RANEY NICKEL REDUCTIONS—PART I

By K. H. Shah, B. D. Tilak and K. Venkataraman, F.A.Sc.

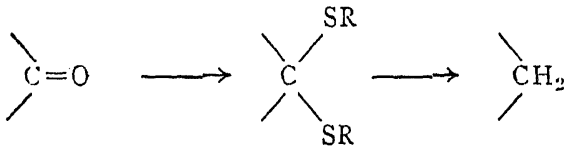
(Department of Chemical Technology, University of Bombay)

Received July 29, 1948

Since Covert and Adkins[1] prepared Raney nickel in a highly active form by treatment of a nickel-aluminium alloy with aqueous sodium hydroxide followed by washing, it has been used for effecting a variety of reactions.[2] Bougault, *et al.*[3] have shown that Raney nickel prepared in the usual manner retains hydrogen and is capable of quantitatively converting thioglycollanilide ($HSCH_2CONH\ C_6H_5$) into acetanilide, and thioglycollic and dithioglycollic acids into acetic acid, without addition of hydrogen. These observations have been considerably extended by Mozingo,[4] who has shown that Raney nickel catalyst removes sulphur from a variety of organic compounds without gaseous hydrogen at moderate temperatures and in the presence of solvents such as alcohol, as follows:

$$RSR' \xrightarrow{Ni\,(H)} RH + R'H$$

Sulphoxides and sulphones are also similarly reduced. An interesting application of the reduction of carbonyl compounds by Raney nickel to the corresponding methylene derivatives has been mentioned.[5] The carbonyl compound is first converted to the mercaptal which is then subjected to treatment with Raney nickel.



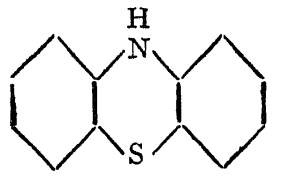
Mozingo[6] has extended the application of Raney nickel to the reduction of compounds other than sulphides, such as ethylenic compounds, aldehydes and ketones. Raney alloy has been directly used in the presence of alkali by Papa[7] for the reduction of several types of compounds. Thus, phenyl ketones, PhCOR, are reduced to the corresponding hydrocarbon $PhCH_2R$, while ketones of the type $Ph\,(CH_2)_x\,COR$, where x is one or more, are reduced to the corresponding carbinol. Various groups attached to the aromatic nucleus are displaced under the conditions used by Papa. For example, halogen is displaced, bromobenzene giving benzene, and *m*-chlorobenzoic acid benzoic acid, in quantitative yields. Simultaneous replacement of halogen by hydrogen and reduction of carbonyl to methylene was also

observed. Sulphonic groups are displaced, *o*- and *m*-sulphobenzoic acids being desulphonated in 40 and 50 per cent. yields to benzoic acid. Alkoxyl groups in disubstituted benzene derivatives are replaced by hydrogen when they are situated in the *o*- and *p*-positions with respect to a *m*-directing group. For example, quantitative replacement of the methoxyl group occurs with *o*- and *p*-methoxybenzoic acids, but the *m*-isomer is recovered unchanged.

Desulphurisation of heterocyclic compounds containing sulphur by means of Raney nickel under mild conditions without the use of hydrogen does not appear to have been widely studied. Among the very few examples of such reductions may be cited the conversion of biotin methyl ester into dethiobiotin methyl ester.[8] While removal of sulphur occurs when excess of Raney nickel is used, it is possible to effect reductions without removing sulphur using smaller quantities of the reagent. Thus nitrodiphenyl sulphides have been reduced to the corresponding amines by using catalytic quantities of Raney nickel.[9] Dibenzyl sulphide was found to be unaffected when treated with Raney nickel in a Parr hydrogenator at room temperature.

