Synthesis of selectively deuterated fulvenes and indenes from enediynes†

Scott W. Peabody, Boris Breiner, Serguei V. Kovalenko, Satish Patil and Igor V. Alabugin*

Department of Chemistry and Biochemistry, Florida State University, Tallahassee, Florida, 32306-4390, USA. E-mail: alabugin@chem.fsu.edu; Fax: +1 850 644 8281; Tel: +1 850 644 5795

A facile enediyne→fulvene→indene transformation provides a route to all possible isotopomers of substituted fulvenes and indenes.

Introduction

Interest in substituted fulvenes and benzofulvenes stems from their potential as building blocks for the preparation of metallocene catalysts,[1] and from the application of fulvenes as electron acceptors in material science and molecular electronics.[2] Fulvenes and benzofulvenes have also been used as key intermediates in the total synthesis of several natural products and patented as anti-inflammatory agents having antipyretic and analgesic activity.[3] Deuterated indenes have received significant attention as mechanistic probes, *e.g.*, in Clemmensen reduction,[4] photochemistry of alkylidenes,[5] hydrogenolysis,[6] rutheniummediated cycloaromatization,[7] *etc.*[8]

Recently, we discovered a photochemical transformation of enediynes to indenes,[9] which is accompanied by four formal hydrogen abstractions from the environment. In order to determine whether these hydrogens are transferred as H-atoms or protons, an important aspect in understanding the DNA-cleaving properties of these molecules, we carried out this reaction in the presence of CH$_3$OD and found that it results in a mixture of indene isotopomers, with varying extent of D incorporation at both of the methylene positions (Scheme 1). In order to understand the details of D-incorporation in the individual steps of the enediynes–indene cascade, we needed to prepare the fulvene and indene isotopomers. Since they were not available through literature routes,[10] we developed a new approach to selectively deuterated fulvenes and indenes, which we report in this paper.

† Electronic supplementary information (ESI) available: experimental procedures, ^{1}H and ^{13}C spectra for compounds **1**, **3–6** and **8–14**. See http://www.rsc.org/suppdata/ob/b4/b417493n/

Results and discussion

In this approach, the fulvene moiety is assembled through a 5-*exo*-dig radical cyclization initiated by Bu$_3$Sn radical addition to diaryl enediynes[11] (Scheme 1) – the first synthetically useful application of reaction of an enediyne moiety with radical reagents, a process which has been only briefly studied so far.[12,13,14] This process lends itself to the preparation of selectively deuterated fulvene isotopomers because the whole sequence introduces two hydrogen atoms into the fulvene moiety in two mechanistically separate and synthetically orthogonal steps (Scheme 2). In the first stage, either H or D is introduced at the exocyclic double bond depending on the choice of the tin reagent (Bu$_3$SnH or Bu$_3$SnD). Subsequent destannylation can be achieved using a source of either protons or deuterons (HCl or DCl), thus introducing either H or D at the endocyclic benzofulvene position.
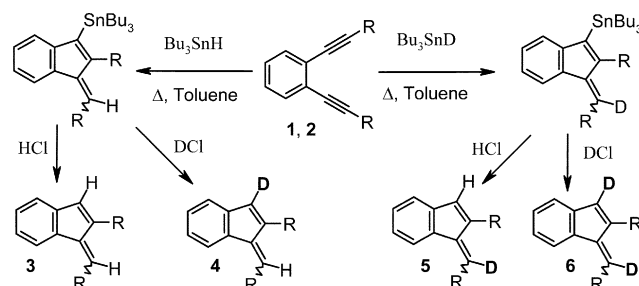
Scheme 2 Synthesis of the four fulvene isotopomers, R = TFP, Ph.

