

Some Applications of Nickel Boride as a Desulphurising Agent. An Improved Route to Triterpene 2-Enes

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Optimum conditions are defined for the desulphurisation of ethylene dithioacetals with nickel boride. Normally a mixture of saturated and unsaturated products is formed. Nickel boride is inferior to Raney nickel for the desulphurisation of thiophens. Hemithioacetals are rapidly cleaved by nickel boride, allowing regeneration of the ketone. Triterpene 2-enes are obtained in excellent yield from 3-ketones by desulphurisation of intermediate benzyl thio(enol ether)s with either nickel boride or Raney nickel.

NICKEL BORIDE is the name given to the black precipitate formed when nickel(II) salts are reduced with borohydride ion.^{1,2} Although the composition of this material corresponds closely to Ni₂B,^{1,2} X-ray powder diffraction analyses have shown it to be amorphous.³ It acts as a selective hydrogenation catalyst,^{1,4,5} and has also been used for the desulphurisation of a variety of simple organic compounds.⁶⁻⁹ It is more conveniently prepared and handled than is Raney nickel.

Initially we sought optimum conditions for the desulphurisation of 3,3-ethylenedithiocholestane and 3,3-ethylenedithio-5 α -lanost-8-ene (I). Addition of sodium borohydride to a solution of nickel(II) chloride in ethanol

containing the cholestane dithioacetal and refluxing the mixture for 7 h gave, after chromatography, a mixture of cholest-2-ene and cholestane (*ca.* 4:1 by t.l.c.). Similarly, the dithioacetal (I) afforded 5 α -lanosta-2,8-diene (II) together with 5 α -lanost-8-ene (III) (4:1) [we shall refer to compounds corresponding to (II) and (III) as the unsaturated and saturated products respectively]. However, 50% of starting material remained even after 18 h. Significantly, the addition of further quantities of nickel(II) chloride and sodium borohydride did not lead to further reaction. This fact, together with the observation (t.l.c.) that desulphurisation was always most rapid at the beginning of an experiment, suggested

¹ R. Paul, P. Buisson, and N. Joseph, *Compt. rend.*, 1951, **232**, 627; *Ind. Eng. Chem.*, 1952, **44**, 1006.

² H. I. Schlesinger, H. C. Brown, A. E. Finholt, J. R. Gilbreath, M. R. Hoekstra, and E. K. Hyde, *J. Amer. Chem. Soc.*, 1953, **75**, 215.

³ L. J. E. Hofer, J. F. Shultz, R. D. Panson, and R. B. Anderson, *Inorg. Chem.*, 1964, **3**, 1783.

⁴ C. A. Brown and H. C. Brown, *J. Amer. Chem. Soc.*, 1963, **85**, 1003, 1005; C. A. Brown, *Chem. Comm.*, 1969, 952; *J. Org. Chem.*, 1970, **35**, 1900.

⁵ E. Adler and J. Marton, *Acta Chem. Scand.*, 1961, **15**, 357, 370.

⁶ W. E. Truce and F. E. Roberts, *J. Org. Chem.*, 1963, **28**, 961.

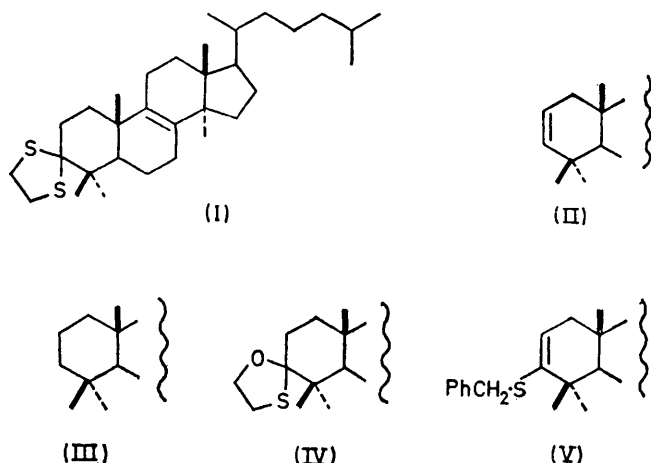
⁷ W. E. Truce and F. E. Perry, *J. Org. Chem.*, 1965, **30**, 1316.

⁸ J. Clark, R. K. Grantham, and J. Lydiate, *J. Chem. Soc. (C)*, 1968, 1122.