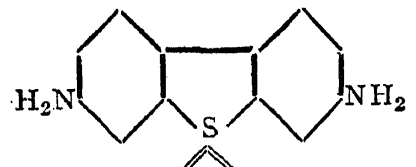
During the course of an investigation of the constitution of the sulphurised vat dyes, Cibanone Yellow R, Cibanone Orange R and Hydron Blue, reduction by Raney nickel was employed for effecting desulphurisation under mild conditions to give sulphur-free degradation products which could then be compared with synthetic products of definite constitution. The valuable data concerning the constitution of these dyes obtained by treatment with Raney nickel will be reported separately.[10] In this paper, the action of Raney nickel on sulphur containing heterocyclic compounds such as thiodiphenylamine (I) and benzidine-sulphone (II), sulphonic acids such as J-acid, and a few other compounds are described.

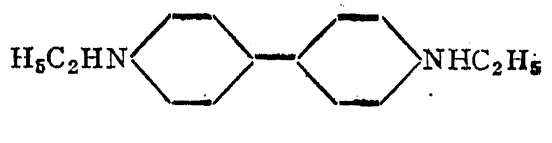
Thiodiphenylamine (I) in alcohol on treatment with Raney nickel gave diphenylamine; and benzidine-sulphone (II) on similar reduction gave N: N′-diethylbenzidine. N-alkylation during reduction by Raney nickel has also been observed by Mozingo.[6]



$C_6H_5NHC_6H_5$

(I)





When J-acid was reduced in aqueous alkaline solution by Raney alloy according to Papa,[7] it gave 6-amino-1-naphthol.

Reduction of β-naphthol in alcoholic alkaline solution gave a mixture of 5:6:7:8-tetrahydro-2-naphthol and 1:2:3:4-tetrahydro-2-naphthol, the latter in a little larger yield. Adkins and Krsek[11] carried out high pressure hydrogenation of β-naphthol in alcohol by means of nickel catalysts prepared by various methods, and obtained both the phenol and alcohol derivatives in proportions depending on the type of catalyst used.

The action of Raney nickel on 2-hydroxy-3-naphthanilide (Brenthol AS); led to 5:6:7:8-tetrahydro-2-hydroxy-3-naphthanilide, identical with the product described by Schröter and Bayer,[12] who prepared it from 5:6:7:8-tetrahydro-2-hydroxy-3-naphthoic acid. The latter compound was obtained by these authors by pressure hydrogenation of 2-hydroxy-3-naphthoic acid, and by Schroeter[13] from 6-hydroxytetralin by means of the Kolbe reaction. Arnold *et al.*[14] also obtained the same acid by the catalytic hydrogenation of ethyl 3-hydroxy-2-naphthoate at 140–150° and under a pressure of 900 lbs., followed by hydrolysis of the ester.

Carbazole has been reported to be resistant to catalytic hydrogenation.[15] Adkins and Coonradt[16] have, however, prepared tetra-, hexa- and dodecahydrocarbazoles in 72, 16 and 85% yields respectively by high pressure reduction of carbazole using Raney nickel or copper chromite catalysts. It has been found in the present work that when carbazole was treated with Raney nickel in boiling morpholine it remained unaffected while reduction in alcohol gave tetrahydrocarbazole (yield, 46%) along with other reduced derivatives. 3-Chlorocarbazole on reduction in alcohol gave a mixture of products from which tetrahydrocarbazole was isolated through the picrate. 3-Aminocarbazole on similar treatment yielded a small quantity of a compound insoluble in dilute hydrochloric acid which was identified as tetrahydrocarbazole, and a very small quantity of an acid-soluble portion which could not be identified.