D-incorporation at the endocyclic position through hydrolytic deuteriodestannylation proceeds with excellent efficiency (see the Supporting Information for the details†). On the other hand, reaction of bis-TFP substituted enediyne **1** with Bu$_3$SnD in toluene, which is the most common solvent for such processes,
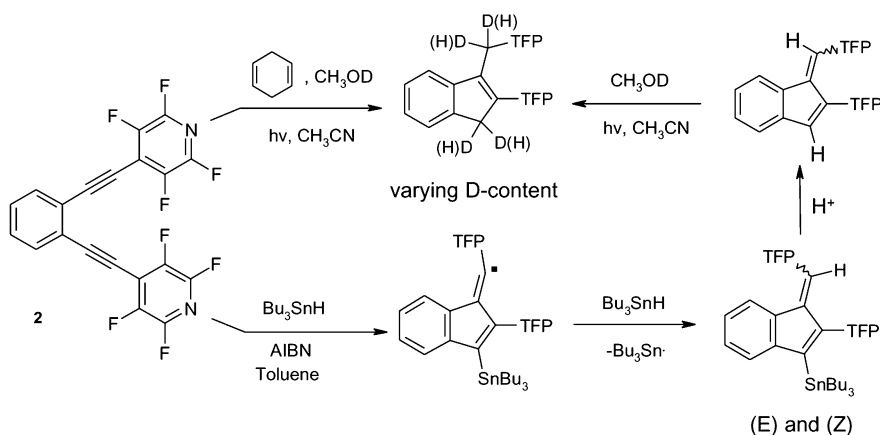
Scheme 1 Photochemical reactions leading to indene isotopomers (top) and tin-promoted radical cyclization leading to fulvene (bottom); TFP = tetrafluoropyridine.

resulted in only ~50% D-incorporation at the exocyclic double bond for the (*E*)-isomer, and ~56% D-incorporation for the (*Z*)-isomer. At a higher Bu$_3$SnD concentration,[15] deuterium incorporation increases (~69% for the (*Z*)-isomer, 66% for the (*E*)-isomer) but still remains incomplete. These results point to H-atom abstraction from the benzylic position of toluene solvent as a competing process (commercial Bu$_3$SnD is 96% deuterated). Despite the much higher concentration of toluene compared to the tin reagent ([PhCH$_3$] ~9 M, [Bu$_3$SnD] ~3 × 10^{-4} M) and the contribution from the primary H/D isotope effect, this observation may seem surprising, taking into consideration the dramatic differences in the X–H bond dissociation energies for Bu$_3$SnH (74 kcal mol^{-1})[16] and toluene (88 kcal mol^{-1}).[17] However, when the difference in reaction energies is translated into the H-abstraction barriers using Marcus theory,[18] one would expect H-abstraction from toluene to proceed only ~10^5 times more slowly. A possible explanation for the small but consistent difference in the extent of deuteration between the (*E*)- and (*Z*)-isomers involves a weak non-covalent interaction between toluene and the electron-deficient TFP moiety leading to precoordination of toluene next to the radical center. This interaction may be more important in formation of the (*E*)-isomer where the toluene molecule can be associated with both TFP moieties. Such interactions should also contribute to the considerable degree of H-atom abstraction from the solvent – a hypothesis which is consistent with the higher amount of D-incorporation (~75%) in the case of R = phenyl even at lower Bu$_3$SnH concentrations.

The efficiency of deuteration can be dramatically increased by using a solvent incapable of hydrogen atom donation. We found that in benzene or α,α,α-trifluorotoluene, the observed amount of H-incorporation can be explained by the 4% of residual Bu$_3$SnH in Bu$_3$SnD.

The fulvene isotopomers can be further transformed to a variety of indenes with the selective introduction of either protium or deuterium. Nucleophilic attack at the exocyclic double bond by an organolithium compound leads to formation of the cyclopentadienyl anion lithium salt. Subsequent addition of either a proton or deuteron to the cyclopentadienyl moiety during workup with either H$_2$O or D$_2$O provides substituted indenes **7–9** (Scheme 3). This procedure combined with the appropriate deuterated fulvene provides a synthetic route to any of the possible indenes illustrated in Scheme 3. Although the initial radical cyclization results in a mixture of (*E/Z*)-isomers, their subsequent transformation to indene converges to a single isomer.

