfinate anion to **3** generates the anionic species **I**, which attacks furanone (±)-**1** to give lactone enolate **II**. Intermediate **II** can intramolecularly evolve into cyclopentene **III** through a 5-*endo*-trig attack onto the activated double bond, which is followed by elimination of one of the sulfonyl groups. This mechanism also accounts for the formation of bisulfone **7** (by protonation of **I**) and the fact that only sub-stoichiometric amounts of the promoter (Tol-SO$_2^-$) are required (0.2 equiv are enough for the reaction to be successful).

The stereochemistry of the resulting adducts is a consequence of the favoured approach of the anionic bisulfone **I** to the less-hindered face of furanones (the −OR group blocks one face of the electrophile). The strong reactivity of vinyl sulfones as Michael acceptors and the leaving-group ability of ArSO$_2^-$ determine the course of the last two steps. The fact that these reactions do not evolve through the route proposed for Lu's reaction (Scheme 1) can be explained by assuming that prototropy involved in the transformation of **III** into **IV** is much slower than the direct elimination of the sulfonyl group from **III**. Alternatively, the last two steps of the catalytic cycle (intramolecular Michael addition and elimination of ArSO$_2^-$) take place simultaneously, which precludes the formation of **IV** and, therefore, its conversion into the 4-sulfonyl adduct.

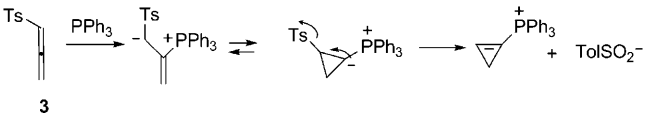
The formation of (±)-**6**, **7** and **8** when nucleophiles other than sulfinates are used as catalysts requires more intricate explanation. One plausible route would involve the formation of TolSO$_2^-$ by reaction of allene **3** with the nucleophile (PPh$_3$ or NaNO$_2$). Once formed, its reaction with allene **3** must be much faster than that of PPh$_3$ or nitrite and, therefore, the catalytic cycle in Scheme 4 must be preferred for the evolution for furanones.

The reaction of **3** with PPh$_3$ provided a complex mixture in which the phosphine was recovered in 86% yield, whereas the allenyl sulfone had completely disappeared (only 8% of its isomeric propargyl sulfone was recovered). Among the products, we could isolate bisulfone **7** (5%), propanetrisulfone (7%) and a significant amount (almost 40% of the initial mass of allene) of unidentified products, the NMR spectrum of which suggests a polymeric structure (Scheme 5).



Scheme 5. Transformation of allenylsulfone in the presence of PPh$_3$.

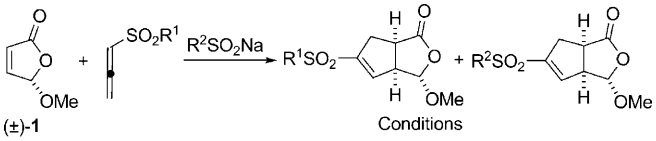
The formation of 1,2,3-trisulfonylpropane clearly demonstrates that Tol-SO$_2^-$ has been formed in the course of the reaction, but the way in which this formation takes place is not easily rationalised. One of the reviewers has suggested that the formation of sulfinate from sulfonylallene in the presence of PPh$_3$ can explain this as shown in Scheme 6.



Scheme 6. Possible explanation for the formation of TolSO$_2^-$ from (±)-**1** and PPh$_3$.

This possibility has been investigated, however, we could not isolate the phosphonium salts that support this hypothesis. Additionally, a similar pathway could contribute to sulfonyl scrambling when allenylsulfones are activated by arylsulfinates possessing a different aryl group.

The ratio of adducts is not strictly the allene/sulfinate ratio used in each case (Scheme 7). It is evident that the



1 equiv	1.2 equiv (R^1=Ph)	0.7 equiv (R^2=Tol)	A	85	15
1 equiv	1.2 equiv (R^1=Tol)	0.7 equiv (R^2=Ph)	A	85	15
1 equiv	1.2 equiv (R^1=Tol)	0.7 equiv (R^2=Ph)	B	61	39
1 equiv	1.2 equiv (R^1=Tol)	0.3 equiv (R^2=Ph)	B	78	22

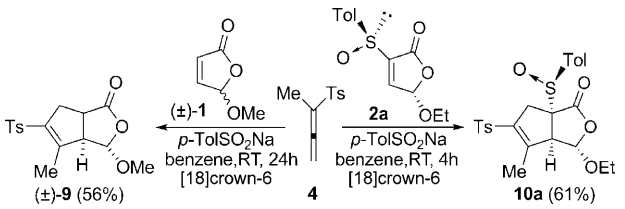
Conditions: A- Benzene and 18crown-6
B- Benzene/H_2O 10:1 and Bn(Bu)$_3$NBr (0.2 equiv)

Scheme 7. Reactions of (±)-**1** with Ar^{1}SO$_2$CH=CH$_2$ and Ar^{2}SO$_2$.

adduct retaining the group present in the allene is predominant.[24]

With the aim of supporting the mechanistic proposal depicted in Scheme 4 we have performed several experiments. Firstly, we generated anions of type **I** by reaction of vinylsulfones (**7** or the 2-phenylsulfonyl derivative) with base and checked if they reacted with (±)-**1** and **2a** to afford (±)-**6** and **8a** or the 4-phenylsulfonyl adducts. The results support the hypothesis that anions of type **I** can be considered as reaction intermediates. The yield obtained in this reaction was lower than those achieved starting from allenylsulfone. The reaction of **I** with its precursor, in competition with the reaction of **I** with the furanones, can explain these results. The proposed mechanism suggests that the use of arylsulfinates that contain a different aryl group to that bore by the starting allenylsulfone would produce a mixture of adducts, that differ in the nature of arylsulfonyl group joined to C-5 and this was also confirmed (see Scheme 7).

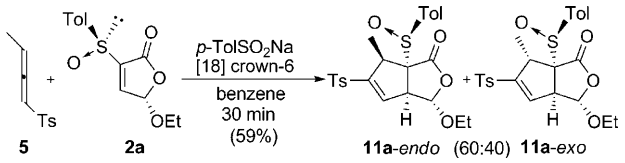
To date, there are only two antecedents of the reaction of 2-methyl-2,3-butadienoates and electron-deficient alkenes catalysed by phosphines and none of them evolved through a normal Lu's reaction mechanism. In 2007, Kwon and Tran reported that reactions of these allenes with benzylidenemalonitrile undergo a [4+2] annulation process through a different mechanism.[25] This year, Yu and co-workers reported the first example of the synthesis of cyclopentenes in moderate yields by [3+2] annulation of α-alkyl-substituted allenoates with fumarates.[13,26] According to the mechanism proposed in Scheme 4, we hypothesised that 1,1-disubstituted allenes such as **4**,[25,27] which would be unable to intervene in normal Lu's reactions (the proton required for prototropy is non-existent, see Scheme 1), would react according to this alternative mechanism to afford adducts with the methyl group at C-4. We verified this hypothesis by studying the reactions of **4** with (±)-**1** and **2a** (Scheme 8) under different conditions.



