Heck Reaction on Protected 3-Alkyl-1,2-dien-1-ols: an Approach to Substituted 3-Alkenylindoles, 2-Alkoxy 3-Alkylidene-2,3-Dihydrobenzofuranes and –Indolidines†

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Abstract

A phosphine free annulation reaction has been exploited for the preparation of substituted 3-alkenylindoles, 2-alkoxy 3-alkylidene-2,3-dihydrobenzofuranes and -indolidines in good to excellent yields. This has been done by reaction of protected 3-alkyl-1,2-dienols with o-iodophenols or protected o-iodoanilines. Two different heterocyclic skeletons were obtained, this depends on the electron-donating properties of the heteroatom involved in the annulation process.

† Electronic Supplementary Information (ESI) available: 1H and 13C NMR spectra of products 4a – f and 5b – g. NOESY spectra of products 4a (E and Z) and 4b. See DOI: 10.1039/b000000x/
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Introduction

The palladium catalysed annulation process is one of the most useful methods to synthesise highly functionalised heterocycles. In recent years this reaction has been exploited as a route to a wide variety of heterocycles and carbocycles using 1,2-, 1,3-, 1,4-dienes, as well as internal alkynes, which were placed to react with aryl or vinyl halides and triflates. Allenes represent a very attractive class of compounds due to their increased reactivity with respect to other classes of dienic substrates. They undergo carbopalladation very readily, and moreover many examples of catalysed annihilations involving 1,2-dienes have so far been reported.

Recently we have described the synthetic use of the Heck coupling applied to 1-alkoxy-functionalised 1,3-dienes, and more recently we have addressed our attention to protected 1,2-dienols as synthetic precursors of α-arylated α,β-unsaturated aldehydes. In particular alkoxy-substituted allenenes are characterised by unique reactivity, and they have been exploited in different reactions with organometallic, nucleophilic, and electrophilic reagents. The synthesis of carbocycles and heterocycles, exploiting lithiated alkoxyallenes have been recently reviewed. The reactivity of 1-alkoxy-π-allylpalladium complexes, obtained from the corresponding alkoxyallenes, has been explored, and the dramatic effect of the alkoxy group on the regioselectivity of the Pd(0) catalysed coupling reactions has been demonstrated. Actually, the most reactive position is that adjacent to the alkoxy group.

The indolic scaffold represents a privileged motif that is found in various natural and synthetic products, many efforts have been consequently directed towards the synthesis of substituted indoles. In particular, vinylindoles represent a valuable class of precursors of biologically important derivatives, such as alkaloids, carbazoles and carbolines. As far as we know, few syntheses of alkyl indoles have so far been reported in the literature. Some procedures utilise the suitable phosphorane and indole-3-carbaldehydes, or the gramine framework coupled with aldehydes. The Heck coupling has also been exploited. Since the proposed procedures resort to the indol scaffold as starting reagent, their applicability to the synthesis of variously substituted targets is limited, as few functionalised indoles are commercially available.

As far as 3-alkylidene-2,3-dihydrobenzofuranes are concerned, they can be the starting point to synthesise several biologically relevant molecules as, for example, the rocaglates that show a potent antitumor activity.

Discussion

In this paper we report the synthesis of highly functionalised benzoheterocycles by Heck reaction using various phenols or protected o-iodoanilines, and protected alkyl-1,2-dien-1-ols. 1,2-Dienols were synthesised as previously described by the reaction of the protected alkyne with 2 equiv of BuLi, as shown in Scheme 1. According to the literature, internal allenones afford a mixture of 1,2-dienol and the starting alkyn.