The reaction of LiAlH$_4$ or LiAlD$_4$ proceeds in a similar fashion with the nucleophile (hydride or deuteride) attacking the exo-

cyclic double bond to form a substituted cyclopentadienyl anion. The cyclopentadienyl anion can then be trapped selectively using either H$_2$O or D$_2$O to form selectively deuterated indenes **10–13** (Scheme 4).[19] In principle, trapping by other electrophiles, *e.g.*, ferrous chloride, to directly form a metallocene complex[20] or by Me$_3$SiCl[11] should also be possible.
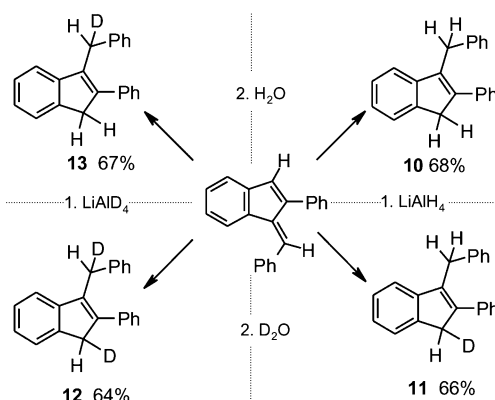
Scheme 4 Reactions of LiAlH$_4$ (LiAlD$_4$) with fulvene.

Conclusion

The enediyne→fulvene→indene sequence provides a choice for selective introduction of hydrogen isotopes through a radical, electrophilic, or nucleophilic form at either of two positions of an indene or a fulvene moiety. Applications of this method for mechanistic studies of photochemical enediyne→indene transformations and of metallocene catalysis will be reported in due course.

Experimental

General

NMR spectra were recorded on a Varian Gemini 300 MHz spectrometer at 300 MHz (^{1}H NMR) and 75.4 MHz (^{13}C NMR), respectively, in CDCl$_3$ unless otherwise noted. ^{19}F NMR was performed on a Bruker 300 MHz spectrometer. Mass spectra were measured on a Jeol JMS-600H. GC analyses were conducted on a Varian CP-3800 GC. 1,2-Diiodobenzene was synthesized according to the reported method.[21] The synthetic procedures for **1** and compounds derived from it are given below. For synthesis of remaining compounds, as well as spectral data, please refer to the Supporting Information.†

1,2-Bis(phenylethynyl)benzene (1)

A mixture of 1,2-diiodobenzene (3.00 g, 9.09 mmol), bis(triphenylphosphine)palladium(II) dichloride (0.7 g, 1.00 mmol), and copper(I) iodide (0.39 g, 2.02 mmol) in Et$_3$N (75 ml) was degassed by the freeze–pump–thaw method. The solution was brought to reflux and phenylacetylene (2.05 g, 20.0 mmol) was added. The reaction mixture was allowed to reflux overnight. The reaction mixture was filtered through Celite, washed with saturated ammonium chloride solution, water, and dried over MgSO$_4$. Column chromatography (silica gel, hexanes) provided 1.95 g (77%) of **1** as an off-white solid, mp 51–52 °C (lit.[10] 51–52 °C); ^{1}H NMR: δ 7.57 (m, 6H), 7.32 (m, 8H); ^{13}C NMR: δ 131.8, 131.6, 128.4, 128.3, 128.0, 125.8, 123.3; 93.6, 88.3; HRMS (EI, 70 eV) calcd. for C$_{22}$H$_{14}$ (M$^+$) 278.10955, found 278.10944.

