Facial Stereoselectivity in Lithium Dialkylcuprate Additions to Functionalized endo-Tricyclo[5.2.1.0^2,6]decadienones

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Abstract: Lithium dialkylcuprate additions to a variety of 6-functionalized endo-tricyclo[5.2.1.0^2,6]decadienones 4 are described. The introduction of an alkyl or aryl ether function containing oxygen, sulfur or selenium leads to a remarkably high endo-stereoselectivity. The observed facial stereoselectivity of these conjugate additions to 4 is interpreted in steric and stereo-electronic terms.

Introduction

Tricyclo[5.2.1.0^2,6]decadienones 1 have found widespread use in the synthesis of naturally occurring cyclopentanoids. The basic strategy underlying this approach is depicted in Scheme 1. Chemical manipulation of 1 followed by thermal or Lewis-acid mediated [4+2] cycloreversion produces functionalized cyclopentanones 3. Owing to their endo structure, most chemical modifications of 1 occur in a highly stereoselective manner ultimately leading to cyclopentenones 3 with a well-defined stereochemistry. The availability of both antipodes of 1 in enantiopure form, either by enzymatic resolution or asymmetric synthesis completes this strategy and makes it extremely useful for the enantioselective synthesis of a variety of natural products.

Scheme 1

Nucleophilic conjugate addition to the enone moiety in 1 has been studied for parent endo-tricyclocdecadienone 4a using a variety of nucleophiles. Independent of the nature of the
nucleophilic complete diastereoselectivity is observed in all cases to give exo-substituted tricyclodecenones 5a (Scheme 2). So far no nucleophilic 1,4-additions to 4a have been reported involving the formation of endo-addition product 6a. This high stereoselectivity is the result of effective shielding of the concave endo-face in endo-tricyclodecadienones 1 by the norbornene C8-C9 bridge which hampers nucleophilic attack at this face and therefore promotes attack at the exo-face of the enone moiety. In contrast to parent tricyclodecadienone 4a, conjugate additions of some selected organometallics to tricyclic ester 4b were found to give mixtures of exo- and endo-addition products 5b and 6b. With lithium dimethyl- and di-n-butylcuprates the exo-addition products 5b (R= Me, n-Bu) are still the predominant products but a considerable amount of endo-products 6b (R= Me, n-Bu) is also formed (exo:endo ratio 4:1). With lithium diphenylcuprate the endo-product 6b (R= Ph) is even the major addition product (ratio 6b/6b = 1:2). These results indicate that the stereochemistry of nucleophilic 1,4-additions to endo-tricyclodecadienones 1 is strongly affected by the substitution pattern at the exo-face of the molecule and the nature of the nucleophilic reagent. The substantial difference observed for the exo:endo ratios in the addition of lithium dimethyl- and di-n-butylcuprates, and lithium diphenylcuprate to 4b indicates that besides steric effects electronic factors may play a significant role in determining the product formation.

In a preceding paper, it was shown that tricyclic carboxylic acid 4c (X= COOH) can be conveniently converted into the corresponding 6-halides 4d (X= Cl, Br, I), 6-alcohol 4e (X= OH), 6-sulfides 4g (X= SMe) and 4h (X= SePh), and 6-selenides 4i (X= SePh) using the thiohydroxamic radical chemistry developed by Barton et al. 6-Methoxytricyclodecadienone 4f is readily obtained from bromide 4d by an elimination/addition reaction using potassium hydroxide in methanol. Thus, a series of 6-substituted endo-tricyclodecenones is available in which substituents differ in the nature of the heteroatom. As tricyclodecadienones 4 actually constitute γ-substituted cyclopentenones constrained in a rigid tricyclic system, these structures have interesting prospects to investigate the electronic and steric effect of γ-substituents of different steric size and electronic nature on conjugate addition reactions to γ-functionalized αβ-enones.

In this paper the first results on a comparative study of the 1,4-addition of lithium dimethyl- and di-n-butylcuprates to endo-tricyclodecadienones 4 containing an ether, thio- or selenoether function are described.

Results

For the purpose of comparison, the nucleophilic addition reactions involving 6-carboxylic ester 4b...
with both lithium dimethyl- and di-n-butylcuprate at -78°C were repeated. In both cases the chemical yields were nearly quantitative with high exo-stereoselectivity which was almost complete for the di-n-butylcuprate addition (Table 1). In comparison with the addition at 0°C carried out earlier, a considerable increase in stereoselectivity was observed at -78°C. The somewhat higher exo-selectivity for lithium di-n-butylcuprate as compared with its dimethyl analogue is merely the result of the slightly greater steric bulk of the former cuprate which disfavors endo-attack.

Replacing the carboxylic ester function in 4b by a methoxy substituent, which is sterically much less demanding (A-values 1.1-1.2 and 0.55-0.75, respectively[5]), has an enormous effect on the exoendo ratio. Both with lithium dimethyl- and di-n-butylcuprate 6-methoxytricyclodecadienone 4f gave a mixture of addition products 5f and 6f in excellent yield, with a preponderance of the endo-addition products 6f. This result clearly shows that steric factors are less important here than electronic features. Increasing the steric size of the 6-methyl ether function by replacing the oxygen atom by sulfur as in 4g (A-value 1.04[9]) led to complete endo-stereoselectivity for the addition of lithium dimethylcuprate. No exo-product was detected. A similar result was obtained for the addition of lithium dimethylcuprate to 4h which contains the somewhat larger thioophenyl group (A-value 1.10-1.24[9]). Addition of lithium di-n-butylcuprate to 4h produced again predominantly the endo-addition product but now a small amount (less than 4%) of

