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An Efficient Synthesis of Functionalised Decalin via Cycloaddition Reaction of D-Glucose Based Dienes and 2-Methoxycarbonyl-p-Benzoquinone⁺

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Abstract : *The cycloaddition reaction of D-glucose based dienes 1 (b,c) with in-situ generated 2-methoxycarbonyl-p-benzoquinone 2 furnished cycloadducts 3 (a, b) with excellent stereo- and regiochemical control. The cyclo- adduct 3b on further transformations furnished fuctionalised decalin 7c in quantitative yield.*

Of the various carbohydrate templates[1], carbohydrate based dienes and dienophiles are currently under investigation in approaches to complex natural products[2]. In one of our ongoing projects on chiral synthesis of highly functionalised decalins as posssible intermediates for the synthesis of labdane and clerodane based diterpenoids, we studied cycloadditon reaction of D-glucose based acyclic[3] and cyclic dienes[4,5] with *in-situ* generated 2-substituted-p-benzoquinones. Acyclic dienes showed *ortho*-regiochemistry[3], whereas, cyclic furanoid vinyl glycals showed meta-regiochemistry[4]. However, irrespective of having hetero- substituent on diene, pyranoid vinyl glycals displayed excellent *ortho*-regiochemistry[5]. In view of these results, and to generate more information on the regiochemical outcome of these cycloaddition reactions, we reasoned that acyclic diene 1 with a heteroalkyl substituent at C-3 position would not only favour the meta-regiochemistry with respect to C-1 substituent, but would also provide an excellent handle for C-8 alkylation of the resulting adduct and the results are reported in the present communication.

Dienes 1 (a-c) were prepared from the easily available 2,3,4,6-tetra-O-benzyl-D-glucose[6] with some minor modifications. The reaction of 2,3,4,6-tetra-O-benzyl-D-glucose with methylenetri-phenylphosphorane in toluene (RT, 48 h) furnished 3,5,7- tri-O-benzyl-1,2,4-trideoxy-D-erythro-hepta-1,3-dienitol **1a** in 85% yield. Acetate diene **1b** and methoxy diene **1c** were prepared from **1a** using standard procedures.

The Diels-Alder reaction of the diene **1a** with **2** was found to be very slow (benzene, RT, 8 days) and furnished an inseparable mixture of products. However, the acetoxy diene **1b** reacted smoothly with *in-situ* generated **2** (benzene, RT, 30 h) to furnish cycloadduct **3a** in 80% yield as a crystalline solid, mp 40-41°C, $[\alpha]_D$ +50(c, 0.133, $CHCl_3$). The cycloadduct **3a** on epimerisation (basic alumina) furnished trans- adduct **4a** $[\alpha]_D$ + 53 (c 0.133, $CHCl_3$). The reaction of methoxy diene **1c** within-situ generated **2** (benzene, RT, 18 h) furnished cycloadduct **3b**[9] as a pale yellow crystalline solid, mp 41-42°C, $[\alpha]_D$ + 58 (c, 1.00, $CHCl_3$) in 73% yield. The cycloadduct **3b** on epimerisation (basic alumina) furnished trans adduct **4b** $[\alpha]_D$ + 31 (c, 1.5, $CHCl_3$) in

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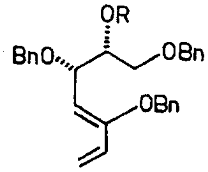
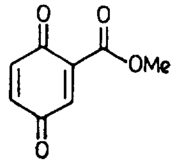
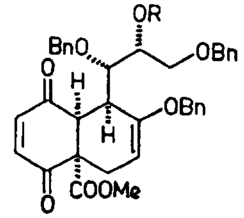
⁺ CDRI Communication No. 5486



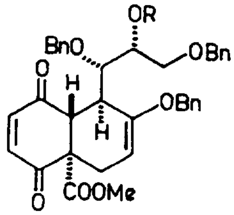
1a R = H
1b R = Ac
1c R = Me



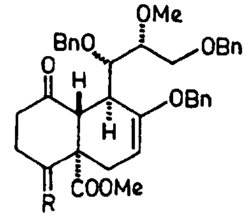
2



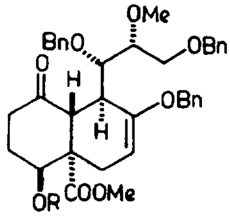
3a R = Ac
3b R = Me



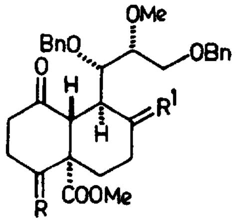
4a R = Ac
4b R = Me



5a R = O
5b R = CH_2



6a R = H
6b R = Ac



7a R = CH_2, R^1 = O
7b R = R^1 = O
7c R = R^1 = CH_2

quantitative yield.

