

FUNCTIONALISATION OF THE 4 $\alpha$ -METHYL GROUP  
OF LANOSTANOL VIA AZIDOFORMATE THERMOLYSIS

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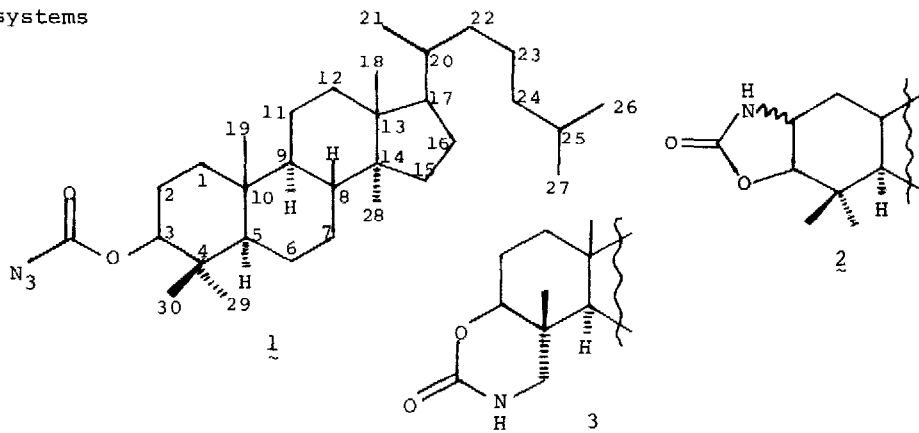
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Encouraged by the observation that thermolysis of alkyl azidoformates yields perhydro-1,3-oxazin-2-ones as well as 1,3-oxazolidin-2-ones<sup>1</sup> we have explored the thermolysis of 3 $\beta$ -lanostanyl azidoformate (1) as a method for functionalising the C-4 methyl groups of 4,4-dimethyl-3 $\beta$ -ol triterpenoid systems



The azidoformate 1<sup>2</sup>, m.p. 135-136<sup>o</sup> (prepared by standard procedures from lanostan-3 $\beta$ -ol via the chloroformate<sup>2</sup>, m.p. 129-131<sup>o</sup>) was thermolysed in methylene chloride solution at 125<sup>o</sup> overnight. The reaction products were separated by chromatography on a column of alumina (Woelm neutral, GIII) from which was eluted first lanostan-3-one (ca.15%), and then compounds A (ca.30%) and B (ca.35%). Although both compounds were homogeneous by t.l.c. analysis

only A was obtained crystalline, m.p. 284-285<sup>0</sup>, B gelled from solutions and upon drying was obtained as a colourless transparent lacquer.

Both A and B had composition C<sub>31</sub>H<sub>53</sub>NO<sub>2</sub><sup>2</sup>. The initial assignment of structures was made on the basis of the following spectroscopic evidence: A had  $\nu_{\max}$  (KBr) 3450, 1780 and 1755 cm<sup>-1</sup>, and a p.m.r. spectrum revealed eight C-methyl groups, consistent with the oxazolidinone 2; whereas B had  $\nu_{\max}$  (KBr) 3450 and 1720 cm<sup>-1</sup>, and only seven C-methyl groups in its p.m.r. spectrum, consistent with the structure 3.

Confirmation of these structural assignments, and the identification of the methyl group functionalised in forming 3 was provided by analysis of their c.m.r. spectra. The carbon-13 chemical shifts<sup>3</sup> for the compounds 1, 2 and 3 and for lanostan-3 $\beta$ -ol are given in the Table. Assignment of the resonances to individual carbon atoms was made using chemical shift additivity relationships<sup>4</sup>, gated decoupling<sup>5</sup> and modulated off-resonance methods<sup>6</sup> as well as spectral comparison with structurally related tetracyclic triterpenoids<sup>7,8</sup>. The effects of steric compression on the axial 4 $\beta$ -methyl group C-30 characterises the high field shift (14 ppm) of this carbon compared with the equatorial 4 $\alpha$ -methyl C-29 (27.9 ppm) in lanostan-3 $\beta$ -ol, 1, 2 and related compounds<sup>7,8</sup>. This observation is the single most important feature establishing the methyl group functionalisation since in 3 the 4 $\beta$ -methyl carbon shifts to high field (12.4 ppm), while a "new" methylene resonance attributable to C-29 (C-4 $\alpha$ ) is observed at 54.1 ppm. The trans-stereochemistry at the junction of the A and the heterocyclic rings in 3 is also illustrated by the shift to high field at C-4 (2.6 ppm)<sup>8</sup>. The oxazolidinone structure 2 is confirmed particularly in the downfield  $\alpha$ - and  $\beta$ -substituent shifts observed at C-2 and C-1, C-3, respectively (see Table).

