ChemComm

Synthesis and domino reactions of 1,1-bis(hydroxymethyl)allenes

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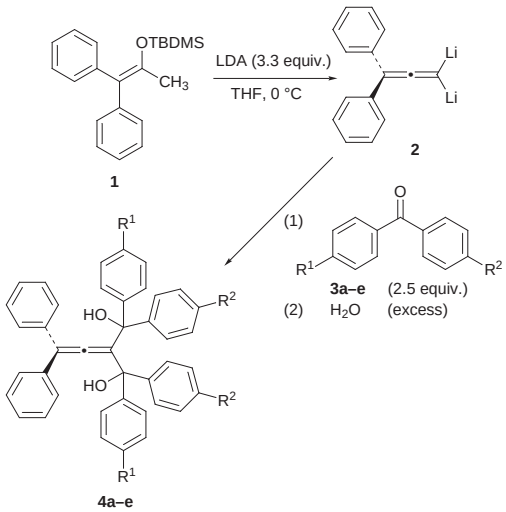
Received (in Cambridge, UK) 15th February 1999, Accepted 12th April 1999

The reaction of dilithiated 1,1-diphenylallene with aryl ketones provides a convenient access to novel 1,1-bis(hydroxymethyl)allenes, which undergo Friedel–Crafts-type domino reactions upon treatment with TsOH.

Domino reactions of alkynes have been used for the efficient synthesis of carbocycles and polycyclic aromatic hydrocarbons (PAHs).[1] Hydroxymethylalkynes have been converted into the more labile allenes and cumulenes which have then been used *in situ* for the preparation of [4]radialenes, macrocycles and 1,2-dihydrocyclobutaarenes.[2] However, only a few domino reactions using allenes as starting materials have been reported so far.[3] Herein, we report a convenient synthesis of 1,1-bis(hydroxymethyl)allenes.[4] These new difunctionalized substrates are used as starting materials in a unimolecular cationic domino reaction. In this context the first, to the best of our knowledge, Nazarov–Friedel–Crafts tandem reaction of an allene is reported which we believe represents a new type of domino process.

1,1-Diphenyl-3,3-dilithioallene **2** was generated in one pot by treatment of the TBDMS enol ether **1** with an excess of LDA in THF, a reaction recently developed by us.[5] The reaction of **2** with 2 equiv. of aryl ketones **3a**–**e** regioselectively provided the colourless bis(hydroxymethyl)allenes **4a**–**e** (Scheme 1, Table 1).† Due to the steric hindrance of the allenic phenyl groups, the sterically crowded allenes **4a**–**e** were regioselectively formed and isolated in high yields.



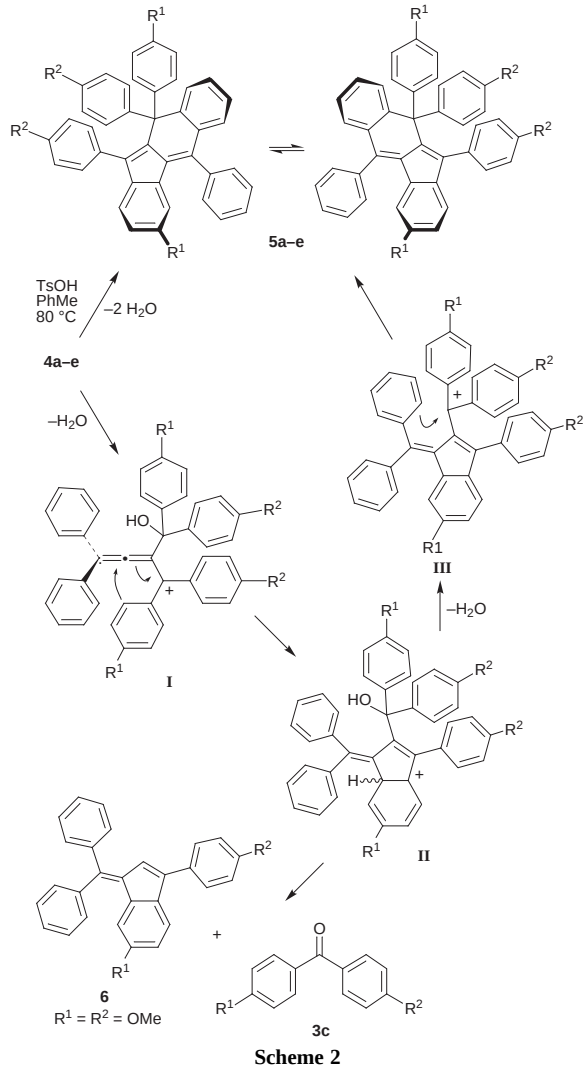
Scheme 1

Table 1 Synthesis of **4** and **5**

			Isolated yield (%)	
4/**5**	R^1	R^2	**4**	**5**
a	H	H	80	85
b	MeO	H	62	73
c	MeO	MeO	75	76
d	Me	Me	76	83
e	Cl	Cl	71	86