⁹ M. A. Paz, A. Bernath, E. Henson, O. O. Blumenfeld, and P. M. Gallop, *Analyt. Biochem.*, 1970, **36**, 527.

that some inhibitory factor (increase in pH, see later) was developing during the reaction.

Hydrolysis of sodium borohydride in aqueous solutions



is greatly accelerated by the addition of acids, boric acid being particularly effective.² The data in the Table

Desulphurisation of 3,3-ethylenedithio-5 α -lanost-8-ene (I) with nickel boride

Reaction medium ^a	5 α -Lanosta-2,8-diene and 5 α -lanost-8-ene formed	
	Total (%) ^b	Ratio ^b
Ethanol	50	4 : 1
Ethanol, citric acid-sodium hydroxide buffer pH 3.2 ^c	0 ^d	
Ethanol, acetic acid-sodium acetate buffer pH 4.3	80	4 : 1
Ethanol, acetic acid-sodium acetate buffer pH 5.6	30	1 : 1
Ethanol, citric acid-sodium hydroxide buffer pH 5.6	30	1 : 1
Ethanol, boric acid-sodium hydroxide buffer pH 7.5	10	1 : 1
Ethanol, boric acid-sodium hydroxide buffer pH 8.4	10	1 : 1
Ethanol, boric acid-sodium hydroxide buffer pH 9.2	0 ^e	
Ethanol, acetic acid	0 ^d	
Ethanol, boric acid	90	4 : 1
Dimethylacetamide	75	1 : 1
Dimethylacetamide, boric acid	80	5 : 1
Diethylene glycol	90	4 : 1

^a Experiments were continued under reflux for 24 h. However, in no case did the reaction mixture appear to change significantly after the first 3 h. ^b Estimated by t.l.c. ^c pH Values are those of the corresponding aqueous systems. ^d No black precipitate formed. ^e Black precipitate formed only slowly.

show that the pH of the reaction medium is the critical factor in desulphurisations with nickel boride. Both the amount of desulphurisation achieved and the relative amount of unsaturated product formed are increased by a lowering of pH, although there is a critical level below

which the reaction will not proceed. The reaction is also favoured by use of a higher temperature.

Similar trends were observed with the cholestane dithioacetal, except that at acid pH values the ratio of cholest-2-ene to cholestane became *ca.* 1:1. This implies that hydrogenation of initially formed cholest-2-ene is occurring. Indeed, when the reaction was conducted in an atmosphere of hydrogen the sole product was cholestane (80%). Furthermore, treatment of 5 α -lanosta-2,8-diene (II) with nickel boride under the standard conditions caused a 10% conversion into 5 α -lanost-8-ene (III).

The most satisfactory conditions for nickel boride desulphurisations were those employing diethylene glycol or ethanol-boric acid as the reaction medium, which were used in all subsequent experiments.

We have also applied nickel boride to two reactions for which the normal reagent is Raney nickel. A general method of chain extension involves desulphurisation of thiophens with Raney nickel.¹⁰ We have found that in general the use of nickel boride leads to inferior results; we record two such cases.

The protection of a carbonyl group as the hemithioacetal is complemented by the possibility of regeneration by use of Raney nickel.¹¹ 5 α -Lanost-8-en-3-one was treated with 2-mercaptoethanol to give two isomeric hemithioacetals (IV). Treatment of these with nickel boride afforded a mixture of 5 α -lanost-8-en-3-one and 5 α -lanost-8-en-3 β -ol, which on oxidation gave the ketone in an overall yield of 87%. Here nickel boride provides an attractive alternative to Raney nickel.

Finally, we report the use of either nickel boride or Raney nickel in an improved synthesis of triterpene 2-enes. Previously such compounds have been best prepared by the pyrolysis of 3 β -benzoates.¹² Treatment of a solution of the triterpene 3-ketone in acetic acid with toluene- α -thiol in the presence of boron trifluoride-ether complex yields the 3-benzylthio-2-ene (V). The latter, on desulphurisation with either nickel boride or Raney nickel, gives an excellent overall yield of the corresponding 2-ene. In principle, this route should provide a general method for the removal of a sterically hindered carbonyl group with introduction of a double bond.

