Mild and efficient methodology for installation of *gem*-diallyl functionality on carbohydrate synthons

Mukund K. Gurjar,* S. V. Ravindranadh and Sukhen Karmakar

National Chemical Laboratory, Pune 411008, India. E-mail: gurjar@dalton.ncl.res.in

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A versatile approach to construct *gem*-diallyl functionality has been described.

As a part of our ongoing efforts directed toward synthesis of natural products containing a spiro-ring system,[1] we were confronted with a need to synthesize a *geminal* (*gem*) diallyl containing carbohydrate backbone (Fig. 1). The *gem*-diallyl groups can undergo ring closing metathesis to produce the spiro-ring system.[2] Such *gem*-diallyl systems are not reported in carbohydrate chemistry, although they can form valuable synthons for many chemical transformations leading to functionalised products.

Incorporation of *gem*-diallyl groups is usually achieved by base catalyzed dialkylation of active methylene groups with allyl halides.[3] However, we realized that this approach may not be appropriate for carbohydrate molecules because of side reactions resulting from various hydroxy groups. We were particularly interested in the application of Keck's one electron C–C bond-forming reaction[4] to generate a *gem*-diallyl system in a carbohydrate unit by quenching the allylic radical generated *in situ*, with allyltri-*n*-butylstannane.

In accordance with our plan, 5-*O*-*tert*-butyldiphenylsilyl-1,2-*O*-isopropylidene-α-D-xylofuranose (**1**) was oxidized with IBX–DMSO (IBX = *o*-iodoxybenzoic acid) and then the resulting 3-ulose derivative was treated with PPh_3=$CHCO_2Et$ in refluxing benzene to give the α,β-unsaturated product (**2**).[5]

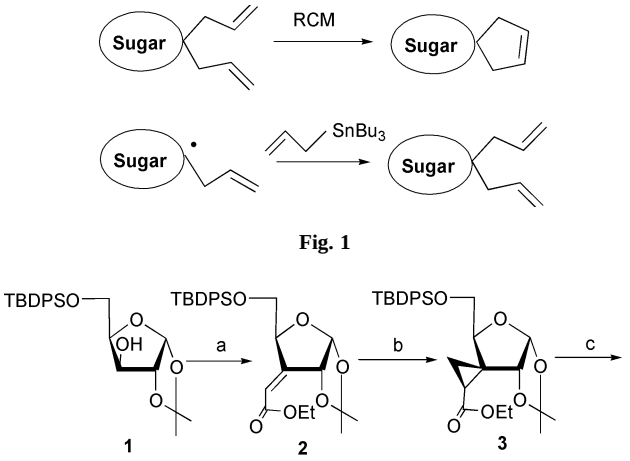
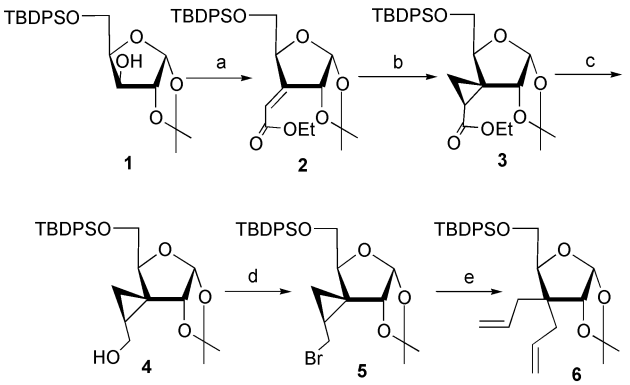


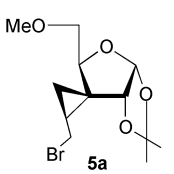
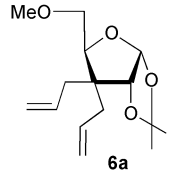
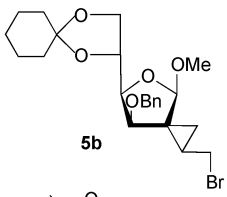
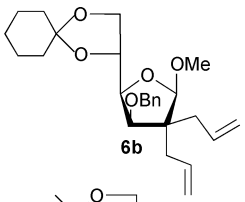
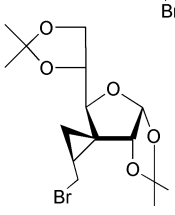
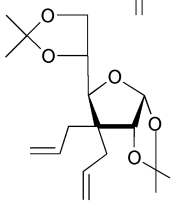
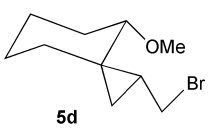
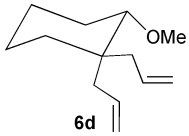
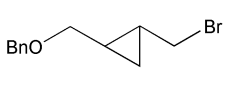
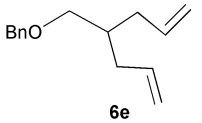
Fig. 1



