Tetrahedron Letters,Vol.29,No.6,pp 635-638,1988
Printed in Great Britain

0040-4039/88 $3.00 + .00
Pergamon Journals Ltd.

SELECTIVE REDUCTION OF AROMATIC / ALIPHATIC NITRO GROUPS BY SODIUM SULFIDE.

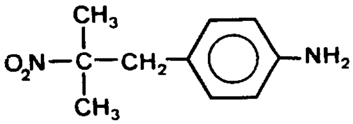
Didier HUBER[1], Guy ANDERMANN[2] and Gérard LECLERC[1]*.

[1] Institut de Pharmacologie (UA 589), Equipe de Pharmacochimie,
Faculté de Médecine, 11, rue Humann, 67000 Strasbourg, France.

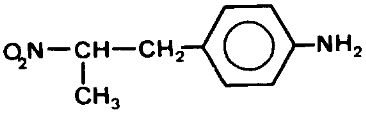
[2] Laboratoires ALCON, Recherche et Développement, BP 15,
68240 Kaysersberg, France.

__*Abstract*__ *- Sodium sulfide can be used to reduce selectively aromatic / aliphatic nitro groups. In the absence of water, the aromatic nitro group can be reduced selectively in the presence of a secondary aliphatic one. However, in the presence of a tertiary aliphatic nitro group, the reduction is accompanied by 50% of the styrene derivative* __*6*__*.*

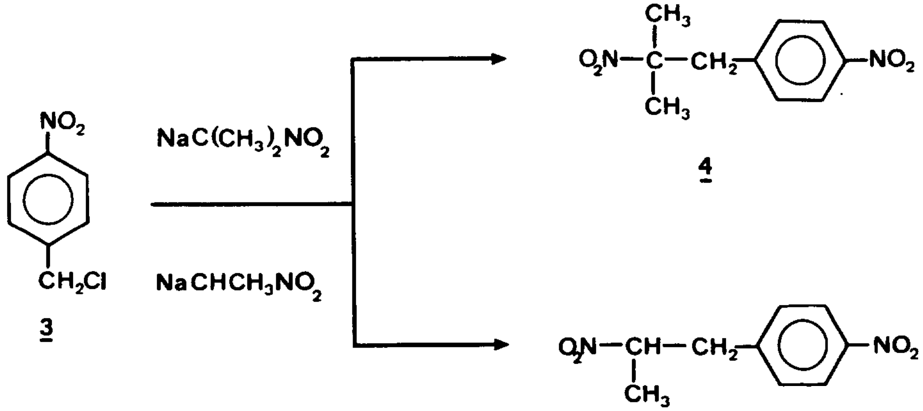
In our studies of molecules with adrenergic properties, we needed large quantities of compounds 1 and 2 as starting material. To obtain these, p-nitro benzyl chloride 3 was treated with the sodium salt of 2-nitropropane or nitroethane to obtain respectively 4 and 5 (Scheme 1).



