An unusual observation in the rhodium carbenoids: [1,4]-migration in the sugar-derived α-diazo-β-ketoesters

Vijaya N. Desai, Nabendu N. Saha and Dilip D. Dhavale *

Department of Chemistry, Garware Research Centre, University of Pune, Pune - 411 007, India. E-mail: ddd@chem.unipune.ernet.in

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In competition with [1,2]-migration, [2,3]-sigmatropic rearrangement and C–H insertion, product formation *via* an unusual [1,4]-migration is also found to be a prominent process in the rhodium carbenoids derived from sugar α-diazo-β-keto esters **2a**–**d**.

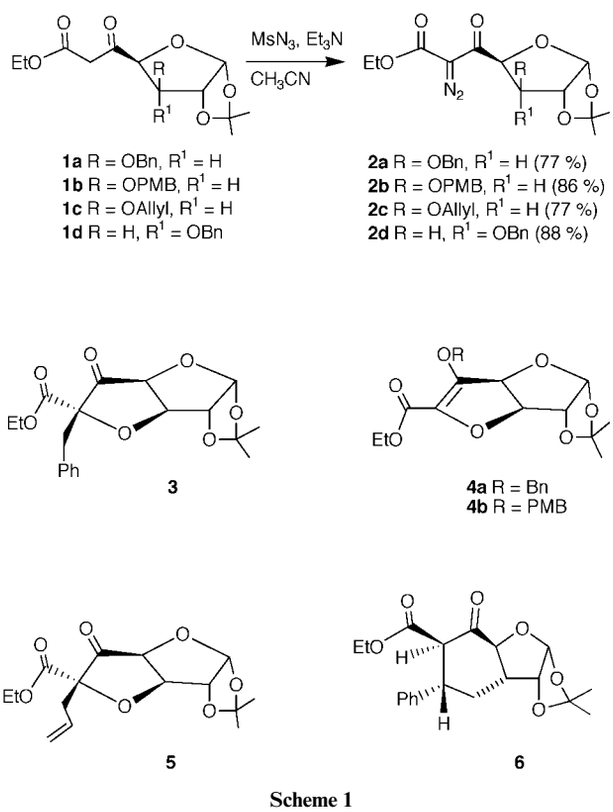
Introduction

The rhodium(II)-catalysed reactions of α-diazocarbonyl compounds and their applications in the selective formation of polycyclic systems have received much attention over the years.[1] In general, the rhodium carbenoids have been utilised in three major reaction pathways which include (a) olefin cyclopropanation, cyclopropenation and Buchner reaction, (b) X–H (X = C, O, N, S, Si) insertion reactions, and (c) ylide formation. Thus, for a given substrate several distinct possibilities are available and the chemoselectivity of such processes is dependent on steric, conformational, electronic factors and the nature of both the substrate and the catalyst. Amongst rhodium(II)-catalysed oxonium-ylide-formation reactions, the product derived from either [2,3]-sigmatropic rearrangement[2] or [1,2]-migration[3] is routinely observed; however, the product formation *via* [1,4]-migration is unusual.[4] Pirrung *et al.*[5] first noticed an example of the [1,4]-migration in rhodium(II)-mediated reaction pathway. The second report, by F. G. West *et al.*, described the isolation of the [1,4]-migration product *albeit* in very low yield in the Cu^{II} carbenoids-derived oxonium ylides. However, the same reaction fails to give the [1,4]-migration product in the presence of rhodium(II) acetate.[6]

Recently, we have reported the synthesis of sugar β-keto ester **1a** and demonstrated its applicability in the synthesis of 6-deoxyheptulosurono-7,4-lactones,[7a] 1,6-dideoxynojirimycin[7b] and coumarinyl *C*-glycosides.[7c] In order to explore the utility of sugar β-keto esters **1a**–**d** in the synthesis of polyether antibiotics, we have examined the rhodium(II)-catalysed reactions of α-diazo-β-keto esters **2a**–**d** and the results thus obtained are presented herein.

Results and discussion

The sugar β-keto esters **1a**–**d** were prepared as reported earlier by us.[7a] The reaction of **1a**–**d** with mesyl azide in the presence of triethylamine in acetonitrile afforded α-diazo-β-keto esters **2a**–**d**, respectively, in good yields (Scheme 1). The individual reactions of **2a**–**d** were performed using rhodium(II) acetate (1 mol%) under different conditions of solvent and temperature. The reaction of **2a** in dichloromethane at room temperature or at reflux afforded a complex mixture of products, while in benzene at 25 °C it was found to be very sluggish and even after 36 h nearly quantitative amounts of starting material were recovered. However, the reaction of **2a** and rhodium(II) acetate (1 mol%) in benzene at reflux for 5 min afforded **3** and **4a** in the ratio 38 : 62 in 77% yield. The appreciable difference in the R_f-values of these two compounds allowed us to separate the products **3** and **4a** in pure form by column chromatography.



