Palladium-catalyzed desulfinylative C–C allylation of Grignard reagents and enolates using allylsulfonyl chlorides and esters

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Abstract
2-Methylprop-2-ene-, prop-2-ene-, 1-methylprop-2-ene-, and (E)-but-2-enesulfonyl chlorides have been used as electrophilic partners in desulfinylative palladium-catalyzed C–C coupling with Grignard reagents and sodium salts of dimethyl malonate and methyl acetoacetate. Neopentyl alk-2-ene sulfonates can also be used as electrophilic partners in desulfinylative allylic arylations and allylic alkylations. The regioselectivity of the allylic arylation and alkylation depends on the nature of the catalyst. With PdCl2(PhCN)2, (E)-crotyl derivatives are formed in high regioselectivity using either 1-methylprop-2-ene- or (E)-but-2-enesulfonyl chloride.

1. Introduction

The search of efficient methods for the construction of carbon–carbon bonds represents an ongoing, central theme of research of organic synthesis.1–11 Transition metal catalyzed cross-coupling of organometallic reagents with halides or triflates constitutes today one of the most powerful methods to generate carbon–carbon bonds.12–17 Arene- and alkanesulfonyl chlorides are inexpensive and readily available compounds. They have been used for more than a century in material sciences and medicinal chemistry.18–23 Recently, we have shown that Stille, carboynylative Stille, 24,25 Suzuki–Miyaura,26 Sonogashira–Hagihara27 type cross-couplings and Mizoroki–Heck28,29 type arylation can be carried out using sulfonyl chlorides as electrophilic partners under desulfinylation conditions.30 In the case of Mizoroki–Heck coupling reaction, Pd[P(t-Bu)3]2 catalyst led to products of aryl–aryl homocoupling, the organomagnesium reagents had to be converted into organozinc reagents for successful desulfinylative C–C cross-coupling reactions (Scheme 1B).58

One-pot syntheses of alk-2-enesulfonyl chlorides 2a–c and alk-2-enesulfonic esters 3a–c were realized applying the ene-reaction of SO2 with allylsilanes 1a–c (Scheme 2A).50–64 Neopentyl esters,53–55 and sulfonamides56 in the presence of nickel catalysts. Since 1929 it is known that Grignard reagents displace sulfonyl chlorides to generate the corresponding sulfones (Scheme 1A).57

Early experiments with sulfonyl chlorides and aryl Grignard reagents in the presence of Pd[P(t-Bu)3]2 catalyst led to products of aryl–aryl homocoupling, the organomagnesium reagents had to be converted into organozinc reagents for successful desulfinylative C–C cross-coupling reactions (Scheme 1B).58

We have now examined the palladium-catalyzed desulfinylative C–C cross-coupling reaction using alk-2-ene-sulfonyl chlorides and neopentyl alk-2-ene sulfonic esters with Grignard reagents (‘hard nucleophiles’) and sodium β-oxoenolates (‘soft nucleophiles’).

2. Results and discussion

One-pot syntheses of alk-2-enesulfonyl chlorides 2a–c and alk-2-enesulfonic esters 3a–c were realized applying the ene-reaction of SO2 with allylsilanes 1a–c (Scheme 2A).50–64 Neopentyl esters,53–55 and sulfonamides56 in the presence of nickel catalysts. Since 1929 it is known that Grignard reagents displace sulfonyl chlorides to generate the corresponding sulfones (Scheme 1A).57

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(E)-crotysulfonate (3d) was prepared from (E)-crotysulfonyl chloride (2d) as shown in Scheme 2.

Our exploratory experiments engaged first sulfonyl chlorides 2a and 2b and various Grignard reagents, PhZnCl, sodium salts of methyl acetacetaldehyde and dimethyl malonate as nucleophiles. Our results are summarized in Tables 1 and 2.