Treatment of allenes **4a**–**e** with TsOH in toluene resulted in elimination of 2 equiv. of water and selective formation of the orange coloured 5,10,10,11-tetraaryl-10*H*-benzo[*b*]fluorenes **5a**–**e** in very good yields (Scheme 2, Table 1).‡ In the case of allene **4b** containing two asymmetric carbon atoms, the cyclization proceeded regioselectively *via* the *p*-methoxyphenyl rather than the phenyl group to give **5b** in good yield. Pentafulvenes related to **5** have been used as intermediates in the synthesis of fullerene fragments.[6] Due to their curved structure, 10*H*-benzo[*b*]fluorenes **5a**–**e** are chiral as demonstrated by separation of the two atropic enantiomers of **5a** by HPLC using a chiral stationary phase.§

The formation of 10*H*-benzo[*b*]fluorenes **5** can be explained by a Nazarov–Friedel–Crafts domino reaction. Carbocation **I** is initially generated by dehydration (Scheme 2). The central allene carbon atom is attacked by the *ortho* carbon atom of one

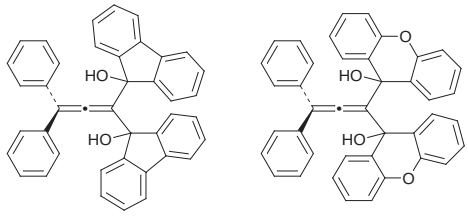


Scheme 2

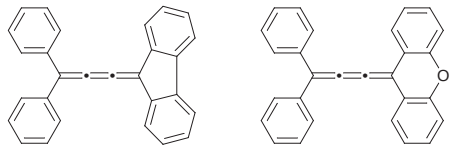
of the aryl groups with formation of a five-membered ring to give intermediate **II**. Aromatization and dehydration subsequently lead to formation of the cationic intermediate **III**. The *ortho* carbon of the allene-derived phenyl group is attacked by the carbocation neighboring the ketone derived aryl groups. Aromatization finally leads to the products **5a**–**e**. The mechanism suggested is supported by the following observation: starting with the *p*-methoxyphenyl-substituted allene **4c**, the benzofulvene **6** is obtained as a minor product in 10% yield. Formation of **6** can be explained by formation of the benzofulvene moiety and subsequent elimination of bis(*p*-methoxyphenyl) ketone or, alternatively, by initial elimination of the ketone, formation of a cumulene (*vide infra*) and subsequent isomerization of the latter.

It is noteworthy that in the domino reaction leading to **5a**–**e** the allenic phenyl group became *sterically* accessible for the cationic π-cyclization only after the previous cyclization involving the rigid allene moiety had occurred. The reaction cascade thus represents a combination of cyclizations as observed for mono(hydroxymethyl)allenes[7a] and for aryl-substituted bis(hydroxymethyl)alkenes $Ar_2C{=}C[C(OH)Ar_2]_2$. The latter have been used as precursors for the generation of (hexaaryltrimethylene)methane dications.[7b]

The reaction of dilithioallene **2** with 2 equiv. of fluorenone and xanthone gave the colourless allenes **4f** and **4g** in 72 and 68% yields, respectively. As minor products, the yellow coloured cumulenes **7a** and **7b** were isolated in 10 and 14%



4f **4g**



7a **7b**

yields. Treatment of the allenes **4f** and **4g** with TsOH resulted in elimination of fluorenone or xanthone and formation of the cumulenes **7a** and **7b** in 85 and 70% yields, respectively, rather than in cyclization. Previously, formation of cumulenes has only been observed for α-unsubstituted (hydroxymethyl)-allenes.[8] In the case of **4f**, the striking difference between the course of the dehydration reactions of the allenes **4a**–**e** and **4f**–**g** can be explained by the fact that cyclization would lead to a strained unsaturated 5,5,6-ring system.[9] In addition, the anti-aromatic character of the fluoren-9-yl cation in the ground state and the rigid character of the ketone-derived subunits of **4f** and **4g** presumably direct the course of the reaction.[10]

P. L. thanks Professor A. de Meijere and Professor D. Seyferth for their support and Professor A. Mannschreck for his help with the separation of the enantiomers of **5a**. Financial support from the Fonds der Chemischen Industrie (Liebig-scholarship and funds for P. L.) is gratefully acknowledged.