Scheme 1

The assignment of the structures was based on IR and NMR spectral data. The IR spectra of the compound with a high R_f-value showed two carbonyl frequencies, at 1779 and 1744 cm^{-1}, indicating the presence of a five-membered-ring ketone (furan-3-one) and the ester carbonyl functionality, respectively. The ^1H NMR spectrum showed an AB quartet at δ 3.26 (J 14.0 Hz) indicating the presence of a CCH_2Ph group instead of OCH_2Ph functionality. The ^{13}C NMR spectrum showed a ketone carbonyl at δ_C 202.3 and the ester carbonyl at δ_C 166.9. These spectral data were found to be consistent with structure **3**. The formation of **3** could be explained *via* a five-membered oxonium ylide followed by [1,2]-migration of the benzyl group as shown in Scheme 2. The stereochemistry of the [1,2]-migration was tentatively assigned as shown in structure **3** on the basis of transition state **A** (Scheme 2) that resembles an oxabicyclo-[3.1.0]hexane ring system with the key, stereochemically defining benzyl group coming from the same side (β-face) as that of the 3-OBn functionality in the final product **3**. In the compound

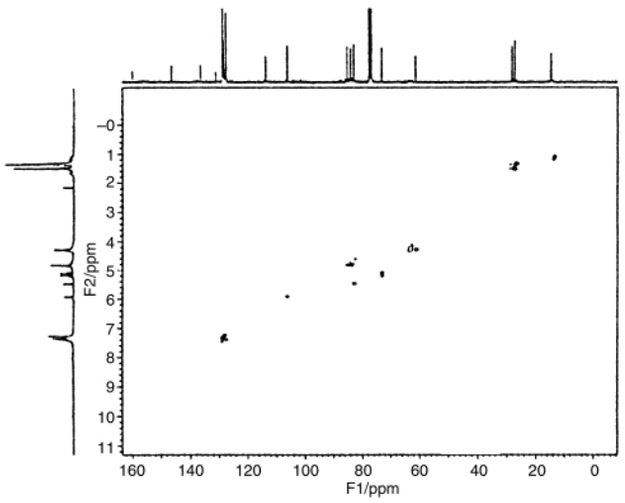
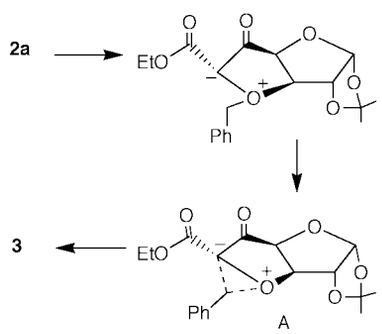


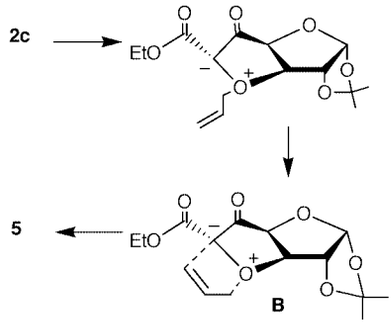
Fig. 1 GHSQC (300 MHz; $CDCl_3$) spectrum of **4a**.



Scheme 2

with low R_f-value, the absence of a carbonyl frequency at ≈1770 cm^{-1} ruled out the presence of a five-membered ring carbonyl (furan-3-one) and the lower ester carbonyl signal observed at 1714 cm^{-1} suggested an α,β-unsaturated ester. In the ^1H NMR spectrum, the appearance of an AB quartet at δ 5.16 (J 12.1 Hz) suggested the OCH_2Ph functionality. The ^{13}C NMR spectrum showed only one ester carbonyl, at δ_C 160.1, but additional signals at δ_C 146.4 and 127.9 indicated the presence of olefinic carbons. Based on spectral and analytical data structure **4a** was assigned to the compound. The formation of compound **4a** *via* [1,4]-migration was unusual, therefore the structure was further confirmed by ^{13}C DEPT and HETCORR 2D NMR experiments (Fig. 1).

In order to ascertain the generality of the [1,4]-migration product, the reaction sequence was carried out with different sugar-derived α-diazo-β-keto esters by changing the C-3 substituent. Thus, when 3-*O*-(4-methoxybenzyl)-α-diazo-β-keto ester **2b** was allowed to react in benzene (reflux; 25 min) the [1,4]-migration product **4b** was the only isolable product, in 80% yield after purification. In its ^1H NMR spectrum, the crude reaction mixture showed no other stereoisomers or regioisomers. The spectral and analytical data were in accord with the assigned structure **4b**. However, when the reaction was performed with 3-*O*-allyl-α-diazo-β-keto ester **2c**, in benzene (reflux, 5 min), the product **5** was obtained in 74% yield. As shown in Scheme 3, this reaction pathway is presumably following the [2,3]-sigmatropic rearrangement as the allylic oxonium ylides have a preference for symmetry-allowed [2,3]-sigmatropic rearrangement over [1,2]-migration.[2a] The assignment of the configuration at C-6 in **5** was decided on the basis of transition state **B** (Scheme 3) that resembles an oxabicyclo[3.3.0]octane ring system in which the migrating group comes from the β-face. In view of the fact that, in metal carbenoid reactions, [2,3]-sigmatropic rearrangements have the lower activation energy as compared with other possible pathways,[4] the reaction



Scheme 3

was performed at lower temperatures. Thus, when the reaction of **2c** was carried out either in dichloromethane (for 1 h) or in benzene (for 3 h) at 35 °C, compound **5** was obtained in 78 and 86% yield, respectively, indicating that the reaction pathway is indeed a [2,3]-sigmatropic rearrangement.