Scheme 8. Reactions of 1,1-disubstituted allene **4** with furanones **1** and **2a**.

The reaction of **4** with (±)-**1** in benzene, with PPh_3 as the nucleophile, did not work but the use of sulfinate in benzene/[18]crown-6 afforded racemic compound (±)-**9** in 56% yield after long reaction times (24 h). As expected, the reactivity of **4** was lower than that of **3** because the methyl group decreases the electrophilic character of the allene for both steric and electronic reasons. Under the same conditions, the reaction of **4** with **2a** required 4 h for completion (also a longer reaction time than that required for **3**) and afforded optically pure **10a** in 61% yield (Scheme 8). These results provide evidence for the positive influence exerted by the sulfinyl group on the reactivity of the alkene. The stereoselectivity was complete in both cases, which suggests that the configuration at C-5 of the furanone ring is responsible for the complete π-facial selectivity observed in these reactions. We have also studied the reaction between **4** and **2b**. The results were unsuccessful, which can be understood by taking into account the long reactions times required and the easier route of decomposition for furanone **2b**.[23]

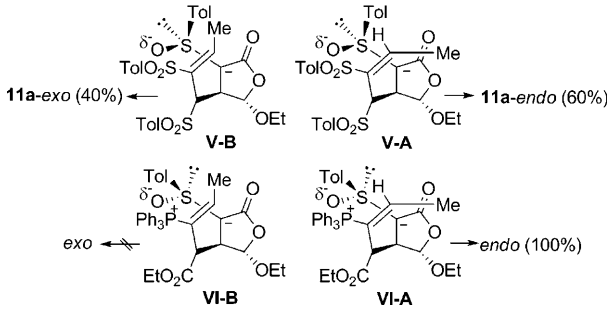
Finally, we studied the behaviour of allene **5**. Reactions with (±)-**1** did not give good results, regardless of the catalyst used. With sulfinate as the promoter and THF as the solvent, unaltered furanone **1** was recovered but allene **5** was isomerised into *p*-tolylsulfonyl-2-butyne. Reaction of **2a** with **5**, catalysed by PPh_3, gave a complex reaction mixture after long reaction times. The starting allene (partially isomerised to the corresponding alkyne) could be recovered, whereas the furanone **2a** was decomposed. When the reaction was catalysed by the sulfinate in benzene/[18]crown-6, it afforded a separable 60:40 mixture of C-4 epimers, **11a**-*endo* and **11a**-*exo*, after 30 min (Scheme 9). This reaction time, shorter than that required for **4** (4 h, Scheme 8), reveals the higher reactivity of **5** (which is expected for steric reasons).



Scheme 9. Reaction of 1,3-disubstituted allene **5** with furanone **2a**.

The fact that (±)-**1** was not able to react with **5**, despite the fact that **5** is more reactive than **4**, can be rationalised by assuming that the isomerisation of **5** to the corresponding alkyne (non-reactive) competes with the normal reaction over long reaction times. The reaction of **5** with **2b** was unsuccessful, and the lactone decomposed.

The low *endo* selectivity observed in the reactions of **2a** with **5** contrasts with the exclusive formation of the *endo* adduct observed in the reactions of **2a** with allenoate.[12] In this case, we postulated that intermediate **VI-A** was favoured with respect to **VI-B** because the latter was destabilised by the Me/SOTol interaction (see Scheme 10). However, this situation would be identical for allenylsulfone **5** (**V-B** will be destabilised with respect to **V-A** by the Me/SOTol interaction), yet the *endo*-selectivity is very low. This suggests that another interaction must be responsible for this behaviour. Taking into account the electrostatic attraction between the sulfinyl oxygen and P^+, the distance between the carbanionic centre and the activated double bond in the transition states (TS) derived from **VI-A** and **VI-B** can become short enough to determine that their steric differences (Me/SOTol versus H/SOTol) could be critical for the in-

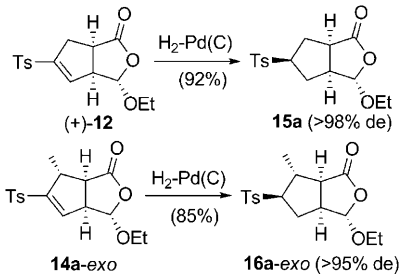


Scheme 10. *Endo/exo* selectivity in reactions of **2a** with allenyl sulfone or ethyl allenoate.

duction of complete *endo* selectivity. In contrast, the strong destabilising interaction of SO_2Ar/SOTol (from both a steric and electronic point of view) will determine a longer distance between the carbanionic centre and the activated double bond in the TS, resulting from **V-A** and **V-B**, thus minimising the magnitude of the steric interactions Me/SOTol and H/SOTol and reducing the stereoselectivity.

Transformation of the adducts: The synthetic usefulness of the obtained adducts depends on their ready desulfurisation reactions. Elimination of the sulfinyl group is important because it would allow optically pure sulfinyl furanones **2a** and **2b** to be considered as more reactive, chiral synthetic equivalents of racemic furanone (±)-**1**. Desulfinylation can be easily performed with aluminium amalgam. We first studied reactions of stereoisomers **8a** and **8b**, which afforded (+)-**12** and (−)-**12**, respectively, in good yields (Scheme 11). The enantiomeric relationship of these compounds reveals that the starting sulfoxides exhibit the opposite configuration at all of their stereogenic carbon atoms. The high optical purity of compounds (+)-**12** and (−)-**12**, established by chiral HPLC,[28] proves that these cycloadditions were completely stereoselective and that the configuration at the C-6a was maintained in the desulfinylation process. Under similar conditions, compounds **10a**, **11a-***exo* and **11a-***endo* were converted into enantiomerically pure compounds **13a**,[29] **14a-***exo* and **14a-***endo*, with good yields and without affecting the sulfonyl group (Scheme 11).