![Scheme 1 Synthesis of protected 1,2-dienols starting from protected alkynols](image)

The reaction of 1-(ethoxymethoxy)hex-1,2-diene (2c) with 2-iodophenol was selected in order to optimise the process. This was done by evaluating the effect of the catalyst, solvent, and base, as well the influence of added phosphines and ionic liquids on the coupling yield and the diastereoselectivity. The E and Z configuration of the double bond of 3-butylidene-2-(ethoxymethoxy)-2,3-dihydrobenzofuran (4a) was determined by a NOESY experiment in which the correlation point between H_a (5.81 ppm) and H_b (6.12 ppm), for the E isomer, or H_a (6.12 ppm) and H_b (7.19 ppm), for the Z isomer, was observed. The E/Z ratio was determined by ^1H NMR analysis on the crude reaction mixture. In particular, the E/Z ratio was deduced by comparing the integration area of the signal centred at 5.81 ppm, pertinent to the H_a proton of the E isomer, with the signal centred at 6.35 ppm, due to the H_b proton of the Z isomer. The results are listed in the Table 1.

### Table 1 Coupling reaction between 1-(ethoxymethoxy)hex-1,2-diene (2c) and 2-iodophenol

<table>
<thead>
<tr>
<th>Entry</th>
<th>Base</th>
<th>Catalyst (%)</th>
<th>Solvent</th>
<th>Time (h)</th>
<th>Yield (%)</th>
<th>E/Z</th>
</tr>
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<tbody>
<tr>
<td>1</td>
<td>nPr</td>
<td>2c</td>
<td>BuLi, THF</td>
<td>-78°C, 2h</td>
<td>60%</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>nPr</td>
<td>2c</td>
<td>BuLi, THF</td>
<td>-78°C, 2h</td>
<td>66%</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>nPr</td>
<td>2c</td>
<td>BuLi, THF</td>
<td>-78°C, 2h</td>
<td>62%</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>nPr</td>
<td>2c</td>
<td>BuLi, THF</td>
<td>-78°C, 2h</td>
<td>68%</td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>nPr</td>
<td>2c</td>
<td>BuLi, THF</td>
<td>-78°C, 2h</td>
<td>65%</td>
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<tr>
<td>6</td>
<td>nPr</td>
<td>2c</td>
<td>BuLi, THF</td>
<td>-78°C, 2h</td>
<td>60%</td>
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<tr>
<td>7</td>
<td>nPr</td>
<td>2c</td>
<td>BuLi, THF</td>
<td>-78°C, 2h</td>
<td>62%</td>
<td></td>
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<tr>
<td>8</td>
<td>nPr</td>
<td>2c</td>
<td>BuLi, THF</td>
<td>-78°C, 2h</td>
<td>68%</td>
<td></td>
</tr>
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</table>

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Examining the results reported in Table 1, it can be observed that the highest stereoselectivity is achieved when the reaction is carried out in pure TBAB (entry 6), while a mixture of DMSO/TBAB (entry 8) is the best compromise in order to attain good yields with reasonable stereoselectivities. The improvement of the reaction stereoselectivity which was observed when changing from pure DMSO to pure TBAB, might be attributed to the effect of the ionic liquid and to a higher polarity of the reaction medium.

Sev eral ionic liquids were tested, in each case either the cation or the anion were changed, the TBA cation seems to be necessary to obtain good reaction outcomes, actually the use of DMSO/bmimBr (entry 17) decreases the yield. On the one hand, reaction yield does not seem to be strongly influenced by the nature of the anion in the ionic liquid, and good yields are always observed, even if bromide appears to be the preferred anion. Im provement of the reaction stereoselectivity which was observed when changing from pure DMSO to pure TBAB, might be attributed to the effect of the ionic liquid and to a higher polarity of the reaction medium.

The Heck coupling was therefore carried out using functionalised 1,2-dienes and protected 2-idoaniline, or 2-iodophenols, which contain both electron-donating and electron-withdrawing substituents. Surprisingly, as shown in Scheme 2, the reaction led to two different scaffolds depending on the nature of the nucleophile (oxygen or nitrogen), and of the withdrawing substituents. Substituted 2-alkoxy-3-alkylidene-2,3-dihydrobenzofuranes or -indolines were obtained. Substituted 2-alkoxy-3-alkylidene-2,3-dihydrobenzofuranes or -indolines 4 a-f in one case, and substituted 3-alkenylandoles 5 a-g in the other, were isolated.

