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NMR Investigation of Bicyclic Nitromusk Compounds.

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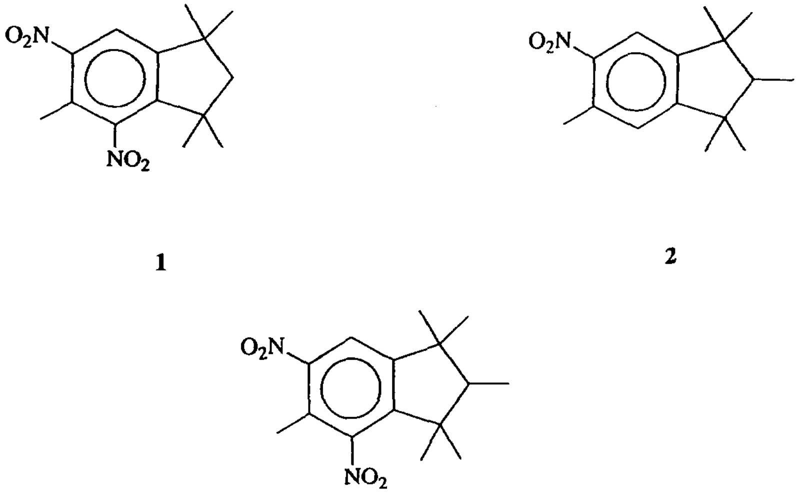
Abstract**:** The NMR spectra of five bicyclic nitromusk compounds (three indans and two tetralins) have been obtained. The results are discussed with respect to the crystal structures determined from the same batches.

Musk compounds belong to a large group of widely varying chemical structures, among which are macrocyclic esters, steroid-related structures, tetralin and indan derivatives and also relatively simple benzene derivatives. Musk compounds form one of the most universally appreciated odour groups. The compounds concerned can be considered to be pure olfactive stimulants which are uncomplicated by other stimuli-generating properties.

Within the course of X-ray crystal studies of a number of these compounds[2] five different batches [denoted hereafter **a**,**b**,**c**,**d** and **e**] of crystals supposed to contain respectively the structures **1**,**2**,**3**,**4** and **5** were investigated. A first crystal structure determination of a crystal of batch **e**, yielded structure **6** [1,1,2,4,4,7-hexamethyl-5,6-dinitrotetralin]. Since at the same time attempts to recrystallise compound **2** were not successful, a NMR investigation of these two batches was carried out. The NMR spectra of **1**, **3** and **4** were also taken thus offering reference spectra. The structures obtained from the crystal structure determination are given in Figure 1 (for the indans **1**, **2** and **3**) and in Figure 2 (for the tetralins **4**, **5** and **6**).

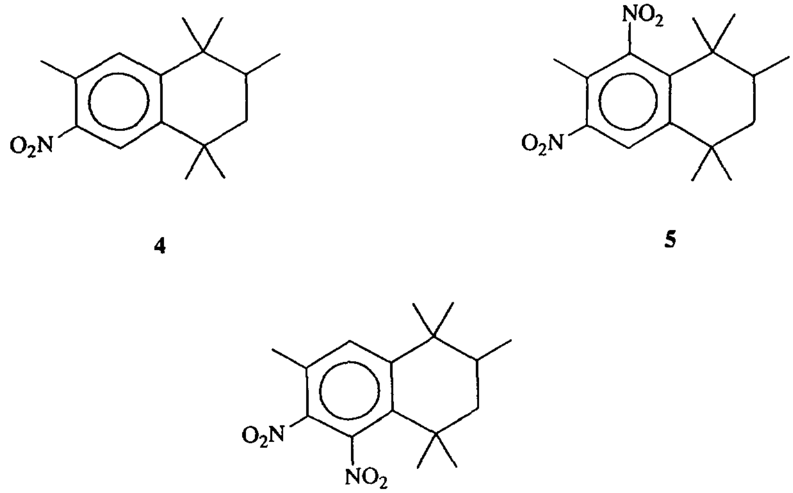


1

2

3

Fig. 1. Chemical structure of the indan compounds.



4

5

6

Fig. 2. Chemical structure of the tetralin compounds.

The ^{1}H-NMR ($CDCl_3$) spectra were obtained at 250 MHz on a Bruker WM 250 instrument. The spectra of the five batches were as followed (s=singulet, d=doublet, t=triplet, q=quartet, m=complex pattern):

(a) 1,1,3,3,5-pentamethyl-4,6-dinitro-indan (Musk Moskene): δ=7.75 (s, phenyl, 1H); δ=2.38 (s, methyl group on the aromatic ring, 3H) δ=2.36 (s, methylene, 2H); δ=1.36 (s, four methyl groups on the non-aromatic ring, 12H). An additional NOE-experiment [radiation on the peak at δ=7.75] revealed no supplementary peaks.

