

## Spectroscopic Properties of *endo*-Substituted D-(+)-Camphor Derivatives

By A. H. BECKETT,\*† ABDUL Q. KHOKHAR,† G. P. POWELL,‡ and J. HUDEC‡

(†*Department of Pharmacy, Chelsea College, London, S.W.3* and ‡*Department of Chemistry, The University, Southampton SO9 5NH*)

**Summary** C.d. and u.v. spectra of several *endo*-substituted aminocamphor derivatives have been measured: the results follow certain trends which are rationalised by spectroscopic rules previously postulated.

A NUMBER of *endo*-substituted camphors were synthesized in connection with work<sup>1</sup> on conformationally rigid derivatives of acetylcholine analogues. Some of these compounds are suitable models for verification of the recently suggested spectroscopic rules for carbonyl compounds.<sup>2</sup>

The spectroscopic data for the compounds in the two solvents methanol and n-hexane parallel one another (Table); therefore only the comparison of the results for the free bases and their hydrochlorides in methanol is discussed.

U.v. spectra: The introduction of an  $\alpha$ -amino-group (**1**; R = NHMe and **1**; R = NHEt) into bornanone (**1**; R = H) causes a red shift (Rule i<sup>2</sup>) due to coupling of the  $\pi$ ,  $\pi^*$  with  $\sigma$ ,  $\sigma^*$  energy levels which is enhanced when the lone pair of the nitrogen can adopt a W arrangement with respect to one of the lobes of the  $\pi$  orbital of the carbonyl group (Rule ii<sup>2</sup>) (*e.g.* in **1**; R = NH<sub>2</sub>).

Protonation of the nitrogen in these examples removes the lone pair thus reducing the red shift of the basic group. The remainder of the red shift is due to C $_{\alpha}$ -N<sup>+</sup>.

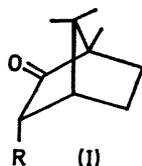
The same value of  $\lambda_{\max}$  for the *NN*-dimethylaminobornanone (**1**; R = NMe<sub>2</sub>) and its hydrochloride, which is also near to the  $\lambda_{\max}$  value of its corresponding trimethylammonium compound (**1**; R = N<sup>+</sup>Me<sub>3</sub>Br<sup>-</sup>) indicates that the lone

## C.d. and u.v. spectra of 3-endo-substituted D-(+)-camphor derivatives

| Compound (1)<br>R  | Spectral data in methanol |                             |            |                             |                  |                             |            |                             | Spectral data in n-hexane |                             |            |    |
|--|---------------------------|-----------------------------|------------|-----------------------------|------------------|-----------------------------|------------|-----------------------------|---------------------------|-----------------------------|------------|----|
|  | Bases                     |                             |            |                             | Hydrochlorides   |                             |            |                             | Bases                     |                             |            |    |
|  | C.d.                      |                             | U.v.       |                             | C.d.             |                             | U.v.       |                             | C.d.                      |                             | U.v.       |    |
| $\lambda_{\max}(\text{nm})$  | $\Delta\epsilon$          | $\lambda_{\max}(\text{nm})$ | $\epsilon$ | $\lambda_{\max}(\text{nm})$ | $\Delta\epsilon$ | $\lambda_{\max}(\text{nm})$ | $\epsilon$ | $\lambda_{\max}(\text{nm})$ | $\Delta\epsilon$          | $\lambda_{\max}(\text{nm})$ | $\epsilon$ |    |
| H  | 297                       | +1.52                       | 290        | 33                          |                  |                             |            | 302                         | +1.69                     | 292                         | 24         |    |
| Et   | 300                       | +1.81                       | 292        | 37                          |                  |                             |            | 310                         | +2.01                     | 295                         | 31         |    |
| NH <sub>2</sub> <sup>a</sup>   | 310                       | +2.31                       | 308        | 54.5                        | 316sh            | +0.61                       | 298.5      | 32                          | 314.5                     | +1.90                       | 304.5      | 39 |
|  |                           |                             |            |                             | 309              | +0.71                       |            |                             |                           |                             |            |    |
| NHMe   | 312                       | +1.53                       | 300        | 44.5                        | 309              | +0.89                       | 298        | 35.5                        | 313                       | +0.84                       | 293        | 36 |
|  |                           |                             |            |                             |                  |                             |            |                             | 305                       | +0.80                       |            |    |
| NHEt <sup>a</sup>  | 313                       | +1.24                       | 300        | 54                          | 310              | +0.79                       | 298        | 37                          | 312                       | +0.78                       | 300        | 37 |
|  |                           |                             |            |                             |                  |                             |            |                             | 304                       | +0.65                       |            |    |
| NMe <sub>2</sub> <sup>a</sup>  | 323                       | +0.41                       | 304        | 29                          | 323              | +0.48                       | 304        | 35                          | 324                       | +0.71                       | 300        | 25 |
|  | 313                       | +0.31                       |            |                             | 312              | +0.57                       |            |                             | 312                       | +0.66                       |            |    |
|  |                           |                             |            |                             |                  |                             |            |                             | 301                       | +0.37                       |            |    |
| CH <sub>2</sub> NHMe   | 300                       | +1.81                       | 296        | 50                          | 301              | +1.30                       | 293        | 40                          | 312                       | +1.58                       | 296        | 60 |
|  |                           |                             |            |                             |                  |                             |            |                             | 303                       | +1.82                       |            |    |
| CH <sub>2</sub> NMe <sub>2</sub>   | 300                       | +1.86                       | 294        | 52                          | 299              | +1.31                       | 292        | 43.5                        | 312                       | +1.57                       | 296        | 49 |
|  |                           |                             |            |                             |                  |                             |            |                             | 303                       | +1.80                       |            |    |
| CH <sub>2</sub> CH <sub>2</sub> NMe <sub>2</sub>                               | 300                       | +1.84                       | 295        | 45                          | 301              | +1.35                       | 293        | 41                          | 312                       | +1.80                       | 294        | 38 |
|  |                           |                             |            |                             |                  |                             |            |                             | 303                       | +2.16                       |            |    |
|  |                           |                             |            |                             | Bromide          |                             |            |                             |                           |                             |            |    |
| N <sup>+</sup> Me <sub>3</sub> Br <sup>-a</sup>                                |                           |                             |            |                             | 312              | +1.04                       | 300        | 37                          |                           |                             |            |    |
| CH <sub>2</sub> N <sup>+</sup> Me <sub>2</sub> Br <sup>-</sup>                 |                           |                             |            |                             | 299              | +1.63                       | 292.5      | 45                          |                           |                             |            |    |
| CH <sub>2</sub> CH <sub>2</sub> N <sup>+</sup> Me <sub>2</sub> Br <sup>-</sup> |                           |                             |            |                             | 300              | +1.54                       | 295.5      | 39                          |                           |                             |            |    |