Table 1. Diastereoselectivity of 1,4-additions of lithium dialkylcuprates to 4

<table>
<thead>
<tr>
<th>substrate</th>
<th>X</th>
<th>R2CuLi</th>
<th>temp.</th>
<th>yield</th>
<th>ratio(exo 5 / endo 6)</th>
</tr>
</thead>
<tbody>
<tr>
<td>4a</td>
<td>H</td>
<td>Me</td>
<td>-78°C</td>
<td>&gt;90%</td>
<td>100 /-</td>
</tr>
<tr>
<td></td>
<td>n-Bu</td>
<td></td>
<td></td>
<td>&gt;90%</td>
<td>100 /-</td>
</tr>
<tr>
<td>4b</td>
<td>CO2Et</td>
<td>Me</td>
<td></td>
<td>90%</td>
<td>86 /14</td>
</tr>
<tr>
<td></td>
<td>n-Bu</td>
<td></td>
<td></td>
<td>90%</td>
<td>95 /5</td>
</tr>
<tr>
<td>4f</td>
<td>OMe</td>
<td>Me</td>
<td></td>
<td>96%</td>
<td>23 /77</td>
</tr>
<tr>
<td></td>
<td>n-Bu</td>
<td></td>
<td></td>
<td>69%</td>
<td>40 /50</td>
</tr>
<tr>
<td>4g</td>
<td>SMe</td>
<td>Me</td>
<td></td>
<td>97%</td>
<td>- /100</td>
</tr>
<tr>
<td>4h</td>
<td>SPh</td>
<td>Me</td>
<td></td>
<td>90%</td>
<td>- /100</td>
</tr>
<tr>
<td></td>
<td>n-Bu</td>
<td></td>
<td></td>
<td>85%</td>
<td>4 /96</td>
</tr>
<tr>
<td>4i</td>
<td>SePh</td>
<td>Me</td>
<td></td>
<td>89%</td>
<td>- /100</td>
</tr>
<tr>
<td></td>
<td>n-Bu</td>
<td></td>
<td></td>
<td>86%</td>
<td>- /100</td>
</tr>
<tr>
<td>4j*</td>
<td>S(O)Me</td>
<td>Me</td>
<td>0°C</td>
<td>98%</td>
<td>- /100</td>
</tr>
<tr>
<td>4k*</td>
<td>S(O)Ph</td>
<td>Me</td>
<td></td>
<td>46%</td>
<td>- /100</td>
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</tbody>
</table>
exo-product was isolated as well. Complete endo-stereoselectivity was observed for both the dimethyl- and n-butylcuprate addition to phenylselenide 4i. Interestingly, due to its higher polarization selenium has a relatively low A-value (1.0-1.2)⁹ despite its considerable size. Based on this consideration the phenyl selenide function is assumed to have about the same steric demand as the thiophenyl ether and ethyl ester functions as present in 4h and 4b, respectively.

Structural assignments

The gross structures of the cuprate addition adducts 5 and 6 were deduced from their IR, NMR and MS data. Unequivocal assignment of the configuration of the newly introduced substituent at C₅, either exo or endo, was possible by comparison of the ¹H-NMR-data of the new structures 5f,h and 6f,g,h,i (R = Me, n-Bu) with those of the known tricyclodecenones 5a,b and 6a,b (R = Me, n-Bu)⁵. Typically, the endo-C₅ protons in all structures 5 absorb at much high field than the exo-C₅ protons in tricyclodecenones 6 (Table 2). This higher field position of the endo-C₅ proton is clearly the result of its considerable shielding by the norbornene C₆-C₈ double bond. Obviously, such a shielding is not possible in tricyclodecenones 6. For 6-methoxy- and 6-methylsulfanyltricyclodecenones 6f, 6g (R=Me) independent proof of the endo-configuration of the methyl group at C₅ was obtained from their 2D ¹H-NMR NOSY spectra (Table 3). The strong interaction observed between the C₅-methyl protons and the olefinic C₅-proton confirms that these protons are indeed within a distance of 3 Å of each other as may be expected for these structures 6f and 6g. Interestingly, the ¹H-NMR spectra of 6-phenylsulfanyltricyclodecenones 6h (R = Me, n-Bu) were nearly identical to those of the corresponding 6-phenylselenyl compounds 6i. Since the structure of 6i (R = Me) has recently been secured unambiguously by X-ray diffraction analysis¹¹, the configuration around C₅ in the 6-sulfanyl compounds 6h (R = Me, n-Bu) is therefore also established. Finally, with the aim to elucidate the structures of the diastereomeric tricyclic sulfoxides 6j, which are readily obtained by oxidation of methyl sulfide 4g followed by lithium dimethylcuprate addition (vide infra), an X ray diffraction of the major diastereomer 6j⁸ was undertaken (Figure 1). As can be seen from Figure 1 this structure again confirms the endo-configuration of the methyl group at C₅¹¹. Interestingly, this X-ray structure shows that the methyl group of the sulfoxide group is positioned over the annelated cyclopentanone ring while the electron pair is directed toward the methylene bridge carbon C₁₀. It is evident that if this conformation has some preference in tricyclodecadienone 4j⁸, which is the precursor for 6j⁸, then addition of lithium dialkylcuprates to the enone system from the exo-face in 4j⁸ will be severely hindered.

Discussion

The results presented above clearly show that steric factors are not always decisive in controlling the stereochemistry of conjugate nucleophilic cuprate addition to 4. In particular, the reversed stereoselectivity found for the lithium dialkylcuprate additions to 6-methoxytricyclodecadienone 4f as compared with tricyclic ester 4b unambiguously proves that electronic features dominate steric factors.

The vinylogous addition of lithium dialkylcuprates to γ-substituted cycloenones has only scarcely been studied for relative simple enones containing an alkyl or alkoxy substituent at the γ-position¹²⁻¹³. In the cases reported, cuprate addition generally occurs with high diastereoselectivity affording
Table 2. Chemical shift of selected protons in 5 and 6

<table>
<thead>
<tr>
<th>product</th>
<th>chemical shift(ppm)</th>
</tr>
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<tbody>
<tr>
<td></td>
<td>$H_{3-exo}$</td>
</tr>
<tr>
<td>5a</td>
<td>exo-Me</td>
</tr>
<tr>
<td></td>
<td>exo-n-Bu</td>
</tr>
<tr>
<td>6a</td>
<td>endo-Me</td>
</tr>
<tr>
<td>5b</td>
<td>exo-Me</td>
</tr>
<tr>
<td></td>
<td>exo-n-Bu</td>
</tr>
<tr>
<td>6b</td>
<td>endo-Me</td>
</tr>
<tr>
<td></td>
<td>endo-n-Bu</td>
</tr>
<tr>
<td>5f</td>
<td>exo-Me</td>
</tr>
<tr>
<td></td>
<td>exo-n-Bu</td>
</tr>
<tr>
<td>6f</td>
<td>endo-Me</td>
</tr>
<tr>
<td></td>
<td>endo-n-Bu</td>
</tr>
<tr>
<td>6g</td>
<td>endo-Me</td>
</tr>
<tr>
<td>5h</td>
<td>exo-n-Bu</td>
</tr>
<tr>
<td>6h</td>
<td>endo-Me</td>
</tr>
<tr>
<td></td>
<td>endo-n-Bu</td>
</tr>
<tr>
<td>6i</td>
<td>endo-Me</td>
</tr>
<tr>
<td></td>
<td>endo-n-Bu</td>
</tr>
<tr>
<td>6j</td>
<td>endo-Me</td>
</tr>
<tr>
<td>6k</td>
<td>endo-Me</td>
</tr>
</tbody>
</table>

predominantly the anti-addition product. This preferred anti-addition is generally explained by invoking steric or electrostatic interactions which clearly disfavors syn-addition at the β-ene carbon in the cyclohexnone$^{13}$.