EXPERIMENTAL

N.m.r. data refer to solutions in deuterochloroform with tetramethylsilane as internal standard, and were recorded with a Perkin-Elmer R10 instrument. Rotations are reported for 0.5% solutions in chloroform and u.v. spectra refer to solutions in absolute ethanol. Column chromatography was performed on Laporte type 0 alumina, and t.l.c. on plates of Merck Silica Gel GF₂₅₄. Ratios of products from the desulphurisation of 3,3-(ethylene dithioacetals) were estimated from t.l.c. plates eluted with cyclohexane-light petroleum (1 : 9 v/v) and developed by spraying with

¹¹ J. Romo, G. Rosenkranz, and C. Djerassi, *J. Amer. Chem. Soc.*, 1951, **73**, 4961.

¹² J. F. McGhie, P. J. Palmer, M. Rosenberger, J. M. Birchough, and J. F. Cavalla, *Chem. and Ind.*, 1959, 1221.

¹⁰ G. M. Badger, H. J. Rodda, and W. H. F. Sasse, *J. Chem. Soc.*, 1954, 4162; T. F. Grey, J. F. McGhie, and W. A. Ross, *ibid.*, 1960, 1502.

2N-sulphuric acid and heating at 110°. Nickel chloride refers to the hexahydrate, and unless otherwise stated light petroleum to the fraction b.p. 40–60°.

3,3-Ethylenedithio-5 α -lanost-8-ene (I).—5 α -Lanost-8-en-3-one (1 g) in glacial acetic acid (50 ml) was treated with ethanedithiol (2 ml) followed by boron trifluoride-ether complex (20 ml). Crystals of the product soon began to form and after 1 h this process was aided by addition of methanol. The dithioacetal formed needles (900 mg, 77%), m.p. 130.5–132.5° (from chloroform-methanol), $[\alpha]_D + 51^\circ$ (Found: C, 76.5; H, 10.7; S, 12.7. C₃₂H₅₄S₂ requires C, 76.4; H, 10.8; S, 12.7%).

Desulphurisations with Nickel Boride.—(i) *General procedure.* The sulphur compound (0.2 mmol) and nickel chloride (10 mmol) in ethanol (150 ml) were stirred under nitrogen and treated dropwise with a solution of sodium borohydride (20 mmol) in water (10 ml). A black precipitate formed immediately. The mixture was then heated under reflux until t.l.c. indicated that reaction was complete. The mixture was filtered through Celite and the filter cake washed thoroughly. The combined filtrates were evaporated to small bulk and extracted with ether to give the product, which was, when necessary, purified by chromatography.

Thus, 3,3-ethylenedithiocholestane gave (7 h; chromatography on alumina with light petroleum) cholest-2-ene and cholestane (4 : 1) (60%), and an uninvestigated more polar product.

3,3-Ethylenedithio-5 α -lanost-8-ene (I) yielded (18 h) 5 α -lanosta-2,8-diene (II) and 5 α -lanost-8-ene (III) (4 : 1), together with starting material (50%).

(ii) *Modified procedures.* The reaction medium was varied as detailed in the Table. Buffers were prepared by dissolving the appropriate acids and bases in 95% ethanol. The pH values quoted are those that would have resulted had the solvent been water.

(iii) *Preferred procedure.* The general procedure was varied by the addition of a large excess of boric acid to the ethanol solution prior to the introduction of the aqueous sodium borohydride.

Reactions with Nickel Boride-Hydrogen.—A warm, vigorously stirred mixture of 3,3-ethylenedithiocholestane (30 mg), nickel chloride (300 mg), and boric acid (1 g) in ethanol (20 ml) and tetrahydrofuran (10 ml) was treated with sodium borohydride (150 mg) in water (5 ml) under hydrogen. After 7 h the mixture was worked up in the usual way to afford pure cholestane (80%), m.p. and mixed m.p. 77–79°.

Under identical conditions the dithioacetal (I) yielded 5 α -lanosta-2,8-diene and 5 α -lanost-8-ene (1 : 1) together with unchanged starting material (40%).

Reaction of 5 α -Lanosta-2,8-diene with Nickel Boride.—Sodium borohydride (250 mg) in water (4 ml) was added dropwise to 5 α -lanosta-2,8-diene (50 mg), nickel chloride (500 mg), and boric acid (2 g) in ethanol (20 ml) and tetrahydrofuran (8 ml). The mixture was refluxed for 12 h. T.l.c. indicated the formation of ca. 10% of 5 α -lanost-8-ene.