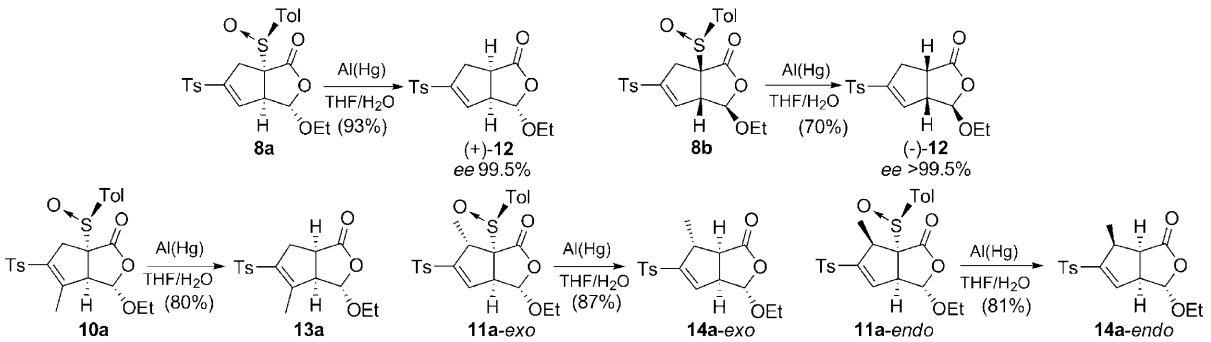
It is of interest to consider the optically pure, bicyclic vinylsulfones shown in Scheme 11 as chiral Michael acceptors, dienophiles and dipolarophiles. The change in position of the substituent (C-5), with respect to that observed in Lu's reactions (C-4), must favour the stereochemical control of reactions with nucleophiles.[30] The attacked position in the sulfones depicted in Scheme 11 (C-4) is closer to the bridge (therefore, more congested) than the position attacked in Lu's adducts (C-5). We have studied the catalytic hydrogenation of sulfones (+)-**12** and **14a-***exo*. The reaction is highly stereoselective and preferentially yields the diastereoisomer resulting from the approach of the reagent to the less-hindered convex face of the bicyclic structure (Scheme 12).



Scheme 12. Palladium-catalysed hydrogenation of compounds (+)-**12** and **14a**-*exo*.

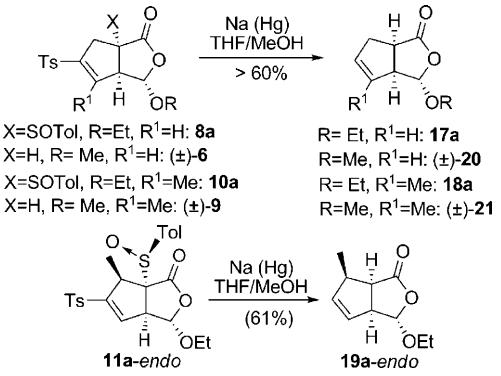
It is noteworthy that the stereocontrol (>95% diastereomeric excess (*de*)) observed in the hydrogenation of the bicyclic sulfones (+)-**12** and **14a-***exo*, with the sulfonyl group at C-5, is much higher than that obtained from analogous 4-esters (64% *de*).[12] This difference confirms that the position of the substituent in the bicyclic system (C-5 for sulfones and C-4 for esters) affects the stereoselectivity and increases the potential interest of adducts obtained from allenylsulfones.

To check whether sulfonylallenes can be considered as synthetic equivalents of non-substituted allenes, it was necessary to perform the reductive desulfonylation of the primary adducts. We treated **8a** with some of the reagents reported for the desulfonylation of vinylsulfones, such as Mg/MeOH and sodium amalgam.[31] The first reagent did not afford the expected results because of the opening of the furanone ring by the MeO^- anion. In contrast, compound **8a** was cleanly transformed into **17a** in 66% yield by treat-



Scheme 11. Selective reductive desulfinylation of primary adducts with aluminium amalgam.

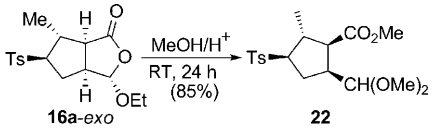
ment with 6% sodium amalgam in a 6:1 THF/MeOH mixture (Scheme 13). Their bicyclic structure predicts a strong control of the stereoselectivity in electrophilic additions and



Scheme 13. Desulfurisation of primary adducts with sodium amalgam.

cycloadditions characteristic of electron-rich alkenes. This reaction involves consecutive desulfinylation and desulfonylation, which is indicated through the detection by TLC of the desulfinylated compound (+)-**12** as an intermediate. The reaction was similarly successful when it was performed on adducts **10a**, **11a**-*endo,* (±)-**6** and (±)-**9** to yield compounds **18a**, **19a**-*endo*, (±)-**20** and (±)-**21**, respectively (Scheme 13).

The compounds shown in Schemes 11–13 can be considered as synthons of optically pure, masked α-formyl cyclopentene- and cyclopentanecarboxylic acids.[32,33] To illustrate this feature, we have transformed **16a**-*exo* into highly functionalised cyclopentane **22**, which contains four contiguous stereocentres (Scheme 14). We followed a mild, inexpensive and efficient one-pot protocol, previously reported by us, for the synthesis of acetals of 4-oxo-but-2-enoates from 5-alkoxyfuran-2(5*H*)-ones.[34]



Scheme 14. Ring opening of **16a**-*exo* to afford a masked α-formyl cyclopentanecarboxylate.

Structural and configurational assignments of all new compounds were based on detailed NMR spectroscopy studies (including two-dimensional NOESY, COSY and HMQC experiments). The absolute configuration of **15a** was unequivocally established from X-ray diffraction of this compound.[35] Details can be found in the Supporting Information.

Conclusion

Allenyl sulfones are activated by phosphines or sulfinates in their reactions with 5-alkoxyfuran-2(5*H*)-ones (and their 3-sulfinyl derivatives) to afford bicyclic adducts in a completely regioselective manner, with total control of the π-facial selectivity. The reaction mechanism is different to that proposed for Lu's reactions and yields 5-sulfonyl substituted adducts (instead of the expected 4-substituted adducts), which enables α-methyl sulfonylallenes to react. Desulfinylation and desulfonylation of the adducts yielded interesting synthons, the bicyclic structures of which efficiently control the stereoselectivity of subsequent reactions and allow the synthesis of optically pure, polyfunctionalised cyclopentyl derivatives.

Experimental Section

General: ^{1}H and ^{13}C NMR spectra were recorded at 300 (^{1}H) and 75.5 MHz [^{13}C, APT (Attached Proton Test)] on a Bruker AC-300 spectrometer in $CDCl_3$, if not otherwise specified. Chemical shifts (δ) are reported in ppm, coupling constants (J) in Hz. TLC were eluted on DC-Alufolien 60 F254 (Merck) and were viewed under UV light at 254 nm or after development with DNPH (2,4-dinitrophenylhydrazine and H_2SO_4, solution in ethanol) or MOPS (10% molybdophosphoric acid, solution in ethanol). Column chromatography was carried out on Merck silica gel 60 (230–400 mesh ASTM). IR spectra were recorded on a Bruker Vector 22 spectrometer as KBr pellets or as films between NaCl plates. HRMS were collected on an Applied Biosystems QSTAR Pulsar I (ESI) or a Waters VG AutoSpec (FAB). Melting points were recorded on a Gallenkamp apparatus in open capillary tubes and are uncorrected. Optical rotations were measured at room temperature (20–23 °C) on a Perkin–Elmer 241 MC polarimeter (concentration in g/100 mL). Microanalyses were carried out on a LECO CHNS-932 in the Laboratory of Elemental Analyses of SIDI, Universidad Autónoma de Madrid and were in good agreement with the calculated values. Enantiomeric excess (*ee*) was determined by HPLC, fitted with a Daicel Chiralpack AD column.