The hypothesised reactivity pattern is illustrated in scheme 2. The addition of arylpalladium compounds to protected alcoxyallenes 2a – e produced the π-allylpalladium intermediate A. Then the following intramolecular nucleophilic substitution afforded the products 4a – f. The elimination of the OR₂ group, assisted by the nitrogen lone pair which gave the intermediate B, could occur, depending on the electron donating properties of the heteroatom X. The final deprotonation at the C of the alkyl chain allowed the formation of the 3-alkenylandoles 5a – g. It should be pointed out that the last step is not possible in the case of terminal 1,2-allen-2-ols. Moreover, when the coupling was carried out with 2-ido-N-acetylaniline (entry 6 in Table 2), the corresponding substituted alkyldieneindoline 4f was isolated first. Besides, when this

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*Reactions conditions: PhIOH, 0.5 mmol; 2e 0.75 mmol; solvent 3 mL; ionic liquid 300 mg, base 0.5 mmol, T = 110 °C. a Isolated products, purified by column chromatography. b Determined by NMR analysis. c Determined by GC analysis.
reaction was not quenched just after the disappearance of the starting materials, the indolidinic derivative 4f was converted into the corresponding N-acetylalkenyldinol 5f (entry 12), that was isolated as the sole pure product after 3 h.

Scheme 2 Proposal of reactivity pattern

The results of the reaction shown are reported in Table 2. The effects on the reaction outcome of the substituents on the aromatic ring, the protecting groups of allenols and the nitrogen, R³ and R², have been evaluated. As far as the o-iodophenols are concerned, good yields were obtained (entries 1–5), regardless of the nature of the R³ substituents that, moreover, slightly affect the stereoselectivity of the reaction. Whereas when the 1-(ethoxymethoxy)but-1,2-diene (2a, entries 2 and 5) was used better stereoselectivities were obtained. In fact a E/Z ratio of 90/10 was observed in the case of the products 4b and 4e. Unprotected 2-iodoaniline did not react, and N-tosyl and N-acetyliodoanilines were tested first. In the first case the coupling proceeded smoothly (1.5 h), and the 1H and 13C NMR spectra of the crude reaction mixture showed the signals of the corresponding alkylideneindoline derivatives. Unfortunately, any chromatographic purification was unsuccessful. As reported above, with N-acetyliodoanilines both the corresponding alkenylindolidines 4f (entry 6) and the 3-alkeny-N-acetyldinol 5f (entry 12) were obtained at different reaction times. N-methyl protected anilines were used next and afforded the corresponding 3-alkeny-N-methyl indoles 5b - e (entries 8–11). The reactions were totally stereoselective and fast, regardless of the R² protecting group (THP in entry 7, MeOCH2 in entries 8 and 12 and MEM in entries 9–11 and 13). Finally, with the aim of confirming the electronic effects of the N-protecting group, N-Benzyliodoaniline was used (entry 13), and the corresponding 3-alkenyldinol 5g was isolated. This shows that the yield and stereoselectivity were comparable to those obtained with N-methylidoaniline.

Table 2 Annulation of protected 3-alkyl-1,2-dien-1-ols and 2-iodophenols and protected 2-iodoanilines

<table>
<thead>
<tr>
<th>Entry</th>
<th>Allenol</th>
<th>Iodophenol or Iodoaniline</th>
<th>Product</th>
<th>Time (h)</th>
<th>Yield (%)</th>
<th>E/Z</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>2c</td>
<td>3a</td>
<td>4a</td>
<td>1</td>
<td>95</td>
<td>72/28</td>
</tr>
<tr>
<td>2</td>
<td>2a</td>
<td>3a</td>
<td>4b</td>
<td>1</td>
<td>93</td>
<td>90/10</td>
</tr>
<tr>
<td>3</td>
<td>2c</td>
<td>3b</td>
<td>OHC-</td>
<td>I</td>
<td>4c</td>
<td>OHC-</td>
</tr>
<tr>
<td>4</td>
<td>2c</td>
<td>3a</td>
<td>I</td>
<td>OH</td>
<td>4d</td>
<td>I</td>
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<tr>
<td>5</td>
<td>2a</td>
<td>3d</td>
<td>MeOOC</td>
<td>I</td>
<td>OH</td>
<td>4c</td>
</tr>
<tr>
<td>6</td>
<td>2a</td>
<td>3c</td>
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<td>2c</td>
<td>3f</td>
<td>I</td>
<td>NHMe</td>
<td>5b</td>
<td>I</td>
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<tr>
<td>9</td>
<td>2d</td>
<td>3h</td>
<td>NC</td>
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<td>NHMe</td>
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<td>I</td>
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<td>3e</td>
<td>I</td>
<td>NHAc</td>
<td>5f</td>
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<tr>
<td>13</td>
<td>2d</td>
<td>3m</td>
<td>I</td>
<td>NHBn</td>
<td>5g</td>
<td>I</td>
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</tbody>
</table>