The exclusive formation of exo-addition products 5a in the cuprate addition to parent tricyclodecadienone 4a is in agreement with this explanation. Whereas the exo-face of the cyclopentenone moiety in 4a is almost unhindered, the norbornene moiety severely hinders cuprate addition at its endo-face resulting in complete exo-addition. Increase of the steric and electrostatic demands at the
Table 3. Observed NOE-effects in $5f, 6f, 6g$ and $6i^*$

[Distance between $H_1$ and the nearest hydrogen of the 5-methyl group (in Å)$^{10}$]

<table>
<thead>
<tr>
<th></th>
<th>$H_1$</th>
<th>$H_2$</th>
<th>$H_{4k}$</th>
<th>$H_{4n}$</th>
<th>$H_5$</th>
<th>$H_7$</th>
<th>$H_8$</th>
<th>$H_9$</th>
<th>$H_{10a}$</th>
<th>$H_{10s}$</th>
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<tbody>
<tr>
<td>$5f$</td>
<td>$&gt;$5</td>
<td>3.2</td>
<td>2.4</td>
<td>3.5</td>
<td>2.5</td>
<td>4.3</td>
<td>$&gt;$5</td>
<td>$&gt;$5</td>
<td>$&gt;$5</td>
<td>$&gt;$5</td>
</tr>
<tr>
<td>$6f$</td>
<td>$&gt;$5</td>
<td>$&gt;$5</td>
<td>2.9</td>
<td>2.5</td>
<td>2.6</td>
<td>3.0</td>
<td>2.4</td>
<td>4.4</td>
<td>$&gt;$5</td>
<td>5.0</td>
</tr>
<tr>
<td>$6g$</td>
<td>$&gt;$5</td>
<td>$&gt;$5</td>
<td>2.9</td>
<td>2.5</td>
<td>2.4</td>
<td>2.9</td>
<td>2.3</td>
<td>4.3</td>
<td>$&gt;$5</td>
<td>5.0</td>
</tr>
<tr>
<td>$6i^*$</td>
<td>$&gt;$5</td>
<td>4.5</td>
<td>3.0</td>
<td>2.6</td>
<td>1.9</td>
<td>2.5</td>
<td>2.3</td>
<td>4.7</td>
<td>4.6</td>
<td>4.4</td>
</tr>
</tbody>
</table>

$^a$ A NOE-effect is expected for protons within 3 Å of the nearest proton of the methyl group. If a NOE-effect is indeed observed, the corresponding distance is underlined.

Figure 1. X-ray structure of $6j^*$

$exo$ face by introducing a $\gamma$-ester function as in $4b$ leads to a decrease in stereoselectivity, however, $exo$-addition is still by far the most preferred process (Table 1). A rather drastic change in stereoselectivity is observed for the cuprate addition to $\gamma$-methoxycyclohexadienone $4f$. The major product obtained now is the endo-addition product $6f$. This high degree of endo-selectivity is certainly not primarily due to steric features since the relative steric demand of the ethoxycarbonyl group is larger than that of a methoxy group ($A$-values: $CO_2Et>OMe$)$^9$. The following explanations for these observations can be envisaged. First, electrostatic repulsion between the electron-rich cuprate reagent and the lone pairs on the oxygen may give rise to a preferred anti-addition. Such an electrostatic repulsion is expected to be more decisive in determining the stereochemistry of cuprate addition to ethers $4f, 4g, 4h$ and $4i$ than to ester $4b$ since the lone pairs on both oxygen atoms in the ester moiety can readily rotate away from the reaction center without increase of the steric hindrance at this $\beta$-ene carbon. Such an operation is not possible for the ethers $4f, 4g, 4h$ and $4i$ without considerably increasing the steric shielding of the $\beta$-ene carbon by either the methyl or phenyl group attached to the ether oxygen or sulfur.

Another possibility is stereoelectronic in nature. Assuming that the first step in the cuprate addition to the enone moiety in $4$ involves the reversible formation of the corresponding cis and trans
Lithium dialkylcuprate additions

d.π*-complexes\(^{14}\), the subsequent step, which involves either the formation of a Cu(III) β-adduct or carbocupration to form the β-alkyl copper enolate, may be strongly affected by the electronic nature of the adjacent γ-substituent. Corey and Boaz\(^{24c}\) suggest that anti-addition may arise from hyperconjugative interaction in which the γ-heteroatom removes electron density from the d(Cu), π\(^g\)*-ene complex or the Cu(III) β-adduct with maximum stabilization occurring in the anti geometry. Unfortunately, experimental data to verify this hypothesis are rather scarce and not yet convincing. This is exemplified by the recent observation that the addition of lithium dimethylcuprate to γ-methylcyclopentenone has a higher anti-selectivity (anti/syn >100:1) than that to γ-methoxycyclopentenone (anti/syn 42:1)\(^{12}\). Although the difference in selectivity is small, this result indicates that stereoelectronic control according to Corey’s model does either not operate or does not play an important role since steric, electrostatic and stereoelectronic factors all promote anti-addition of the cuprate to the γ-methoxycyclopentenone which should result in at least the same high anti-stereoselectivity as observed for the γ-methoxycyclopentenone.

An alternative stereoelectronic analysis involves interaction of the incipient bond at Cp with the nonequivalent faces of the enone system. This interaction is due to the differences in the relative stabilities of the diastereomeric transition states. According to this hypothesis (Cieplak’s model\(^{15}\)), which has been successfully used for the explanation of facial selectivity in 1,2-additions\(^{16}\), stereoelectronic control is primarily determined by interaction of the emerging σ*-orbital associated with the incipient bond at Cp and a suitably aligned σ-bond at Cy. Transition state stabilization at either face is now dependent on the electron-donating ability of the respective σ-bonds at Cy, ultimately resulting in bond formation at the face anti to the most electron-rich σ-bond. Applying this stereoelectronic hypothesis to γ-methoxy substituted enones syn-addition is expected to be the preferred process as the σ-donating ability of a C-O bond is poor compared with a C-H or C-C bond\(^{17}\). Hence, the stereoelectronic control exerted by a methoxy group opposes both its steric and electrostatic effect on π-diastereofacial selectivity. This may be an explanation for the incomplete stereoselectivity observed\(^{12}\) for the addition of lithium dimethylcuprate to γ-methoxycyclopentenone.