[3+2] Cycloaddition reactions

Procedure A: A solution of triphenylphosphine (see Table 1 and 2) in benzene (1.3 mL) was added to a stirred solution of furanone (±)-**1**, **2a** or **2b** (0.26 mmol) and *p*-tolyl-1-allenyl sulfone **3** (see Table 1 and 2) in benzene (1.3 mL), under positive pressure of argon, at room temperature. After the time indicated in each case the solvent was removed under vacuum and the crude reaction mixture was analysed by ^{1}H NMR spectroscopy and immediately purified by flash column chromatography. The eluent used for purification and the yield of the isolated product are indicated in each case.

Procedure B: To a stirred solution of furanone (±)-**1**, **2a** or **2b** in THF (0.1 M) *p*-tolyl allenyl sulfone **3**–**5** (1.5 equiv) and anhydrous *p*-$TolSO_2Na$ (0.3–0.7 equiv) were added at room temperature. The reaction was monitorised by TLC, the solvent was removed under vacuum and the crude reaction was analysed by ^{1}H NMR spectroscopy and immediately purified by flash column chromatography. The reaction time, the eluent used for purification and the yield of the isolated product are indicated in each case.

Procedure C: Allene (1.5 equiv), [18]crown-6 (0.3–0.7 equiv, see Tables 1 and 2) and anhydrous *p*-$TolSO_2Na$ (0.3–0.7 equiv) were added to a stirred solution of furanone in benzene (0.1 M) at room temperature. The reaction was monitored by TLC, the solvent was removed under vacuum and the crude reaction was analysed by ^{1}H NMR spectroscopy, before purification by flash column chromatography. The reaction time, the eluent used in the purification and the yield of obtained product are indicated in each case.

Compound (±)-6: Following procedure C with (±)-**1**, **3** and *p*-$TolSO_2Na$ (0.3 equiv) were stirred for 3 h. Purification by column chromatography (hexane/ethyl acetate, 2:1) as a colourless oil (63%). ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 7.73$ and 7.34 (AA′BB′ system, 4H), 6.60 (m, 1H), 5.28 (s,

1H), 3.59 (m, 1H), 3.49 (s, 3H), 3.37 (td, $J=8.7$, 1.9 Hz, 1H), 2.97 (ddt, $J=16.8$, 8.7, 2.5 Hz, 1H), 2.85 (dq, $J=16.8$, 1.9 Hz, 1H), 2.44 ppm (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta=177.8$ (C), 147.7 (C), 145.3 (C), 136.7 (CH), 135.1 (C), 130.1 (2×CH), 128.0 (2×CH), 105.4 (CH), 56.8 (CH_3), 53.8 (CH), 41.3 (CH), 34.8 (CH_2), 21.7 ppm (CH_3); IR (film): $\tilde{\nu}=$ 1779, 1596, 1318, 1153, 943 cm^{-1}; HRMS (EI): m/z calcd for $C_{15}H_{16}O_5S$: $[M]^+$ 308.0718; found: 308.0719.

Compound 8a: Following procedure A or C, with sulfinylfuranone **2a** and sulfonylallene **3**, compound **8a** was obtained after 1 and 0.5 h, respectively. Isolation by column chromatography (hexane/dichloromethane/diethyl ether, 4:2:1) gave a white solid (68%, procedure A; 85%, procedure C). Compound **8a** was also obtained from **2a** and but-2-yn-1-yl-4-methylphenyl sulfone after 2 h, following procedure C, in 60% yield. M.p. 70–72°C (with decomposition); $[\alpha]_D^{20}=+124.7$ ($c=0.60$ in $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): $\delta=7.66$ and 7.33 (AA′BB′ system, 4H), 7.47 and 7.30 (AA′BB′ system, 4H), 6.48 (m, 1H), 5.45 (d, $J=0.7$ Hz, 1H), 4.03 (m, 1H), 3.91 (m, 1H), 3.68 (m, 1H), 3.20 (dt, $J=16.8$, 2.2 Hz, 1H), 2.51 (dt, $J=16.8$, 1.9 Hz, 1H), 2.44 (s, 3H), 2.43 (s, 3H), 1.28 ppm (t, $J=7.1$ Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta=171.9$ (C), 146.3 (C), 145.5 (C), 143.3 (C), 135.3 (CH), 135.1 (C), 134.9 (C), 130.2 (CH), 129.6 (CH), 128.0 (CH), 125.8 (CH), 103.8 (CH), 72.7 (C), 66.0 (CH_2), 55.6 (CH), 33.2 (CH_2), 21.7 (CH_3), 21.6 (CH_3), 14.8 ppm (CH_3); IR (KBr): $\tilde{\nu}=$ 1771, 1596, 1321, 1206, 1156, 935 cm^{-1}; HRMS (FAB): m/z calcd for $C_{23}H_{25}O_6S_2$: 461.1093 $[M+H]^+$; found: 461.1110 $[M+H]^+$.

Compound 8b: Following general procedure A with sulfinylfuranone **2b** (0.19 mmol), sulfonylallene **3** (0.29 mmol) and PPh_3 (0.06 mmol in 1 mL) were stirred for 1 h. Isolation by column chromatography (hexane/dichloromethane/diethyl ether, 4:2:1) as a white solid (42%). M.p. 60–62°C (with decomposition); $[\alpha]_D^{20}=+115.8$ ($c=0.78$ in $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): $\delta=7.76$ and 7.36 (AA′BB′ system, 4H), 7.47 and 7.29 (AA′BB′ system, 4H), 6.57 (dt, $J=2.5$, 2.0 Hz, 1H), 5.11 (d, $J=1.5$ Hz, 1H), 3.70 (m, 1H), 3.40 (t, $J=2.0$ Hz, 2H), 3.26 (q, $J=7.1$ Hz, 2H), 2.45 (s, 3H), 2.40 (s, 3H), 0.84 ppm (t, $J=7.1$ Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta=172.3$ (C), 145.6 (2×C), 143.0 (C), 136.3 (CH), 134.8 (2×C), 130.3 (CH), 129.7 (CH), 128.1 (CH), 125.7 (CH_3), 105.3 (CH), 75.7 (C), 65.8 (CH_2), 51.7 (CH), 39.0 (CH_2), 21.7 (CH_3), 21.5 (CH_3), 14.3 ppm (CH_3); IR (KBr): $\tilde{\nu}=1765$, 1626, 1596, 1353, 1155, 1085, 929 cm^{-1}; elemental analysis calcd (%) for $C_{23}H_{24}O_6S_2$: C 59.98, H 5.25, S 13.92; found: C 59.69, H 5.36, S 13.48.