*a* Reactions conditions: ArI, 0.5 mmol; protected allenol 0.75 mmol; DMSO 3 mL; TBAB 300 mg, NaOAc 0.5 mmol, T = 110 °C. *b* Isolated products, purified by column chromatography. *c* Determined by NMR analysis. *d* Determined by GC analysis.

**Conclusions**
In summary a phosphine free Pd(0)-catalysed heteroannulation process involving 2-alkyl-1,2-dienols and o-iodophenols, or o-iodoanilines, has been proposed. Two different frameworks have been achieved, which depend on the electronic features of the nucleophile attacking the Pd π-allyl complex. When o-iodophenols, or o-iodoanilines protected with an electron-withdrawing group, are used, 2-alkoxy-3-alkylidene-2,3-dihydrobenzofuranes or indolines, respectively, were obtained in good yield. On the other hand, when N-methyl and N-benzylidoanilines were used, the nucleophile stereoselectively promoted the elimination of the alkoxy leaving group, affording the corresponding substituted alkenylindoles.

Experimental

General

Flasks and all equipments used for the generation and reaction of moisture-sensitive compounds were dried by electric heat gun under Ar. THF and CH 2Cl2 were distilled from sodium benzophenone ketyl and CaH 2, respectively. BuLi (1.6 M in hexanes) was obtained from Aldrich. All commercially obtained reagents and solvents were used as received. Products 1-(Ethoxymethoxy)hex-2-yne (1a) were added dropwise. The solution was cooled to 0° C. Then H, bs, CH3), 3.60 (2 H, q, J = 6.8 Hz, CH2), 2.20 (2 H, t, J = 6.7 Hz, CH2), 3.57 (2 H, q, J = 6.0 Hz, CH2O), 4.16 (2 H, s, CH2), 4.69 (2 H, s, OCH2CH3). δc (50.2 MHz; CDCl3, MeSi) 13.16 (1 × q), 14.81 (1 × q), 20.44 (1 × t), 21.74 (1 × t), 54.37 (1 × t), 63.18 (1 × t), 75.31 (1 × s), 86.38 (1 × s), 92.92 (1 × s). MS (EI, 70 eV): m/z (%) = 127 (2) [M+ - Et]2, 97 (35), 81 (54), 67 (100), 59 (52).

1-(Ethoxymethoxy)hex-2-yne (1c) Following the general procedure previously described 1.08 g of 2-(but-2-yn-1-yl)benzene were dissolved in CH 2Cl2. 1.48 g of a pale yellow oil were obtained (95%). Found C, 69.75; H, 11.00%. Calc. for C9H12O2: C, 69.19; H, 9.32%. δH (500 MHz; CDCl3, MeSi) 1.32 (3 × t), 3.30 – 4.10 (7 H, m, CH2), 3.60 (2 H, q, J = 6.8 Hz, CH2), 1.55 (2 H, sest, J = 7.0 Hz, CH2), 2.20 (2 H, t, J = 6.7 Hz, CH2), 3.57 (2 H, q, J = 6.0 Hz, CH2O), 4.16 (2 H, s, CH2), 4.69 (2 H, s, OCH2CH3). δc (50.2 MHz; CDCl3, MeSi) 13.16 (1 × q), 14.81 (1 × q), 20.44 (1 × t), 21.74 (1 × t), 54.37 (1 × t), 63.18 (1 × t), 75.31 (1 × s), 86.38 (1 × s), 92.92 (1 × s). MS (EI, 70 eV): m/z (%) = 127 (2) [M+ - Et]2, 97 (35), 81 (54), 67 (100), 59 (52).