2-Phenyl-1-(phenylmethylene)-1*H*-indene (3)

A solution of diyne **1** (94 mg, 0.336 mmol) in anhydrous toluene (5 ml) was brought to reflux in a dry three-neck flask. A solution of tributyltin hydride (120 mg, 0.412 mmol) and AIBN (6 mg, 0.037 mmol) in anhydrous toluene (5 ml) was added by
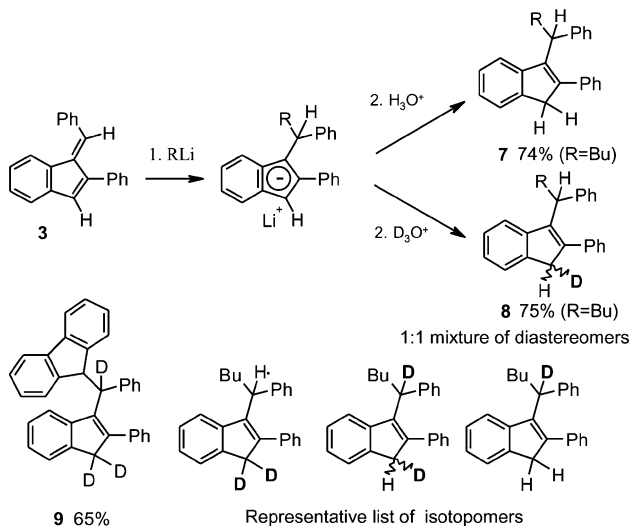
Scheme 3 Synthesis of substituted indene isotopomers.

syringe pump over 1 h and the reaction mixture was allowed to reflux for 2 h. The toluene was evaporated *in vacuo* and the reaction mixture was redissolved in dichloromethane (5 ml). Concentrated HCl (5 ml) was added and the reaction was stirred vigorously for 1 h. The organic layer was washed with water, and dried over $MgSO_4$. Flash chromatography (40 g silica gel, hexanes) afforded 77 mg (82%) of (*E/Z*)-**3** as a yellow oil. NMR and GC data provided a 6 : 1 *E* : *Z* ratio. 10 mg of pure (*E*)-isomer was isolated in the first few fractions of the separation. ^{1}H NMR: δ 7.47 (m, 11H), 7.32 (s, 1H), 7.29 (m, 1H), 7.22 (td, *J* = 7.4 Hz, *J* = 0.9 Hz, 1H), 6.96 (td, *J* = 7.5 Hz, *J* = 1.3 Hz, 1H), 6.88 (s, 1H); ^{13}C NMR: δ 144.3, 143.2, 140.3, 136.8, 136.0, 134.7, 134.7, 129.6, 129.6, 129.3, 128.4, 128.3, 128.2, 128.2, 127.4, 124.9, 123.3, 120.7; pure (*Z*)-isomer was isolated by preparative thin layer chromatography. ^{1}H NMR: δ 7.77 (s, 1H), 7.70 (m, 1H), 7.31 (m, 2H), 7.22 (m 3H), 7.01 (m, 13H); HRMS (EI, 70 eV) calcd. for $C_{22}H_{16}$ (M[+]) 280.12520, found 280.12520.

2-Phenyl-1-(phenylmethylene)-3-deutero-1*H*-indene (4)

Synthesized analogously to **3**, using DCl instead of HCl and yielding 73 mg (75%) of (*E/Z*)-**4** as a yellow oil. ^{1}H NMR: δ 7.47 (m, 11H), 7.32, (s, 1H), 7.29 (m, 1H), 7.22 (td, *J* = 7.4 Hz, *J* = 0.9 Hz, 1H), 6.96 (td, *J* = 7.5 Hz, *J* = 1.3 Hz, 1H), 6.88 (s, 0.08H); ^{13}C NMR: δ 144.3, 143.2, 140.3, 136.8, 136.0, 134.7, 134.7, 129.6, 129.6, 129.3, 128.4, 128.3, 128.2, 128.2, 127.4, 124.9, 123.3, 120.7; HRMS (EI, 70 eV) calcd. for $C_{22}H_{15}D$ (M[+]) 281.13148, found 281.13244.