Crucial for the success was the slow addition of the nucleophilic reagent to a premixed THF solution of the sulfonyl chloride with the palladium catalyst. The formation of sulfones can be completely suppressed by the dropwise addition of Grignard reagent. Temperature can be varied between 20 °C and 78 °C without affecting yield in products of alllylation 4 significantly (Table 1, compare entries 1 and 2 and entries 7 and 8). Using 2-methylprop-2-ene sulfonyl chloride (2a), allylation of aryl and alkyl Grignard reagents have been successful, although alkyl Grignard reagents showed slower reactions (entries 5–7) than aryl derivatives (entries 1–4). With PhZnCl and 2a, coupling occurs also but was significantly slower than with PhMgCl (entry 8). With 2b, coupling with o-tolylMgCl and p-methoxyphenylMgBr were faster and better yielded (Table 2, entries 9–10) than the reaction with n-octylMgBr (entry 11), which provided undes-1-ene in 66% yield. In all cases Pd[P(t-Bu)3]2 in 5 mol % and THF led to better reaction rates and yields than other palladium catalysts as illustrated with 2a and 2b and Grignard reagents (Tables 1 and 2). But in the case of soft nucleophiles, Pd[PPh3]4 was found to be better catalyst (Table 2, entries 12 and 15) than Pd[P(t-Bu)3]2 (entry 13). The sodium salt of methyl acetacetae has also been allylated successfully (entries 14 and 16).

We then explored whether 2-methylprop-2-ene sulfonylic ester 3a would also be suitable for the desulfonyllative C–C coupling with Grignard reagents. For that neopentyl ester 3a was reacted with o-tolylMgCl in the presence of various catalysts (5 mol %) in boiling THF. Our results are summarized in Table 3.

The fastest and best yield (72%) reaction used Pd[PPh3]4 as catalyst (Table 3, entry 1). With NiCl2(dpdp) the yield was slightly lower (68%) and with [Ir(COD)Cl]2, the reaction did not occur. Interestingly, Fe(acac)3 is also able to catalyze the desulfonyllative coupling (Table 3, entry 3) provided that it is reacted first with t-BuMgCl 0.5 h. The sodium salt of methyl acetacetate has also been allylated successfully (entries 14 and 16).

With these successes in hand we then explored whether our conditions could be applied to the regioselective crotylation of metallic nucleophiles. Our results are summarized in Table 4 for the reactions of (E)-crotysulfonyl chloride (2d) and o-tolylMgCl using various palladium and nickel catalysts. Yields were not measured in all our assays, but judging from the 1H NMR spectra of the crude reaction mixtures, they were all better than 50%. In all cases the linear product 5a was favored (product of no allylic rearrangement).

The regioselectivity (product ratio 5a/6a) was the best (96:4, yield 52%) using Pd2(dba)3 and xanthos ligand 66–71 (entry 6). The best regioselectivity (95:5) and yield (75%) were realized using PdCl2(PhCN)2 as catalyst, for a reaction in THF at room temperature (entry 16). As for the desulfonyllative methallation (Table 1), Pd[P(t-Bu)3]2 led to the fastest reaction and highest yield (78%), but with a lower regioselectivity (entry 8).

Application of Hermann’s palladacycle (27,28) (entry 14) did not lead to any significant improvement of the regioselectivity. In the

**Table 1**

Study of the effect of palladium catalysts on the reactivity of Grignard reagents with sulfonyl chloride 2b