Nickel Boride Desulphurisation of Thiophens.—(i) 9-[5-(3-Carboxypropyl)-2-thienyl]-9-oxononanoic Acid. Sodium borohydride (1 g) in water (5 ml) was added dropwise to the thiophen (200 mg), nickel chloride (2 g), and boric acid (4 g) in ethanol (100 ml). The mixture was refluxed for

4 h and then worked up. The product in benzene (15 ml) and acetic acid (6 ml) was treated at 10° with Kiliani's chromic acid (6 ml). After 10 min the reaction was worked up to yield 9-oxoheptadecanedioic acid (90 mg), characterised as the dimethyl ester, m.p. [from light petroleum (b.p. 60–80°)] 55.5–57° (lit.,¹³ 60°).

(ii) 3-(2-Furyl)-1-(2-thienyl)prop-2-en-1-one.—The thiophen (400 mg) was treated as in (i). The product from the oxidation was chromatographed on alumina (50 g). Elution with benzene-light petroleum (3 : 2 v/v) gave 1-(2-furyl)-heptan-3-one (70 mg, 20%), ν_{\max} 1720 cm⁻¹ (ketone), τ 2.78 (1H, d, *J* 2 Hz, furan 5-H), 3.79 (1H, q, *J* 2 and 3 Hz, furan 4-H), and 4.05 (1H, d, *J* 3 Hz, furan 3-H), *m/e* 180 (M⁺), 123, 95, 94, 85, 81, and 57. Further elution with benzene-light petroleum (4 : 1 v/v) afforded 3-(2-furyl)-1-(2-thienyl)propan-1-one (40 mg, 10%), ν_{\max} 1670 (ketone) and 1418 (thiophen) cm⁻¹, λ_{\max} 261 and 286 nm, τ 2.41 and 2.95 (2H and 1H respectively, each complex, thiophen protons), 2.76 (1H, d, furan 5-H), 3.77 (1H, q, furan 4-H), and 3.99 (1H, d, furan 3-H), *m/e* 206 (M⁺), 111, 95, 94, 83, and 81.

Reaction of 5 α -Lanost-8-en-3-one with 2-Mercaptoethanol.—5 α -Lanost-8-en-3-one (1 g) in glacial acetic acid (20 ml) was treated with 2-mercaptoethanol (1.5 ml) followed by boron trifluoride-ether complex (4 ml) at 40°, and then left overnight. The product was filtered off and chromatographed on alumina (80 g). Elution with light petroleum gave 3,3-ethylenedithio-oxy-5 α -lanost-8-ene (isomer I) (500 mg, 44%), m.p. 147.5–148.5° (from ethanol-ethyl acetate), $[\alpha]_D + 51^\circ$, ν_{\max} 1265 and 1080 cm⁻¹ (Found: C, 78.8; H, 11.1; S, 6.6. C₃₂H₅₄OS requires C, 78.95; H, 11.2; S, 6.6%). Further elution with benzene-light petroleum (1 : 9) afforded isomer II (120 mg, 11%), m.p. 148–149° (from ethanol-ethyl acetate), $[\alpha]_D + 42^\circ$ (Found: C, 79.1; H, 11.05; S, 6.5%).

Reaction of 3,3-Ethylenedithio-oxy-5 α -lanost-8-ene with Nickel Boride.—The ethylene monothioacetal isomer I (50 mg), nickel chloride (500 mg), and boric acid (2 g) in ethanol (25 ml) and tetrahydrofuran (10 ml) were stirred under nitrogen while sodium borohydride (250 mg) in water (5 ml) was slowly added. After a further 15 min the product was isolated in the usual manner. The resulting mixture of 5 α -lanost-8-en-3-one and 5 α -lanost-8-en-3 β -ol in benzene (4 ml) and acetic acid (1 ml) was treated with Kiliani's chromic acid (1 ml) at 10° for 30 min to give pure 5 α -lanost-8-en-3-one (38 mg, 87%), m.p. and mixed m.p. 116–118° (lit.,¹⁴ 119.5–120.5°).

3-Benzylthio-5 α -lanosta-2,8-diene.—5 α -Lanost-8-en-3-one (200 mg) in acetic acid (20 ml) was treated with toluene- α -thiol (0.3 ml) followed by boron trifluoride-ether complex (1 ml), and the solution was left overnight. The product was filtered off and recrystallised twice from chloroform-methanol to afford needles of the diene (180 mg, 72%), m.p. 111–113°, $[\alpha]_D + 106^\circ$, ν_{\max} 3085, 3060, 3030, and 695 cm⁻¹, τ 2.70 (5H, s, Ph), 4.42br (1H, s, 2-H), and 6.09 (2H, s, PhCH₂S) (Found: C, 83.3; H, 10.6; S, 6.0. C₃₇H₅₆S requires C, 83.4; H, 10.6; S, 6.0%).