2-Phenyl-1-(phenyldeuteromethylene)-1*H*-indene (5)

Synthesized analogously to **3**, using tributyltin deuteride instead of tributyltin hydride and yielding 69 mg (69%) of (*E/Z*)-**5** as a yellow oil. ^{1}H NMR: δ 7.47 (m, 11H), 7.32, (s, 0.14H), 7.29 (m, 1H), 7.22 (td, *J* = 7.4 Hz, *J* = 0.9 Hz, 1H), 6.96 (td, *J* = 7.5 Hz, *J* = 1.3 Hz, 1H), 6.88 (s, 1H); ^{13}C NMR: δ 144.3, 143.2, 140.3, 136.8, 136.0, 134.7, 134.7, 129.6, 129.6, 129.3, 128.4, 128.3, 128.2, 128.2, 127.4, 124.9, 123.3, 120.7; HRMS (EI, 70 eV) calcd. for $C_{22}H_{15}D$ (M[+]) 281.13148, found 281.13237.

2-Phenyl-3-deutero-1-(phenyldeuteromethylene)-1*H*-indene (6)

Synthesized analogously to **3**, using DCl instead of HCl, tributyltin deuteride instead of tributyltin hydride, and yielding 65 mg (65%) of (*E/Z*)-**6** as a yellow oil. ^{1}H NMR: δ 7.47 (m, 11H), 7.32, (s, 0.15H), 7.29 (m, 1H), 7.22 (td, *J* = 7.4 Hz, *J* = 0.9 Hz, 1H), 6.96 (td, *J* = 7.5 Hz, *J* = 1.3 Hz, 1H), 6.88 (s, 0.05H); ^{13}C NMR: δ 144.3, 143.2, 140.3, 136.8, 136.0, 134.7, 134.7, 129.6, 129.6, 129.3, 128.4, 128.3, 128.2, 128.2, 127.4, 124.9, 123.3, 120.7; HRMS (EI, 70 eV) calcd. for $C_{22}H_{14}D_2$ (M[+]) 282.13775, found 282.13836.

1-(5-Phenylpentyl)-2-phenylindene (7)

n-BuLi (277 mg of a 1.6 M solution in hexane, 1.0 mmol) was added dropwise to a solution of **3** (280 mg, 1.0 mmol) in THF (5 ml) at −30 °C. The reaction mixture was warmed to room temperature and stirred for 2 h. Saturated aqueous ammonium chloride solution (5 ml) was added and the product was extracted with diethyl ether. The combined organic layer was dried over $MgSO_4$ and concentrated to a residue that was purified by column chromatography (silica gel, 20 : 1 hexane–chloroform), affording 251 mg (74%) of **7** as a yellow oil. ^{1}H NMR: δ 7.25 (m, 14 H), 4.28 (t, *J* = 7.8 Hz, 1H), 3.97 (d, *J* = 22.5 Hz, 1H), 2.17 (m, 2H), 1.11 (m, 6H), 0.90 (m, 3H); ^{13}C NMR: δ 144.9, 144.7, 143.7, 143.5, 143.2, 140.3, 137.9, 129.6, 129.5, 129.0, 128.9, 128.7, 128.4, 128.3, 127.6, 127.0, 125.8, 124.2, 123.4, 121.9, 42.3, 42.1, 42.0, 32.1, 30.2, 22.6, 13.9; HRMS (EI, 70 eV) calcd. for $C_{26}H_{26}$ (M[+]) 338.2035, found 338.2049.

1-(5-Phenylpentyl)-3-deutero-2-phenylindene (8)

Synthesized analogously to **7**, using DCl instead of HCl and yielding 181 mg (74%, yield) of **8** as a yellow oil. ^{1}H NMR: δ 7.57 (m, 1H), 7.48 (m, 6H), 7.38 (m, 4H), 7.30 (m, 1H), 7.25. (m, 2H), 4.48 (t, *J* = 7.9, 14H), 3.95 (br s, 0.5H), 3.77 (br s, 0.5H), 2.30 (m, 2H), 1.29 (m, 4H), 0.88 (m, 3H); ^{13}C NMR: δ 144.8, 143.7, 143.5, 143.2, 140.4, 138.0, 128.4, 128.3, 128.3, 129.0, 127.6, 127.0, 125.9, 125.9, 124.2, 123.5, 122.0, 42.1, 42.0 (t, *J* = 19.3 Hz), 32.2, 30.3, 22.6, 13.9; HRMS (EI, 70 eV) calcd. for $C_{26}H_{25}D$ (M[+]) 339.20973, found 339.20917.