1



2



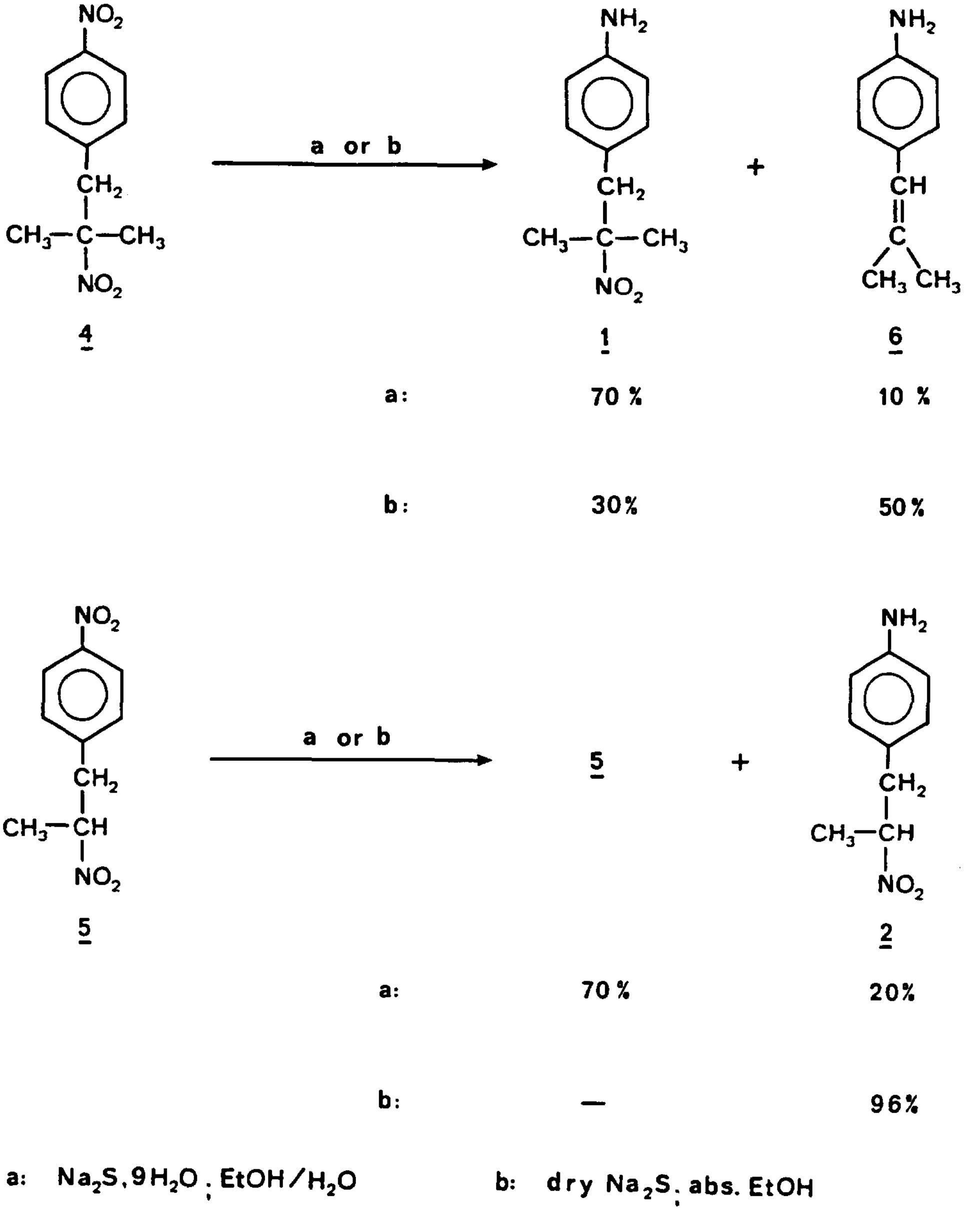
Scheme 1

To obtain target anilines 1 and 2, we had to reduce selectively the aromatic nitro groups of 4 and 5 in the presence of an aliphatic one. Both aliphatic and aromatic compounds can be reduced to amines, though the reaction has been more commonly applied to aromatic nitro compounds, because of their greater availability and versatility. Aliphatic nitro compounds can be reduced to amines with aluminium amalgam, iron, zinc, lithium aluminium hydride or by catalytic hydrogenation using PtO_2 or Raney nickel[1]. Among catalysts used in converting aromatic nitro compounds to anilines by hydrogenation are : platinium oxide, rhodium-platinium oxide, palladium, Raney nickel and copper chromite[2]. Zinc, iron and $SnCl_2$ can be used too. Aliphatic and aromatic nitro compounds can both be reduced to amines with thiol-activated sodium borohydride[3], or with graphite and hydrazine hydrate[4].

We first reduced 4 with $SnCl_2$, as described by Hodgson et al.[5], to obtained compound 1 in a 55% yield. To enhance this yield, we then envisaged a reagent also used by Hodgson et al[6], Na_2S in $EtOH/H_2O$, to reduce the 1-nitro group of 1,2-dinitronaphtalenes. Na_2S with ammonium chloride has also been reported to reduce selectively the ortho nitro group of 2,4-dinitrophenol.[7] We tried to obtain 1 and 2 by reducing 4 and 5 with sodium sulfide under various conditions and found that the reactivity was sensitive to experimental conditions. When 4[8] was treated with $Na_2S,9H_2O$ in a 1/1 mixture of ethanol/water (Scheme 2), we obtained 1 in a 70% yield, which fell to 10% for the ethylenic by-product 6. Under these conditions, slight aliphatic nitro group elimination occurred. When 4[9] was treated with dehydrated Na_2S, obtained by dehydrating sodium sulfide nonahydrate, the ratio between 1 and 6 was different. We increased the proportion of 6 (50%) at the expense of 1 (30%), observing mainly the elimination of the aliphatic nitro group and the reduction of the aromatic nitro group. There are various explanations for this elimination mechanism. It might involve radical species which have also been invoked in the reduction of nitroolefins into olefins[10,11], or an E1cB mechanism might account for it[12].