Strikingly different results were obtained on changing the configuration of the OBn group at C-3. The reaction of D-allose-derived 3-*O*-benzyl-α-diazo-β-keto ester **2d** in benzene (reflux; 5 min) resulted in formation of the C–H insertion product **6** in 80% yield. The presence of a six-membered ketone was obvious from the IR spectrum at 1760 cm^{-1} and the ^{13}C NMR spectrum at δ_C 195.8. The structure was characterised by spectral and analytical data and confirmed by 2D NMR COSY (Fig. 2) and HETCORR (Fig. 3) experiments. The large coupling-constant-value of 10.5 Hz between H-6 and H-7 indicated the relative *trans* diaxial relationship of these protons. The absolute stereochemistry of the C–H insertion, at C-6 and C-7, was decided by DPFGNOE wherein irradiation of H-3 at δ 3.82 showed NOE enhancement for the H-7 signal at δ 5.15, indicating their spatial proximity. In structure **2d**, the OBn substituent at C-3 is α-orientated and the proton is β-oriented, therefore the proton at C-7 was assigned the β-orientation based on observed NOEs with H-3 and hence the C-6 proton was placed α-oriented as shown in structure **6**. The competition between rearrangement or migration reaction *versus* C–H insertion could be related to the steric strain involved in the formation of the five-membered oxonium ylide. The relative *trans* geometry of the substituents at C-3 and C-4 disfavours the *trans* ring fusion of two five-membered rings in transition state **C** (Scheme 4). As a result the C–H insertion pathway, which proceeds *via* a seven-membered transition state **D** as shown in Scheme 4, results in the six-membered-ring product **6**.

It has been observed that the [1,4]-migration products **4a** and **4b** are formed from the substrates **2a** and **2b**, respectively. Although the different mechanisms involved in the formation of products **3**, **5** and **6** are well documented in the literature,[1] an explanation for the [1,4]-migration product is lacking. We assume that the metal-bound oxonium ylide **7** or **8** (Scheme 5), generated from substrate **2a** or **2b**, plays an important role in the reaction selectivity. The product formation *via* **8** can be ruled out as the distance between the migration origin and terminus is large, while in **7** we hypothesised a somewhat different four-centred transition state **9**, in which the C–Rh bond is aligned with the O–CH_2Ar bond. As the reaction proceeds, the migration of CH_2Ar from oxygen to Rh is completed giving Rh^{II} species **10**. Such a type of involvement of rhodium metal in [1,2]-shifts of ylides has been proposed.[2] Free rotation about the Rh–C-6 bond brings CH_2Ar close to the ketone carbonyl, permitting [1,4]-migration at this juncture to give the product.[8] The exclusive formation of **4b** in case of 3-*O*-(4-methoxybenzyl)-substituted compound **2b** could be due to the increase in electron density at the benzyl carbon which renders better coordination with the rhodium, or it may reflect the stabilisation of the partial positive charge on the migrating group during rearrangement.

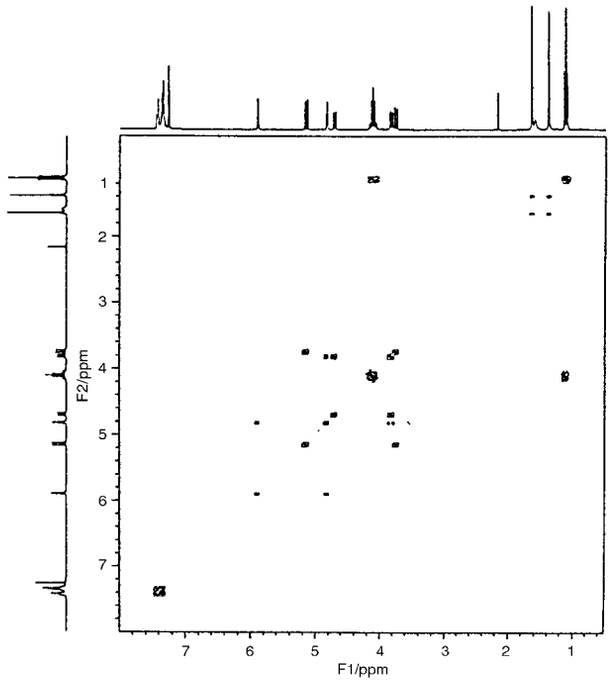


Fig. 2 2D COSY spectrum of compound **6**.

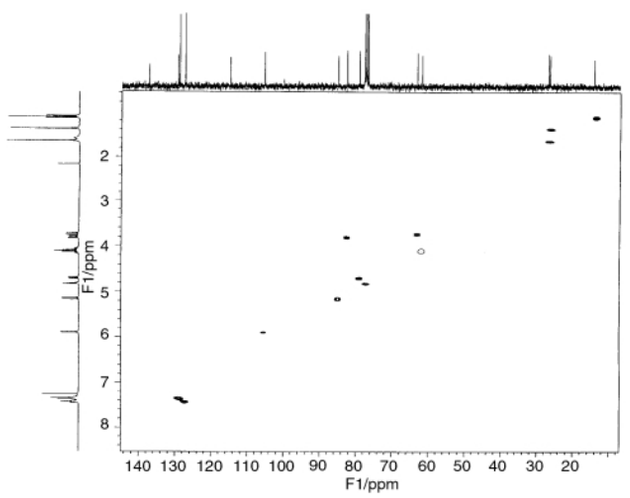
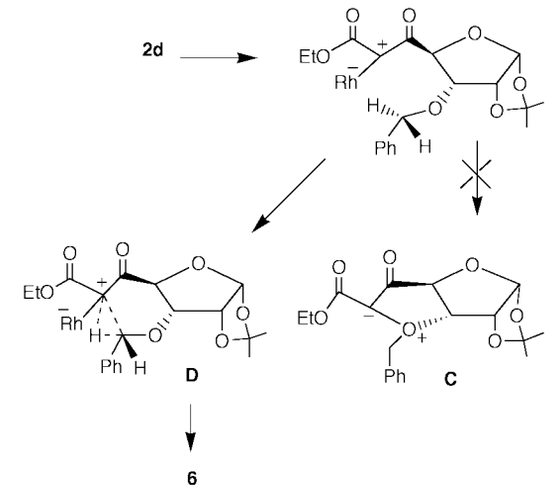


Fig. 3 GHSQC (300 MHz; $CDCl_3$) spectrum of **6**.