Procedure for the protection of alkynols

In a 250 mL three-necked round bottom flask the alkyln (10.0 mmol) was dissolved in anhydrous CH2Cl2 (100 mL) and the solution was cooled to 0° C. Then 1.75 g of a pale yellow oil were obtained (94%). Found C, 63.80; H, 9.61%. Calc. for C10H16O2: C, 64.49; H, 9.74%. δH (200 MHz; CDCl3, MeSi) 0.94 (3 H, t, J = 6.7 Hz, CH2), 2.12 (2 H, sest, J = 7.1 Hz, CH2), 2.12 (2 H, t, J = 6.7 Hz, CH2), 3.40 (2 H, s, OCH2CH3). δc (50.2 MHz; CDCl3, MeSi) 15.00 (1 × q), 20.20 (1 × t), 21.67 (1 × t), 56.00 (1 × t), 58.37 (1 × t), 66.64 (1 × t), 71.35 (1 × t), 75.17 (1 × s), 86.24 (1 × s), 93.10 (1 × t). MS (EI, 70 eV): m/z (%) = 127 (1) [M+ - Me]2, 81 (68), 73 (28), 59 (100), 53 (40).

1-(2-Methoxeythoxy)prop-1-ynyl)benzene (1e) Following the general procedure previously described 1.08 g of 2-alkyl-1,2-dienols and o-iodophenols, or o-iodoanilines protected with an electron-withdrawing group, are used, 2-alkoxy-3-alkylidene-2,3-dihydrobenzofuranes or indolines, respectively, were obtained in good yield. On the other hand, when N-methyl and N-benzylidoanilines were used, the nucleophile stereoselectively promoted the elimination of the alkoxy leaving group, affording the corresponding substituted alkenylindoles.

1-(Ethoxymethoxy)but-2-yn-1-ol and

1.97 g of chloromethoxyethane were dissolved in CH 2Cl2. 1.96 g of a pale yellow oil were obtained (76%). Found C, 65.01; H, 9.50%. Calc. for C8H16O2: C, 65.60; H, 9.44%. δH (500 MHz; CDCl3, MeSi) 1.21 (3 H, t, J = 7.1 Hz, CH2), 1.82 (3 H, bs, CH3), 3.60 (2 H, q, J = 7.1 Hz, CH2), 4.20 (2 H, s, CH2O), 4.72 (2 H, s, OCH2O); δc (50.2 MHz; CDCl3, MeSi) 2.79 (1 × q), 14.551 (1 × q), 53.97 (1 × t), 62.87 (1 × t), 74.35 (1 × s), 83.00 (1 × s), 92.68 (1 × t). MS (EI, 70 eV): m/z (%) = 128 (1) [M+], 82 (19), 59 (18), 53 (100), 52 (17).
(0.1 eq., 1.0 mmol, 0.25 g) were added. The reaction mixture was stirred overnight at r.t. under Ar, then the solvent was partly evaporated. The mixture was diluted with EtO then washed with brine (2 × 20 mL), dried over K2CO3, filtered and evaporated under reduced pressure, to give 1.43 g of a pale yellow oil (93%). The crude reaction product, was used in the subsequent step without further purification. Spectral data corresponded to those reported in literature.41

General procedure for the isomerization of alkenes to allenes. In a Schlenk vessel alkyn (10.0 mmol) was dissolved in anhydrous THF (20 mL) and cooled to −95 °C, then n-BuLi (2.0 eq., 20.0 mmol, 12.5 mL) was added. The reaction mixture was stirred for 2 h at −95 °C, then a solution of THF / H2O was added (20 mL). The mixture was extracted with Et2O (2 × 20 mL), then washed with brine (2 × 20 mL), dried (K2CO3), filtered and evaporated under reduced pressure. The product was purified by column chromatography.

