A Stable, Non-aromatic, Adduct derived from '*ipso*'-Nitration

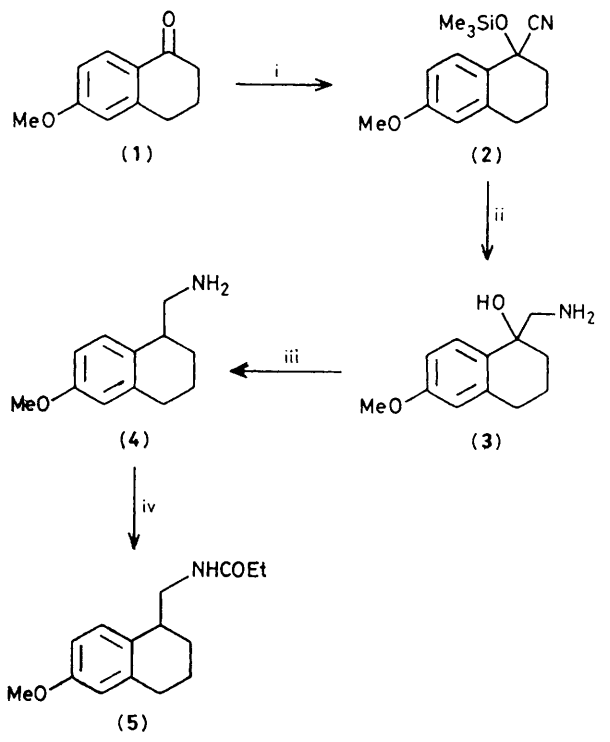
Nigel R. A. Beeley,*[a] Gérard Cremer,[a] Alain Dorlhène,[a] Bernard Mompon,[a] Claudine Pascard,[b] and Elise Tran Huu Dau[b]

[a] *L.E.R. Synthelabo, 31, avenue P. Vaillant-Couturier, 92220 Bagneux, France*

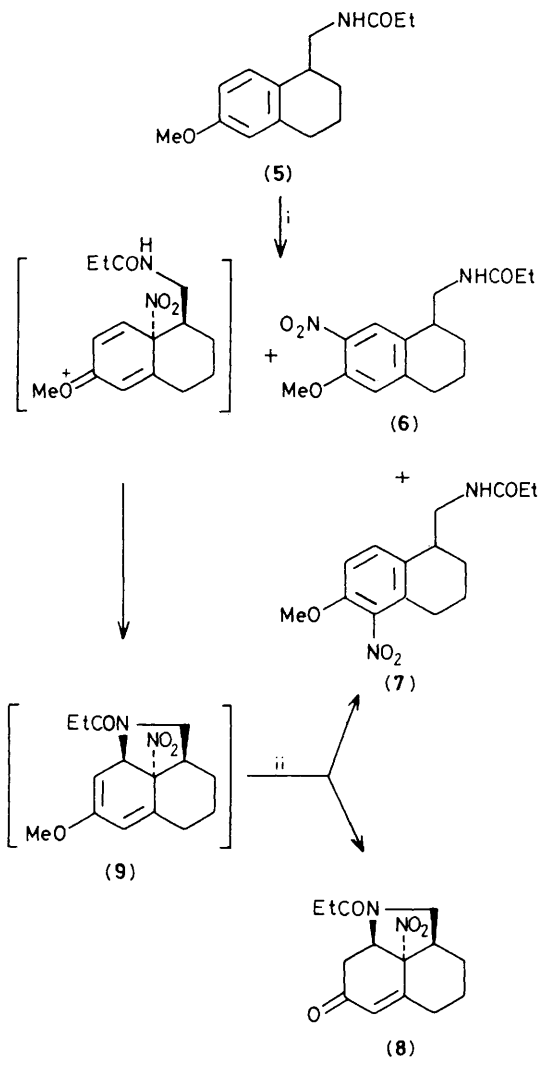
[b] *I.C.S.N.–C.N.R.S., 91190, Gif-sur-Yvette, France*

Nitration of *N*-[(6-methoxy-1,2,3,4-tetrahydronaphthalen-1-yl)methyl]propanamide (**5**) gave not only the expected products (**6**) and (**7**) but also the tricyclic adduct (**8**), the structure of which was confirmed by a single crystal *X*-ray analysis.

As part of a programme directed towards the synthesis of novel cardiovascular agents *N*-[(6-methoxy-1,2,3,4-tetrahydronaphthalen-1-yl)methyl]propanamide (**5**) was prepared as in Scheme 1. Treatment of 6-methoxy-1-tetralone (**1**) with



Scheme 1. i, Me_3SiCN, $ZnCl_2$; ii, $LiAlH_4$; iii, H^+/H_2/Pd on C; iv, $(EtCO)_2O$.



Scheme 2. i, HNO_3–TFA; ii, TFA.

trimethylsilyl cyanide[1] gave the trimethyl silyl cyanohydrin (**2**) (100%, low melting solid)† which was reduced by lithium aluminium hydride to the corresponding amino-alcohol (**3**) (75% overall yield, m.p. 133 °C).† Hydrogenation (0.016 M aqueous HCl/H_2/10% Pd on C) effected reductive elimination to give the hydrochloride salt of (**4**) (85%, m.p. 190 °C).† Conversion of (**4**) into (**5**) (100%, m.p. 76—77 °C)† was unexceptional.