The behaviour of anthraquinone and 2-methylanthraquinone on treatment with Raney nickel in boiling (1) alcohol, (2) morpholine and (3) aqueous alkali, was studied as a preliminary part of the investigation of the constitution of Cibanone Yellow R and Cibanone Orange R, which are derived from 2-methyl or 2-chloromethylanthraquinone by thionation. Reduction of anthraquinone in the presence of alcohol gave a mixture of products from which octahydroanthraquinone, m.p. 185–86°, was isolated after repeated crystallisations. Reduction in morpholine gave a mixture of different substances from which a colourless crystalline compound, m.p. 226–232°,

and a compound crystallising in pale yellow needles, m.p. 182–83°, were isolated by chromatographic separation. The identity of these products has not yet been established. Treatment of anthraquinone with Raney nickel in boiling aqueous alkali gave a colourless crystalline compound, m.p. 267°, as one of the components of the reaction mixture, which analysed for 9:10-dihydroxyperhydroanthracene ($C_{14}H_{24}O_2$). When 2-methylanthraquinone was reduced in alcohol, a new sterioisomeric form of 2-methyloctahydroanthraquinone, m.p. 137°, was obtained. Reduction of 2-methylanthraquinone in boiling aqueous alkali gave a small quantity of a colourless compound crystallising in needles, m.p. 240–45°, and a mixture of compounds which were liquid at room temperature. A complete analysis of these products will be reported later.

Thioindigo on treatment with Raney nickel in morpholine has given interesting degradation products which are under investigation.

Experimental

Desulphurisation of thiodiphenylamine (*I*).—Thiodiphenylamine (1 g.), Raney nickel, prepared according to Mozingo's method, (10 g.) and alcohol (75 c.c.) were heated under reflux for 4 hours and the mixture was filtered. The Raney nickel residue was washed twice with hot alcohol. The alcoholic extracts were concentrated and cooled and the product (0·55 g.) which separated crystallised from aqueous alcohol in leaflets, m.p. 54°, alone or mixed with an authentic specimen of diphenylamine.

Desulphurisation of benzidine-sulphone (*II*).—Benzidine sulphone (1 g.) was treated with Raney nickel as above. The reduction product (0·55 g.; yield, 70%) crystallised from hot alcohol in needles, m.p. 115° C., and was identical with N:N′-diethylbenzidine. Bamberger and Tichivinsky[17] give m.p. 115–6°. Found: N, 11·8. $C_{16}H_{20}N_2$ requires N, 11·7%).

Desulphurisation of J-acid.—J-acid (10 g.) was dissolved in 10% aqueous sodium hydroxide (450 c.c.), the solution was heated to 90° and Raney alloy (60 g.) was added slowly under stirring (*cf.* Papa, *et. al.*[7]). After the addition of the catalyst, the mixture was further heated for 2 hours. The reaction mixture was filtered and sulphur dioxide was bubbled through the filtrate. 6-Amino-1-naphthol, which separated together with alumina, was extracted with ether. Acetic anhydride (2·5 c.c.) and acetic acid (5 c.c.) were added to the ether-extract and after removal of ether, the solution was heated under reflux for ten minutes and then poured over crushed ice. The diacetyl derivative of 6-amino-1-naphthol separated as a yellow solid which was filtered, washed with cold water and was boiled for 1 minute with ammonia

for the removal of the *o*-acetyl group.[18] It was again acidified with acetic acid and the solid (0·2 g.) thus obtained was washed and crystallised from water, when N-acetyl-6-amino-1-naphthol separated as needles, m.p., 98–99°. Sander[18] quotes m.p. 100°. (Found: N, 7·1. $C_{13}H_{11}O_2N$ requires N, 7·0%).