The observation of predominant anti stereochemistry in the cuprate addition to 6-methoxytricyclodecadienone 4f, while for ester 4b syn addition to the ester function is the main process, does not seem to be in accordance with Cieplak’s hypothesis as now both sterically and stereoelectronically syn-addition would be the preferred reaction mode. However, it should be realized that anti-addition in 4f may primarily be the result of strong repulsive electrostatic interaction between the electron-rich cuprate reagent and the methoxy oxygen lone pairs which may be of much higher weight than stereoelectronic effects. For the tricyclic thio- and selenoethers 4g, h and i complete or almost complete diastereofacial endo-selectivity is observed. This increase in endo-selectivity as compared with the methoxy analogue may be merely the result of increased steric hindrance at the exo-face of the enone moiety in 4g, h and i relative to 4f. However, as the C-S and C-Se σ bonds are more electron donating than a C-C σ bond anti-addition is now also the preferred addition mode when adopting Cieplak’s model. Hence, in contrast to 4f for tricyclodecadienones 4g, h and i steric, electrostatic and stereoelectronic effects all combine to favor the endo-addition product.

The tricyclic thioethers 4g and 4h offer a unique opportunity to further evaluate conceivable electronic effects of the γ-substituent on the cuprate additions. Transformation of the thioethers in the corresponding sulfoxides is usually a convenient reaction which changes the electronic nature of the
original sulfur substituent. Due to presence of oxygen the sulfoxide function is much more polar than a sulfide group and exerts a considerably stronger electron withdrawing inductive effect. Hence, if an appreciable electronic interaction of the γ-substituent with either the enone moiety or the incoming nucleophile would play a significant role in these cuprate additions to tricyclodecadienones 4 such an effect should certainly be reflected in either the stereoselectivity or the rate of the addition reaction.

Tricyclic methyl- and phenylsulfoxides 4j and 4k were readily obtained in high yield by selective oxidation of the corresponding thioethers 4g and 4h with sodium periodate. In both cases a mixture of diastereoisomers was isolated which could be readily separated by flash chromatography.

Addition of lithium dimethylcuprate to both sulfoxides 4j* and 4k* (diastereomERICALLY pure compounds; see experimental) was considerably slower than to the corresponding sulfides 4g and 4h. At -78 °C no reaction was observed at all for 4j* and 4k*, whereas for sulfides 4g and 4h addition of the cuprate was complete within half an hour. The temperature had to be raised to 0 °C to obtain an acceptable rate. At this temperature complete conversion of the enone was observed after 2-3 hr reaction time to give essentially only one addition product as was shown by thin layer chromatography (Table 1). The relatively low yield obtained for 6k* is probably due to its thermal instability. NMR-analysis clearly revealed that cuprate addition to both 4j* and 4k* proceeds with high stereoselectivity to give exclusively the endo-5-methyltricyclodecadienones 6j* and 6k* (R= CH3), respectively. No exo-product could be detected.

The considerably decreased reactivity of tricyclic sulfoxides 4j* and 4k* as compared with the corresponding sulfides presents strong evidence for significant electronic participation of the γ-substituent in the cuprate additions to the tricyclic enones 4. By increasing the electron withdrawing ability of this substituent in going from the sulfide to the sulfoxide cuprate addition becomes apparently less favorable. The increased steric demand and electrostatic repulsive effect of the sulfoxide function as compared with the sulfide group are not relevant in this comparison as in both cases addition takes place entirely from the endo-face anti to the γ-substituent. Hence, the change in reactivity must be entirely accounted for by some electronic effect which may be attributed to electronic interaction of the sulfoxide function with the incoming nucleophile (Cieplak model). Due to the poorer electron donating ability of the C-S=O bond in comparison with C-S bond addition of the nucleophile to 4 is expected to be more facile for 4g and 4h than for 4j* and 4k* since σ-σ* overlap will be less effective in the latter cases. The alternative stereoelectronic model involving electronic interaction of the sulfoxide function with the cuprate enolate complex as suggested by Corey14 does not seem to give a satisfactory explanation for the observed decrease in rate. On the contrary, invoking this approach, the increased electron withdrawing ability of the sulfoxide function is expected to enhance the cuprate addition rate. However, at this stage, it cannot be ruled out that both the stereochemistry and reactivity observed for cuprate additions to 4 may in some way be associated with the nature of the nucleophile, i.e. the copper reagent. Experiments to verify whether the nature of the nucleophile has a significant effect on both the stereochemistry and reaction rate of conjugate additions to 4 are currently underway.

In conclusion a strong directing effect of the γ-substituent on the stereoselectivity of lithium dialkylcuprate additions to γ-substituted tricyclodecadienones 4 has been established. The introduction of an alkyl or aryl ether function containing oxygen, sulfur or selenium leads to a remarkably high endo-stereoselectivity despite the severe steric hindrance exerted by the norbornene C8-C9 double bond at the endo-face of the cyclopentenone moiety. This high facial stereoselectivity observed for tricyclodecadienones 4f-k is
typically associated with the electronic features of the substituents which may interact electronically with either the enone-cuprate complex or with the incoming nucleophile.

**Experimental**

**General remarks**

Melting points were measured with a Reichert Thermopan microscope and are uncorrected. IR spectra were recorded on a Perkin-Elmer 298 infrared spectrometer. $^1$H and $^{13}$C-NMR spectra were recorded on a Bruker AM-400 spectrophotometer, using TMS as an internal standard. For mass spectra a double focussing VG 7070E mass spectrophotometer was used. Capillary GC analyses were performed using a Hewlett-Packard 5890A gas chromatograph, containing a cross-linked methyl silicone column (25m).

Flash chromatography was carried out at a pressure of ca. 1.5 bar, a column length of 15-25 cm and a column diameter of 1-4 cm, using Merck Kieselgel 60H. Elemental analyses were performed on a Carlo Erba Instruments CHNS-O 1108 Elemental analyzer. All solvents used were dried and distilled according to the standard procedures.

**General procedure for cuprate addition to 4:**

A solution of RLi (ca. 2 equiv.) in hexane was gradually added to a suspension of dry CuI (ca. 1 equiv.) in dry ether at temp. below 0 °C (ice-salt) under a nitrogen atmosphere. After stirring for 15 min. at this temp., the mixture was cooled down to 78 °C. A solution of 4 (ca. 0.5 equiv.) in ether was then added. The mixture was stirred at -78 °C until the reaction was complete according to TLC (ca. 30 min.), then quenched with aqueous ammonium chloride and the aqueous phase extracted with ether (3x). The combined organic phases were washed with water (3x), dried (Na$_2$SO$_4$) and the solvent evaporated under reduced pressure. Analytical samples were obtained by flash chromatography and/or crystallization.

**exo-3-Methyl-endo-tricyclo[5.2.1.0$^{2,6}$]dec-8-en-5-one carboxylic acid ethyl ester 5b (R= Me) and endo-3-methyl-endo-tricyclo[5.2.1.0$^{2,6}$]dec-8-en-5-one carboxylic acid ethyl ester 6b (R= Me)**

Following the general procedure [MeLi (1.4 ml of 1.6 M solution in hexane, 2.2 mmol), CuI (216 mg, 1.1 mmol), 4b (110 mg, 0.5 mmol)] gave, after work-up and flash chromatography (n-hexane /EtOAc= 90/10), 105 mg (90 %) of a mixture of 5b and 6b in 86:14 ratio according to cap. GC.