(3,3-Dideutero-2-phenylindenyl)deutero(fluorenyl)phenylmethane (9)

A solution of **1** (200 mg, 0.719 mmol) in anhydrous toluene (10 ml) was brought to reflux in a dry three-neck flask. A solution of tributyltin deuteride (251 mg, 0.863 mmol) and AIBN (6 mg, 0.037 mmol) in anhydrous toluene was added by syringe pump over 1 h and the reaction mixture was allowed to reflux for 2 h. The toluene was evaporated *in vacuo* and the reaction mixture was dissolved in dichloromethane (5 ml). 20% DCl in D_2O (5 ml) was added and the reaction was stirred vigorously for 1 h. The organic layer was washed with water and extracted with dichloromethane. The combined organic layer was dried over magnesium sulfate and concentrated to a residue that was dried by dissolving in anhydrous toluene and evaporating the solvent *in vacuo*. The residue was flushed with argon and dissolved in THF (3 ml). *n*-BuLi (1.03 ml of a 1.6 M solution in hexane, 1.0 mmol) was added dropwise to a solution of fluorene (275 mg, 1.65 mmol) in THF (5 ml) at −78 °C and slowly brought to −30 °C over 2 h while stirring. The enediyne reaction mixture was added dropwise and the solution was brought to 0 °C over 2 h while stirring. D_2O (5 ml) was added, the reaction mixture was brought to room temperature, and the product was extracted with diethyl ether. The combined organic layers were dried over $MgSO_4$ and concentrated to a residue that was purified by column chromatography (silica gel, 20 : 1 hexane–chloroform) and recrystallized from a mixture of ethanol and water to afford 209 mg (65%) of **9** as white crystals, mp 94 °C. ^{1}H NMR: δ 7.93 (d, *J* = 7.6 Hz, 1H), 7.74 (d, *J* = 7.6 Hz, 1H), 7.70 (d, *J* = 7.6 Hz, 1H), 7.48 (d, *J* = 7.2 Hz, 1H), 7.41 (m, 2H), 7.27 (m, 8H), 7.12 (m, 3H), 7.00 (t, *J* = 7.4 Hz, 1H), 6.90 (m, 2H), 6.69 (m, 2H), 7.62 (d, *J* = 7.6 Hz, 1H), 5.22 (br s, 1H), 4.17 (d, *J* = 11.4 Hz, 0.32H), 3.66 (br s, 0.08H), 3.55 (br s, 0.08H); ^{13}C NMR: δ 146.2, 145.7, 145.0, 144.2, 144.2, 143.1, 142.0, 142.0, 141.1, 140.9, 140.7, 140.7, 137.7, 129.3, 128.4, 128.2, 128.1, 127.2, 127.0, 126.8, 126.6, 126.5, 126.3, 126.1, 126.1, 126.0, 124.4, 123.9, 122.5, 119.5, 49.1, 48.1; HRMS (EI, 70 eV) calcd. for $C_{35}H_{23}D_3$ (M[+]) 449.22383, found 449.22380.

1-Benzyl-2-phenyl-1*H*-indene (10)

A solution of **3** (80 mg, 0.285 mmol) in THF (10 ml) was cooled to −30 °C. $LiAlH_4$ (16 mg, 0.421 mmol) was added and the mixture was warmed to room temperature over 2 h. The reaction mixture was cooled to 0 °C and H_2O (5 ml) was added dropwise. The product was extracted with dichloromethane and the combined organic layers were dried over sodium sulfate and concentrated to a residue that was purified by column chromatography (silica gel, hexanes) to afford 55 mg (68%) of **10** as an opaque white oil. ^{1}H NMR: δ 7.50 (m, 1H), 7.45 (m, 2H), 7.37 (m, 2H), 7.22 (m, 9H), 4.14 (s, 2H), 3.87 (s, 2H); ^{13}C NMR: δ 146.5, 142.8, 142.5, 139.5, 137.1, 136.6, 128.5, 128.5, 128.2, 128.0, 127.1, 126.4, 126.0, 124.7, 123.4, 120.2, 41.3 (t, *J* = 20.6 Hz) 32.4; HRMS (EI, 70 eV) calcd. for $C_{22}H_{18}$ (M[+]) 282.14085, found 282.14269.