Reduction of β-naphthol.—β-Naphthol (2 g.), Raney nickel (20 g.), alcohol (100 c.c.) and sodium hydroxide (1 g.) were boiled under reflux for 8 hours. After removal of nickel, the solution was acidified and warmed to remove alcohol and then extracted with ether. The ether layer was washed with water and then shaken thrice with 5% sodium hydroxide solution. The alkaline extracts were collected together, acidified and then extracted with ether. After removal of ether, the alkali-soluble reduction product was left behind as an oil (0·54 g.). On shaking the oil with benzoyl chloride in aqueous sodium hydroxide, the benzoyl derivative of 5:6:7:8-tetrahydro-2-naphthol was obtained which on crystallisation from aqueous alcohol gave m.p. 95–96°. Heilbron[19] gives m.p. 96°. The ether extracts containing the alkali insoluble 1:2:3:4-tetrahydro-2-naphthol gave a brown oil (0·7 g.) after removal of the solvent. When heated with phenyl isocyanate it gave the corresponding phenylurathane which crystallised from light petroleum (60–80°) and benzene as needles, m.p. 98–99°. Bamberger and Lodter[20] give m.p. 99°.

Reduction of Brenthol AS

Brenthol AS (2 g.), Raney nickel (20 g.), methyl alcohol (40 c.c.) and sodium hydroxide (1 g.) were heated under reflux for 5 hours. The mixture was filtered while hot and the nickel residue was washed twice with methyl alcohol. On cooling, the unreacted Brenthol AS separated. The more soluble portion after crystallisation from methyl alcohol gave 5:6:7:8 tetrahydro-2-hydroxy-3-naphthanilide as colourless needles, m.p. 185–87°, unaltered by further recrystallisation from the same solvent. Schröter and Bayer[12] quote m.p. 183°. (Found: C, 76·4; H, 6·1; N, 5·5. $C_{17}H_{17}O_2N$ requires C, 76·4; H, 6·4; N, 5·2%.)

Reduction of Carbazole

Method A.—Carbazole (2 g.), Raney nickel (20 g.) and morpholine (50 c.c.) were heated under reflux for 8 hours and filtered and the residue was extracted with hot morpholine. The filtrate and the washings were collected and poured over a mixture of ice and hydrochloric acid. The solid obtained on crystallisation was found to be unreacted carbazole.

Method B.—Carbazole (4 g.), Raney nickel (80 g.) and ethyl alcohol (250 c.c.) were heated under reflux for 6 hours. After the separation of nickel, the alcohol in the reaction mixture was removed by distillation. The reduction product was isolated by means of ether and when purified according to Adkins and Coonradt,[16] gave 0·3 g. of unreacted carbazole, 1·9 g. (yield, 46%) of tetrahydrocarbazole, m.p. 110° and 0·2 g. of a mixture of octa and dodecahydrocarbazole. The tetrahydrocarbazole after crystallisation from aqueous alcohol gave lustrous flakes, m.p. 112°, alone or mixed with authentic tetrahydrocarbazole. It was further characterised by the preparation of its picrate which crystallised from alcohol in red brown needles, m.p. 142–43°. Adkins and Coonradt[16] give m.p. 145–145·5°.

Reduction of 3-chlorocarbazole

3-Chlorocarbazole (1 g.), Raney nickel (10 g.) and alcohol (50 c.c.) were refluxed for 5 hours and then filtered. The filtrate on concentration and cooling, gave a white solid (0·65 g.), m.p. 125–35°, which did not contain chlorine. It was recrystallised from aqueous alcohol but the m.p. was unaltered. The substance was, therefore, treated with picric acid and the picrate obtained was crystallised from alcohol, m.p. 145°, unaltered when recrystallised from the same solvent. Adkins and Coonradt[16] give the m.p. of tetrahydrocarbazole picrate as 145–145·5°. The picrate on decomposition with 1% ammonia, gave tetrahydrocarbazole as a white solid which crystallised from aqueous alcohol in lustrous white flat needles, m.p. 119–20°. Perkin and Plant[21] give m.p. 116°.

Reduction of 3-aminocarbazole

3-Aminocarbazole (2 g.), Raney nickel (20 g.) and dioxan (60 c.c.) were heated under reflux for 8 hours. After removal of nickel, the solvent was removed by distillation and the residue was extracted with ether. The ether extract was shaken repeatedly with 15% hydrochloric acid. It was then washed, dried and ether was removed. The pinkish white solid (0·14 g.) obtained gave a picrate, m.p. 142°, alone or mixed with authentic tetrahydrocarbazole-picrate. The small quantity of acid-soluble portion obtained could not be identified.