<table>
<thead>
<tr>
<th>Entry</th>
<th>NuM</th>
<th>Cat. (5 mol %)</th>
<th>Time</th>
<th>Product (yield)</th>
</tr>
</thead>
<tbody>
<tr>
<td>2a</td>
<td>o-tolylMgCl</td>
<td>Pd[P(t-Bu)3]2</td>
<td>0.5 h</td>
<td>4a (87%)</td>
</tr>
<tr>
<td>2b</td>
<td>PhMgCl</td>
<td>Pd[P(t-Bu)3]2</td>
<td>0.5 h</td>
<td>4b (82%)</td>
</tr>
<tr>
<td>2c</td>
<td>m-tolylMgCl</td>
<td>Pd[P(t-Bu)3]2</td>
<td>0.5 h</td>
<td>4c (62%)</td>
</tr>
<tr>
<td>2d</td>
<td>p-MeOCH2MgBr</td>
<td>Pd[P(t-Bu)3]2</td>
<td>0.5 h</td>
<td>4d (79%)</td>
</tr>
<tr>
<td>2e</td>
<td>BnMgCl</td>
<td>Pd[P(t-Bu)3]2</td>
<td>0.5 h</td>
<td>4e (75%)</td>
</tr>
<tr>
<td>2f</td>
<td>PhCH2CH2MgCl</td>
<td>Pd[P(t-Bu)3]2</td>
<td>0.5 h</td>
<td>4f (62%)</td>
</tr>
<tr>
<td>2g</td>
<td>n-BuMgCl</td>
<td>Pd[P(t-Bu)3]2</td>
<td>1 h</td>
<td>4g (28%)</td>
</tr>
<tr>
<td>2h</td>
<td>PhZnCl</td>
<td>Pd[P(t-Bu)3]2</td>
<td>0.5 h</td>
<td>4h (57%)</td>
</tr>
<tr>
<td>2i</td>
<td>o-tolylMgCl</td>
<td>Pd[P(t-Bu)3]2</td>
<td>0.5 h</td>
<td>4i (76%)</td>
</tr>
<tr>
<td>2j</td>
<td>p-MeOCH2CH2MgBr</td>
<td>Pd[P(t-Bu)3]2</td>
<td>0.5 h</td>
<td>4j (85%)</td>
</tr>
<tr>
<td>2k</td>
<td>n-octylMgBr</td>
<td>Pd[P(t-Bu)3]2</td>
<td>3 h</td>
<td>4k (66%)</td>
</tr>
<tr>
<td>12a</td>
<td>MeOOC-CH=C(Me)OONa</td>
<td>Pd[PPh3]4</td>
<td>0.5 h</td>
<td>4k (76%)</td>
</tr>
<tr>
<td>12b</td>
<td>MeOOC-CH=C(Me)ONa</td>
<td>Pd[PPh3]4</td>
<td>0.5 h</td>
<td>4k (48%)</td>
</tr>
<tr>
<td>12c</td>
<td>MeOOC-CH=C(Me)ONa</td>
<td>Pd[PPh3]4</td>
<td>0.5 h</td>
<td>4m (78%)</td>
</tr>
<tr>
<td>12d</td>
<td>MeOOC-CH=C(Me)ONa</td>
<td>Pd[PPh3]4</td>
<td>0.5 h</td>
<td>4m (92%)</td>
</tr>
<tr>
<td>12e</td>
<td>MeOOC-CH=C(Me)ONa</td>
<td>Pd[PPh3]4</td>
<td>0.5 h</td>
<td>4m (89%)</td>
</tr>
</tbody>
</table>

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**Table 2**

Allylic alkylation and arylation using 2-methylprop-2-ene sulfonyl chloride (2a) and prop-2-ene sulfonyl chloride (2b) and various nucleophiles giving products of desulfonyllative C–C cross-coupling 4

**Scheme 2.** Syntheses of alk-2-ene sulfonyl chlorides and neopentyl alk-2-ene sulfonylates.

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Table 3
Effect of the transition metal catalyst on the cross-coupling of neopentyl 2-methylprop-2-enesulfonate (3a) with o-tolylMgCl

<table>
<thead>
<tr>
<th>Entry</th>
<th>Catalyst (equiv)</th>
<th>Reaction time</th>
<th>Yielda</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>NiCl2(dppe)</td>
<td>2 h</td>
<td>72%</td>
</tr>
<tr>
<td>2</td>
<td>NiCl2(dppe)</td>
<td>3 h</td>
<td>68%</td>
</tr>
<tr>
<td>3</td>
<td>Fe(acac)3</td>
<td>24 h</td>
<td>65%</td>
</tr>
<tr>
<td>4</td>
<td>[Ir(COD)Cl]2</td>
<td>2 h</td>
<td>0%</td>
</tr>
</tbody>
</table>

Conditions: 0.65 mmol of sulfonic ester (1 mmol) with Grignard reagent (1.5–2.5 mmol) was made in refluxing THF (5 mL) with catalyst (0.05 mmol).