Notes and references

† *Preparation* of **4a**. A THF solution (10 ml) of **1** (950 mg, 2.95 mmol) was added to a THF solution of LDA which was prepared by addition of BuLi (1.6 M solution in hexane) to a THF solution (30 ml) of Pr^i_2NH (3.3 equiv.) at 0 °C. The solution was stirred at 20 °C for 6 h during which time the colour of the solution became deep red. A THF solution (10 ml) of benzophenone (1.34 g, 7.38 mmol) was added at −78 °C by syringe. The temperature was allowed to rise to 20 °C within 12 h to give a deep blue solution. The mixture was poured into water (50 ml) and was extracted with Et_2O. The combined yellow coloured organic layers were dried ($MgSO_4$), filtered and the solvent removed *in vacuo*. Purification by column chromatography (Et_2O–light petroleum 1 : 5 → 1 : 1) afforded the allene **4a** (1.31 g, 80%) as a colourless solid, mp 110 °C (decomp.); δ_H($CDCl_3$, 200 MHz): 3.82 (s, 2 H, OH), 6.32 (m, 4 H, Ph), 7.10–7.40 (m, 26 H, Ph); δ_C($CDCl_3$, 50 MHz): 82.90 (C, *C*OH), 114.85, 116.11 (C, *C*=C=*C*), 126.79, 127.91, 128.04 (CH, Ph), 127.18, 127.29, 127.83 (CH, Ph), 136.56, 146.56 (C, Ph), 205.26 (C, C=*C*=C); ν_{max}(KBr)/cm^{-1} 3385 (w), 3057 (w), 1949 (m, C=C=C), 1598 (w), 1493 (m), 1447 (m), 1348 (w), 1177 (w), 1031 (m), 698 (s). *m/z* (CI, H_2O): 539 (M^{+}+1 − H_2O), 521 (M^{+}+1 − $2H_2O$), 357 (100%, $Ph_2C{=}C{=}CPh_2$ + 1). (Calc. for $C_{41}H_{32}O_2$: C, 88.46; H, 5.79. Found: C, 88.23; H, 5.75%.) All new compounds gave correct spectroscopical data and elemental analyses and/or high resolution mass data.

‡ *Preparation* of **5a**: Allene **4a** (200 mg, 0.36 mmol) and TsOH (60 mg) were heated in toluene (30 ml) at 80 °C for 2 h. The colour of the solution changed from light yellow to deep orange. The crude mixture was purified by column chromatography (Et_2O–light petroleum = 1 : 5 → 1 : 1) to give **5a** (159 mg, 85%) as orange coloured crystals, mp 176 °C (decomp.); δ_H($CDCl_3$, 200 MHz) 6.20 (d, *J* 7, 1 H, Ar), 6.56 (m, 2 H, Ar), 6.71 (d, *J* 7, 1 H, Ar), 6.11 (dd, *J* 7, *J* 1.5, 1 H, Ar), 6.41 (m, 2 H, Ar), 6.58 (m, 3 H, Ar), 6.85–7.25 (m, 18 H, Ar); δ_C($CDCl_3$, 50 MHz): 57.42 (C, *C*Ph_2), 119.89, 123.25, 124.70, 126.05, 126.23, 127.33, 127.34, 127.81, 127.99, 128.08, 128.20, 128.77, 128.99, 129.28, 130.14, 130.15, 130.37 (CH, Ar), 133.57, 133.81, 134.32, 135.51, 137.78, 139.80, 140.13, 142.24, 145.54, 145.82, 147.23 (C, Ar); ν_{max}(KBr)/cm^{-1} 3056 (m), 3024 (m), 2924 (m), 1600 (m), 1492 (m), 1448 (m), 1368 (w), 1076 (w), 1032 (w), 760 (s), 744 (s), 724 (s), 700 (s); *m/z* (FAB) 521 (100%, M^{+} + 1). (Calc. for $C_{41}H_{28}$: C, 94.58; H, 5.42. Found: C, 94.27; H, 5.50%.)

§ Conditions (a) stationary phase: tris(phenylcarbamoyl)cellulose/SiO_2; eluent: EtOH; UV detection: λ = 320 nm; polarimetric detection: λ = 436 nm; *c* = 1 mg ml^{-1} (injection of 50 μl); *P* = 63 bar; *T* = 25 °C; flow: 0.5 ml min^{-1}; t_1 = 9 min; k_1' = 0.44. The results were independently confirmed by the use of different conditions: (b) stationary phase: triacetylcellulose/SiO_2; eluent: MeOH; UV detection: λ = 278 nm; polarimetric detection: λ = 405 nm; *c* = 1 mg ml^{-1} (injection of 150 μl); *P* = 68 bar; *T* = 25 °C; flow: 1.0 ml min^{-1}; t_1 = 12.6 min; k_1' = 0.60.

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Communication 9/01208G