

A Convenient Reduction of Activated Olefins by Zinc–Copper Couple

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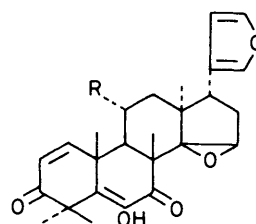
Activated olefins of the types $\text{Ph}_2\text{C}=\text{CXY}$, $\text{R}_2\text{C}=\text{CXY}$, $\text{PhRC}=\text{CXY}$, and $\text{RCH}=\text{CXY}$ (where X and Y are electronegative substituents or one of them is a hydrogen atom) have been reduced to the corresponding saturated compounds in excellent yields by treatment with zinc–copper couple in boiling methanol.

A number of reports have been made on the reductive properties of the zinc–copper couple. Kupchan and Maruyama¹ reported the reductive elimination of epoxides to give olefins in a one-step stereoselective reaction in which a *cis*-epoxide gave predominantly the *trans*-olefin, while *trans*-epoxides generated the *cis*-olefin as the major product. Further reductions of epoxides were carried out by Ekong *et al.*² These workers also reported the reduction of α,β -unsaturated ketones and diosphenolic compounds to the corresponding 'saturated' † compounds, notably in the reduction of anthothocol (1) and cedrelone (2). Other methods for the selective reduction of double bonds include the use of sodium borohydride on α,β -unsaturated acids and esters^{3,4} and, in recent years, L- and K-selectride and *t*-butyl alcohol by Fortunato and Ganem,⁵ 10% palladium-on-carbon and triethyl- or tri-*n*-butyl-amine by Cortese and Heck,⁶ and lithium amide by Melamed and Feit.⁷

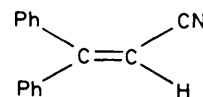
We recently⁸ reported the use of zinc–copper couple in the stereospecific and quantitative reduction of carbon–carbon triple bonds to the corresponding olefins. Our method for reduction of the acetylenes was found to be much better than the palladium-catalysed reduction of acetylenes by Cortese and Heck;⁶ their method reduced *e.g.* hex-1-yne to give hex-1-ene as only 49% of a mixture of products, and the catalyst could further reduce the olefin to a mixture of hexane and other products, whereas with zinc–copper couple different acetylenes gave the alkene in near quantitative yield, no other reduction products being formed.⁸

As a continuation of our study of reactions with zinc–copper couple, we have now found that activated olefins can be conveniently and selectively reduced by this reagent to the corresponding saturated compounds in near quantitative yields. Various activated olefins (7)–(18) were treated with zinc–copper couple in methanol under reflux for periods not exceeding 24 h. Work-up gave the saturated compound without problems [those which arose in the low temperature work (-78°C) of Melamed and Feit⁷ and Fortunato and Bruce⁵ (-70°C) are avoided].

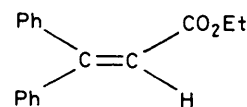
Furthermore, we found no problem in reducing compounds with only one electron-withdrawing group such as (13) and (16), whereas similar compounds [(3) and (4)] could not be reduced by the Melamed and Feit method, which only works when there are two electron-withdrawing groups attached to the double bond. Also, ethyl cinnamate (10), which was reduced by the L-selectride method⁵ to a mixture of twenty-one compounds, is readily reduced in excellent yield to the corresponding saturated compound, no by-products being detected. We have also observed that compounds



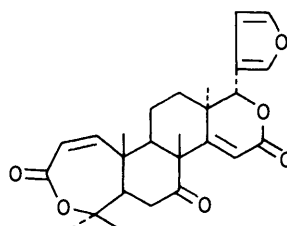
(1) R = OAc
 (2) R = H



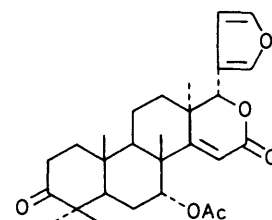
(3)



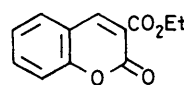
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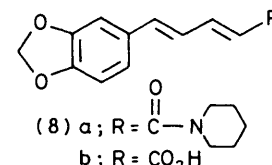
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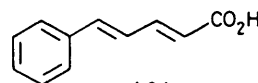
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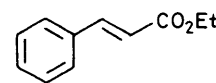
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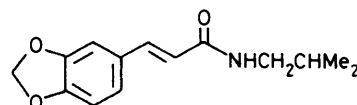
(8) a; R = C(=O)N(CH2)6
 b; R = CO2H



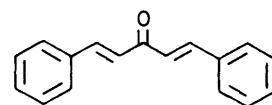
(9)



(10)



(11)



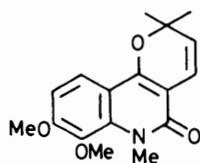
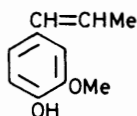
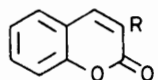
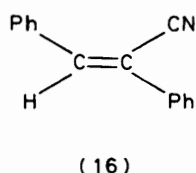
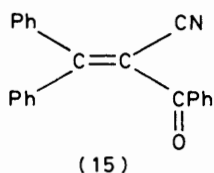
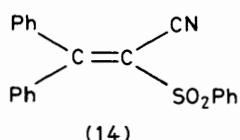
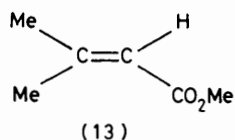
(12)

† The term 'saturated' is used in this paper in a limited sense and refers to the saturation of the double bond being reduced even though X and Y are unsaturated functions both in the starting materials and in the products.



containing two conjugated double bonds with a conjugated electronegative group, such as (8a) and (8b), are readily reduced to the saturated derivatives. The range of compounds reduced in this way is given in the Table.