Reduction of Anthraquinone

Method A.—Anthraquinone (1·5 g.), Raney nickel (10 g.) and alcohol (60 c.c.) were boiled under reflux for 3 hours and then filtered while hot. The alcoholic solution after concentration and cooling gave yellow needles, m.p. 168–72° (0·67 g.), raised to 185–6° after three recrystallisations from alcohol, Skita[22] gives the m.p. of octahydroanthraquinone as 185–6°,

(Found: C, 77·2; H, 7·3. $C_{14}H_{16}O_2$ requires C, 77·8; 7·4%.) After prolonged standing (six months), the analytical specimen turned orange and softened above 150° and melted at 170–74°.

Method B.—Anthraquinone (2 g.), Raney nickel (20 g.) and morpholine (60 c.c.) were heated under reflux for 12 hours and then filtered hot. The filtrate was poured over ice and concentrated hydrochloric acid, and the solid (0·96 g.) which separated was filtered, washed and dried. The substance dissolves in alkaline sodium hydroxide solution giving a colourless solution from which it could be recovered by air oxidation. The reduction product was dissolved in chloroform and passed through an activated alumina solution and the pale green major fraction after concentration gave a crystalline solid, m.p. 226–32°. The chloroform mother-liquor after concentration and addition of alcohol gave pale yellow flat needles, m.p. 182–3° unaltered by further crystallisation from the same solvent (Found: C, 75·9; H, 7·1%).

Method C.—Anthraquinone (2 g.), Raney nickel (20 g.), sodium hydroxide (2 g.) and water (100 c.c.) were heated under reflux for 8 hours. The mixture was acidified with hydrochloric acid and then filtered and the residue was washed and dried. It was extracted with chloroform (200 c.c.) and the chloroform solution after concentration and cooling gave colourless flat elongated plates, m.p. 257–62°, raised to 267–8° after recrystallisation from alcohol. (Found: C, 75·5; H, 11·0. $C_{14}H_{24}O_2$ requires C, 75·0; H, 10·7%.) The substance is insoluble in hot aqueous sodium hydroxide and alkaline hydrosulphite. The mother-liquor, after the separation of the above crystalline product, gave a sticky solid (0·85 g.) after removal of the solvent.

Reduction of 2-methylanthraquinone

Method A.—2-Methylanthraquinone (2 g.) when reduced as in Method A for anthraquinone, gave a yellow reduction product (0·8 g.), m.p. 95–99°, which after two crystallisations from alcohol gave m.p. 137°. Elementary analysis of the product is in agreement with methyl octa hydroanthraquinone. Skita[22] quotes m.p. of 2-methyl-1:2:3:4:5:6:7:8-octahydroanthraquinone as 158–9°. (Found: C, 78·0; H, 7·5. $C_{15}H_{18}O_2$ requires C, 78·3; H, 7·8%.) The reduction product on standing turns orange as in the case of the reduction product from anthraquinone.

Method B.—2-Methylanthraquinone (2 g.) was treated as in Method B for anthraquinone. The sticky product (0·9 g.) obtained after three recrystalllisations from alcohol, gave a substance melting constantly at 170–72°, undepressed when mixed with 2-methylanthraquinone.

Method C.—2-Methylanthraquinone (4 g.) was treated as in Method C for anthraquinone. The nickel residue was extracted with benzene and the benzene extract after concentration and cooling gave a colourless crystalline solid. It softened above 235° and melted at 242–6°. The melting point was unaltered by further recrystallisation from benzene and light petroleum. The mother-liquor after the separation of the above crystalline product gave a viscous orange yellow liquid (2·1 g.) on removal of the solvent. It was redissolved in benzene and chromatographed through alumina. Several fractions separated on eluting the chromatogram with benzene but led only to oily products which could not be further purified.