* a Yield of the coupled product was determined after flash chromatography.

We then applied our best conditions found for the desulfinylative crotylation reported in Table 4 to the reaction of 1-methylprop-2-enesulfonyl chloride (2c) and various nucleophiles. Our results are summarized in Table 5, together with those obtained for the reactions of 2d with further nucleophiles.

Except for the Pd(Ph3P)4-catalyzed reactions of m-tolylMgCl with either the branched (2c) or linear sulfonyl chloride (2d) that both led to a 1:1 mixture of 5b + 6b in mediocre yields (Table 5, entries 3 and 6), the major products of desulfinylative C–C cross-coupling are the linear (E)-crotyl derivatives 5.

As for reaction of 2d with o-tolylMgCl (Table 4, entry 16) the best regioselectivity and yield were obtained with PdCl2(PhCN)2 as catalyst (Table 5, entries 1, 2, 4, 5). Using Pd(Ph3P)4 catalysts that gave the best yield reactions 2a, 2b with sodium enolates, the regioselectivity (5 vs 6) remained bad for the desulfinylative allylations of the sodium salts of dimethyl maleonate (entries 7 and 9) and of methyl acetooacetate (entries 8 and 10) with 2c and 2d. These results suggest that the mechanism of C–C bond formation in these reactions involves the formation of (π-allyl)(ligand)palladium intermediates that are attacked then by the nucleophiles. This
hypothesis is supported by the observation that the regioselectivity does not depend on the nature of the starting sulfonil chloride (2c vs 2d). With PdCl2(PhCN)2 as catalyst, the regioselectivity in favor of the linear products of (E)-crotyl derivatives suggests that a steric factor is controlling the C–C bond forming process. In the case of Pd[PPh3]4-catalyzed reaction it seems that the (crotyl)Pd(ligand) intermediate does not make any great difference for the Nu insertion into the non-substituted (less steric hindrance) and the methyl substituted center of the allyl/palladium moiety. For more than 30 years it has been known that the regioselectivity of allylic alkylation, allylic vinylation and allylic arylation depends on the nature of the catalyst.

Although many more experiments should be carried out to approach a mechanistic interpretation of our results, we propose at this stage that (allyl)palladium intermediates 7 and 8 are formed by reactions of 2c or 2d with PdCl2(PhCN)2 and Pd[PPh3]4, respectively (Scheme 3). Intermediates 7 is expected to be more electrophilic than 8 and favors an anti mode of addition of the nucleophiles (Nu−) onto the least sterically hindered allyl carbon center. In the case of 8, the nucleophile undergoes first an oxidative addition or Sn2 displacement reaction at the palladium center. The resulting intermediate 9 undergoes then a reductive elimination reaction forming the C–C bond, a process, which is less demanding in terms of steric hindrance between secondary and tertiary allylic centers.

Depending on the nature of the leaving group of the allyl and 3-buten-2-y1 electrophiles and ligand significant degree of retention of regiochemistry and stereochemistry has been observed for palladium-catalyzed allylic alkylation.

We thus examined the desulfinylative allylation of m-tolyliMgCl with 1-methylprop-2-ene-sulfonyl chloride (2c) and neopentyl (2d) 109-117 This was also the case for the reaction of (E)-but-2-ene-sulfonyl chloride (2d) with the sodium salt of dimethyl malonate in the presence of [Ir(COD)Cl]2 in THF at room temperature that produced a 1:4 mixture of products of allylation (Scheme 5).

3. Conclusion

Allylic arylation and alkylation of Grignard reagents and sodium salts of dimethyl malonate and methyl acetoacetate can be carried out under smooth conditions in the presence of a palladium catalyst and using 2-alkenesulfonil chlorides as electrophilic reagents. The latter undergo fast desulfinylations generating (allyl)palladium intermediates. The regioselectivity of the quenching of these intermediates by the nucleophilic reagents depends on the nature of the catalyst, but not on the nature of the starting alk-2-ene-sulfonyl chloride. For instance using either 1-methylprop-2-ene-sulfonyl chloride or (E)-but-2-ene-sulfonyl chloride the linear products are favored over the branched isomers (regioselectivity 95:5 or better) for arylMgCl and using 5 mol % of PdCl2(PhCN)2 in THF at room temperature. When branched isomers are targeted [Ir(COD)Cl]2-catalyzed allylic alkylation of (E)-but-2-ene-sulfonyl chlorides with the sodium salt of dimethyl malonate can be employed.