We conclude that 3 $\beta$ -azidoformate thermolysis functionalises the 4 $\alpha$ -methyl group of the lanostane system, and thus provides a useful complement to the recently described nitroxide photolysis procedure<sup>9</sup> whereby the 4 $\beta$ -methyl groups of 4,4-dimethyl sterols may be functionalised. More recently we have successfully applied this functionalisation procedure to a series of analogous decalin derivatives.

Carbon-13 Chemical Shifts in Selected Lanostanol Derivatives

Carbon position	Lanostan-3 $\beta$ -ol	1	2	3
C-1	37.2 <sub>2</sub>	36.7 <sub>6</sub>	41.4 <sub>5</sub>	36.5 <sub>2</sub>
C-2	27.3 <sub>7</sub>	23.6 <sub>3</sub>	52.0 <sub>0</sub>	23.0 <sub>6</sub>
C-3	78.3 <sub>5</sub>	85.7 <sub>4</sub>	91.1 <sub>3</sub>	81.7 <sub>8</sub>
C-4	36.7 <sub>9</sub>	36.6 <sub>5</sub>	36.7 <sub>1</sub>	34.0 <sub>4</sub>
C-5	54.5 <sub>1</sub>	54.5 <sub>6</sub>	55.3 <sub>2</sub>	52.7 <sub>6</sub>
C-6	19.9 <sub>0</sub>	19.9 <sub>0</sub>	20.2 <sub>6</sub>	19.7 <sub>7</sub>
C-7	28.6 <sub>7</sub>	28.4 <sub>8</sub>	28.3 <sub>2</sub>	28.1 <sub>8</sub>
C-8	38.2 <sub>4</sub>	38.2 <sub>2</sub>	37.9 <sub>5</sub>	38.1 <sub>6</sub>
C-9	48.1 <sub>7</sub>	48.0 <sub>6</sub>	48.0 <sub>4</sub>	48.0 <sub>1</sub>
C-10	38.5 <sub>7</sub>	37.7 <sub>9</sub>	39.1 <sub>1</sub>	36.7 <sub>3</sub>
C-11	21.4 <sub>1</sub>	21.2 <sub>0</sub>	20.5 <sub>2</sub>	21.4 <sub>7</sub>
C-12	33.2 <sub>8</sub>	33.2 <sub>6</sub>	33.1 <sub>5</sub>	33.2 <sub>6</sub>
C-13	44.8 <sub>0</sub>	44.8 <sub>0</sub>	44.8 <sub>0</sub>	44.6 <sub>9</sub>
C-14	47.4 <sub>7</sub>	47.4 <sub>1</sub>	47.4 <sub>1</sub>	47.3 <sub>3</sub>
C-15	31.8 <sub>3</sub>	31.7 <sub>7</sub>	31.6 <sub>9</sub>	31.5 <sub>8</sub>
C-16	27.7 <sub>0</sub>	27.7 <sub>3</sub>	27.7 <sub>3</sub>	27.5 <sub>9</sub>
C-17	50.4 <sub>9</sub>	50.5 <sub>0</sub>	50.4 <sub>6</sub>	50.4 <sub>4</sub>
C-18	14.2 <sub>1</sub> <sup>a</sup>	14.2 <sub>1</sub> <sup>a</sup>	15.7 <sub>0</sub> <sup>a</sup>	13.9 <sub>7</sub> <sup>a</sup>
C-19	15.4 <sub>8</sub> <sup>a</sup>	16.1 <sub>0</sub> <sup>a</sup>	16.0 <sub>7</sub> <sup>a</sup>	14.1 <sub>6</sub> <sup>a</sup>
C-20	35.8 <sub>2</sub>	35.8 <sub>2</sub>	35.7 <sub>9</sub>	35.7 <sub>9</sub>
C-21	18.5 <sub>0</sub>	18.4 <sub>8</sub>	18.4 <sub>5</sub>	18.4 <sub>5</sub>
C-22	36.2 <sub>5</sub>	36.2 <sub>5</sub>	36.1 <sub>9</sub>	36.1 <sub>9</sub>
C-23	23.8 <sub>7</sub>	23.8 <sub>7</sub>	23.8 <sub>4</sub>	23.8 <sub>4</sub>
C-24	39.1 <sub>6</sub>	39.1 <sub>3</sub>	39.1 <sub>1</sub>	39.1 <sub>1</sub>
C-25	27.7 <sub>0</sub>	27.7 <sub>3</sub>	27.7 <sub>3</sub>	27.7 <sub>0</sub>
C-26	22.6 <sub>3</sub>	22.6 <sub>0</sub>	22.6 <sub>3</sub>	22.6 <sub>0</sub>
C-27	22.3 <sub>3</sub>	22.3 <sub>3</sub>	22.3 <sub>3</sub>	22.3 <sub>0</sub>
C-28	16.1 <sub>0</sub> <sup>a</sup>	16.4 <sub>0</sub> <sup>a</sup>	16.3 <sub>7</sub> <sup>a</sup>	16.0 <sub>7</sub> <sup>a</sup>
C-29	27.9 <sub>4</sub>	27.8 <sub>3</sub>	27.7 <sub>3</sub>	54.1 <sub>0</sub>
C-30	13.7 <sub>6</sub>	13.7 <sub>8</sub>	14.2 <sub>8</sub>	12.4 <sub>3</sub>
C=O	-	155.7 <sub>0</sub>	159.8 <sub>0</sub>	153.2 <sub>4</sub>

