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

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The reaction of dilithiated 1,1-diphenylallene with aryl ketones provides a convenient access to novel 1,1-bis(hy-droxymethyl)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



 Table 1 Synthesis of 4 and 5

4a-e

	R ¹	R ²	Isolated yield (%)	
4/5			4	5
а	Н	Н	80	85
b	MeO	Н	62	73
с	MeO	MeO	75	76
d	Me	Me	76	83
e	Cl	Cl	71	86

Scheme 1

sterically crowded allenes **4a**–**e** were regioselectively formed and isolated in high yields.

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 10H-benzo $[\bar{b}]$ 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



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 Ar₂C=C[C(OH)Ar₂]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%



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 antiaromatic 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

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Notes and references

 \dagger 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 Pri₂NH (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 Et₂O. The combined yellow coloured organic layers were dried (MgSO₄), filtered and the solvent removed in vacuo. Purification by column chromatography (Et₂O-light petroleum 1 : $5 \rightarrow 1$: 1) afforded the allene **4a** (1.31 g, 80%) as a colourless solid, mp 110 °C (decomp.); $\delta_{\rm H}$ (CDCl₃, 200 MHz): 3.82 (s, 2 H, OH), 6.32 (m, 4 H, Ph), 7.10-7.40 (m, 26 H, Ph); δ_C(CDCl₃, 50 MHz): 82.90 (C, COH), 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); v_{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, H₂O): 539 (M⁺+1 - H₂O), 521 (M⁺+1 - 2H₂O), 357 (100%, Ph₂C=C=CPh₂ + 1). (Calc. for C₄₁H₃₂O₂: 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 (Et₂O–light petroleum = 1:5 → 1:1) to give **5a** (159 mg, 85%) as orange coloured crystals, mp 176 °C (decomp.); δ_H(CDCl₃, 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(CDCl₃, 50 MHz): 57.42 (C, CPh₂), 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 C₄₁H₂₈: C, 94.58; H, 5.42. Found: C, 94.27; H, 5.50%.)

§ Conditions (a) stationary phase: tris(phenylcarbamoyl)cellulose/SiO₂; eluent: EtOH; UV detection: $\lambda = 320$ nm; polarimetric detection: $\lambda = 436$ 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/SiO₂; eluent: MeOH; UV detection: $\lambda = 278$ nm; polarimetric detection: $\lambda = 405$ 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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