4. Experimental section

4.1. Methods

Unless stated otherwise, reactions were conducted in flame-dried glassware under a vacuum. THF was distilled before to use from sodium and benzenophene. Catalysts and ligands were purchased from Strem Chemical, Inc. All commercially available reagents are used without further purification. Solvents after reactions and extraction were evaporated in a rotatory evaporator under vacuum (solvents were removed cooling at –20 °C, in the case of low boiling point or low molecular mass compounds). TLC for reaction monitoring was performed on 60 F254 (Merck) with detection by UV light and charring with KMnO4 or Pancaldi reagent. 1H and 13C NMR spectra were recorded by using Bruker-DPX-400 or Bruker-ARK-400 spectrometer at 400 MHz and 100.6 MHz, respectively, and are reported relative to MeSi (δ 0.0) or to the solvents residual 1H-signal (CDCl3, δ(H) 7.27). Data for 1H NMR spectra are reported as follows: chemical shift (δ ppm), multiplicity, coupling constant (Hz), and integration. Data for 13C NMR spectra reported in terms of chemical shift. IR spectra were recorded on a Perkin–Elmer-1420 spectrometer and are reported in frequency of absorption (cm−1). High Resolution MALDI-TOF mass spectra were obtained from the Institute of Molecular and Biology Chemistry, Swiss Institute of Technology Mass Spectral Facility. Compounds 1c, 2a, 2b, 1d were prepared from known methods.

4.2. 1-Methylprop-2-ene-1-sulfonyl chloride (2c)

(CF3SO2)2NSiMe3 (0.78 mmol, 0.2 equiv) in anhyd CH2Cl2 (5 mL) was degassed by freeze-thaw cycles on the vacuum line. SO2 (78 mmol, 20 equiv), dried through column packed with P2O5 and Al2O3, was transferred on the vacuum line to the MeCN solution frozen at –196 °C. The mixture was allowed to melt and to warm to –40 °C. After 30 min at this temperature but-2-enyl(trimethyl)silane (1c)
(3.9 mmol, 1 equiv) in MeCN (1 mL) was added slowly. The mixture was stirred at \(-40 ^\circ C\) for 6 h. After cooling to \(-78 ^\circ C\), the excess of SO\(_2\) and the solvent were evaporated under reduced pressure (10\(^{-3}\) Torr) to dryness (ca. 1 h). Halogenating agent (NCS 4.7 mmol, 1.2 equiv, dissolving in MeCN) was added to reaction mixture at \(-20 ^\circ C\). After 2 h at this temperature, allylsulfonyl chloride formed. The residue was purified by flash chromatography (9:1 PE/EtOAc) to yield 68% as colorless oil. IR (film): 3060, 2930, 1720, 1400, 1175, cm\(^{-1}\). 1\(^{1}H\) NMR (400 MHz, CDCl\(_3\)): \(\delta = 5.82 \text{ (qn, 1H, } J=7.83 \text{ Hz, H–C(3)}, 3.82 \text{ (m, 2H, H–C(4)): 4.25 (m, 1H, H–C(2))), 1.72 (d, } 6.41 \text{ Hz, H–C(4)), 0.91 (s, 9H, H–C(3))). 1^{13}C\) NMR (100.6 MHz, CDCl\(_3\)): \(\delta = 136.5, 117.5, 79.7, 54.3, 32.2, 26.5, 18.5. CIMS (NH}_3\): \(m/z=224 \text{ (100, } [M+18]), 154 (10, } [M-52]), 71 \text{ (80, } [M-135]). HRMS (MALDI-TOF): (C\(_9\)H\(_{18}\)O\(_3\)SNa\(^{+}\)), calcd: 229.0874; found: 229.0874.