$^1$H-NMR (400 MHz, CDCl$_3$): 5b (R= Me): 5 0.60 A of AB (dd, $J_{8,9}=$5.6 Hz, $J_{1,9}$ resp. $J_{7,8}=$2.9 Hz, 1H, H$_8$ or H$_9$), 6.20 B of AB (dd, $J_{8,9}=$5.6 Hz, $J_{1,9}$ resp. $J_{7,8}=$3.2 Hz, 1H, H$_8$ or H$_9$), 4.24 (q, $J=$7.1 Hz, 2H, -COOCH$_2$CH$_3$), 3.49-3.46 (m, 2H, H$_7$ and H$_8$ or H$_9$), 3.19-3.16 (m, 1H, H$_6$ or H$_7$), 2.31 A of AB (dd, $J_{4,5,6}=$17.3 Hz, $J_{4,5}=$10.7 Hz, $J_{4,6}=$1.6 Hz, 1H, H$_6$), 2.25 B of AB (dd, $J_{4,5,6}=$17.3 Hz, $J_{4,5}=$7.9 Hz, 1H, H$_7$ or H$_8$), 2.09-1.99 (m, 1H, H$_8$ or H$_9$), 1.69 A of AB (d, $J_{10a,10b}=$8.8 Hz, 1H, H$_{10a}$), 1.41 B of AB (d, $J_{10a,10b}=$8.8 Hz, 1H, H$_{10b}$), 1.52 (t, $J=$7.1 Hz, 3H, CH$_3$CH$_2$), 1.04 (d, $J=$7.0 Hz, 3H, CH$_3$) 6b (R= Me): 5 6.35 A of AB (dd, $J_{8,9}=$5.7 Hz, $J_{1,9}$ resp. $J_{7,8}=$3.1 Hz, 1H, H$_8$ or H$_9$), 6.16 B of AB (dd, $J_{8,9}=$5.7 Hz, $J_{1,9}$ resp. $J_{7,8}=$2.9 Hz, 1H, H$_7$ or H$_8$), 4.24-4.16 (m, 2H, -COOCH$_2$CH$_3$), 3.49 (d, $J_{8,9}=$5.1 Hz, 1H, H$_8$ or H$_9$), 3.46 (bs, 1H, H$_1$ or H$_2$), 3.33-3.21 (m, 1H, H$_1$ or H$_2$), 2.53-2.38 (m, 1H, H$_3$), 2.32 A of AB (dd, $J_{4,5,6}=$18.4 Hz, $J_{4,5}=$9.4 Hz, $J_{4,6}=$1.5 Hz, 1H, H$_6$), 1.84 B of AB (dd, $J_{4,5,6}=$18.4 Hz, $J_{4,5,6}=$11.9 Hz, $J_{4,5,6}=$1.0 Hz, 1H, H$_6$), 1.57 A of
AB (d, J_{10a}=8.7 Hz, 1H, H_{10a}). 1.42 B of AB (d, J_{10a}=8.7 Hz, 1H, H_{10a}). 1.29 (t, J=7.1 Hz, 3H, CH\textsubscript{2}CH\textsubscript{3}), 1.21 (d, J=6.9 Hz, 3H, CH\textsubscript{3}).

exo-3-n-Butyl-endo-tricyclo[5.2.1.0\textsubscript{2,6}][4.8]dec-8-en-5-one carboxylic acid ethyl ester 5b (R= n-Bu) and endo-3-n-butyl-endo-tricyclo[5.2.1.0\textsubscript{2,6}][4.8]dec-8-en-5-one carboxylic acid ethyl ester 6b (R= n-Bu)

Following the general procedure [BuLi (1.4 ml of 1.6 M solution in hexane, 2.2 mmol), CuI (216 mg, 1.1 mmol), 4b (110 mg, 0.5 mmol)] gave, after work-up and flash chromatography (n-hexane /EtOAc= 90/10), 125 mg (90 %) of a mixture of 5b and 6b in 95:5 ratio according to \(^1\)HNMR (400 MHz) and cap. GC.

\[^1\]H-NMR (400 MHz, CDCl\textsubscript{3}): 5b (R= n-Bu): 8 6.30 A of AB (dd, J\textsubscript{1,10a}=5.6 Hz, J\textsubscript{1,10b}=2.9 Hz, 1H, H\textsubscript{1}), 6.18 B of AB (dd, J\textsubscript{1,10a}=5.6 Hz, J\textsubscript{1,10b}=3.2 Hz, 1H, H\textsubscript{1}), 4.24 (q, J=7.2 Hz, 2H, -COOCH\textsubscript{2}CH\textsubscript{3}), 3.46 (bs, 1H, H\textsubscript{1} or H\textsubscript{10a}), 3.40 (dd, J\textsubscript{1,10a}=4.6 Hz, J\textsubscript{5,6}=2.1 Hz, 1H, H\textsubscript{5}), 3.16-3.14 (m, 1H, H\textsubscript{1} or H\textsubscript{10a}), 2.40 A of AB (ddd, J\textsubscript{5,6}=16.9 Hz, J\textsubscript{4,5}=12.5 Hz, J\textsubscript{4,5}=2.1 Hz, 1H, H\textsubscript{4}), 2.24 B of AB (dd, J\textsubscript{4,5}=5.7 Hz, J\textsubscript{4,5}=3.2 Hz, 1H, H\textsubscript{4} or H\textsubscript{5}), 1.91-1.82 (m, 1H, H\textsubscript{3}), 1.59-1.48 and 1.34-1.19 (2 x m, 1H and 5H, (CH\textsubscript{2})\textsubscript{5}CH\textsubscript{3}), 1.42 B of AB (d, J\textsubscript{10a}=8.7 Hz, 1H, H\textsubscript{10a}). 1.32 (t, J=7.2 Hz, 3H, CH\textsubscript{2}CH\textsubscript{3}), 0.88 (t, J=7.0 Hz, 3H, CH\textsubscript{3}). 6b (R= n-Bu): 8 6.32 A of AB (dd, J\textsubscript{1,10a}=5.7 Hz, J\textsubscript{1,10b}=2.9 Hz, 1H, H\textsubscript{1} or H\textsubscript{10a}), 6.14 B of AB (dd, J\textsubscript{1,10a}=5.7 Hz, J\textsubscript{1,10b}=2.9 Hz, 1H, H\textsubscript{1} or H\textsubscript{10a}), 3.47 (bs, 1H, H\textsubscript{1} or H\textsubscript{10a}), 3.45 (dd, J\textsubscript{1,10a}=5.1 Hz, J\textsubscript{5,6}=1.5 Hz, 1H, H\textsubscript{5}), 3.22-3.19 (m, 1H, H\textsubscript{1} or H\textsubscript{10a}), 2.40-2.27 AB (m, 2H, H\textsubscript{4} and H\textsubscript{5}), 1.93-1.77 (m, 2H, H\textsubscript{3} and 1H of -(CH\textsubscript{2})\textsubscript{5}CH\textsubscript{3}), 1.58 A of AB (dd, J\textsubscript{10a}=8.8 Hz, J\textsubscript{1,10a}=J\textsubscript{7,10a}=1.5 Hz, 1H, H\textsubscript{10a}). 1.40 B of AB (d, J\textsubscript{10a}=8.8 Hz, 1H, H\textsubscript{10a}), 1.42-1.15 (m, 5H of -(CH\textsubscript{2})\textsubscript{5}CH\textsubscript{3}), 1.29 (t, J=7.1 Hz, 3H, CH\textsubscript{2}CH\textsubscript{3}), 0.90 (t, J=7.1 Hz, 3H, CH\textsubscript{3}).