Compound (±)-**9**: Following procedure C, furanone (±)-**1**, allene **4** (1.5 equiv), p-$TolSO_2Na$ (0.7 equiv) and [18]crown-6 (0.7 equiv) were stirred for 24 h. Purification by column chromatography (hexane/ethyl acetate, 2:1) gave **9** as a white solid (56%). M.p. 148–150°C; ^{1}H NMR (300 MHz, $CDCl_3$): $\delta=7.73$ and 7.33 (AA′BB′ system, 4H), 5.26 (s, 1H), 3.50 (s, 3H), 3.44 (m, 1H), 3.18 (td, $J=8.2$, 2.3 Hz, 1H), 2.96 (m, 2H), 2.43 (s, 3H), 2.24 ppm (brs, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta=178.0$ (C), 147.0 (C), 144.9 (C), 137.4 (C), 137.0 (C), 130.0 (2×CH), 127.4 (2×CH), 104.7 (CH), 59.6 (CH), 56.7 (CH_3), 38.4 (CH), 36.9 (CH_2), 21.6 (CH_3), 13.4 ppm (CH_3); IR (KBr): $\tilde{\nu}=1774$, 1632, 1319, 1149, 936 cm^{-1}; elemental analysis calcd (%) for $C_{16}H_{18}O_5S$: C 59.61, H 5.63, S 9.95; found: C 59.63, H 5.66, S 9.91.

Compound 10a: Following procedure C, furanone **2a**, allene **4** (1.5 equiv), p-$TolSO_2Na$ (0.7 equiv) and [18]crown-6 (0.7 equiv) were stirred for 4 h. Purification by column chromatography (hexane/ethyl acetate, 2:1) gave **10a** as a white solid (61%). M.p. 135–137°C (with decomposition); $[\alpha]_D^{20}=+108.5$ ($c=0.60$ in $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): $\delta=7.64$ (m, 2H), 7.47 (m, 2H), 7.32–7.27 (m, 4H), 5.42 (d, $J=$ 1.0 Hz, 1H), 3.90 (m, 1H), 3.88 (m, 1H), 3.69 (m, 1H), 3.17 (m, 1H), 2.60 (m, 1H), 2.44 (s, 3H), 2.43 (s, 3H), 2.17 (brs, 3H), 1.28 ppm (t, $J=$ 7.1 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta=172.1$ (C), 146.2 (C), 145.0 (C), 143.2 (C), 136.9, (C) 136.1 (C), 135.2 (C), 130.1 (CH), 129.6 (CH), 127.4 (CH), 125.7 (CH), 103.3 (CH), 69.7 (C), 65.9 (CH_2), 60.7 (CH), 35.6 (CH_2), 21.6 (2×CH_3), 14.9 (CH_3), 13.4 ppm (CH_3); IR (KBr): $\tilde{\nu}=$ 1774, 1638, 1596, 1322, 1154, 961 cm^{-1}; elemental analysis calcd (%) for $C_{24}H_{26}O_6S_2$: C 60.74, H 5.52, S 13.51; found: C 60.48, H 5.58, S 13.35.

Compound 11: Following procedure C, compound **2a**, **5** (1.5 equiv), p-$TolSO_2Na$ (0.7 equiv) and [18]crown-6 (0.7 equiv) were stirred for 30 min. Isomers **11a** were separated by column chromatography (hexane/ethyl acetate, 2:1).

Compound 11a-*endo*: Major component, white solid (31%); $R_f=0.30$ (hexane/ethyl acetate 3:2); m.p. 102–104°C (with decomposition); $[\alpha]_D^{20}=$ +93.3 ($c=1.6$ in $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): $\delta=7.62$ and 7.33 (AA′BB′ system, 4H), 7.50 and 7.25 (AA′BB′ system, 4H), 6.30 (dd, $J=$ 2.8, 1.9 Hz, 1H), 5.29 (d, $J=2.2$ Hz, 1H), 3.96 (m, 1H), 3.87 (m, 1H), 3.62 (m, 1H), 3.41 (m, 1H), 2.46 (s, 3H), 2.42 (s, 3H), 1.24 (t, $J=7.1$ Hz, 3H), 0.93 ppm (d, $J=7.3$ Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta=169.1$ (C), 150.1 (C), 145.3 (C), 143.3 (C), 135.8 (C), 135.4 (CH), 134.4 (C), 130.0 (2×CH), 129.6 (2×CH), 128.1 (2×CH), 126.2 (2×CH), 103.8 (CH), 76.3 (C), 66.1 (CH_2), 54.1 (CH), 41.6 (CH), 21.7 (CH_3), 21.5 (CH_3), 15.7 (CH_3), 14.8 ppm (CH_3); IR (KBr): $\tilde{\nu}=1771$, 1596, 1318, 1155, 939 cm^{-1}; elemental analysis calcd (%) for $C_{24}H_{26}O_6S_2$: C 60.74, H 5.52, S 13.51; found: C 60.60, H 5.55, S 13.32.

Compound 11a-*exo*: Minor component, white solid (28%); $R_f=0.20$ (hexane/ethyl acetate 3:2); m.p. 136–138°C (with decomposition); $[\alpha]_D^{20}=$ +155.0 ($c=1.0$ in $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): $\delta=7.69$ and 7.34 (AA′BB′ system, 4H), 7.61 and 7.29 (AA′BB′ system, 4H), 6.57 (dd, $J=$ 2.1, 0.9 Hz, 1H), 5.02 (d, $J=0.8$ Hz, 1H), 3.48 (m, 1H), 3.43 (td, $J=2.1$, 0.8 Hz, 1H), 3.23 (q, $J=7.1$ Hz, 2H), 2.44 (s, 3H), 2.41 (s, 3H), 1.73 (d, $J=7.0$ Hz, 3H), 0.88 ppm (t, $J=7.0$ Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta=170.8$ (C), 151.6 (C), 145.5 (C), 143.5 (C), 135.6 (C), 135.5 (CH), 135.4 (C), 130.3 (2×CH), 129.8 (2×CH), 127.9 (2×CH), 127.3 (2×CH), 103.9 (CH), 74.0 (C), 65.9 (CH_2), 52.9 (CH), 47.3 (CH), 21.7 (CH_3), 21.6 (CH_3), 16.4 (CH_3), 14.3 ppm (CH_3); IR (KBr): $\tilde{\nu}=1754$, 1321, 1153, 1086, 924 cm^{-1}; MS (FAB): m/z: 475 $[M+H]^+$; HRMS (FAB): m/z calcd for $C_{24}H_{27}O_6S_2$: 475.1249 $[M+H]$; found: 475.1259 $[M+H]^+$.

