Photocycloaddition of Cyanoethylenes onto 1,4-Dihydro- and 1,4,5,6-Tetrahydro-pyridines

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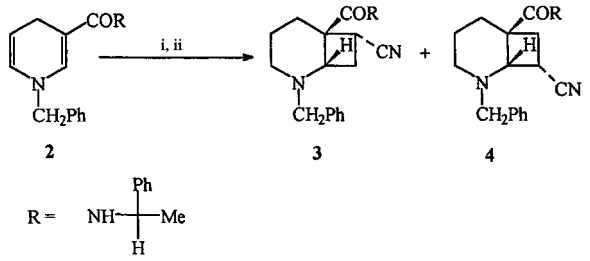
The photochemical cycloaddition of cyanoethylenes onto the title compounds to give 2-azabicyclo[4.2.0]octanes shows a different degree of selectivity depending on the position of the chiral centre of the starting material, with a maximum effect in the case of the 4-position.

Previously we reported that some enantiomeric induction is observed during the photoaddition of acrylonitrile onto 1,4-dihydropyridines carrying an easily removable tetra-acetylglucoside substituent at the 1-position.[1].

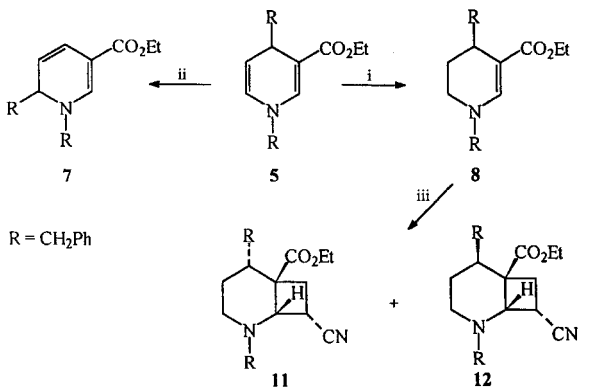
In view of the continued interest in asymmetric synthesis, we now report a further insight into the above reaction, by considering the effect of the location of the chiral centre with respect to the C(2)–C(3) double bond. Photochemical addition of acrylonitrile onto dihydropyridine **2** followed by catalytic hydrogenation of the reaction mixture yielded two pairs of the diastereoisomeric amides, **3** and **4**, with a low diastereoisomeric excess (d.e.) (5–15%).



Scheme 1 *Reagents and conditions:* i, CH_2=CHCN, *hv*; ii, H_2

We then considered the 1,4-dibenzyl-1,4-dihydropyridine **5**, but found it not suitable for our aims since upon irradiation it rearranges to the 1,6-dibenzyl-1,6-dihydropyridine **7**. However, catalytic hydrogenation of **5** gave the tetrahydro derivative **8**, which by acrylonitrile photoaddition gave nearly exclusively the 8-cyano-2-azabicyclo[4.2.0]octanes **11** and **12**, showing a high degree of regio- and stereo-chemical control due to the 4-substituent. The structures of compounds **11** and **12** were assigned on the basis of ^{1}H and ^{13}C NMR chemical shift considerations and NOE experiments.

In view of the synthetic potential of this reaction, a deeper insight into the mechanism was required. To this purpose we verified that the reaction requires a non-symmetrically substituted electron-deficient alkene. In fact, neither fumaronitrile



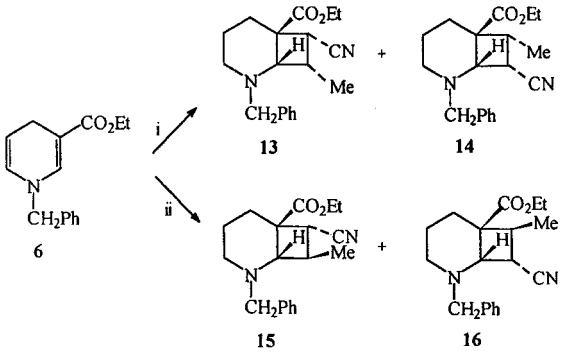
Scheme 2 *Reagents and conditions:* i, H_2/Pd; ii, *hv*; iii, CH_2=CHCN, *hv*

*To receive any correspondence.

nor vinyl ether underwent photoaddition onto 1,4-dihydropyridines. In addition, when we irradiated ethyl 1-benzyl-1,4-dihydronicotinate in the presence of (*Z*)- or (*E*)-but-2-enenitrile we obtained, after hydrogenation, the 2-azabicyclo[4.2.0]octanes **13, 14** or **15, 16**, respectively. It is worth noting that the cross-over products, *i.e.* **13**, **14** from the *E*-isomer or **15**, **16** from the *Z*-isomer, were not formed.

The structures of the above compounds were assigned on the basis of NMR, NOE and observed and calculated[10] LIS data.

In conclusion, alkene geometry is retained during the photoaddition onto the pyridine system, suggesting a concerted process and excluding long-lived radicals as intermediates.



Scheme 3 *Conditions:* i, irradiation with (*Z*)-but-2-enenitrile, catalytic hydrogenation; ii, irradiation with (*E*)-but-2-enenitrile, catalytic hydrogenation

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Techniques used: ^{1}H and ^{13}C NMR, IR, polarimetry, MS and HRMS

References: 10

Schemes: 4

Figure 1: Stereoview of the conformation of **14**

Table 1: ^{1}H NMR data for 2-azabicyclo[4.2.0]octanes **3**, **4**, **11–18**

Table 2: ^{13}C NMR data for 2-azabicyclo[4.2.0]octanes **3**, **4**, **11–18**

Table 3: Observed and calculated LIS data for **13–18** (**17** and **18** are stereoisomers of **14**/**16**).

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