The endo-meta-cycloaddtion of the dienes **1b** and **1c** with **2** is evident from the ^{1}H NMR spectrum of **3b**, which displayed a multiplet at 2.70 for H-9, a doublet of doublets at 3.74 ($J_{9,11}$= 4.00 Hz, $J_{11,12}$= 8.00 Hz) for H-11 and a doublet at 4.10 ppm ($J_{9,10}$=4.00 Hz) for H-10. The appearence of the ring junction proton, H-10, in **4b** at 3.65 ppm ($J_{9,10}$=10.00 Hz) not only confirmed its trans-stereochemistry but also supported the meta-regiochemistry in cycloadduct **3b**. The stereochemistry of **3b** was further confirmed by using nOe difference experiments. nOe was performed by applying multiple irradiation techniques in order to remove INDOR effects. On irradiation of the H-9 multiplet at 2.70 ppm, nOe was observed for the H-10 doublet at 4.10 ppm, similarly, irradiation of H-10 at 4.10 ppm gave nOe for H-9 only. The above results confirm that H-9 and H-10 are cis to each other.

The trans adduct **4b** on reduction (Zn, AcOH) furnished diketone **5a** in quantitative yield. Sodium borohydride, which is known to show chemoselectivity towards anhydrides[7] and 1,4-diketones[8], on reaction with **5a** (DMF, RT, 3h) furnished **6a** as a single compound in 80% yield. Acetylation of **6a** (Ac_2O, Py) furnished acetate **6b** in quantitative yield. In the borohydride reduction of **5a**, the hydride attack is not only on the C-4 ketone but it is from the less hindered-face of the molecule, which is evident from the ^{1}H and ^{13}C NMR spectrum of **6b**. The appearance of the H-4 proton of **6b** at 5.30 ppm ($J_{3a,4a}$, 12.00 Hz, $J_{3e,4a}$=6.00 Hz) in the proton NMR and appearance of the C-5 carbon at 55.15 ppm, almost 5 ppm upfield as compared to the C-5 carbon of 5a in the carbon NMR confirmed the stereo- and chemoselective nature of the hydride reduction. The Wittig olefination of **5a** with methylenetriphenylphosphorane (toluene, O°C, 4h) furnished C-4 exomethylene compound **5b**[9]. Deprotection of **5b** (AcOH:THF:H_2O, 1:1:1,RT,20h) furnished 7**a**. The reaction of **7a** with methylenetriphenyl-phosphorane (toluene, O°C, 4h) furnished diexomethylene compound 7c[9]. In an alternate synthesis of **7c**,**5a** was deprotected (AcOH:THF:H_2O,1:1:1,6h) to furnish triketone **7b**[9]. Witting olefination of **7b** with methylenetriphenylphosphorane (toluene, O°C,4h) furnished 7c. Compounds **5b**,**7a**,**7c**,**7b** were formed in quantitative yield.

In conclusion, dienes **1b** and **1c** showed excellent stereo- and regiochemical control in the cycloaddition reaction. The trans-adduct **4b** displayed excellent chemo- and stereoselectivity towards borohydride reduction. Double alkylation of **4b** via Wittig reaction furnished advanced decalin skeleton of diterpenoids. Further studies are in progress and will be reported in due course.

Acknowledgements

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References

1.a) Hanessian, S., Total Synthesis of Natural Products: The Chiron Approach, Baldwin, J.E.; Ed., Pergamon, Oxford, 1983; b) Inch, T.D., Tetrahedron, **40**, 3161 (1984).

2. Al-Afed, Y., Al-Tel, T.H., Schroder, C.S., Volter, W., Ang. Chem. Int. Ed. Eng., **33**, 1499 (1994) and references cited therein.

3. Mukhopadhyay, A., Ali, S.M., Husain, M., Suryawanshi, S.N., Bhakuni, D.S., Tetrahedron. Lett., **30**, 1853 (1989).

4.a) Mukhopadhyay, A., Suryawanshi, S.N., Bhakuni, D.S., Ind. J. Chem., **26B**, 501 (1987), b) Suryawanshi, S.N., Dhami, T.S., Bhakuni, D.S., Tetrahedron Lett., 32, 1519 (1991).