When the aliphatic nitro group was attached to a secondary carbon atom (compound 5), the results were different. Treating 5[13] with sodium sulfide nonahydrate in a 1/1 mixture of EtOH/water (Scheme 2), gave 2 (20%). When 5[14] was reduced with anhydrous sodium sulfide in absolute ethanol, aniline 2 (96%) was obtained in a nearly quantitative yield. Interestingly, nitrocyclohexane was recovered unchanged when treated with $Na_2S,9H_2O$ or dry Na_2S.

In conclusion, we observed that the selectivity of sodium sulfide in reducing aromatic nitro compounds depends on the experimental conditions. With or without water, aromatic nitro groups were reduced. The conditions for optimum selective reduction differed when the aliphatic nitro group was



Scheme 2

attached either to a secondary carbon atom ($Na_2S,9H_2O$ in ethanol/water or Na_2S in abs. ethanol can be used) or to a tertiary one ($Na_2S,9H_2O$ in ethanol/water was used).

ACKNOWLEDGEMENTS

We thank R. HALTER for his technical collaboration and J.D. Ehrhardt for mass spectra interpretations.

References and Notes

1. S.L. Ioffe, V.A. Tartakovskii and S.S. Novikov, *Russ. Chem. Rev.* 35, 19 (1966)
2. Rylander, *Catalytic Hydrogenation over Platinum Metals*, Academic Press, New York, 1967.
3. Y. Maki, H. Sugiyama, K. Kikuchi and S. Seto, *Chem. Let.*, 1093 (1975).
4. B.H. Han, D.H. Shin and S.Y. Cho, *Tetrahedron. Lett.*, 26, 6233 (1985).
5. H.H. Hodgson, E.W. Smith, *J. Chem. Soc.*, 671 (1935).
6. H.H. Hodgson, H.S. Turner, *J. Chem. Soc.*, 318 (1948).
   H.H. Hodgson, W. Walter, *J. Chem. Soc.*, 1346 (1933).
7. W.W. Hartman, H.L. Silloway, *Org. Synth.*, 3, 83 (1955).
8. Compound 4 (1.12g; 5 mmoles) was treated with $Na_2S,9H_2O$ (3.12g; 130 mmoles) in 15 ml of 1/1 mixture of ethanol/water for 3h at 60°C. After that time, the solvent was evaporated. Water (20ml) was added and extracted with ethyl acetate. The organic layer was dried over $MgSO_4$ and evaporated. The crude sample (800mg) was purified on a silica gel column using CH_2Cl_2 as solvent to give 680mg of 1 (70%) and 80mg of 6 (10%). Compound 1: MS: M^+:194; ^1H NMR (60 MHz, $CDCl_3$): (s,6H, $2(CH_3)$); 3.0(s,2H, CH_2); 3.6(s,2H, NH_2); 6.4-6.9(m,4H, Ar); Compound 6: MS: M^+:147; ^1H NMR: 1.8(d,2H, $2(CH_3)$); 3.5(s,2H, NH_2); 6.2(s,1H, CH); 6.5-7.1(m,4H, Ar).
9. Compound 4 (1.12g; 5mmoles) was treated with 3.12g of dried Na_2S (dehydrated at 170°C)in 20ml of abs. ethanol for 3h at 60°C. After work-up as described in 8, 950mg of crude sample were obtained. Silica gel chromatography yielded 295mg of 1 (30%) and 365mg of 6 (50%).
10. N. Ono, S. Kawai, K. Tanaka, A. Kaji, *Tetrahedron. Lett.*, 20, 1733 (1979).
11. N. Kornblum, S.D. Boyd, H.W. Pinnick, R.G. Smith, *J. Am. Chem. Soc.*, 93, 4316 (1971).
12. D.J. McLennan, *Q. Rev. Chem. Soc.*, 21, 490 (1967).
13. Compound 5 (1.89g; 9 mmoles) was treated with 5.64g of $Na_2S,9H_2O$ in 30ml of 1/1 mixture of ethanol/water for 3h at room temperature. After usual work-up and silica gel column[6], 315mg of 2 (20%) were obtained. Compound 2: MS: M^+:180; ^1H NMR 1.5(d,6H, CH_3); 3.0(m,2H, CH_2); 3.6(s,2H, NH_2); 4.7(m,1H, CH); 6.5-7.0(m,4H, Ar).
14. Compound 5 (1.89; 9mmoles) was treated with 5.64g of Na_2S for 3h. After work-up and chromatography 1.55g of 2 (96%) were obtained.

(Received in France 7 November 1987)