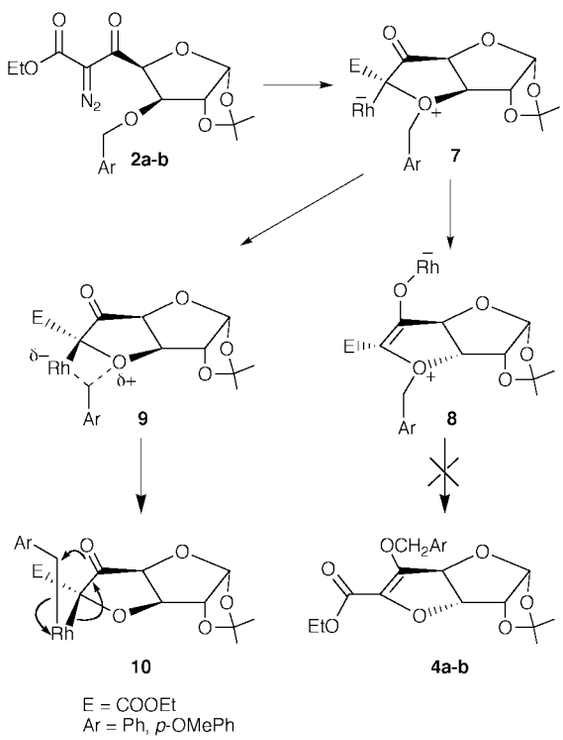
In conclusion, a novel rhodium carbenoid-mediated [1,4]-migration pathway has been found to be a prominent process in oxonium ylides. It has also been demonstrated that the pathway is dependent on the nature of the diazocarbonyl precursor. Further investigations into the substrate reactivity and the scope of this reaction in the synthesis of polyether antibiotics are in progress.

Experimental

NMR spectra of $CDCl_3$ solutions were recorded with a Bruker AMX 500 MHz and a Varian VXR 300S MHz spectrometer. Chemical shifts are reported in ppm (δ) downfield of TMS. IR spectra were recorded with a Perkin-Elmer 1600 FTIR spectrophotometer. Optical rotations were measured at 25 °C with a Perkin-Elmer 241 polarimeter and $[a]_D$-values are given in units of 10^{-1} deg cm^2 g^{-1}. C, H analyses were performed on a Hosli Carbon-Hydrogen analyser. Mps were taken on a Thomas-Hoover capillary melting point apparatus and are uncorrected. All the reactions were conducted in oven-dried glassware under dry nitrogen. TLC was carried out on Polygram Sil G/UV 254 precoated plastic sheets, and flash chromatography was



Scheme 4



Scheme 5

carried out using Kieselgel 60 (230–400 mesh) with petroleum spirit (PS) (boiling range 60–80 °C)–ethyl acetate as eluent. Rhodium acetate was purchased from Fluka and was dried under high vacuum (0.01 mmHg) at 100 °C for 4 h before use. Dichloromethane, acetonitrile and benzene were dried according to standard procedures. Ethyl 3-*O*-benzyl-6-deoxy-1,2-*O*-isopropylidene-α-D-*xylo*-hept-5-ulofuranuronate **1a** and ethyl 3-*O*-benzyl-6-deoxy-1,2-*O*-isopropylidene-α-D-*ribo*-hept-5-ulofuranuronate **1d** were prepared according to our previous report.[7a]

Ethyl 6-deoxy-1,2-*O*-isopropylidene-3-*O*-(4-methoxybenzyl)-α-D-*xylo*-hept-5-ulofuranuronate 1b

A solution of 1,2-*O*-isopropylidene-3-*O*-(4-methoxybenzyl)-α-D-*xylo*-pentodialdose (2 g, 6.49 mmol) and ethyl diazoacetate (1.0 mL, 9.74 mmol) in dry CH_2Cl_2 (100 mL) was cooled to −50 °C under N_2. A solution of BF_3–diethyl ether (0.25 mL, 1.95 mmol) in dry CH_2Cl_2 (10 mL) was added dropwise with control of the evolution of N_2 (30 min). The reaction mixture was stirred at −50 °C for 3 h and quenched with a saturated