### 4.5. Neopentyl (\(E\))-but-2-ene-1-sulfonate (3d)

Applying the same procedure as for 3a, starting from 2d. FC (8:2 PE/EtOAc): 89% of 3d, light yellow oil. IR (film): 2960, 1480, 1350, 1160, 960, 935, 840, 630 cm\(^{-1}\). 1\(^{1}H\) NMR (400 MHz, CDCl\(_3\)): \(\delta = 5.81 \text{ (m, 1H, H–C(2)), 5.47 (m, 1H, H–C(3)), 3.79 (s, 2H, H–C(1’)), 3.70 (d, } J=7.31 \text{ Hz, H–C(2)), 1.71 (d, 3H, } J=6.41 \text{ Hz, H–C(4)), 0.91 (s, 9H, H–C(3))). 1^{13}C\) NMR (100.6 MHz, CDCl\(_3\)): \(\delta = 136.5, 117.5, 79.7, 54.3, 32.2, 26.5, 18.5. CIMS (NH}_3\): \(m/z=224 \text{ (100, } [M+18]), 154 (10, } [M-52]), 71 \text{ (80, } [M-135]). HRMS (MALDI-TOF): (C\(_9\)H\(_{18}\)O\(_3\)SNa\(^{+}\)), calcd: 229.0874; found: 229.0874.

### 4.6. General procedure 1 for the desulfinylative allylation of Grignard reagents with sulfonyl chlorides

In a round bottom flask dried under vacuum was placed under \(N_2\), the corresponding sulfonyl chloride (1 equiv), catalyst (5 mol %) in THF (4 mL) at 25 \(^\circ\)C. Grignard reagent (1.5 equiv) was added dropwise to this solution over 5–10 min. The reaction mixture was stirred until complete disappearance of starting material. The reaction mixture was added to satd aq soln of NH\(_4\)Cl (15 mL) and extracted with ether (15 mL, three times). The combined organic layers were dried (Na\(_2\)SO\(_4\)), filtered, and concentrated under reduced pressure. The residue was purified by flash chromatography.

### 4.7. General procedure 2 for the desulfinylative allylation of sodium enolates with sulfonyl chlorides

NaH (1.5 equiv) and either dimethyl malonate or methyl acetooacetate (1.5 equiv) were mixed in THF (3 mL) and stirred at 0 \(^\circ\)C for 20 min. This solution was then added dropwise to a round bottom flask containing sulfonyl chloride (1 equiv), catalyst (0.05 equiv) in THF (3 mL) at 25 \(^\circ\)C. The reaction mixture was stirred until disappearance of starting material. The mixture was added to cold H\(_2\)O (15 mL) and extracted with ether (15 mL, three times). The combined organic layers were dried (Na\(_2\)SO\(_4\)), filtered, and concentrated under reduced pressure. The residue was purified by flash chromatography.

### 4.8. 1-Methyl-2-(2-methyl-2-propenyl)benzene (4a)

Using the general procedure 1 for the reaction using 1.0 M soln of o-tolylmagnesium chloride (1.0 mL, 1.0 mmol, 1.5 equiv) with 2a (0.1 g, 0.65 mmol, 1 equiv): 82 mg (87%), colorless oil. 1\(^{1}H\) NMR
4.13. 1-(4-Methylpent-4-enyl)benzene (4f)  

Using the general procedure 1 for the reaction using 1.0 M solution of PhMgCl (0.56 mL, 1.0 mmol, 1.5 equiv) with 2a (0.1 g, 0.65 mmol, 1 equiv): 70 mg (82%), colorless oil. Using the general procedure 1 for the reaction using 0.5 M solution of phenylzinc bromide (2.0 mL, 1.0 mmol, 1.5 equiv) with 2a (0.1 g, 0.65 mmol, 1 equiv): 54 mg (57%), colorless oil. 1H NMR (400 MHz, CDCl3): δ = 7.16 (m, 4H, arom.), 4.84 (s, 1H, H–C(3)), 2.30 (s, 3H, Me–arom.), 1.77 (s, 3H, Me–C(2)). 13C NMR (100.6 MHz, CDCl3): δ = 144.6, 130.5, 130.2, 127.7, 127.2, 111.9, 42.2, 23.1, 19.8. CIMS (NH3): m/z = 146 (40, [M]), 131 (100, [M − 15]), 91 (33, [M − 55]).

