

## Enantiospecific Synthesis of the Hexahydrofuran Unit of Erythrokyrine, a Pentaenoyltetramic Acid Metabolite

Raymond C. F. Jones\* and Mark Tankard

Chemistry Department, Nottingham University, Nottingham NG7 2RD, UK

A hexahydrofuro[3,2-*b*]furan unit suitably functionalised for incorporation into the synthesis of erythrokyrine has been prepared in homochiral form from diacetone-D-glucose.

The 3-acyltetramic acids form a structurally diverse family of biologically active natural products sharing the 3-acylpyrrolidine-2,4-dione moiety (**1**). Amongst the 3-polyenoyl sub-class, the highly toxic pigment erythrokyrine (**2**), isolated from *Penicillium islandicum*,<sup>1</sup> is unique in carrying a hexa-

hydrofuro[3,2-*b*]furan at the terminus of a pentaenoyl chain.<sup>2</sup> Continuing our interest in the 3-acyltetramic acids,<sup>3</sup> we report herein the first synthesis of the homochiral furofuran unit (**3**) suitable for incorporation into the synthesis of erythrokyrine.

The recently defined relative and absolute stereochemistry



supported by analytical and spectroscopic data, including NMR COSY measurements. Comparison of the  $^1\text{H}$  and  $^{13}\text{C}$  NMR information for (**3a**) with that reported<sup>4</sup> for the furofuran portion of erythrokyrine indicated excellent correlation for C-22 to C-26 (erythrokyrine numbering).<sup>‡</sup> We have thus completed the first synthesis in homochiral form of the hexahydrofuro[3,2-*b*]furan unit of erythrokyrine.

Halogenation under the conditions used involves diastereoisomeric alkoxyphosphonium salts (**9d**).<sup>11</sup> A possible rationale for the formation of (**3a**) in both reactions invokes intramolecular participation<sup>12</sup> in the minor epimer of (**9d**) leading directly to (**3a**) via oxycation (**12**) (with an *exo*-Me at C-25) and cleavage of the isopropylidene moiety on work-up. Attack by bromide ion on the major epimer of (**9d**) affords bromide (**11**) and thence, by acid treatment, furofuran (**3a**) of the same configuration.<sup>§</sup>

We thank the SERC for a studentship (M.T.) and the referees for helpful comments.

Received, 6th February 1990; Com. 0100547I

<sup>‡</sup> Selected data for (**3a**): m.p. 63.5–65 °C;  $\delta_{\text{H}}$  ( $\text{CDCl}_3$ ) 1.33 (3H, d, *J* 6 Hz, H-26), 1.55 (1H, ddd, *J* 13.5, 11, and 4.5 Hz, H-24a), 2.28 (1H, dd, *J* 13.5 and 4.5 Hz, H-24b), 4.22 (2H, m, H-25, 21), 4.5 (1H, t, *J* 4.5 Hz, H-23), and 4.63 (2H, m, H-22, 19a);  $\delta_{\text{C}}$  ( $\text{CDCl}_3$ ) 19.8 (C-26), 40.3 (C-24), 77.2 (C-25), 82.9 (C-23), and 84.2 (C-22).

<sup>§</sup> This rationale implies that the major alcohol (**9c**) has the (*R*)-configuration, which is consistent with chelation control in the reduction of ketone (**9b**).

## References

- 1 B. H. Howard and H. Raistrick, *J. Biochem.*, 1954, **57**, 212; Y. Ueno, Y. Kato, and M. Enomoto, *Jpn. J. Exp. Med.*, 1975, **45**, 525.
- 2 J. Shoji, S. Shibata, U. Sankawa, H. Taguchi, and Y. Shibamura, *Chem. Pharm. Bull.*, 1965, **13**, 1240.
- 3 R. C. F. Jones and J. M. Patience, *Tetrahedron Lett.*, 1989, **30**, 3217, and references cited therein.
- 4 J. A. Beutler, B. D. Hilton, P. Clark, M. S. Tempesta, and D. G. Corley, *J. Nat. Prod.*, 1988, **51**, 562.
- 5 P. H. J. Carlsen, T. Katsuki, V. S. Martin, and K. B. Sharpless, *J. Org. Chem.*, 1981, **46**, 3936.
- 6 W. Meyer zu Reckendorf, *Meth. Carbohydr. Chem.*, 1972, **6**, 129.
- 7 R. U. Lemieux and R. V. Stick, *Aust. J. Chem.*, 1975, **28**, 1799.
- 8 W. A. Szarek, G. W. Hay, D. M. Vyas, E. R. Ison, and L. J. J. Hronowski, *Can. J. Chem.*, 1984, **62**, 671; J. H. P. Verheyden, A. C. Richardson, R. S. Bhatt, B. D. Grant, W. L. Fitch, and J. G. Moffatt, *Pure Appl. Chem.*, 1978, **50**, 1363; D. M. Clode, *Chem. Rev.*, 1979, **79**, 491.
- 9 A. Calveo-Mateo, M.-J. Camarasa, A. Diaz-Ortiz, F. G. De las Heras, and A. Alemany, *J. Chem. Soc., Perkin Trans. 1*, 1988, 2861.
- 10 H. Ohruai, G. H. Jones, J. G. Moffatt, M. L. Maddox, A. T. Christensen, and S. K. Byram, *J. Am. Chem. Soc.*, 1975, **97**, 4602; G. H. Jones, J. G. Moffatt, R. S. Ranganathan, N. P. Damodaran, G. B. Howarth, M. D. Edge, H. Ohruai, and C. M. Gupta, in 'Asymmetry in Carbohydrates,' ed. R. E. Harmon, Marcel Dekker, New York, 1979, p. 127; H. Ohruai and S. Emoto, *J. Org. Chem.*, 1977, **42**, 1951.
- 11 J. D. Slagle, T. T.-S. Huang, and B. Franzus, *J. Org. Chem.*, 1981, **46**, 3526; R. Appel, *Angew. Chem., Int. Ed. Engl.*, 1975, **14**, 801.
- 12 R. K. Makie, in 'Organophosphorus Reagents in Organic Synthesis,' ed. J. I. G. Cadogan, Academic Press, London, 1979.