solution of sodium bicarbonate. The organic layer was separated and the aqueous layer was extracted with dichloromethane (20 mL × 3). The combined organic layer was dried (Na_2SO_4) and evaporated on a rotary evaporator. The residue thus obtained on column chromatography yielded β-*keto ester* **1b** as an oil (1.913 g, 75%), R_f 0.23 (PS–ethyl acetate 7:3); $[\alpha]_D$ −49.17 (*c* 0.4, $CHCl_3$); ν_{max} (neat)/cm^{-1} 1724 (CO_2Et), 1745 (C=O); δ_H ($CDCl_3$; 200 MHz) 1.25 (3H, t, *J* 6.2 Hz, CH_2CH_3), 1.32 (3H, s, CH_3), 1.45 (3H, s, CH_3), 3.52 (1H, d, *J* 18.0 Hz, $COCH_2CO$), 3.72 (1H, d, *J* 18.0 Hz, $COCH_2CO$), 3.80 (3H, s, OCH_3), 4.2 (2H, q, *J* 6.2 Hz, OCH_2CH_3), 4.26 (1H, d, *J* 3.6 Hz, 3-H), 4.40 (1H, d, *J* 2.0 Hz, OCH_2Ph), 4.50 (1H, d, *J* 12.0 Hz, OCH_2Ph), 4.56 (1H, d, *J* 3.3 Hz, 2-H), 4.70 (1H, d, *J* 3.6 Hz, 4-H), 6.05 (1H, d, *J* 3.3 Hz, 1-H), 6.87 (2H, d, *J* 8.0 Hz, ArH), 7.20 (2H, d, *J* 8.0 Hz, ArH); δ_C ($CDCl_3$; 22.5 MHz) 13.8, 25.9, 26.5, 47.1, 54.8, 60.7, 72.1, 81.8, 83.0, 84.6, 105.7, 112.2, 113.5, 128.5, 129.1, 159.2, 166.6, 200.7 (Calc. for $C_{20}H_{26}O_8$: C, 60.90; H, 6.64. Found: C, 61.08; H, 6.85%).

Ethyl 3-*O*-allyl-6-deoxy-1,2-*O*-isopropylidene-α-D-*xylo*-hept-5-ulofuranuronate 1c

The reaction of 3-*O*-allyl-1,2-*O*-isopropylidene-α-D-*xylo*-pentodialdose (1.5 g, 6.58 mmol) and ethyl diazoacetate (1.05 mL, 9.87 mmol) in dry CH_2Cl_2 (100 mL) at −10 °C for 3 h as per the procedure for **1b** gave β-*keto ester* **1c** as an oil (1.811 g, 88%). R_f 0.39 (PS–ethyl acetate 7:3); $[\alpha]_D$ −61.0 (*c* 0.4, $CHCl_3$); ν_{max} (Nujol)/cm^{-1} 1723 (CO_2Et), 1747 (C=O); δ_H ($CDCl_3$; 300 MHz) 1.27 (3H, t, *J* 7.1 Hz, CH_2CH_3), 1.33 (3H, s, CH_3), 1.47 (3H, s, CH_3), 3.55 (1H, d, *J* 16.8 Hz, $COCH_2CO$), 3.74 (1H, d, *J* 16.8 Hz, $COCH_2CO$), 3.94 (1H, ddt, *J* 1.5, 5.7, 12.6 Hz, $OCH_2CH{=}CH_2$), 4.05 (1H, ddt, *J* 1.1, 5.5, 12.6 Hz, $CH_2CH{=}CH_2$), 4.12–4.30 (3H, m, OCH_2CH_3, 3-H), 4.56 (1H, d, *J* 3.5 Hz, 2-H), 4.69 (1H, d, *J* 3.6 Hz, 4-H), 5.18–5.28 (2H, m, $CH_2{=}CH$), 5.70–5.85 (1H, m, $CH_2{=}CH$), 6.06 (1H, d, *J* 3.5 Hz, 1-H); δ_C ($CDCl_3$; 22.5 MHz) 13.8, 26.1, 26.7, 47.1, 60.6, 71.3, 79.2, 83.5, 84.9, 105.9, 112.2, 117.4, 133.4, 166.5, 200.8 (Calc. for $C_{13}H_{22}O_7$: C, 53.78; H, 7.64. Found: C, 53.90; H, 7.86%).

General procedure for the synthesis of α-diazo-β-keto esters 2a–d

To a solution of α-diazo-β-keto ester (1 mmol) in dry acetonitrile (30 mL) were added triethylamine (2 mmol) and methanesulfonyl azide (1.1 mmol). The reaction mixture was stirred at room temperature for 3 h and quenched with aq. sodium hydroxide (2 M; 1 mL). The organic layer was separated and the aqueous layer was extracted with ethyl acetate (20 mL × 3). The combined organic layer was dried (Na_2SO_4), and evaporated on a rotary evaporator to give a thick oil, which on column chromatography (PS–ethyl acetate 19:1) yielded the α-diazo-β-keto ester.

Ethyl 3-*O*-benzyl-6-deoxy-6-diazo-1,2-*O*-isopropylidene-α-D-*xylo*-hept-5-ulofuranuronate 2a. *Thick oil*; 77% yield; R_f 0.42 (PS–ethyl acetate 7:3); $[\alpha]_D$ +1.6 (*c* 0.44, $CHCl_3$); ν_{max} (neat)/cm^{-1} 1680 (C=O), 1712 (C=O), 2141 (N=N); δ_H ($CDCl_3$; 500 MHz) 1.24 (3H, t, *J* 7.1 Hz, CH_2CH_3), 1.34 (3H, s, CH_3), 1.49 (3H, s, CH_3), 4.04–4.20 (2H, m, OCH_2CH_3), 4.34 (1H, d, *J* 12.3 Hz, CH_2Ph), 4.46 (1H, d, *J* 3.9 Hz, 3-H), 4.63 (1H, d, *J* 3.6 Hz, 2-H), 4.68 (1H, d, *J* 12.3 Hz, OCH_2Ph), 5.42 (1H, d, *J* 3.8 Hz, 4-H), 6.12 (1H, d, *J* 3.6 Hz, 1-H), 7.22–7.34 (5H, m, Ph); δ_C ($CDCl_3$; 22.5 MHz) 14.2, 26.6, 27.2, 61.6, 71.9, 75.8, 81.8, 82.6, 83.6, 105.6, 112.6, 128.1, 128.2, 128.3, 137.0, 160.7, 185.2 (Calc. for $C_{19}H_{22}N_2O_7$: C, 58.45; H, 5.68. Found: C, 58.55; H, 5.81%).