Similarly, 5 α -euph-8-en-3-one afforded 3-benzylthio-5 α -eupha-2,8-diene, m.p. 90.5–91.5°, $[\alpha]_D + 82^\circ$ (Found: C, 83.2; H, 10.6; S, 6.0. C₃₇H₅₆S requires C, 83.4; H, 10.6; S, 6.0%). Urs-12-en-3-one gave 3-benzylthioursa-2,12-diene, m.p. 166–166.5°, $[\alpha]_D + 91.5^\circ$ (Found: C, 83.7; H, 10.2; S, 5.9. C₃₇H₅₄S requires C, 83.7; H, 10.25; S, 6.0%).

¹³ L. Canonica and T. Bacchetti, *Atti Acad. naz. Lincei, Rend. Classe Sci. fis. mat. nat.*, 1953, **15**, 278 (*Chem. Abs.*, 1955, **49**, 8121).

¹⁴ L. Ruzicka, R. Denss, and O. Jeger, *Helv. Chim. Acta*, 1945, **28**, 759.

Olean-12-en-3-one gave 3-benzylthio-oleana-2,12-diene, m.p. 138.5—139°, $[\alpha]_D + 92^\circ$ (Found: C, 84.0; H, 10.2; S, 5.75. $C_{37}H_{54}S$ requires C, 83.7; H, 10.25; S, 6.0%). 3-Oxo-olean-12-en-28-oic acid afforded 3-benzylthio-oleana-2,12-dien-28-oic acid, m.p. 273—274°, $[\alpha]_D + 90.6^\circ$ (Found: C, 79.1; H, 9.3; S, 5.6. $C_{37}H_{52}O_2S$ requires C, 79.2; H, 9.35; S, 5.7%). Methyl 3-oxo-olean-12-en-28-oate afforded methyl 3-benzylthio-oleana-2,12-dien-28-oate, m.p. 190—191°, $[\alpha]_D + 72.9^\circ$ (Found: C, 79.2; H, 9.4; S, 5.4. $C_{38}H_{54}O_2S$ requires C, 79.4; H, 9.5; S, 5.6%). Friedelin (friedelan-3-one) gave 3-benzylthiofriedel-3-ene, m.p. 235—236°, $[\alpha]_D + 17.4^\circ$ (Found: C, 83.3; H, 10.5; S, 5.9. $C_{37}H_{56}S$ requires C, 83.4; H, 10.6; S, 6.0%).

Desulphurisation of Benzyl Thio(enol ether)s.—(i) *With Raney nickel.* Raney nickel sludge (W2; 3 g) was refluxed with acetone (30 ml) for 2 h. 3-Benzylthio-oleana-2,12-diene (300 mg) in acetone (15 ml) was added and the mixture was refluxed for 20 h, then filtered through Celite. The crude product from the filtrate was washed through an alumina column (20 g) with light petroleum to yield oleana-2,12-diene (204 mg, 88%), m.p. 149.5—150.5°, $[\alpha]_D + 145^\circ$

(lit.,¹⁵ m.p. 148—150°, $[\alpha]_D + 139^\circ$). Similarly, ursal-2,12-diene, m.p. 120—121°, $[\alpha]_D + 135.3^\circ$ (lit.,¹⁵ m.p. 119—120°, $[\alpha]_D + 137^\circ$), methyl oleana-2,12-dien-28-oate, m.p. 182—182.5°, $[\alpha]_D + 111.7^\circ$ (Found: C, 82.2; H, 10.8. $C_{31}H_{48}O_2$ requires C, 82.2; H, 10.7%), and friedel-3-ene, m.p. 253—254°, $[\alpha]_D + 55.6^\circ$ (lit.,¹⁶ m.p. 253—256°, $[\alpha]_D + 59.0^\circ$), were prepared from the corresponding benzyl thio(enol ether)s.

(ii) *With nickel boride.* 3-Benzylthio-5 α -lanosta-2,8-diene (100 mg) and nickel chloride (480 mg) in ethanol (80 ml) were treated dropwise with sodium borohydride (64 mg) in water (8 ml). The mixture was refluxed for 1 h and then worked up to give 5 α -lanosta-2,8-diene (72 mg, 93%), m.p. 81—82.5°, $[\alpha]_D + 119^\circ$ (lit.,¹² m.p. 83—84°, $[\alpha]_D + 124^\circ$).

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