Summary

Treatment of sulphur-containing heterocyclic compounds such as thiodiphenylamine (I) and benzidine-sulphone (II) with Raney nickel in a suitable solvent gave the sulphur-free compounds diphenylamine and N: N′-diethylbenzidine (reduction in ethyl alcohol).

β-Naphthol gave a mixture of 1:2:3:4-tetrahydro-2-naphthol and 5:6:7:8-tetrahydro-2-naphthol on reduction with Raney nickel in alcoholic alkaline solution. Naphthol AS (2-hydroxy-3-naphthanilide) yielded 5:6:7:8-tetrahydro-2-hydroxy-3-naphthanilide and J-acid gave 6-amino-1-naphthol on treatment with Raney nickel.

Carbazole was unaffected when treated with Raney nickel in morpholine, but gave tetrahydrocarbazole when reduced in alcohol. 3-Chloro- and 3-aminocarbazole also gave tetrahydrocarbazole on reduction in alcohol and dioxan respectively.

Anthraquinone and 2-methylanthraquinone gave octahydro-derivatives on reduction in alcohol. Reduction in morpholine and in aqueous alkali gave several reduction products which are under investigation.

Acknowledgments

We are grateful to the Imperial Chemical Industries (Dyestuff Group) for the award of a Fellowship to one of us, which has enabled him to take part in this investigation. Our thanks are also due to Mr. T. S. Gore for the microanalyses recorded in this paper.

References

1. Covert and Adkins .. *J. A. C. S.*, 1932, **54**, 4116.
2. Spring and Baxter .. *Annual Rep.*, 1945, **42**, 101.
3. Bougault *et al.* .. *Bull. Soc. Chim.*, 1938, **5**, 1699; 1940, **7**, 781.
4. Mozingo *et al.* .. *J. A. C. S.*, 1943, **65**, 1013.
5. Wolfrom and Karabinos .. *Ibid.*, 1944, **66**, 909.
   Soffer *et al.* .. *Ibid.*, 1945, **67**, 1435.
6. Mozingo *et al.* .. *Ibid.*, 1944, **66**, 1859.
7. Papa *et al.* .. *J. Org. Chem.*, 1942, **7**, 587 ; 1944, **9**, **1**; 1945, **10**, 232.
8. V. du. Vigneaud *et al.* .. *J. Biol. Chem.*, 1942, **146**, 475.
9. Gilman and Broadbent .. *J. A. C. S.*, 1947, **69**, 2053.
10. See following and subsequent papers.
11. Adkins and Krsek .. *J. A. C. S.*, 1948, **70**, 412.
12. Schröter and Bayer .. *D. R. P.*, 629, 698.
13. Schroeter .. *Annalen*, 1922, **426**, 147.
14. Arnold *et al.* .. *J. A. C. S.*, 1941, **63**, 1314.
15. von Braun and Ritter .. *Ber.*, 1922, **55**, 3792.
    von Braun and Schoring .. *Ibid.*, 1925, **58**, 2156.
16. Adkins and Coonradt .. *J. A. C. S.*, 1941, **63**, 1563.
17. Bamberger and Tichivinsky .. *Ber.*, 1902, **35**, 4182.
18. Sander .. *Ibid.*, 1925, **58**, 829.
19. Heilbron .. *Dictionary of Organic Compounds*, 1943, **3**, 698.
20. Bamberger and Lodter .. *Ber.*, 1890, **23**, 211.
21. Perkin and Plant .. *J. C. S.*, 1921, **119**, 1825.
22. Skita .. *Ber.*, 1925, **58**, 2692.

744-48 Printed at The Bangalore Press, Bangalore City, by G. Srinivasa Rao, Superintendent and Published by The Indian Academy of Sciences, Bangalore