General procedure for reductive desulfinylation with aluminium amalgam: Aluminium amalgam (obtained from the amount of aluminium kitchen foil indicated in each case) was added in small portions to a vigorously stirred 0.01 M solution of sulfinylcycloadduct **8a**, **8b**, **10a**, **11a**-*endo* or **11a**-*exo* in a 9:1 mixture of THF/water. The reaction was monitored by TLC and when the starting material was no longer observed the reaction mixture was filtered through Celite and the solid was washed with dichloromethane. The solvent was removed under reduced pressure and the product was isolated by column chromatography with the eluent indicated in each case.

Compound (+)-12: After following the general desulfination procedure with cycloadduct **8a** (0.15 mmol, 70 mg) and aluminium foil (277 mg), isolation by column chromatography (hexane/ethyl acetate, 3:1) gave (+)-**12** as a white solid (93%). M.p. 110–112°C; $[\alpha]_D^{20}=+98.3$ ($c=0.88$ in $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): $\delta=7.74$ and 7.35 (AA′BB′ system, 4H), 6.61 (m, 1H), 5.38 (s, 1H), 3.86 (m, 1H), 3.67–3.56 (m, 2H), 3.39 (td, $J=8.7$, 1.9 Hz, 1H), 2.98 (ddt, $J=16.8$, 8.7, 2.5 Hz, 1H), 2.85 (dq, $J=$ 16.8, 1.9 Hz, 1H), 2.44 (s, 3H) 1.23 ppm (t, $J=7.0$ Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta=177.9$ (C), 147.6 (C), 145.3 (C), 136.8 (CH), 135.2 (C), 130.2 (CH), 128.1 (CH), 104.3 (CH), 65.4 (CH_2), 53.9 (CH), 41.5 (CH), 34.8 (CH_2), 21.7 (CH_3), 14.8 ppm (CH_3); IR (film): $\tilde{\nu}=1778$, 1596, 1351, 1153, 940 cm^{-1}; elemental analysis calcd (%) for $C_{16}H_{18}O_5S$: C 59.61, H 5.63, S 9.95; found: C 59.66, H 5.63, S 9.96; HPLC (70:30 hexane/isopropyl alcohol, flow 1 mL min^{-1}): $ee=99.5\%$, retention time (t_R) = 11.9 min.

Compound (−)-12: After following the general desulfination procedure with cycloadduct **8b** (0.13 mmol, 60 mg) and aluminium foil (300 mg), isolation by column chromatography (hexane/ethyl acetate, 3:1) gave (−)-**12** as a white solid (70%). M.p. 106–108°C; $[\alpha]_D^{20}=-96.4$ ($c=0.70$ in $CHCl_3$); elemental analysis calcd (%) for $C_{16}H_{18}O_5S$: C 59.61, H 5.63, S 9.95; found: C 59.55, H 5.56, S 10.27; HPLC (70:30 hexane/isopropyl alcohol, flow 1 mL min^{-1}): $ee=99.5\%$, $t_R=9.5$ min.

Compound 13a: After following the general desulfination procedure with cycloadduct **10a** (0.15 mmol, 70 mg) and aluminium foil (277 mg), isolation by column chromatography (hexane/ethyl acetate, 3:1) gave **13a** as a white solid (80%). M.p. 110–112°C; $[\alpha]_D^{20}=+59.2$ ($c=0.60$ in $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): $\delta=7.72$ and 7.33 (AA′BB′ system, 4H), 5.36 (s, 1H), 3.85 (dq, $J=9.4$, 7.1 Hz, 1H), 3.62 (dq, $J=9.4$, 7.1 Hz, 1H), 3.44 (m, 1H), 3.20 (td, $J=8.5$, 2.1 Hz, 1H), 2.96 (m, 2H), 2.43 (s, 3H), 2.24 (brs, 3H), 1.23 ppm (t, $J=7.1$ Hz, 3H); ^{13}C NMR (75 MHz,

$CDCl_3$): δ = 178.1 (C), 147.1 (C), 144.9 (C), 137.3 (C), 137.0 (C), 130.0 (CH), 127.4 (CH), 103.6 (CH), 65.3 (CH_2), 59.7 (CH), 38.6 (CH), 36.9 (CH_2), 21.6 (CH_3), 14.8 (CH_3), 13.4 ppm (CH_3); IR (KBr): $\tilde{\nu}$ = 1777, 1632, 1318, 1148, 938 cm^{-1}; elemental analysis calcd (%) for $C_{17}H_{20}O_5S$: C 60.70, H 5.99, S 9.53; found: C 60.71, H 6.03, S 9.62.

Compound 14a-*endo*: After following the general desulfination procedure with cycloadduct **11a-*endo*** (0.15 mmol, 71 mg) and aluminium foil (235 mg), isolation by column chromatography (hexane/ethyl acetate, 3:1) gave **14a**-*endo* as a colourless, gummy solid (81%). $[\alpha]_D^{20}$ = +24.9 (c = 1.9 in $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.74 and 7.34 (AA′BB′ system, 4H), 6.61 (m, 1H), 5.29 (d, J = 1.4 Hz, 1H), 3.86 (m, 1H), 3.60 (m, 1H), 3.52 (m, 1H), 3.42–3.33 (m, 2H), 2.44 (s, 3H), 1.27 (d, J = 6.8 Hz, 3H), 1.22 ppm (t, J = 7.0 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 174.4 (C), 151.0 (C), 145.0 (C), 137.9 (CH), 136.4 (C), 130.0 (CH), 128.0 (CH), 103.9 (CH), 65.4 (CH_2), 52.5 (CH), 45.7 (CH), 41.4 (CH), 21.6 (CH3), 14.8 (CH_3), 14.6 ppm (CH_3); IR (film): $\tilde{\nu}$ = 1776, 1597, 1315, 1052, 948 cm^{-1}; HRMS (ESI): m/z calcd for $C_{17}H_{21}O_5S$: 337.1104 $[M+H]^+$; found: 337.1120 $[M+H]^+$; m/z calcd for $C_{17}H_{20}O_5NaS$: 359.0923 $[M+Na]^+$; found: 359.0920 $[M+Na]^+$.