<sup>a</sup> Analytical data published.<sup>1</sup> Other compounds in Table had correct analytical and spectral data.

pair is no longer involved, since the orientation is unfavourable for coupling because of the non-bonded interactions between the methyl group and the C-5 *endo*-position.<sup>§</sup> The extinction coefficients of all the above compounds follow Rule iii.<sup>§</sup>



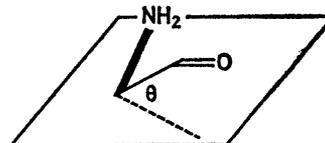
The spectral data of  $\beta$ - and  $\gamma$ -aminoketones (1; R = CH<sub>2</sub>NHMe, CH<sub>2</sub>NMe, and CH<sub>2</sub>CH<sub>2</sub>NMe<sub>2</sub>, respectively) indicate that the C-N bond and the lone pair have now hardly any effect (*c.f.* 1; R = Et) on the position of  $\lambda_{\max}$  because of conformationally incorrect orientation for coupling.

C.d. spectra: The  $\Delta\epsilon$  value of  $\alpha$ -aminobornanone (1; R = NH<sub>2</sub>) exhibits "octant" behaviour as predicted by Rules ii, iii, and iv<sup>§</sup> (see above).

The introduction of *N*-methyl, *N*-ethyl, and *N*-dimethyl substituents (1; R = NHMe, NHEt, and NMe<sub>2</sub>, respectively) into bornanone (1; R = H) produces increasing conformational restraint which results in incorrect orientation of the lone pair for coupling and thus leads to an increasing "antioctant" trend. This may also be in part due to

decreasing availability of the lone pair for back-donation<sup>¶</sup> because of Bohlmann coupling.<sup>§</sup>

The  $\Delta\epsilon$  values of  $\beta$ - and  $\gamma$ -aminoketones, (1; R = CH<sub>2</sub>NHMe, CH<sub>2</sub>NMe, and CH<sub>2</sub>CH<sub>2</sub>NMe<sub>2</sub>, respectively) are similar to that of  $\alpha$ -ethylbornanone (1; R = Et) indicating that the "antioctant" contribution of the C-N bond is counterbalanced by the "octant" contribution of the nitrogen lone pair in the various possible conformations of the side chain. The protonation of these compounds removes the "octant" contribution of the lone pair, thus resulting in "antioctant" behaviour.



The enhancement of the value of  $\Delta\epsilon$  of bornanone (1; R = H) by the introduction of the  $\alpha$ -amino-group (1; R = NH<sub>2</sub>) [ $\Delta(\Delta\epsilon) + 0.8$ ] is not so great as that produced by the introduction of the 5 $\alpha$ -amino-group into 3 $\beta$ -acetoxycholestan-6-one<sup>4</sup> [ $\Delta(\Delta\epsilon) - 3.2$ ]; this is probably due to the dihedral angle between the carbonyl group and C <sub>$\alpha$</sub> -N bond being *ca.* 60° in the former case and 116° in the latter (Figure 1).

(Received, February 1st, 1971; Com. 116.)

<sup>§</sup> The introduction of the *N*-methyl group into *N*-methylaminobornanone increases the red shift, possibly due to an increase in the energy of the  $\sigma$  orbital of the N-C <sub>$\alpha$</sub>  bond (lowering of  $\sigma^*$ ) with attendant larger coupling of the  $\pi$  and  $\pi^*$  levels.

<sup>¶</sup> Unpublished work (G. P. Powell, M. T. Hughes, and J. Hudec) shows that the lone pair interacts with the  $\pi^*$  orbital by back-donation. The reverse applies to the  $\sigma^*$  orbital of the C-N bond which withdraws electrons from the  $\pi$  orbital.

<sup>1</sup> A. H. Beckett, N. T. Lan, and G. R. McDonough, *Tetrahedron*, 1969, 25, 5689 and 5693.

<sup>2</sup> J. Hudec, *Chem. Comm.*, 1970, 829.

<sup>3</sup> F. Bohlmann, *Chem. Ber.*, 1958, 91, 2157; T. Masamune and M. Takasugi, *Chem. Comm.*, 1967, 625; T. Masamune, *ibid.*, 1968, 244; H. P. Hamlow, S. Okuda, and N. Nagakawa, *Tetrahedron Letters*, 1964, 2553.

<sup>4</sup> G. Snatzke and A. Veithen, *Annalen*, 1967, 703, 159.