Ethyl 6-deoxy-6-diazo-1,2-*O*-isopropylidene-3-*O*-(4-methoxybenzyl)-α-D-*xylo*-hept-5-ulofuranuronate 2b. *Thick oil*; 86% yield; R_f 0.19 (PS–ethyl acetate 7:3); $[\alpha]_D$ +14.81 (*c* 0.42, $CHCl_3$); ν_{max} (neat)/cm^{-1} 1713 (CO_2Et), 1777 (C=O), 2142 (N=N); δ_H ($CDCl_3$; 90 MHz) 1.25 (3H, t, *J* 7.1 Hz, CH_2CH_3), 1.34 (3H, s, CH_3), 1.50 (3H, s, CH_3), 3.80 (3H, s, OCH_3), 4.00–4.20 (2H, m, OCH_2CH_3), 4.26 (1H, d, *J* 12.0 Hz, OCH_2Ar), 4.43 (1H, d, *J* 3.8 Hz, 2-H), 4.61 (1H, d, *J* 4.2 Hz, 3-H), 4.62 (1H, d, *J* 12.0 Hz, OCH_2Ar), 5.40 (1H, d, *J* 4.0 Hz, 4-H), 6.12 (1H, d, *J* 3.8 Hz, 1-H), 6.85 (2H, d, *J* 8.6 Hz, ArH), 7.16 (2H, d, *J* 8.6 Hz, ArH); δ_C ($CDCl_3$; 22.5 MHz) 13.8, 26.5, 26.9, 54.9, 61.2, 71.5, 75.2, 81.7, 82.7, 83.5, 105.4, 112.2, 113.6, 129.0, 129.4, 159.4, 160.5, 184.9 (Calc. for $C_{20}H_{24}N_2O_8$: C, 57.13; H, 5.75. Found: C, 56.91; H, 6.04%).

Ethyl 3-*O*-allyl-6-deoxy-6-diazo-1,2-*O*-isopropylidene-α-D-*xylo*-hept-5-ulofuranuronate 2c. *Thick oil*; 77% yield; R_f 0.36 (PS–ethyl acetate 7:3); $[\alpha]_D$ +8.85 (*c* 0.76, $CHCl_3$); ν_{max} (neat)/cm^{-1} 1673 (C=O), 1713 (C=O), 2139 (N=N); δ_H ($CDCl_3$; 90 MHz) 1.31 (6H, t, *J* 7.1 Hz, CH_2CH_3, CH_3), 1.45 (3H, s, CH_3), 3.50–4.03 (2H, m, $OCH_2CH{=}CH_2$), 4.23 (2H, q, *J* 7.1 Hz, OCH_2CH_3), 4.37 (1H, d, *J* 3.7 Hz, 3-H), 4.51 (1H, d, *J* 3.0 Hz, 2-H), 4.95–5.26 (2H, m, $CH_2{=}CH$), 5.37 (1H, d, *J* 3.7 Hz, 4-H), 5.45–5.81 (1H, m, $CH_2{=}CH$), 5.98 (1H, d, *J* 3.0 Hz, 1-H); δ_C ($CDCl_3$; 22.5 MHz) 14.0, 26.3, 26.9, 42.5, 61.4, 71.0, 75.3, 82.6, 83.7, 105.3, 112.3, 117.4, 133.4, 160.9, 185.2 (Calc. for $C_{15}H_{20}N_2O_7$: C, 52.93; H, 5.92. Found: C, 52.80; H, 6.15%).

Ethyl 3-*O*-benzyl-6-deoxy-6-diazo-1,2-*O*-isopropylidene-α-D-*ribo*-hept-5-ulofuranuronate 2d. *Thick oil*; 88% yield; R_f 0.5 (PS–ethyl acetate 7:3); $[\alpha]_D$ +64.7 (*c* 0.25, $CHCl_3$); ν_{max} (neat)/cm^{-1} 1660 (C=O), 1720 (CO_2Et), 2140 (N=N); δ_H ($CDCl_3$; 300 MHz) 1.32 (3H, t, *J* 7.1 Hz, CH_2CH_3), 1.38 (3H, s, CH_3), 1.67 (3H, s, CH_3), 4.22 (1H, dd, *J* 8.4, 4.4 Hz, 3-H), 4.25–4.33 (2H, m, OCH_2CH_3), 4.56 (1H, d, *J* 12.0 Hz, CH_2Ph), 4.60 (1H, d, *J* 3.4 Hz, 2-H), 4.74 (1H, d, *J* 12.0 Hz, OCH_2Ph), 5.41 (1H, d, *J* 8.6 Hz, 4-H), 5.81 (1H, d, *J* 3.4 Hz, 1-H), 7.28–7.39 (5H, m, Ph); δ_C ($CDCl_3$; 22.5 MHz) 14.3, 26.8, 27.1, 61.8, 72.7, 78.3, 78.4, 79.6, 104.9, 113.8, 128.0, 128.0, 128.4, 128.6, 137.5, 160.1, 187.7 (Calc. for $C_{19}H_{22}N_2O_7$: C, 58.45; H, 5.68. Found: C, 58.18; H, 5.63%).