1-(Ethoxymethoxy)but-1,2-diene (2a) (EP/EE 95/5, 1% Et3N) pale yellow oil (0.84 g, 66%). Spectral data corresponded to those reported in literature.18

2-(Buta-1,2-dienyloxy)tetrahydro-2H-pyrane (2b) (EP/EE 98/2, 1% Et3N; diastereomeric mixture 60/40) pale yellow oil (0.92 g, 60%). Spectral data corresponded to those reported in literature.11

1-(Ethoxymethoxy)hexa-1,2-diene (2c) (EP/EE 95/5, 1% Et3N) pale yellow oil (0.96 g, 62%). Found C, 69.60; H, 10.32%. Calc. for C13H16O3: C, 70.89; H, 7.32%.

2-(Ethoxymethoxy)propa-1,2-dienylbenzene (2e) (EP/EE 95/5, 1% Et3N) pale yellow oil (1.12 g, 51%). Found C, 70.95; H, 7.34%. Calc. for C15H18O2: C, 70.89; H, 7.32%. νmax(neat)/ cm −1 2978, 2357, 1748, 1532, 1419, 922.
(E)- and (Z)-2-(ethoxymethoxy)-3-ethylidene-2,3-dihydrobenzofuran (4b) (EP/EE 93/7, 1% Et2N) pale yellow oil (102.4 mg, 93%). Found C, 71.35; H, 7.29%. Calc for C15H18O3: C, 70.89; H, 7.32%. m/zfound(neat)/cm−1 2982, 1730, 1588, 1465, 925. δH major isomer (200 MHz; CDCl3, Me2Si) 0.90 (3 H, t, J = 7.1 Hz, CH3), 1.95 (3 H, dd, J = 7.3, 1.5 Hz, CH2CH=CH2), 3.63 (2 H, quint, J = 7.1 Hz, CH2CH2O), 3.82 (2 H, quint, J = 7.1 Hz, CH2CH2O), 4.83 (1 H, d, J = 6.8 Hz, OCH2O), 5.11 (1 H, d, J = 6.8 Hz, OCH2O), 5.90 (1 H, qd, J = 7.4, 1.5 Hz, CH=CH2), 6.12 (1 H, q, J = 1.4 Hz, OCHO). 6.89 (2 H, m, Ar), 7.20 (1 H, td, J = 7.3, 1.5 Hz, Ar), 7.52 (1 H, d, J = 7.3 Hz, Ar), δC major isomer (50.2 MHz; CDCl3, Me2Si) 14.2 (1 × q), 14.9 (1 × q), 63.9 (1 × t), 92.7 (1 × t), 103.3 (1 × d), 110.2 (1 × d), 120.9 (1 × d), 122.2 (1 × s), 124.2 (2 × d), 129.3 (1 × d), 135.7 (1 × s), 161.1 (1 × s). MS (EI, 70 eV): m/z (%) = 220 (18) [M]+, 147 (25), 145 (43), 115 (30), 59 (100). MS (E) (EI, 70 eV): m/z (%) = 220 (15) [M]+, 147 (20), 145 (38), 115 (33), 59 (100).

(3,5-dihydrobenzofuran-5-carboxaldehyde (4c) (EP/EE 93/7, 1% Et2N) (E/Z=60/40) pale yellow oil (147 mg, 99%). Found C, 66.48; H, 7.29%. Calc for C15H18O3: C, 66.65; H, 7.24%. m/zfound(neat)/cm−1 3010, 2902, 1725, 1583, 1455, 1030, 935, 747. δH major isomer (200 MHz; CDCl3, Me2Si) 0.98 (3 H, m, CH3CH2C), 1.25 (3 H, m, CH2CH2O), 1.60 (2 H, sext, J = 6.3 Hz, CH2CH=CH2), 2.28 (2 H, t, J = 7.1 Hz, CH2CH2O, isomer Z), 2.52 (2 H, q, J = 7.1 Hz, CH2CH2CH3, isomer E), 3.63 (1 H, m, CH2CH2O), 3.80 (1 H, m, CH2CH2O), 3.93 (3 H, s, CH3O).

