

a one pot procedure to give a 3:1 mixture of ketones. Major ketone isomer **8** was isolated in 61% yield and hydrogenated to give calystegine B₂ ($[\alpha]_{\text{D}}^{20} +23.8$ (c 0.31, H₂O)). NMR data and optical rotation were in accordance with those reported for the natural product.¹³

The same sequence was then applied to the synthesis of calystegine B₃ and B₄ (Scheme 2). Subjecting galactose-derived iodoglycoside **9** to the domino reaction gave a 2:1 mixture of amino dienes. Major diastereomer **10**† was isolated in 59% yield and then converted into cycloheptene **12**. Hydroboration and oxidation gave a 3:1 mixture of ketones and the major isomer **13** was isolated in 64% yield. Hydrogenation then furnished calystegine B₃ ($[\alpha]_{\text{D}}^{20} +75.6$ (c 0.55, H₂O)) with NMR data and optical rotation in accordance with the data for the natural compound.¹³ Subjecting mannose-derived iodoglycoside **14** to the domino reaction gave a 8:1 mixture of amino dienes and the major diastereomer **15**‡ was isolated in 71% yield. The stereochemical outcome in these allylations is noteworthy. In all three cases the major product is the (R)-benzylamine which is the correct stereochemistry for the calystegines. The major product **15** from mannose is consistent with predictions from the Felkin-Anh model while the major isomers from glucose and galactose are not. This, however, does correspond with our previous experience on zinc-mediated alkylations of glucose and mannose substrates.^{4a} Finally, amine **15** was converted into cycloheptene **17** which was hydroborated and oxidised to give a 3:1 ratio of ketones. The major isomer **18** was isolated in 63% yield and deprotected to give calystegine B₄ ($[\alpha]_{\text{D}}^{20} -46.4$ (c 0.18, H₂O)). NMR data and optical rotation were similar to those reported for the natural product.⁷

In conclusion, a general strategy for preparation of the calystegines has been devised. Calystegine B₃ and B₄ have been prepared for the first time and their absolute configuration confirmed. These syntheses should hold great promise for making the calystegines and their analogues more readily available for biological investigations.

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Notes and references

- † All Cbz-protected compounds showed mixtures of rotamers by NMR.
‡ Spectral data for **10**: δ_{H} (CDCl₃) 7.35–7.22 (m, 20H), 5.98 (ddd, 1H, *J* 17.9, 10.0, 8.5), 5.65 (m, 1H), 5.31 (bd, 1H, *J* 10.0), 5.15 (bd, 1H, *J* 17.5),

5.00 (m, 2H), 4.92 (d, 1H, *J* 11.1), 4.84 (d, 1H, *J* 11.1), 4.72 (d, 1H, *J* 11.1), 4.56 (d, 1H, *J* 12.8), 4.53 (d, 1H, *J* 12.4), 4.29 (d, 1H, *J* 11.9), 4.18 (bs, 1H), 3.90 (d, 1H, *J* 13.2), 3.83 (dd, 1H, *J* 7.8, 3.2), 3.67 (d, 1H, *J* 13.2), 3.56 (bs, 1H), 2.66 (bs, 1H), 2.45 (m, 1H), 2.29 (m, 1H); δ_{C} (CDCl₃) 140.5, 139.1, 139.0, 138.7, 135.8, 135.1, 128.2–126.6 (20C), 118.9, 116.7, 82.6, 81.5, 80.1, 74.7, 74.5, 69.7, 56.7, 50.7, 34.5.

§ Spectral data for **15**: δ_{H} (CDCl₃) 7.43–7.25 (m, 20H), 6.00 (ddd, 1H, *J* 17.7, 10.4, 8.1), 5.79 (m, 1H), 5.39 (bd, 1H, *J* 17.5), 5.34 (bd, 1H, *J* 10.4), 5.10 (bd, 1H, *J* 17.9), 5.09 (bd, 1H, *J* 9.8), 4.83 (d, 1H, *J* 11.5), 4.75 (d, 2H, *J* 11.5), 4.71 (d, 1H, *J* 11.9), 4.58 (d, 1H, *J* 11.1), 4.44 (d, 1H, *J* 11.9), 4.29 (m, 1H), 3.89 (m, 1H), 3.83 (d, 1H, *J* 12.8), 3.82 (m, 1H), 3.77 (d, 1H, *J* 12.8), 3.08 (dt, 1H, *J* 8.0, 3.9), 2.51 (m, 1H), 2.36 (m, 1H); δ_{C} (CDCl₃) 140.6, 138.8, 138.6, 138.5, 136.4, 136.2, 128.8–125.9 (20C), 118.1, 117.0, 82.3, 81.1, 79.4, 74.4, 73.1, 70.4, 57.1, 51.7, 34.6.

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