Ethyl 3,6-anhydro-6-benzyl-1,2-*O*-isopropylidene-α-D-*gluco*-hept-5-ulofuranuronate 3 and ethyl 3,6-anhydro-5-*O*-benzyl-1,2-*O*-isopropylidene-α-D-*xylo*-hept-5-enofuranuronate 4a

A solution of α-diazo β-keto ester **2a** (0.150 g, 0.385 mmol) and $Rh_2(OAc)_4$ (0.002 g, 0.002 mmol) in benzene (5 mL) under N_2 atmosphere was refluxed for 5 min. On cooling, the reaction mixture was directly loaded onto a silica gel column and purified by eluting with PS–ethyl acetate (9.5:0.5) to afford, first, *bicycle* **3** as a thick oil (0.066 g, 48%), R_f 0.69 (PS–ethyl acetate 7:3); $[\alpha]_D$ +54.0 (*c* 1.0, $CHCl_3$); ν_{max} (neat)/cm^{-1} 1779 (C=O), 1744 (C=O); δ_H ($CDCl_3$; 500 MHz) 1.27 (3H, t, *J* 6.5 Hz, CH_2CH_3), 1.30 (3H, s, CH_3), 1.39 (3H, s, CH_3), 3.26 (2H, AB quartet, *J* 14.0 Hz, CCH_2Ph), 4.17–4.24 (4H, m, 3-H, 4-H, OCH_2CH_3), 4.87 (1H, d, *J* 3.5 Hz, 2-H), 5.94 (1H, d, *J* 3.5 Hz, 1-H), 7.17–7.25 (5H, m, Ph); δ_C ($CDCl_3$; 125 MHz) 13.9, 26.6, 27.3, 40.6, 62.4, 79.1, 82.7, 85.3, 86.9, 107.7, 113.4, 127.1, 128.4, 130.4, 133.8, 166.9, 202.3 (Calc. for $C_{19}H_{22}O_7$: C, 62.97; H, 6.12. Found: C, 62.76; H, 6.39%).

Further elution gave the isomeric bicycle **4a** as a white solid (0.041 g, 29%), mp 75–77 °C; R_f 0.57 (PS–ethyl acetate 7:3); $[\alpha]_D$ +26.81 (*c* 0.45, $CHCl_3$); ν_{max} (Nujol)/cm^{-1} 1714 (C=O); δ_H ($CDCl_3$; 300 MHz) 1.33 (3H, t, *J* 7.1 Hz, CH_2CH_3), 1.36 (3H, s, CH_3), 1.51 (3H, s, CH_3), 4.3 (2H, q, *J* 7.1 Hz, OCH_2CH_3), 4.84 (1H, d, *J* 7.0 Hz, 4-H), 4.85 (1H, d, *J* 3.0 Hz, 2-H), 5.16 (2H, AB quartet, *J* 12.1 Hz, OCH_2Ph), 5.48 (1H, d, *J* 7.0 Hz, 3-H), 5.93 (1H, d, *J* 3.0 Hz, 1-H), 7.31–7.43 (5H, m, Ph); δ_C ($CDCl_3$; 75 MHz) 14.3, 26.9, 27.8, 61.2, 73.0, 82.8, 83.9, 85.1, 106.1, 113.7, 127.3, 127.9, 128.2, 128.6, 136.5, 146.4, 160.1 (Calc. for $C_{19}H_{22}O_7$: C, 62.97; H, 6.12. Found: C, 62.59; H, 6.72%).

Ethyl 3,6-anhydro-1,2-*O*-isopropylidene-5-*O*-(4-methoxybenzyl)-α-D-*xylo*-hept-5-enofuranuronate 4b

A solution of α-diazo-β-keto ester **2b** (0.150 g, 0.357 mmol) and $Rh_2(OAc)_4$ (0.003 g, 0.007 mmol) in benzene (5 mL) under N_2 atmosphere was refluxed for 25 min. On cooling, the reaction mixture was directly loaded onto a silica gel column and purified by eluting with PS–ethyl acetate (9:1) to afford **4b** as a thick oil (0.113 g, 80%), R_f 0.31 (PS–ethyl acetate 7:3); $[\alpha]_D$ +15.47 (*c* 0.42, $CHCl_3$); ν_{max} (neat)/cm^{-1} 1716 (C=O); δ_H ($CDCl_3$; 300 MHz) 1.33 (3H, t, *J* 7.1 Hz, CH_2CH_3), 1.37 (3H, s, CH_3), 1.51 (3H, s, CH_3), 3.81 (3H, s, OCH_3), 4.29 (2H, q, *J* 7.1 Hz, OCH_2CH_3), 4.83 (1H, d, *J* 3.9 Hz, 2-H), 4.84 (1H, d, *J* 4.8 Hz, 3-H), 5.09 (2H, AB quartet, *J* 11.7 Hz, OCH_2Ar), 5.48 (1H, d, *J* 6.4 Hz, 4-H), 5.94 (1H, d, *J* 3.5 Hz, 1-H), 6.89 (2H, d, *J* 8.7 Hz, ArH), 7.34 (2H, d, *J* 8.7 Hz, ArH); δ_C ($CDCl_3$; 75 MHz) 14.3, 26.8, 27.8, 55.3, 61.1, 72.9, 82.8, 83.9, 85.1, 106.1, 113.6, 113.9 (s), 128.7, 129.2 (s), 130.6, 146.4, 159.9, 160.0 (Calc. for $C_{20}H_{24}O_8$: C, 61.21; H, 6.17. Found: C, 61.10; H, 6.45%).