On exposure of (**5**) to nitrating conditions [trifluoroacetic acid (TFA)–HNO_3 (d = 1.42, 1 equiv.)] a less polar compound (**8**) (13%, m.p. 120 °C)‡ was isolated by h.p.l.c. as a single diastereoisomer along with the expected products (**6**) (33%, m.p. 118 °C)† and (**7**) (8.4%, m.p. 174 °C)† (Scheme 2). Initial ambiguities in the spectral data for (**8**)‡ demanded a single crystal X-ray analysis, the results of which are shown in Figure 1.§

Previous observations of *ipso*-nitration¶ have been mainly concerned with the reagent acetyl nitrate[4] or variations

† All compounds had satisfactory spectral data.

‡ For (**8**), numbering not systematic: i.r. (1% in $CDCl_3$), 1690, 1660, and 1550 cm^{-1}; ^1H n.m.r. (200 MHz, $CDCl_3$), δ 6.25 (s, 4-H), 4.65 (dd, J 2, 5 Hz, 1-H), 3.65 (dd, J 8.5, 8 Hz, 10-Hα), 3.5 (dd, J 2, 18 Hz, 2-Hα), 3.44 (m, 9-H), 3.31 (dd, J 8, 12 Hz, 10-Hβ), 2.72 (dd, J 5, 18 Hz, 2-Hβ), 2.5 (m, 6-Hα), 2.1—2.4 (m, 6-H and 2 × 15-H), 1.6—2.1 (m, 7-Hα, Hβ, 8-Hα, Hβ), 1.14 (t, 3 H × 16-H); ^{13}C n.m.r. (25.2 MHz, $CDCl_3$), 61.62 (C-1), 23.87, 32.68, 36.48 (C-2, C-6, C-15), 195.33 (C-3), 131.39 (C-4), 149.91 (C-5), 21.59, 22.96 (C-7, C-8), 43.69 (C-9), 48.17 (C-10), 89.92 (C-12), 173.83 (C-14), 9.02 p.p.m. (C-16).

§ *Crystal data:* $C_{14}H_{18}N_2O_4$, M = 278, monoclinic, space group $P2_1/c$, Z = 4, a = 11.068(4), b = 7.363(3), c = 17.378(7) Å, β = 101.10(8)°. Data were measured with a Philips PW 1100 diffractometer using the ω–2θ scan technique with graphite monochromated Cu-K_α radiation (λ = 1.5418 Å). The structure was solved by direct methods (ref. 2). Hydrogen atoms were located from difference Fourier maps and fixed. The least-squares refinement (ref. 3) based on 1579 observed reflections, with anisotropic temperature factors for the non-hydrogen atoms resulted in an R factor of 0.057.

The atomic co-ordinates for this work are available on request from the Director of the Cambridge Crystallographic Data Centre, University Chemical Laboratory, Lensfield Road, Cambridge CB2 1EW. Any request should be accompanied by the full literature citation for this communication.

The structure factor table is available as Supplementary Publication No. SUP 23742 (10 pp.) from the British Library Lending Division. For details of how to obtain this material, see Instructions for Authors, *J. Chem. Soc., Perkin Trans.* 1, 1983, Issue 1, p. xvii.

¶ Although the term *ipso* is ambiguous in our case, *ipso*-nitration has been widely used to describe this reaction.

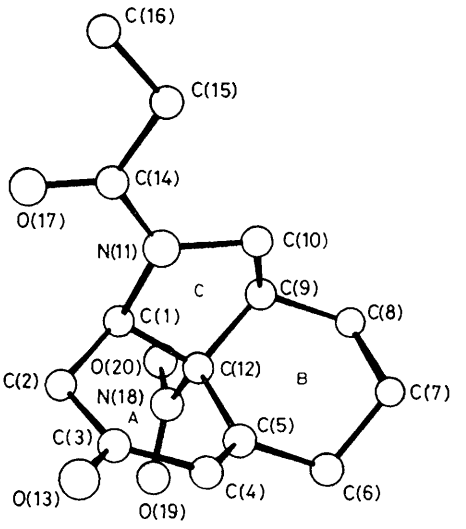
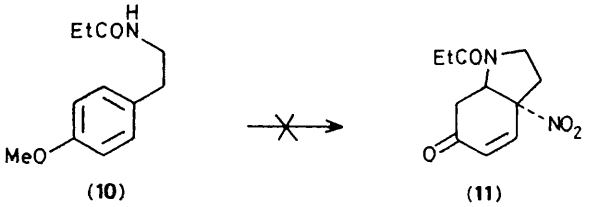


Figure 1. Structure of (**8**) showing the numbering scheme.



Scheme 3

thereof. A recent ^{15}N labelling study of the nitration of 4-nitrophenol[5] has confirmed speculation as to whether this reaction is common to other nitrating conditions.**[6] Our own work represents direct evidence for the importance of this pathway under normal nitrating conditions.

Surprisingly, exposure of (**5**) to propionic anhydride–HNO_3 gave only (**6**) (32.3%) and (**7**) (25%) suggesting that the pathway leading to a stable product *i.e.* cleavage of the enol ether (**9**) (Scheme 2) is not available.

Because (**8**) appears to be formed at the expense of (**7**) the intriguing possibility arises that *ipso*-nitration may offer a solution to the problem of obtaining regiospecificity in this type of reaction,[7] particularly if the proposed sigmatropic rearrangement of such adducts is generally valid.[8]

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** Exposure of (**10**) to HNO_3–TFA gave none of the bicycle (**11**) (Scheme 3).

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