Scheme 1 *Reagents and conditions*: (a) (i) IBX (1.5 eq.), DMSO, rt, 10 h; (ii) PPh_3=CHCOOEt, (1.5 eq.), benzene, 80 °C, 3 h, 70% after two steps; (b) Me_2SOCH_3I (1.1 eq.), NaH (1.1 eq.), DMSO, rt, 3 h, 60%; (c) DIBAL-H (2.5 eq.), −78 °C, 0.5 h, 85%; (d) PPh_3 (2.0 eq.), CBr_4 (2.2 eq.), pyridine (2.5 eq.), 0 °C, 90%; (e) allyltri-*n*-butylstannane (2 eq.), AIBN (5 mol %), benzene, 80 °C,12 h, 80%.

Cyclopropanation of **2** was effected with Me_2SOCH_3I–NaH in dry DMSO to give **3**, as a single diastereomer.[6] Although the stereochemical identification of **3** was of no consequence to the present study, we believe the approach of the ylide occurs from the β-face due to the stereo-controlling effect of the adjacent 1,2-*O*-isopropylidene group. In the ^1H NMR spectrum of **3**, the protons of the cyclopropyl group, as expected, appeared in the high field region. Conversion of the ester function in **3** into the hydroxymethyl group was accomplished by using DIBAL-H at −78 °C to produce **4** in 85% yield. Compound **4** on treatment with CBr_4–PPh_3 in CH_2Cl_2 at rt gave the bromo derivative (**5**) in 90% yield. The ^1H, ^{13}C NMR and MS studies substantiated the assigned structure **4**. Treatment of **5** with allyltri-*n*-butylstannane in the presence of a catalytic amount of AIBN in refluxing benzene under argon atmosphere for 12 h gave the *gem*-diallyl compound **6** in 80% yield.† In the ^1H NMR

Table 1 Compounds **5a**–**e** were prepared essentially by the route shown in Scheme 1 and their structures elucidated by spectral data. Yields are given for isolated products.

Entry	Substrate	Product	Yield (%)
1	 **5a**	 **6a**	72
2	 **5b**	 **6b**	63
3	 **5c**	 **6c**	76
4	 **5d**	 **6d**	75
5	 **5e**	 **6e**	70

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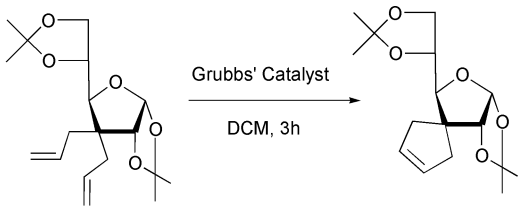

Scheme 2

spectrum of **6**, the characteristic olefinic proton signals of two allylic groups appeared in in the region of 5.0 and 5.7 ppm while the allylic methylene protons were located in the region of 2.2 ppm. In addition, the assigned structure of **6** was further suggested by the ^{13}C NMR, MS and elemental analysis. Table 1 provides other examples in this series which substantiates the versatility of this methodology. Only entry 5 describes an aliphatic example.

The ring closing metathesis reaction of **6c** with Grubbs catalyst in CH_2Cl_2 at rt gave the spiro-ring compound **7** in 80% yield.[7] The structure of **7** was established based on ^{1}H, ^{13}C NMR and MS (Scheme 2).[8]

In summary this communication describes a mild and efficient methodology to construct *gem*-diallylic substituted carbohydrate synthons as precursors for spiro-cyclic systems. The preparation of unsymmetrical *gem*-diallyl substituents at the quaternary carbon will be the next endeavour of this methodology.

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Notes and references

† Typical experimental procedure: A solution of the cyclopropylmethyl bromide derivative **5a**–**e** (0.4 mmol), allyltri-*n*-butylstannane (0.8 mmol) and AIBN (5 mol %) in dry benzene (3 mL) was degassed by bubbling argon for 30 min. The reaction mixture was heated under reflux for 12 h and concentrated *in vacuo*. A KF solution (5 mL) and diethyl ether (10 mL) were added, stirred for 1 h, filtered and washed with ether. The ether layer was separated, dried over anhydrous Na_2SO_4 and concentrated. The crude product was purified on silica gel using ethyl acetate–hexane to afford the desired diallyl product.