<sup>a</sup> Cannot distinguish between these resonances.

## REFERENCES

1. P.F. Alewood, M. Benn and R. Reinfried, Canad. J. Chem., 52, 4083 (1974), and references therein.
2. The molecular formulae of all new compounds reported were established by high resolution mass measurements.
3.  $^{13}\text{C}$  spectra were determined (for 0.1M solutions in deuteriochloroform with tetramethylsilane as internal reference) in the Fourier mode using a Bruker HFX-270 spectrometer operating at 67.89 MHz.
4. See for example, J. B. Stothers, "Carbon-13 NMR Spectroscopy", Academic Press, New York (1972).
5. O.A. Gansow and W. Schittenhelm, J. Amer. Chem. Soc., 93, 4294 (1971)
6. E. Wenkert, A.O. Clouse, D.W. Cochran and D. Doddrell, J. Amer. Chem. Soc. 91, 6879 (1969); A.J. Jones and M.H. Benn, Can. J. Chem., 51, 486 (1973).
7. S.A. Knight, Tetrahedron Letts., 83 (1973); idem., Org. Mag. Res., 6 603 (1974).
8. (a) G. Lukacs, F. Khuong-Huu, C.R. Bennett, B.L. Buckwalter and E. Wenkert, Tetrahedron Letts., 3515 (1972); (b) F. Khuong-Huu, M. Sangaré, V.M. Charl, A. Bekaert, M. Devys, M. Barbier and G. Lukacs, ibid., 1787 (1975), (c) M. Angaré, F. Khuong-Huu, D. Herlem, A. Millet, B. Septe, G. Berenger and G. Lukacs, ibid., 1791 (1975)
9. J.A. Nelson, S. Chou and T.A. Spencer, J. Amer. Chem. Soc., 97, 648 (1975).