Compound 14a-*exo*: After following the general desulfination procedure with cycloadduct **11a-*exo*** (0.12 mmol, 58 mg) and aluminium foil (80 mg), isolation by column chromatography (hexane/ethyl acetate, 3:1) gave **14a**-*exo* as a colourless, gummy solid (87%). $[\alpha]_D^{20}$ = +105.0 (c = 1.4 in $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.71 and 7.33 (AA′BB′ system, 4H), 6.59 (brs, 1H), 5.36 (s, 1H), 3.84 (m, 1H), 3.65–3.55 (m, 2H), 3.13 (q, J = 7.1 Hz, 1H), 2.97 (d, J = 7.1 Hz, 1H), 2.43 (s, 3H), 1.31 (d, J = 7.1 Hz, 3H), 1.22 ppm (t, J = 7.1 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 177.3 (C), 152.3 (C), 145.1 (C), 136.8 (CH), 135.8 (C), 130.1 (CH), 127.9 (CH), 104.0 (CH), 65.3 (CH_2), 51.9 (CH), 50.1 (CH), 43.7 (CH), 21.7 (CH_3), 20.4 (CH_3), 14.8 ppm (CH_3); IR (film): $\tilde{\nu}$ 1775, 1597, 1316, 1151, 945 cm^{-1}; HRMS (ESI): m/z calcd for $C_{17}H_{21}O_5S$: 337.1104 $[M+H]^+$; found: 337.1121 $[M+H]^+$; m/z calcd for $C_{17}H_{20}O_5NaS$: 359.0923 $[M+Na]^+$; found: 359.0917 $[M+Na]^+$.

Catalytic hydrogenation (15a): A solution of (+)-**12** (0.17 mmol) in ethyl acetate (3 mL) containing 10% Pd(C) (25 mg) was stirred under positive pressure of hydrogen at room temperature for 1 h. The suspension was filtered through Celite, the solid residue was washed with ethyl acetate and the solvent was removed in vacuo. Compound **15a** was recrystallised from dichloromethane/diethyl ether as a white solid (92%). M.p. 198–200 °C; $[\alpha]_D^{20}$ = +80.8 (c = 1.0 in $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.76 and 7.36 (AA′BB′ system, 4H), 5.31 (d, J = 0.7 Hz, 1H), 3.86 (m, 1H), 3.60 (m, 1H), 3.54 (m, 1H), 3.19 (m, 1H), 2.81 (m, 1H), 2.45 (s, 3H), 2.38 (m, 1H), 2.29 (m, 1H), 2.00 (dt, J = 13.3, 10.2 Hz, 1H), 1.21 ppm (t, J = 7.0 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 177.9 (C), 145.2 (C), 134.8 (C), 130.0 (CH), 128.6 (CH), 106.0 (CH), 65.3 (CH_2), 64.9 (CH), 47.0 (CH), 42.9 (CH), 30.3 (CH_2), 29.7 (CH_2), 21.6 (CH), 14.9 ppm (CH_3); IR (KBr): $\tilde{\nu}$ = 1756, 1322, 1142, 1043, 939 cm^{-1}; elemental analysis calcd (%) for $C_{16}H_{20}O_5S$: C 59.24, H 6.21, S 9.88; found: C 59.10, H 6.12, S 9.94.

Compound 16a-*exo*: Following the above procedure, a solution of **14a-*exo*** (23 mg, 0.07 mmol) in ethyl acetate (1.5 mL) and 10% Pd(C) (10 mg) was stirred for 2 h. Purification by column chromatography (hexane/ethyl acetate, 2:1) gave **16a**-*exo* as a white solid (85%). M.p. 138–139 °C; $[\alpha]_D^{20}$ = +48.8 (c = 0.5 in $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.76 and 7.36 (AA′BB′ system, 4H), 5.24 (s, 1H), 3.83 (m, 1H), 3.57 (m, 1H), 3.16 (m, 1H), 2.85–2.63 (m, 3H,), 2.46 (s, 3H), 2.31 (m, 1H), 1.96 (m, 1H), 1.19 (t, J = 7.2 Hz, 3H), 1.15 ppm (d, J = 6.8 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 177.4 (C), 145.2 (C), 134.9 (C), 130.0 (CH), 128.7 (CH), 106.0 (CH), 71.6 (CH), 65.3 (CH_2), 51.6 (CH), 45.4 (CH), 39.0 (CH), 31.3 (CH_2), 21.6 (CH_3), 21.2 (CH_3), 14.8 ppm (CH_3); IR (KBr): $\tilde{\nu}$ = 1771, 1598, 1301, 1284, 1146, 927 cm^{-1}; elemental analysis calcd (%) for $C_{17}H_{22}O_5S$: C 60.33, H 6.55; found: C 60.30, H 6.58.

General procedure for reductive desulfination and desulfonylation with sodium amalgam: NH_4Cl and 6% sodium amalgam (see individual entries for quantities) were added in small portions to a 0.01 M solution of sulfone **8a**, **10a**, **11a**-*endo*, (±)-**6** or (±)-**9** in anhydrous THF, cooled in an ice bath. After the addition of the first amalgam portions, anhydrous MeOH (see individual entries for volume) was added. The reaction was monitored by TLC and sodium amalgam was sequentially added in small portions until no starting material remained or the corresponding sulfinyl compounds were observed. The reaction mixture was filtered through Celite and the solid residue was washed with dichloromethane. The filtrates were combined and the solvent was removed under reduced pressure.

Compound 17a: After following the general procedure above with **8a** (93 mg, 0.20 mmol), NH_4Cl (1 g), methanol (3.3 mL) and 6% sodium amalgam (1 g), purification by column chromatography (hexane/diethyl ether, 6:1) gave **17a** as a colourless oil (66%). $[\alpha]_D^{20}$ = +139.0 (c = 0.30 in $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 5.86 (dq, J = 5.7, 2.2 Hz, 1H), 5.68 (dq, J = 5.7, 2.1 Hz, 1H), 5.30 (s, 1H), 3.88 (m, 1H), 3.61 (m, 1H), 3.43 (m, 1H), 3.27 (td, J = 7.2, 3.4 Hz, 1H), 2.75 (m, 2H), 1.24 ppm (t, J = 7.1 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 180.4 (C), 133.2 (CH), 128.0 (CH), 105.9 (CH), 65.0 (CH_2), 54.1 (CH), 41.0 (CH), 36.6 (CH_2), 14.9 ppm (CH_3); IR (film): $\tilde{\nu}$ = 1777, 1646, 1351, 1240, 1113, 952, 931 cm^{-1}; elemental analysis calcd (%) for $C_9H_{12}O_3$: C 64.27, H 7.19; found: C 64.31, H 7.21.