6-Methoxy-exo-5-n-butyl-endo-tricyclo[5.2.1.0\textsubscript{2,6}][4.8]dec-8-en-3-one 5f (R= Me) and 6-methoxy-endo-5-n-butyl-endo-tricyclo[5.2.1.0\textsubscript{2,6}][4.8]dec-8-en-3-one 6f (R= Me)

Following the general procedure [MeLi (1.4 ml of 1.6 M solution in hexane, 2.2 mmol), CuI (216 mg, 1.1 mmol), 4f (90 mg, 0.5 mmol)] gave, after work-up and flash chromatography (n-hexane /EtOAc= 80/20), 92 mg (96 %) of a colorless oil consisting of 23% of 5f and 77% of 6f according to \(^1\)HNMR (400 MHz) and cap. GC.

\[^1\]H-NMR (400 MHz, CDCl\textsubscript{3}): 5f (R= Me): 8 6.25 (m, 1H, H\textsubscript{1} or H\textsubscript{10}), 6.13 B of AB (dd, J\textsubscript{1,10}=5.5 Hz, J\textsubscript{1,10}=2.9 Hz, 1H, H\textsubscript{1} or H\textsubscript{10}), 3.39 (s, 3H, OCH\textsubscript{3}), 3.21 - 3.14 (m, 2H, H\textsubscript{1} and H\textsubscript{10}), 2.81 (d, J=4.7 Hz, 1H, H\textsubscript{2}), 2.27 (m, 1H, H\textsubscript{4}), 2.19 (m, 1H, H\textsubscript{5}), 1.98 A of AB (d, J\textsubscript{10a}=8.4 Hz, 1H, H\textsubscript{10a}), 1.80 - 1.68 (m, 2H, H\textsubscript{10a} and H\textsubscript{10b}), 1.15 (d, J=6.8 Hz, 3H, CH\textsubscript{3}); 6f (R= Me): 8 6.25 (m, 1H, H\textsubscript{1} or H\textsubscript{10}), 6.18 B of AB (dd, J\textsubscript{1,10}=5.7 Hz, J\textsubscript{1,10}=2.9 Hz, 1H, H\textsubscript{1} or H\textsubscript{10}), 3.36 (s, 3H, OCH\textsubscript{3}), 3.21-3.14 (m, 2H, H\textsubscript{4} and H\textsubscript{5}), 2.75 (d, J=5.0 Hz, 1H, H\textsubscript{2}), 2.64 (m, 1H, H\textsubscript{3}), 2.49 A of AB (dd, J\textsubscript{1,10}=18.6 Hz, J\textsubscript{1,10}=9.8 Hz, 1H, H\textsubscript{10}), 2.00 A of AB (d, J\textsubscript{10a}=8.4 Hz, 1H, H\textsubscript{10a}), 1.80-1.68 (m, 2H, H\textsubscript{10a} and H\textsubscript{10b}), 1.18 (d, J=7.0 Hz, 3H, CH\textsubscript{3}) \textit{IR} (CH\textsubscript{2}Cl\textsubscript{2}): v 3010-2860 (C-H), 1740 (C=O), 1090 cm\textsuperscript{-1}. EI/MS: m/e (%) 127 (100, M\textsuperscript{+1}-C\textsubscript{5}H\textsubscript{4}), 66 (31, C\textsubscript{2}H\textsubscript{4}). El/HRMS m/e: 127.0751 [calc.for C\textsubscript{9}H\textsubscript{10}O\textsubscript{2}M(+1)-C\textsubscript{2}H\textsubscript{4}H\textsubscript{4}: 127.0759].

exo-5-n-Butyl-6-methoxy-endo-tricyclo[5.2.1.0\textsubscript{2,6}][4.8]dec-8-en-3-one 5f (R= n-Bu) and endo-5-n-buty]-6-methoxy-endo-tricyclo[5.2.1.0\textsubscript{2,6}][4.8]dec-8-en-3-one 6f (R= n-Bu)

Following the general procedure [n-BuLi (1.5 ml of 1.6 M solution in hexane, 2.3 mmol), CuI (222 mg, 1.2
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mmol), 4f (100 mg, 0.57 mmol), gave, after work-up and flash chromatography (n-hexane /EtOAc= 80/20), 95 mg (69 %) of colorless oil consisting of 40% of 5f and 60% of 6f according to 1H NMR (400 MHz) and cap GC.

1H NMR (400 MHz, CDCl3): 5f (R= n-Bu): δ 6.24 A of AB (dd, Jg=5.5 Hz, 1H, Hg or Hh), 6.19 B of AB (dd, Jg=5.5 Hz, 1H, Hg or Hh), 3.44 (2 x bs, 2H, H1 and H2), 2.95 (d, J1,2=4.6 Hz, 1H, H2), 2.37-2.20 (m, 2H, H4a and H4b), 2.00-1.93 (m, 2H, H5 and H10a), 1.79-1.67 and 1.39-1.24 (2 x m, 8H), 0.91 (t, J=6.8 Hz, 3H, CH3). IR (CH2Cl2): ν 3010-2860 (C-H), 1740 (C=O) cm⁻¹. EI/MS: m/e (%) 169 (100, M+1-C4H3). 66 (100, C2H5). EI/HRMS m/e: 169.1227 [calc for C4H7O2(M+1-C4H3): 169.1229].