5. Rani, A., Mukhopadhyay, A., Paul, S., Roy, R., Suryawanshi, S.N., Bhakuni, B.S., Carbohydrate Lett., 1, 207 (1995).

6. Pougny, J.R., Nassr, M.A.M., Sinay, P., J. Chem. Soc. Chem. Commun. 375 (1981).

7.a) Bloomfield, J.J., Lee, S.J., J. Org. Chem., **32** 3919 (1967); b) Sun, K.M., Giuliano, R.M., Fraser Reid, B., J. Org. Chem., **50**, 4774 (1985).

8. Suryawanshi, S.N., Mukhopadhyay, A., Dhami, T.S., Bhakuni, D.S., Ind. J. Chem. **29B**, 1001 (1990).

9. The elemental analysis and spectral data for the new compounds were in accordance with the structures assigned, and only selected data are listed 3b: ^{1}H NMR (400 MHz, CDCl$_3$) 2.52 (m, 1H), 2.70 (m, 1H), 2.90 (dd, J=16.00, 4.00 Hz, 1H), 3.10 (s, 3H), 3.52 (dd, J=12.00, 8.00 Hz, 1H), 3.62 (s, 3H), 3.65 (dd, J=12.00, 4.00Hz, 1H), 3.74 (dd, J=8.00, 4.00 Hz, 1H), 4.10 (d, J=4.00 Hz, 1H), 4.20 (d, J=12.00 Hz, 1H), 4.40 (m, 1H), 4.42 (d, J=12.00 Hz, 1H), 4.55 (d, J=12.00 Hz, 1H), 4.65 (m, 1H), 4.70 (s, 2H), 4.90(d, J=12.00Hz, 1H), 6.50 (s, 2H), 7.30 (m, 15H); ^{13}C NMR (400 MHz, CDCl$_3$) 27.00 (t), 39.40 (d), 51.25 (q), 52.95 (d), 57.48 (q), 60.16 (s), 69.46 (t), 69.89 (t), 73.22 (t), 73.90(t), 76.86 (d), 84.85 (d), 90.88 (d), 127.08-128.32 (15d), 136.27 (d), 138.30 (s), 138.70 (2s), 140.69 (d), (s), 169.87 (s), 195.99 (s), 196.57 (s); 5b: ^{1}H NMR (400 MHz, CDCl$_3$) 2.35 (m, 1H), 2.45 (m, 4H), 2.65 (m, 1H), 2.82 (dd, J=15.00, 9.00 Hz, 1H), 3.15 (d, J=10.00 Hz, 1H), 3.35(s, 3H), 3.55 (s, 3H), 3.60 (m, 1H), 3.70 (m, 3H), 4.50 (ABq, J=12.00 Hz, 2H), 4.55 (d, J=12.00 Hz, 1H), 4.72 (ABq, J=12.00 Hz, 2H), 4.88 (m, 1H), 5.10 (d, J=12.00 Hz, 1H), 5.15 (d, J=15.00 Hz, 2H), 7.30 (m, 15H), ^{13}C NMR (400 MHz, CDCl$_3$) 31.05 (t), 38.00 (d), 40.24 (t), 52.25 (q), 53.45 (d), 55.41 (s), 57.01(q), 129.20 (15d), (s) 138.46 (s), 139.41 (s), 145.51 (s), 156.35 (s), 173.45(s), 207.10 (s); 7c: ^{1}H NMR (400 MHz, CDCl$_3$) 2.35 (m, 2H), 2.50 (m, 6H), 2.65 (d, J=8.00 Hz, 1H), 3.40 (s, 3H), 3.55 (s, 3H), 3.56 (m, 3H), 3.65 (dd, J=12.00, 6.00 Hz, 1H), 3.90(dd, J=12.00, 3.00 Hz, 1H), 4.50 (s, 2H), 4.70 (s, 2H), 4.85(bs, 2H), 5.05 (d, J=7.50 Hz, 2H), 7.30 (m, 10H), ^{13}C NMR (400 MHz, CDCl$_3$) 27.65 (t), 30.36 (t), 31.17 (t), 39.66 (t), 40.91 (d), 51.96 (q), 53.58 (d), 53.68 (s), 57.12 (q), 57.12 (t), 72.63 (t), 73.40 (t), 79.51 (d),82.23 (d),112.02 (t),116.50(t), 126.94-129.47 (10d), 138.40 (s) 138.65 (s), 143.30(s),146.28 (s), 173.56 (s), 207.43 (s).

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