(3,5-dihydrobenzofuran-5-carboxaldehyde (4c) (EP/EE 93/7, 1% Et2N) (E/Z=60/40) pale yellow oil (147 mg, 99%). Found C, 66.48; H, 7.29%. Calc for C15H18O3: C, 66.65; H, 7.24%. m/zfound(neat)/cm−1 3010, 2902, 1725, 1583, 1455, 1030, 935, 747. δH major isomer (200 MHz; CDCl3, Me2Si) 0.98 (3 H, m, CH3CH2C), 1.25 (3 H, m, CH2CH2O), 1.60 (2 H, sext, J = 6.3 Hz, CH2CH=CH2), 2.28 (2 H, t, J = 7.1 Hz, CH2CH2O, isomer Z), 2.52 (2 H, q, J = 7.1 Hz, CH2CH2CH3, isomer E), 3.63 (1 H, m, CH2CH2O), 3.80 (1 H, m, CH2CH2O), 3.93 (3 H, s, CH3O).

(E)- and (Z)-3-Butylidene-2-(ethoxyethoxy)-methyl-2,3-dihydrobenzofuran-5-carboxaldehyde (4c) (EP/EE 93/7, 1% Et2N) (E/Z=60/40) pale yellow oil (147 mg, 99%). Found C, 66.48; H, 7.29%. Calc for C15H18O3: C, 66.65; H, 7.24%. m/zfound(neat)/cm−1 3010, 2902, 1725, 1583, 1455, 1030, 935, 747. δH major isomer (200 MHz; CDCl3, Me2Si) 0.98 (3 H, m, CH3CH2C), 1.25 (3 H, m, CH2CH2O), 1.60 (2 H, sext, J = 6.3 Hz, CH2CH=CH2), 2.28 (2 H, t, J = 7.1 Hz, CH2CH2O, isomer Z), 2.52 (2 H, q, J = 7.1 Hz, CH2CH2CH3, isomer E), 3.63 (1 H, m, CH2CH2O), 3.80 (1 H, m, CH2CH2O), 3.93 (3 H, s, CH3O).
CH₃(CHOH)₂CH₂CO₂H, 2.27 (2 H, q, J = 7.1 Hz, CH₂CH₂), 3.71 (3 H, s, CH₃N), 6.19 (1 H, dt, J = 16.4, 6.8 Hz, CH₂CH₂=CH), 6.53 (1 H, d, J = 16.2 Hz, CH₂CH₂=CH), 7.08 (1 H, s, CHN), 7.29 (3 H, m, Ar), 7.87 (1 H, d, J = 6.7 Hz, Ar). δC(50.2 MHz; CDCl₃, Me₄Si) 14.1 (1 × q), 26.5 (1 × t), 32.5 (1 × q), 109.2 (1 × d), 113.9 (1 × s), 119.3 (1 × d), 119.9 (1 × d), 120.9 (1 × d), 121.7 (1 × d), 126.0 (1 × s), 126.6 (1 × d), 129.0 (1 × d), 137.3 (1 × s). MS (EI, 70 eV): m/z (%) = 185 (78 [M⁺], 170 (100), 154 (24), 144 (23), 115 (13).

(E)-3-(But-1-enyl)-1-methyl-1H-indole-5-carboxonitrile (5e) (EP/EE 95/5, 1% Et₃N) pale yellow oil (91 mg, 87%). Found C, 77.65; H, 7.61, N, 7.61%. Calc. for C₁₅H₁₇NO₂: C, 77.81; H, 7.59, N, 7.60%. 70 eV/70 eV).

(E)-3-(But-1-enyl)-1-methyl-1H-indole-5-carboxonitrile (5f) (EP/EE 95/5, 1% Et₃N) pale yellow oil (110 mg, 85%). Found C, 77.65; H, 7.61, N, 7.61%. Calc. for C₁₅H₁₇NO₂: C, 77.81; H, 7.59, N, 7.60%. 70 eV/70 eV.

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Notes and references