4.14. 1- Allyl-2-methylbenzene (4h)  

Using the general procedure 1 for the reaction using 1.0 M solution of o-tolylmagnesium chloride (1.1 mL, 1.1 mmol, 1.5 equiv) with sulfonyl chloride 2b (0.1 g, 0.72 mmol, 1 equiv): 72 mg (76%), colorless oil. 1H NMR (400 MHz, CDCl3): δ = 7.35–7.10 (m, 4H, arom.), 6.01 (m, 1H, H–C(2)), 5.12 (m, 2H, H–C(3)), 3.44 (d, J = 6.39 Hz, 2H, H–C(1)), 2.34 (s, 3H, Me–arom.). CIMS (NH3): m/z = 132 (40, [M]), 91 (100, [M − 41]).

4.15. 4-Allylanisole (4i)  

Using the general procedure 1 for the reaction using 0.5 M solution of p-methoxyphenylmagnesium bromide (2.2 mL, 1.1 mmol, 1.5 equiv) with 2b (0.1 g, 0.72 mmol, 1 equiv): 90 mg (85%), colorless oil. 1H NMR (400 MHz, CDCl3): δ = 7.06 (d, J = 8.56 Hz, 2H, arom.), 6.80 (d, J = 8.56 Hz, 2H, arom.), 5.91 (m, 1H, H–C(2)), 4.97 (m, 2H, H–C(3)), 3.71 (s, 3H, OMe), 3.26 (d, J = 6.59 Hz, 2H, H–C(1)). CIMS (NH3): m/z = 148 (21, [M]), 147 (100, [M − 1]), 132 (19, [M − 16]), 91 (44, [M − 57]).

4.16. Dimethyl 2-(2-methyl-2-propenyl)malonate (4k)  

Using the general procedure 2 for the reaction using NaH (40 mg, 0.97 mmol, 1.5 equiv), dimethyl malonate (0.13 g, 0.97 mmol, 1.5 equiv) with 2a (0.1 g, 0.65 mmol, 1 equiv): 92 mg (97%), colorless oil. 1H NMR (400 MHz, CDCl3): δ = 4.76 (s, 1H, H–C(3)), 4.69 (s, 1H, H–C(3)), 3.74 (s, 6H, OMe), 3.59 (t, J = 7.7 Hz, 1H, H–C(3)), 2.59 (d, J = 7.7 Hz, 2H, H–C(1)), 1.72 (s, 3H, Me–C(2)). 13C NMR (100.6 MHz, CDCl3): δ = 170.6, 139.8, 116.6, 49.2, 48.6, 38.1, 23.2. CIMS (NH3): m/z = 204 (19, [M + 18]), 171 (100, [M − 15]), 155 (11, [M − 31]).

4.17. Methyl 2-acetyl-4-methyl-4- pentenoate (4l)  

Using the general procedure 2 for the reaction using NaH (40 mg, 0.97 mmol, 1.5 equiv), dimethyl malonate (0.11 g, 0.97 mmol, 1.5 equiv) with 2a (0.1 g, 0.65 mmol, 1 equiv): 86 mg (83%), colorless oil. 1H NMR (400 MHz, CDCl3): δ = 5.68 (t, J = 8.6 Hz, 2H, arom.), 4.80 (s, 1H, H–C(4)), 4.73 (s, 1H, H– C(1)), 3.81 (s, 3H, OMe), 3.28 (s, 2H, H–C(3)), 1.69 (s, 3H, Me–C(2)). 13C NMR (100.6 MHz, CDCl3): δ = 158.0, 145.5, 131.8, 129.8, 113.7, 111.6, 55.3, 43.8, 21.9. CIMS (NH3): m/z = 180 (2, [M + 18]), 163 (9, [M − 1]), 162 (75, [M]), 146 (32, [M − 16]).