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8 Compound **6**: ^{1}H NMR (200 MHz) data: δ 1.08 (s, 9 H, ^{t}Bu), 1.29, 1.54 (2s, 6 H, 2 × Me, 1.87–2.54 (m, 4H, 2 × CH_2-CH=), 3.82 (m, 2 H, H-5 and H-5′), 4.03 (t, 1 H, J = 6.4 Hz, H-4), 4.25 (d, 1 H, J = 3.4 Hz, H-2), 5.0 (m, 4 H, 2 × CH_2=), 5.70 (d, 1 H, J = 3.4 Hz, H-1), 5.80 (m, 2 H, 2 × CH=), 7.35–7.77 (m, 10 H, 2 × Ph); ^{13}C NMR (50.32 MHz) data: δ 19.3, 26.5, 27.0, 35.6, 36.5, 50.0, 62.9, 84.7, 85.6, 104.2, 111.0, 117.7, 127.8, 129.8, 133.3, 133.5, 134.5, 135.0, 135.7.

Compound **6a**: ^{1}H NMR (200 MHz) data: δ 1.31, 1.53 (2s, 6 H, 2 × Me), 1.91–2.50 (m, 4 H, 2 × CH_2-CH=), 3.35 (s, 3 H, OMe), 3.52 (m, 2 H, H-5 and H-5′), 4.06 (dd, 1H, J = 3.9, 7.3 Hz, H-4), 4.26 (d, 1 H, J = 3.9 Hz, H-2), 5.06 (m, 4 H, 2 × CH_2=), 5.70 (d, 1 H, J = 3.9, H-1), 5.84 (m, 2 H, 2 × CH=); ^{13}C NMR (75.47 MHz) data: δ 26.3, 26.8, 35.3, 35.8, 49.8, 59.2, 71.7, 83.2, 85.3, 104.2, 112.2, 118.0, 134.0, 134.4.

Compound **6b**: ^{1}H NMR (500 MHz) data: δ 1.58 (m, 10 H, 5 × CH_2), 2.05- 2.4 (m, 4 H, 2 × CH_2-CH=), 3.31 (s, 3 H, OMe), 3.9 (d, 1 H, J = 4.4 Hz, H-3), 3.95 (dd, 1 H, J = 5.9, 8.3 Hz, H-4), 4.08 (m, 2 H, H-6 and H-6′), 4.31 (m, 1 H, H-5), 4.49, 4.74 (2d, 2 H, J = 11.0 Hz, CH_2Ph), 4.71 (s, 1 H, H-1), 5.06 (m, 4 H, 2 × CH_2=), 5.77 (m, 2 H, 2 × CH=); ^{13}C NMR (125.75 MHz) data: δ 23.9, 24.1, 25.2, 35.0, 35.3, 36.5, 52.6, 55.9, 67.2, 73.2, 74.2, 80.4, 84.4, 109.2, 109.6, 117.5, 117.7, 127.6, 128.0, 128.3, 135.0, 138.5.

Compound **6c**: ^{1}H NMR (200 MHz) data: δ 1.27, 1.33, 1.45, 1.50 (4s, 12 H, 4 × Me), 2.15–2.45 (m, 4 H, 2 × CH_2-CH=), 3.72 (m, 1 H, H-4), 3.78 (m, 1 H, H-5), 4.09 (m, 2 H, H-6 and H-6′), 4.24 (d, 1 H, J = 3.4 Hz, H-2), 5.03 (m, 4 H, 2 × CH_2=), 5.57 (d, 1 H, J = 3.4 Hz, H-1), 5.9 (m, 2 H, 2 × CH=); ^{13}C NMR (50.32 MHz) data: δ 25.5, 26.4, 26.8, 27.1, 36.1, 37.0, 50.6, 69.0, 73.5, 85.2, 86.0, 104.4, 109.5, 111.3, 117.6, 134.8, 135.5.

Compound **6d**: ^{1}H NMR (200 MHz) data: δ 1.30 (m, 8 H, 4 × CH_2), 1.92–2.30 (m, 4 H, CH_2-CH=), 2.94 (dd, 1 H, J = 3.4, 7.8 Hz, CH), 3.27 (s, 3 H, OMe), 4.94 (m, 4 H, 2 × CH_2=), 5.77 (m, 2 H, 2 × CH=); ^{13}C NMR (50.32 MHz) data: δ 21.0, 22.9, 24.1, 31.4, 36.8, 39.8, 40.9, 56.3, 82.3, 117.0, 117.2, 135.1.

Compound **6e**: ^{1}H NMR (200 MHz) data: δ 1.76 (m, 1 H, methine), 2.10 (m, 4 H, 2 × CH_2-CH=), 3.33 (dd, 2 H, J = 5.9, 11.2 Hz, CH_2O), 4.46 (d, 2 H, J = 11.7 Hz, CH_2Ph), 5.00 (m, 4 H, 2 × CH_2=), 5.73 (m, 2 H, 2 × CH=), 7.26 (m, 5 H, Ph); ^{13}C NMR (50.32 MHz) data: δ 35.4, 38.3, 72.4, 73.1, 116.3, 127.5, 128.3, 136.7.