Compound 18a: After following the general procedure above with **10a** (60 mg, 0.13 mmol), NH_4Cl (650 mg), MeOH (1.9 mL) and 6% sodium amalgam (1.6 g), purification by column chromatography (hexane/diethyl ether, 9:1) gave **18a** as a colourless oil (63%). $[\alpha]_D^{20}$ = +45.3 (c = 0.60 in $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 5.42 (m, 1H), 5.33 (s, 1H), 3.88 (m, 1H), 3.62 (m, 1H), 3.24 (m, 2H), 2.67 (m, 2H), 1.78 (brs, 3H), 1.25 ppm (t, J = 7.1 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 180.6 (C), 136.3 (C), 127.1 (CH), 104.3 (CH), 64.9 (CH_2), 56.7 (CH), 41.7 (CH), 35.9 (CH_2), 14.9 (CH_3), 14.3 ppm (CH_3); IR (film): $\tilde{\nu}$ = 1760, 1655, 1234, 1105, 928 cm^{-1}; HRMS (ESI): m/z calcd for $C_{10}H_{15}O_3$: 183.1015 $[M+H]^+$; found: 183.1026 $[M+H]^+$; m/z calcd for $C_{10}H_{14}O_3Na$: 205.0835 $[M+Na]^+$; found: 205.0838 $[M+Na]^+$.

Compound 19a-*endo*: After following the general procedure above with **11a-*endo*** (42 mg, 0.09 mmol), NH_4Cl (450 mg), MeOH (1.3 mL) and 6% sodium amalgam (1.2 g), purification by column chromatography (hexane/diethyl ether, 6:1) gave **19a**-*endo* as a colourless oil (61%). $[\alpha]_D^{20}$ = +3.8 (c = 0.40 in $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 5.71 (dt, J = 5.6, 2.0 Hz, 1H), 5.63 (dt, J = 5.6, 2.2 Hz, 1H), 5.20 (d, J = 1.1 Hz, 1H), 3.87 (dq, J = 9.5, 7.0 Hz, 1H), 3.59 (dq, J = 9.5, 7.0 Hz, 1H), 3.47 (m, 1H), 3.28 (dd, J = 9.1, 8.0 Hz, 1H), 3.20 (m, 1H), 1.24 (t, J = 7.0 Hz, 3H), 1.23 ppm (d, J = 7.2 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 176.6 (C), 139.4 (CH), 126.7 (CH), 105.6 (CH), 64.9 (CH_2), 55.0 (CH), 44.5 (CH), 42.3 (CH), 16.0 (CH_3), 14.9 ppm (CH_3); IR (film): $\tilde{\nu}$ = 1775, 1646, 1166, 1117, 950 cm^{-1}; HRMS (ESI): m/z calcd for $C_{10}H_{15}O_3$: 183.1015 $[M+H]^+$; found: 183.1022 $[M+H]^+$; m/z calcd for $C_{10}H_{14}O_3Na$: 205.0835 $[M+Na]^+$; found: 205.0837 $[M+Na]^+$.

Compound (±)-20: After following the general procedure above with (±)-**6** (64 mg, 0.21 mmol), NH_4Cl (1 g), methanol (3 mL) and 6% sodium amalgam (1.8 g), purification by column chromatography (hexane/diethyl ether, 6:1) gave (±)-**20** as a colourless oil (60%). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 5.86 (dq, J = 5.7, 2.2 Hz, 1H), 5.68 (dq, J = 5.7, 2.1 Hz, 1H), 5.20 (s, 1H), 3.51 (s, 3H), 3.43 (m, 1H), 3.25 (td, J = 7.2, 3.4 Hz, 1H), 2.75 ppm (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 180.3 (C), 133.3 (CH), 127.9 (CH), 107.0 (CH), 56.5 (CH_3), 54.0 (CH), 40.9 (CH), 36.6 ppm (CH_2).

Compound (±)-21: After following the general procedure above with (±)-**9** (64 mg, 0.20 mmol), NH_4Cl (1 g), methanol (3 mL) and 6% sodium amalgam (1.8 g), purification by column chromatography (hexane/diethyl ether, 6:1) gave (±)-**21** as a colourless oil (60%). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 5.43 (m, 1H), 5.22 (s, 1H), 3.51 (s, 3H), 3.24 (m, 2H), 2.68 (m, 2H), 1.68 ppm (brs, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 180.5, 136.2, 127.1, 105.5, 56.6, 56.5, 41.5, 35.8, 14.3 ppm.

Synthesis of acetal-ester 22: A solution of **16a**-*exo* (17 mg, 0.05 mmol) in methanol (2 mL) containing 1% sulfuric acid was allowed to stand for 24 h at room temperature. The reaction mixture was neutralised with solid $NaHCO_3$ (60 mg) and stirred for 30 min. The solid was filtered off and the solvent was removed in vacuo. The crude ester acetal was purified by column chromatography (hexane/diethyl ether, 1:1) to give **22** as a colourless oil (82%). $[\alpha]_D^{20}$ = −26.5 (c = 1.0 in $CHCl_2$); ^{1}H NMR (300 MHz, CD_2Cl_2): δ = 7.76 and 7.39 (AA′BB′ system, 4H), 4.32 (d, J =

8.1 Hz, 1H), 3.63 (s, 3H), 3.26 (s, 3H), 3.20 (s, 3H), 3.08 (q, $J=9.0$ Hz, 1H), 2.69 (m, 1H), 2.51 (m, 2H), 2.45 (s, 3H), 2.13 (m, 1H), 1.94 (m, 1H), 1.03 ppm (d, $J=6.6$ Hz, 3H); ^{13}C NMR (75 MHz, CD_2Cl_2): $\delta=173.3$ (C), 145.5 (C), 136.3 (C), 130.4 (CH), 129.1 (CH), 104.6 (CH), 69.8 (CH), 54.5 (CH_3), 53.8 (CH), 53.7 (CH_3), 52.0 (CH_3) 43.2 (CH), 39.0 (CH), 30.2 (CH_2), 21.9 (CH_3), 19.8 ppm (CH_3); IR (film): $\tilde{\nu}=1732$, 1597, 1301, 1285, 1145, 1058 cm^{-1}; HRMS (ESI): m/z calcd for $C_{18}H_{26}O_6SNa$: 393.1342 $[M+Na]^+$; found: 393.1356 $[M+Na]^+$.

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[23] The low yield obtained from reaction of **2b**, compared with that obtained from **2a**, could be a consequence of the lower stability of substrate **2b** and adduct **8b** in relation to the corresponding **a** isomers, under the reaction conditions.
[24] We have attributed this behaviour to solubility problems with $NaSO_2Ar$ in benzene, which determines that the actual concentration of this sulfinate is lower than that expected from the added amount. When the reactions are performed under phase-transfer conditions (conditions B in Scheme 7), the solubility problems are presumed to be reduced and the ratio of adducts (SO_2Tol/SO_2Ph) was similar to that of the starting allene/sulfinate ratio.
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[29] Although no adducts of **2b** with allenes **4** and **5** were obtained, the enantiomers of **13a** and **14a** could be accessible by this route.

[30] Preliminary studies of these reactions have been performed. Reaction of racemic (±)-**6** with diethyl malonate only provides one diastereoisomer, which results from the approach of the nucleophile to the convex face of the bicyclic system. The application of these products to the synthesis of a range of known and novel structures is under investigation.

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[35] CCDC-755291 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

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