Ethyl 6-allyl-3,6-anhydro-1,2-*O*-isopropylidene-α-D-*gluco*-hept-5-ulofuranuronate 5

The reaction of α-diazo-β-keto ester **2c** (0.100 g, 0.294 mmol) and $Rh_2(OAc)_4$ (0.001 g, 0.003 mmol) in benzene (5 mL) was performed as per the procedure for the reaction of **2a**, to give **5** (0.68 g, 74%) as a thick oil.

Reaction in benzene at 35 °C. To a solution of α-diazo-β-keto ester **2c** (0.100 g, 0.294 mmol) and $Rh_2(OAc)_4$ (0.001 g, 0.003 mmol) in benzene (5 mL) was stirred for 3 h at 35 °C. Solvent was evaporated off and the residue was chromatographed (PS–ethyl acetate 9.5:0.5) to afford **5** (0.079 g, 86%) as a thick oil.

Reaction in dichloromethane at 35 °C. To a solution of α-diazo-β-keto ester **2c** (0.100 g, 0.294 mmol) and $Rh_2(OAc)_4$ (0.001 g, 0.003 mmol) in dichloromethane (5 mL) was stirred for 1 h at 35 °C. Solvent was evaporated off and the residue was chromatographed (PS–ethyl acetate 9.5:0.5) to afford **5** as a *thick oil* (0.72 g, 78%), R_f 0.48 (PS–ethyl acetate 7:3); $[\alpha]_D$ +31.64 (*c* 0.3, $CHCl_3$); ν_{max} (neat)/cm^{-1} 1779 (C=O), 1744 (C=O); δ_H ($CDCl_3$; 300 MHz) 1.27 (3H, t, *J* 7.1 Hz, CH_2CH_3), 1.36 (3H, s, CH_3), 1.48 (3H, s, CH_3), 2.60 (1H, ddt, *J* 1.1, 7.1, 14.3 Hz, $CH_2CH{=}CH_2$), 2.75 (1H, br dd, *J* 7.1, 14.3 Hz, $CH_2CH{=}CH_2$), 4.21 (2H, dq, *J* 1.8, 7.1 Hz, OCH_2CH_3), 4.50 (1H, d, *J* 3.6 Hz, 3-H), 4.78 (1H, d, *J* 3.6 Hz, 4-H), 4.98 (1H, d, *J* 3.3 Hz, 2-H), 5.13–5.21 (2H, m, $CH_2{=}CH$), 5.60–5.74 (1H, m, $CH_2{=}CH$), 5.99 (1H, d, *J* 3.3 Hz, 1-H); δ_C ($CDCl_3$; 75 MHz) 14.1, 26.8, 27.5, 39.2, 62.5, 79.2, 82.9, 85.7, 86.0, 108.1, 113.6, 120.8, 130.3, 167.1, 201.3 (Calc. for $C_{15}H_{20}O_7$: C, 57.68; H, 6.46. Found: C, 57.88; H, 6.74%).

3,7-Anhydro-6-deoxy-6-ethoxycarbonyl-1,2-*O*-isopropylidene-7-(*S*)-phenyl-α-D-*allo*-heptofuran-5-ulose 6

The reaction of α-diazo-β-keto ester **2a** (0.390 g, 1.00 mmol) and $Rh_2(OAc)_4$ (0.004 g, 0.001 mmol) in benzene (5 mL) was performed as per the procedure for **2a** to give **6** as a *white solid* (0.29 g, 80%), mp 131–132 °C; R_f 0.36 (PS–ethyl acetate 7:3); $[\alpha]_D$ +48.53 (*c* 0.5, $CHCl_3$); ν_{max} (Nujol)/cm^{-1} 1760 (C=O), 1720 (C=O); δ_H ($CDCl_3$; 300 MHz) 1.12 (3H, t, *J* 7.1 Hz, CH_2CH_3), 1.39 (3H, s, CH_3), 1.65 (3H, s, CH_3), 3.75 (1H, dd, *J* 1.5, 10.5 Hz, 6-H), 3.82 (1H, dd, *J* 3.3, 10.2 Hz, 3-H), 4.05–4.17 (2H, m, OCH_2CH_3), 4.70 (1H, dd, *J* 1.5, 10.2 Hz, 4-H), 4.83 (1H, t, *J* 3.3 Hz, 2-H), 5.15 (1H, d, *J* 10.5 Hz, 7-H), 5.91 (1H, d, *J* 3.3 Hz, 1-H), 7.32–7.45 (5H, m, Ph); δ_C ($CDCl_3$; 75 MHz) 13.9, 26.0, 26.5, 61.5, 62.8, 77.0, 79.0, 82.3, 84.8, 105.1, 114.7, 127.2, 128.7, 129.2, 137.1, 166.0, 195.8 (Calc. for $C_{19}H_{22}O_7$: C, 62.97; H, 6.12. Found: C, 62.66; H, 5.96%).

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