endo-5 Methyl 6 methylsulfanyl endo-tricyclo[5.2.1.02,6]dec 8 en-3-one 6g
Following the general procedure [MeLi (1.4 ml of 1.6 M solution in hexane, 2.2 mmol), Cul (216 mg, 1.1 mmol), 4g (75 mg, 0.39 mmol)], gave, after work-up and flash chromatography (n-hexane /EtOAc= 90/10), 79 mg of 6g (97 %) as a colorless crystalline solid.

endo-5-Methyl-6-phenylsulfanyl endo-tricyclo[5.2.1.02,6]dec-8-en-3-one 6h (R= Me)
Following the general procedure [MeLi (0.8 ml of 1.6 M solution in hexane, 1.3 mmol), Cul (112 mg, 0.59 mmol), 4h (100 mg, 0.38 mmol)], gave, after work-up and flash chromatography (n-hexane /EtOAc= 95/5), 93 mg (90 %) of 6h as a colorless crystalline solid.

endo-5-n-Butyl-6-phenylsulfanyl endo-tricyclo[5.2.1.02,6]dec-8-en-3-one 6h (R= n-Bu)
Following the general procedure [n-BuLi (1.2 ml of 1.6 M solution in hexane, 1.9 mmol), Cul (180 mg, 0.95 mmol), 4h (100 mg, 0.38 mmol), gave, after work-up and flash chromatography (n-hexane /EtOAc= 95/5), 93 mg (90 %) of 6h as a colorless crystalline solid.

endo-5-Methyl-6-phenylsulfanyl endo-tricyclo[5.2.1.02,6]dec-8-en-3-one 6h (R= Me)
Following the general procedure [MeLi (0.8 ml of 1.6 M solution in hexane, 1.3 mmol), Cul (112 mg, 0.59 mmol), 4h (100 mg, 0.38 mmol)], gave, after work-up and flash chromatography (n-hexane /EtOAc= 95/5), 93 mg (90 %) of 6h as a colorless crystalline solid.
mmol), 4h (140 mg, 0.55 mmol), gave, after work-up and flash chromatography (n-hexane /EtOAc= 95/5), 145 mg (85 %) of m and 5 mg (ca. 3%) of S.

6h (R= n-Bu): m.p.: 50 °C. 1H-NMR (400 MHz, CDCl₃): δ 7.54 and 7.36 (2 x m, 5H, Ph-H), 6.28 A of AB (dd, Jₓᵧ=5.4 Hz, J₁ₓ₁=3.1 Hz, 1H, Hₓ or Hᵧ), 6.12 B of AB (dd, Jₓᵧ=5.6 Hz, J₁ₓ₁=3.0 Hz, 1H, Hₓ or Hᵧ), 3.20 and 3.08 (2 x bs, 2H, Hₓ and Hᵧ), 2.99 (d, J₁ₓ₁=4.9 Hz, 1H, Hₓ), 2.58 (m, 1H, Hᵧ), 2.44 A of AB (d, J₁ₓ₁ₓ₁=8.5 Hz, 1H, H₁ₓ₁), 2.22 A of AB (dd, Jₓᵧₓₓ₁=18.4 Hz, Jₓᵧᵧₓ₁=9.5 Hz, 1H, Hₓ), 1.72 (m, 2H, Hₓ and Hᵧ), 1.51 and 1.25-1.06 (12 x m, 6H, (CH₂ₓ)₃CH₃), 0.84 (t, J=7.0 Hz, 3H, CH₃).

IR (CHCl₃): ν 3010-2820 (C-H), 1725 (C=O) cm⁻¹. EI/MS: m/e (%) 312 (0.6, M⁺), 247 (100, M⁺+1-C₅H₆), 190 (71, M⁺+1-C₅H₆-C₅H₅), 66 (20, C₅H₆). EI/HRMS m/e: 312.1547 [calc. for C₁₅H₂₃O₂(M⁺): 312.1548].

endo-5-Methyl-6-phenylselenyl-endo-tricyclo[5.2.1.0²⁶]deca-8-en-3-one 6i
Following the general procedure [MeLi (1 ml of 1.6 M solution in hexane, 1.6 mmol), CuI (200 mg, 1 mmol), 4i (150 mg, 0.55 mmol)], gave, after work-up and flash chromatography (n-hexane /EtOAc= 95/5), 140 mg (89 %) of 6i as a white solid.

6i: m.p.: 61-62 °C (distisopropylether). 1H-NMR (400 MHz, CDCl₃): δ 7.66-7.29 (m, 5H, Ph-H), 6.31 A of AB (dd, Jₓᵧ=5.6 Hz, J₁ₓ₁=3.0 Hz, 1H, Hₓ or Hᵧ), 6.12 B of AB (dd, Jₓᵧ=5.6 Hz, J₁ₓ₁=2.9 Hz, 1H, Hₓ or Hᵧ), 3.27 and 3.12 (2 x bs, 2H, Hₓ and Hᵧ), 2.81 2.71 (m, 1H, Hₓ), 2.39 A of AB (d, J₁ₓ₁ₓ₁=8.6 Hz, 1H, H₁ₓ₁), 0.98 (d, 3H, CH₃).

13C-NMR (100 MHz, CDCl₃): δ 218.8 (quat.), 137.7/137.5/136.0/129.2/129.1 (tert.), 128.2/63.6 (quat.), 62.8 (tert.), 53.4 (sec.), 52.4 (tert.), 49.4 (sec.), 48.3 (tert.), 14.6 (prim.). IR (CH₂Cl₂): ν 3080-3020 (C-H, unsat.), 1730 (C=O) cm⁻¹. EI/MS: m/e (%) 318 (9, M⁺), 252 (77, M⁺+1-C₅H₆), 161 (45, M⁺-SePh), 133 (59, M⁺-SePh-CO), 95 (100, M⁺-SePh-C₅H₅), 66 (53, C₅H₆). EI/HRMS m/e: 318.0524 [calc. for C₁₅H₁₆O₈Se (M⁺): 318.0523].

6 Metbylsulfonyl endo-tricyclo[5.2.1.0²⁶]deca-4,8-dien-3-one 4j
A solution of NaIO₄ (3 equiv.) in water (20 ml) was added dropwise to a solution of sulfide 4g (1.5 mmol) in methanol (25 ml) with stirring at room temp. After 1 hour the reaction mixture was filtered and methanol was evaporated under reduced pressure to give an oil. Flash chromatography (EtOAc/methanol = 80/20) gave 183 mg 4jB (58%) and 102 mg 4jA (33%) as colorless crystalline solids.