4.18. Dimethyl 2-allylmalonate (4m)  

Using the general procedure 2 for the reaction using NaH (43 mg, 1.07 mmol, 1.5 equiv), dimethyl malonate (0.13 g, 1.07 mmol, 1.5 equiv) with 2b (0.1 g, 0.72 mmol, 1 equiv): 114 mg (92%), colorless oil. The spectral data (1H NMR and 13C NMR) of the product are identical with those described in the literature for this compound. 1H NMR (400 MHz, CDCl3): δ = 5.71 (m, 1H, H–C(2)), 5.12 (m, 2H, H–C(3)), 3.74 (s, 6H, OMe), 3.48 (t, J = 7.2 Hz, 2H, H–C(3)), 2.67 (t, J = 7.4 Hz, 2H, H–C(1)). CIMS (NH3): m/z = 173 (9, [M + 1]), 172 (100, [M]), 140 (6, [M − 32]).

4.19. Methyl 2-acetylpent-4-enoate (4n)  

Using the general procedure 2 for the reaction using NaH (43 mg, 1.07 mmol, 1.5 equiv), methyl acetoacetate (0.13 g, 1.07 mmol, 1.5 equiv) with 2b (0.1 g, 0.72 mmol, 1 equiv): 100 mg (89%), colorless oil. 1H NMR (400 MHz, CDCl3): δ = 5.76 (m, 1H, H– C(4)), 5.10 (m, 2H, H–C(5)), 3.74 (s, 3H, OMe), 3.54 (t, J = 7.1 Hz, 1H, H–C(2)), 2.59 (m, 2H, H–C(3)), 2.21 (s, 3H, Me–C(4)). CIMS (NH3): m/z = 174 (5, [M + 18]), 156 (100, [M]), 142 (9, [M − 14]).

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4.20. (E)-1-(But-2-enyl)-2-methylbenzene (5a)\textsuperscript{131} and 1-(but-3-en-2-yl)-2-methylbenzene (6a)\textsuperscript{101}

Using the general procedure 1 for the reaction using 1.0 M solution of α-tolylmagnesium chloride (1.0 mL, 1.0 mmol, 1.5 equiv) with 2ε (0.1 g, 0.65 mmol, 1 equiv) 65 mg (69%), colorless oil. Using the general procedure 1 for the reaction using 1.0 M solution of α-tolylmagnesium chloride (1.0 mL, 1.0 mmol, 1.5 equiv) with 2d (0.1 g, 0.65 mmol, 1 equiv): 71 mg (75%), colorless oil. \textsuperscript{1}H NMR (400 MHz, CDCl\textsubscript{3}) of 5a: \(\delta = 7.21 \text{ (s, 4H, arom.)}, 5.62 \text{ (m, 1H, H–C(2))}, 5.48 \text{ (m, 1H, H–C(3))}, 3.33 \text{ (d, 2H, 6.61 Hz, H–C(1))}, 2.33 \text{ (s, 3H, Me–arom.)}, 1.71 \text{ (d, 3H, 6.38 Hz, H–C(4))}. \)

\textsuperscript{1}H NMR (400 MHz, CDCl\textsubscript{3}) of 6a: \(\delta = 7.21 \text{ (s, 4H, arom.)}, 6.02 \text{ (m, 1H, H–C(3))}, 5.10 \text{ (m, 2H, H–C(4))}, 3.73 \text{ (m, 1H, 6.98 Hz, H–C(2))}, 2.33 \text{ (s, 3H, Me–arom.)}, 1.38 \text{ (d, 3H, 6.98 Hz, H–C(1))}. \) CIMS (NH\textsubscript{3}): \(m/z = 147 \text{ ([M + 1]}^+)\), \(170 \text{ ([M]}^+)\), 151 (5, [M–19])\textsuperscript{19}, 126 (12, [M–44])\textsuperscript{19}.

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**References and notes**