1-Benzyl-2-phenyl-1*H*-indene (11)

Synthesized analogously to **10**, using D_2O instead of H_2O and yielding 53 mg (66%) of **11** as an opaque white oil. ^{1}H NMR: δ 7.50 (m, 1H), 7.45 (m, 2H), 7.37 (m, 2H), 7.22 (m, 9H), 4.15 (s, 2H), 3.87 (m, 1H); ^{13}C NMR: δ 146.5, 142.8, 142.5, 139.5, 137.1, 136.6, 128.5, 128.5, 128.2, 128.0, 127.1, 126.4, 126.0, 124.7,

123.4, 120.2, 41.3 (t, J = 20.6 Hz) 32.4; HRMS (EI, 70 eV) calcd. for $C_{22}H_{17}D$ (M^+) 283.14713, found 283.14597.

1-Benzyl-2-phenyl-1*H*-indene (12)

Synthesized analogously to **10**, using LiAlD$_4$ instead of LiAlH$_4$, D$_2$O instead of H$_2$O, and yielding 52 mg (64%) of **12** as an opaque white oil. ^{1}H NMR (300 MHz, CDCl$_3$) δ ^{1}H NMR: δ 7.50 (m, 1H), 7.45 (m, 2H), 7.37 (m, 2H), 7.22 (m, 9H), 4.12 (m, 1H), 3.87 (s, 2H); ^{13}C NMR: δ 146.5, 142.8, 142.6, 139.4, 137.1, 136.5, 128.5, 128.5, 128.3, 128.0, 127.1, 126.4, 126.0, 124.7, 123.4, 120.2, 41.4, 31.8 (t, J = 19.1 Hz); HRMS (EI, 70 eV) calcd. for $C_{22}H_{17}D$ (M^+) 283.14713, found 283.14597.

1-Benzyl-2-phenyl-1*H*-indene (13)

Synthesized analogously to **10**, using LiAlD$_4$ instead of LiAlH$_4$, and yielding 54 mg (67%) of **13** as an opaque white oil. ^{1}H NMR: δ 7.50 (m, 1H), 7.45 (m, 1H), 7.37 (m, 1H), 7.22 (m, 9H), 4.12 (m, 1H), 3.86 (m, 0.5H); ^{13}C NMR: δ 146.6, 142.8, 142.5, 139.4, 137.1, 136.5, 128.5, 128.5, 128.3, 128.0, 127.1, 126.4, 126.1, 124.7, 123.4, 120.2, 41.1 (t, J = 19.8), 31.8 (t, J = 19.1); HRMS (EI, 70 eV) calcd. for $C_{22}H_{16}D_2$ (M^+) 284.15340, found 284.15255.

Acknowledgements

References

1 (*a*) H. Alt and A. Köppl, *Chem. Rev.*, 2000, **100**, 1205; (*b*) S. Lin and R. Waymouth, *Acc. Chem. Res.*, 2002, **35**, 765.

2 K. Kondo, H. Goda, K. Takemoto, H. Aso, T. Sasaki, K. Kawakami, H. Yoshida and K. Yoshida, *J. Mat. Chem.*, 1992, **2**, 1097.

3 (*a*) J. Vicente, J. Abad and J. Gil-Rubio, *Organometallics*, 1995, **14**, 2677; (*b*) A. Korte, J. Legros and C. Bolm, *Synlett*, 2004, **13**, 2397.