(b) 1,1,2,3,3,6-hexamethyl-5-nitro-indan: δ=7.77 (s, phenyl adjacent to the nitro group, 1H); δ=7.06 (s, phenyl adjacent to the methyl group, 1H); δ=2.59 (s, methyl group on the aromatic ring, 3H); δ=1.90 (q, methyn, 1H); δ=1.29 (s, two methyl groups on the non-aromatic ring closest to the nitro group, 6H); δ=1.09 (s, two methyl groups on the non-aromatic ring closest to the aromatic methyl group, 6H); δ=1.01 (d, methyl group on the non-aromatic ring, 3H).

(c) 1,1,2,3,3,5-hexamethyl-4,6-dinitro-indan: δ=7.79 (s, phenyl, 1H); δ=2.38 (s, methyl group on the aromatic ring, 3H); δ=1.95 (q, methyn, 1H); δ=1.31 (s, methyl group on the non-aromatic ring, 3H); δ=1.21 (s, two methyl groups on the non-aromatic ring, 6H); δ=1.15 (s, methyl group on the non-aromatic ring, 3H); δ=1.01 (d, methyl group on the non-aromatic ring, 3H).

(d) 1,1,2,4,4,7-hexamethyl-6-nitrotetralin: δ=7.93 (s, phenyl adjacent to the nitro group, 1H); δ=7.25 (s, phenyl adjacent to the methyl group, 1H); δ=2.54 (s, methyl group on the aromatic ring, 3H); δ=1.85 (m, methyn, 1H); δ=1.62 (q, methylene equatorial, 1H); δ=1.40 (q, methylene axial, 1H); δ=1.32 (d, two methyl groups on the non-aromatic ring, 6H); δ=1.25 (s, methyl group on the non-aromatic ring, 3H); δ=1.06 (s, methyl group on the non-aromatic ring, 3H); δ=0.99 (d, methyl group on the non-aromatic ring, 3H).

(e) 1,1,2,4,4,7-hexamethyl-6,8-dinitrotetralin: δ=7.92 (s, phenyl, 1H); δ=2.28 (s, methyl group on the aromatic ring, 3H); δ=1.86 (m, methyn, 1H); δ=1.71 (t, methylene equatorial, 1H); δ=1.56 (t, methylene axial, 1H); δ=1.36 (s, methyl group on the non-aromatic ring, 3H); δ=1.29 (s, two methyl groups on the non-aromatic ring, 6H); δ=1.21 (s, methyl group on the non-aromatic ring, 3H); δ=0.99 (d, methyl group on the non-aromatic ring, 3H). An additional NOE-experiment [radiation on the peak at δ=2.28] revealed no supplementary peaks.

The spectra of the batches (**a**,**b** and **c**) for the indan compounds (**1**,**2** and **3**) corroborate with the respective crystal structures[3]. Furthermore spectrum **a** confirms that Musk Moskene (**1**) has the structure as shown above and not the 2,6-dinitro-3-*tert*-butyl-4-isopropyltoluene structure assigned by Barbier[4] in 1932.

For the mononitro tetralin compound **4** the NMR spectrum (**d**) corroborates with the crystal structure[5]. The NMR spectrum of the dinitro tetralin compound (**e**) corroborates with structure **5** and no indication for structure **6** is found.

No other crystals suitable for X-ray diffraction were found in batch **e**. Attempts to recrystallise samples of this batch by slow evaporation using different solvents (for example ethanol, methanol or 1:1 ehtanol/methanol) at room temperature failed. Finally a few crystals having structure **5** were obtained after recrystallisation of a sample of batch **e** by sublimation[5]. Further nitration of the mononitro compound (batch **d**) will give a small amount of the *ortho*-dinitrotetralin **6** next to a large yield of the *meta*-dinitrotetralin **5**, but no sufficient explanation can be given at this moment why the former has been forming single crystals more easily.

Caution.

From about 1980 onwards, the use of nitro musks has been put into question on the suspicion that they might have phototoxic and photoallergic properties and might possibly even cause liver cancer. The photosensitivity of Musk Moskene (**1**) has been mentioned in a paper by Cronin[6].

Acknowledgement.

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References and Notes.

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7. In both papers the crystal structures of a number of acyl derivatives is discussed. For these compounds no NMR spectra have been determined.

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