4j: m.p.: 135 °C. 1H-NMR (400 MHz, CDCl₃): δ 7.65 (d, Jₓᵧ=5.8 Hz, 1H, Hₓ), 6.35 (d, Jₓᵧ=5.8 Hz, 1H, Hᵧ), 6.09 A of AB (dd, Jₓᵧ=5.5 Hz, J₁ₓ₁=3.1 Hz, 1H, Hₓ or Hᵧ), 6.05 B of AB (dd, Jₓᵧ=5.5 Hz, J₁ₓ₁=2.9 Hz, 1H, Hₓ or Hᵧ), 3.47 and 3.31 (2 x bs, 2H, Hₓ and Hᵧ), 2.81 (d, J₁ₓ₁=4.6 Hz, 1H, Hₓ), 2.56 (s, 3H, SOCH₃), 2.15 A of AB (d, J₁ₓ₁ₓ₁=9.3 Hz, 1H, H₁ₓ₁), 1.87 B of AB (d, J₁ₓ₁ₓ₁=9.3 Hz, 1H, H₁ₓ₁). IR (CH₂Cl₂): ν 3010-2860 (C-H), 1705 (C=O) cm⁻¹. EI/MS: m/e (%) 208 (0.5, M⁺), 145 (100, M⁺-SOCH₃), 127 (15, M⁺-C₅H₆CH₂), 117 (59, M⁺-SOCH₃-CO), 79 (84, M⁺-SOCH₃-C₅H₅), 66 (11,C₅H₆). EI/HRMS m/e: 208.0559 [calc. for C₁₁,H₁₂SO₂(M⁺): 208.0558].
end-5-Methyl-6-methylsulfinyl-endo-tricyclo[5.2.1.02,7]deca-8-en-3-one 6j

A solution of MeLi (1.2 ml of a 1.6 M solution in hexane, 1.9 mmol) in hexane was gradually added to a suspension of dry CuI (200 mg, 1 mmol) in dry ether at temp. below 0 °C (ice-salt) in a nitrogen atmosphere. After stirring for 15 min., a solution of 4j (100 mg, 0.48 mmol) in THF was added. The mixture was then stirred at 10 °C until the reaction was complete according to TLC (ca. 2h). The mixture was quenched with aqueous ammonium chloride and the aqueous phase extracted with ether (3×). The combined organic phases were washed with water (3×), dried (Na₂SO₄) and the solvent was evaporated under reduced pressure. Flash chromatography (EtOAc/methanol = 9/1) gave 107 mg (98 %) of 6j as a colorless crystalline solid.

6-Phenylsulfinyl-endo-tricyclo[5.2.1.0²,7]deca-8,14-dien-3-one 4k

A solution of NaIO₄ (3 equiv.) in water (20 ml) was added dropwise to a solution of sulfide 4h (450 mg, 1.77 mmol) in methanol (25 ml) with stirring at room temp. After 1 hour the reaction mixture was filtered and methanol was evaporated under reduced pressure to gave an oil. Flash chromatography (EtOAc/methanol = 80/20) gave 300 mg of 4k (63%) and 100 mg of 6k (31%) as colorless crystalline solids.
1H, H₈ or H₉). 5.87 B of AB (dd, J₈,₉=5.5 Hz, J₉,₁₀ resp. J₇,₈=2.9 Hz, 1H, H₈ or H₉), 3.41 (bs, 1H, H₁ or H₇), 3.33 (d, J₁,₂=4.6 Hz, 1H, H₂), 3.00 (bs, 1H, H₁ or H₃), 2.40 A of AB (d, J₁₀,₁₀=9.1 Hz, 1H, H₁₀), 1.91 B of AB (d, J₁₀,₁₀=9.1 Hz, 1H, H₁₀), 13C-NMR (100 MHz, H-dec., CDCl₃): δ 206.1 (quat.), 155.8/141.1 (tert.), 140.3 (quat.), 136.1/133.5/131.9/129.1x2/125.5x2 (tert.), 80.9 (quat.), 53.0 (tert.), 51.1 (sec.), 46.4/46.0 (tert.) IR (CH₂Cl₂): υ 3010-2820 (C-H), 1710 (C=O, conj.) cm⁻¹. ESI/MS: m/e (%) 270 (0.5, M⁺), 145 (100, M⁺-SOPh), 117 (85, M⁺-SOPh-C₅H₄), 79 (85, M⁺-SOPh-C₅H₄), 66 (7, C₃H₆⁺). ESI/HRMS m/e: 270.0715 [calc for C₁₇H₁₄SO₂(M⁺): 270.0715].

A solution of MeLi (0.6 ml of a 1.6 M solution in hexane, 0.95 mmol) in hexane was gradually added to a suspension of dry CuI (100 mg, 0.5 mmol) in dry ether at temp. below 0 °C (ice-salt) under a nitrogen atmosphere. After stirring for 15 minutes, a solution of 4k (50 mg, 0.18 mmol) in THF was added. The mixture was stirred at 10 °C until the reaction was complete according to TLC (ca. 2h). The mixture was then quenched with aqueous ammonium chloride and the aqueous phase extracted with ether (3x). The combined organic phases were washed with brine (3x) and the solvent was evaporated under reduced pressure. Flash chromatography (EtOAc/methanol = 80/20) gave 48 mg (46%) of 6k as a colorless solid.

6k™: m.p.: 103 °C. 1H-NMR (400 MHz, CDCl₃): δ 7.69 and 7.54 (2 x m, SH, ph-H), 6.44 A of AB (dd, J₈,₉=5.3 Hz, J₉,₁₀ resp. J₈,₉=2.9 Hz, 1H, H₈ or H₉), 3.63 and 3.28 (2 x bs, 2H, H₄ and H₅), 2.95 (d, J₁,₂=4.7 Hz, 1H, H₂), 2.73 (m, 1H, H₃), 1.75 B of AB (dd, J₈,₉=18.8 Hz, J₉,₁₀=11.2 Hz, 1H, H₁₀), 1.76 B of AB (d, J₁₀,₁₀=9.1 Hz, 1H, H₁₀), 1.09 (d, J=7.0 Hz, 3H, CH₃). IR (CH₂Cl₂): υ 3010-2820 (C-H), 1710 (C=O) cm⁻¹. ESI/MS: m/e (%) 287 (0.7, M⁺+1), 221 (3, M⁺+1-C₅H₄), 161 (90, M⁺-SOPh), 133 (47, M⁺-SOPh-C₅H₄), 95 (92, M⁺-C₅H₄-SPh), 66 (30, C₃H₆⁺). ESI/HRMS m/e: 286.1028 [calc for C₁₇H₁₄SO₂(M⁺): 286.1028].

References and notes


Lithium dialkylcuprate additions


10. Structures were minimized, using the Allinger force field method (MM2-M in MODEL). Use of the services and facilities of the Dutch National NWO/SURF expertise Center CAOS/CAMM, University of Nijmegen, The Netherlands, under grant numbers SON 326-052 and STW NCH99.1751, is gratefully acknowledged.


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