4 S. Galton and R. Abbas, *J. Org. Chem.*, 1973, **38**, 2008.

5 M. Suarez, R. Duguid and H. Morrison, *J. Am. Chem. Soc.*, 1989, **111**, 6384.

6 V. Ranade and R. Prins, *Chem. Eur. J.*, 2000, **6**, 313.

7 J. O'Connor, S. Friese and M. Tichenor, *J. Am. Chem. Soc.*, 2002, **124**, 3506.

8 (*a*) Cycloalkene–cycloalkene transformations *via* platina(IV) cyclobutane derivatives: B. Williams and P. Jennings, *Inorg. Chim. Acta*, 1997, **265**, 23; (*b*) sigmatropic rearrangements: A. Padwa, S. Goldstein, R. Loza and M. Pulwer, *J. Org. Chem.*, 1981, **46**, 1858; (*c*) dioxygenase-catalysed hydroxylation: D. Boyd, N. Sharma, N. Bowers, R. Boyle, J. Harrison, K. Lee, T. Bugg and D. Gibson, *Org. Biomol. Chem.*, 2003, **1**, 1298; (*d*) rearrangements:E. Friedrich and D. Taggart, *J. Org. Chem.*, 1975, **40**, 720; (*e*) addition of thiols: H. Szmant and J. Baeza, *J. Org. Chem.*, 1980, **45**, 4902.

9 (*a*) I. V. Alabugin and S. V. Kovalenko, *J. Am. Chem. Soc.*, 2002, **124**, 9052; (*b*) theoretical study: I. V. Alabugin and M. Manoharan, *J. Am. Chem. Soc.*, 2003, **125**, 4495.

10 H. W. Whitlock, P. E. Sandvick, L. E. Overman and P. B. Reichard, *J. Org. Chem.*, 1969, **34**, 879.

11 S. V. Kovalenko, S. Peabody, M. Manoharan, R. S. Clark and I. V. Alabugin, *Org. Lett.*, 2004, **6**, 2457.

12 B. König, W. Pitsch, M. Klein, R. Vasold, M. Prall and P. Schreiner, *J. Org. Chem.*, 2001, **66**, 1742.

13 J. Johnson, D. Bringley, E. Wilson, K. Lewis, L. Beck and A. Matzger, *J. Am. Chem. Soc.*, 2003, **125**, 14708.

14 J. Scott, S. Parkin and J. Anthony, *Synlett*, 2004, **1**, 161.

15 A solution of Bu$_3$SnD was added to a solution of other reagents using a syringe pump to minimize the formation of acyclic addition products. "Low concentration" refers to a total toluene volume of 33 ml, while "high concentration" refers to 3 ml of toluene. The H/D ratios from ^{1}H NMR and high-resolution MS are in perfect agreement with each other. See Supplementary Information† for details.

16 T. J. Burkey, M. Majewski and D. Griller, *Adv. Free Radical Chem. (Greenwich, Conn.)*, 1990, **1**, 159.

17 D. D. M. Wagner and D. Griller, *J. Am. Chem. Soc.*, 1986, **108**, 2218.

18 (*a*) For the interconnection of reaction and activation energies in hydrogen transfer reactions, see: J. P. Roth, J. C. Yoder, T.-J. Won and J. M. Mayer, *Science*, 2002, **294**, 2524; (*b*) I. V. Alabugin, M. Manoharan, B. Breiner and F. Lewis, *J. Am. Chem. Soc.*, 2003, **125**, 9329; (*c*) for the seminal theoretical treatment, see: R. A. Marcus, *J. Phys. Chem.*, 1968, **72**, 891.

19 From a practical point of view, it is important to work up the reaction mixtures expediently since prolonged exposure to base leads to facile hydrogen exchange at the endocyclic methylene group. This exchange is especially fast in bis-TFP indenes where it can be used for selective D-labeling at this position.

20 (*a*) J. Leblanc and C. Moise, *J. Organomet. Chem.*, 1976, **120**, 65; (*b*) G. Knox and P. Pauson, *J. Chem. Soc.*, 1961, 4615.

21 L. Friedman and F. M. Logullo, *J. Org. Chem.*, 1969, **34**, 3089.