We found that when the double bond was activated by a



lactone, as in 14,15-deoxybacunone (5) and dihydro-14,15-deoxygedunin (6), no reduction took place even over long periods and with large quantities of the couple. This is not due to steric hindrance in the vicinity of the double bond, however, as coumarin (17a) is similarly not reduced, while 3-ethoxycarbonylcoumarin (17) is readily converted into the saturated derivative; clearly an electron-withdrawing group between the double bond and the lactone carbonyl is necessary for the reduction to occur.

Although the styrene chromophore is present in most of these compounds, it does not contribute to their reduction as shown by the fact that the double bond on the side chain in isoeugenol (17b) is unaffected.

Experimental

Zinc-copper couple was prepared as indicated elsewhere.^{2,5} M.p.s were taken on a K \ddot{o} fler hot-stage apparatus and are uncorrected. Refractive indices were taken on a universal refractometer. ¹H N.m.r. spectra were taken on a Perkin-Elmer R12 B spectrometer with deuteriochloroform as solvent, unless otherwise stated, and tetramethylsilane as internal standard. The n.m.r. data are given as δ values. Wherever used, silica gel for columns refers to Merck silica gel, mesh 0.063–0.200 nm. Products were isolated in all cases by the following procedure: the exhausted zinc-copper couple was filtered off (filter paper) and repeatedly washed with methanol (the reaction solvent); the filtrate was then diluted with distilled water and extracted with either chloroform or methylene dichloride (3 \times 50 ml). The combined extracts were dried (Na₂SO₄ or MgSO₄) and evaporated under reduced pressure.

Tetrahydropiperine and Tetrahydropiperic Acid.—Piperic acid (8b) [5-(3,4-methylenedioxyphenyl)penta-2,4-dienoic acid] (1 g, 0.0045 mol) and zinc-copper couple (prepared from

Table. Reduction of olefins (8)–(18) by zinc-copper couple

Olefin	Amount used (10 ⁻³ mol)	Time (h)	Product yield (%)
(8a)	3.5	3	98
(8b)	4.5	3	98
(9)	5.6	6	96
(10)	5.6	5	84
(11)	4.0	5	97
(12)	4.0	5	95
(13)	8	24	88
(14)	2.8	4	98
(15)	3.0	4	98
(16)	5.0	5	98
(17)	8.0	6	94
(18)	3.0	96	85
(17a)	7	24	

zinc dust; 30 g, 1 mol) were refluxed for 3 h in methanol (95%, 100 ml). Work-up as above gave a crude product which was recrystallized from benzene to give tetrahydropiperic acid (0.97 g, 98%), m.p. 95–96 °C; δ (CDCl₃) 1.50–1.90 (4 H, m, CH₂CH₂CH₂CO₂H), 2.30–2.80 (4 H, m, ArCH₂ · · · CH₂CO₂H), 5.85 (2 H, s, OCH₂O), 6.60 (3 H, s, Ar), and 9.5 (1 H, br s, CO₂H, disappears on deuteration).

Similarly piperine (1-piperoylpiperidine) (8a) (1 g, 0.0035 mol) and zinc-copper couple were refluxed for 3 h. Work-up as usual gave a crude product which was hydrolysed to tetrahydropiperic acid.

1,5-Diphenylpentan-3-one.—1,5-Diphenylpenta-1,4-dien-3-one (12) (1 g, 0.0040 mol) was refluxed with zinc-copper couple (prepared from 30 g of zinc dust) in methanol–water (3 : 1; 120 ml) for 5 h. Work-up gave a crude product which was passed through a silica-gel column and then recrystallized (methanol) to give 1,5-diphenylpentan-3-one (0.96 g, 95%), m.p. 67–70 °C.

2,3-Diphenylpropionitrile.—2,3-Diphenylacrylonitrile (16) (1 g, 0.0048 mol) and zinc-copper couple (30 g, 1 mol of zinc dust) were refluxed in methanol (95%; 100 ml) for 5 h. After usual work-up, the crude product was passed through a silica-gel column and then recrystallized (hexane) to give 2,3-diphenylpropionitrile (0.99 g, 98%), m.p. 66–68 °C.

3,3-Diphenyl-2-phenylsulphonylpropionitrile.—3,3-Diphenyl-2-phenylsulphonylacrylonitrile^{9a} (14) (1 g, 0.0028 mol) and zinc-copper couple (30 g of zinc dust) were refluxed in methanol–water (3 : 1) for 4 h. Work-up gave an oily product which was recrystallized from ethanol to give the propionitrile (0.99 g, 98%), m.p. 170–172 °C; δ (CDCl₃) 4.75 (1 H, d, Ph₂CHCH), 5.05 (1 H, d, Ph₂CHCH), 7.35 (10 H, s, Ar), and 7.10–7.80 (5 H, m, Ar).

2-Benzoyl-3,3-diphenylpropionitrile.—2-Benzoyl-3,3-diphenylacrylonitrile^{9b} (15) (1 g, 0.003 mol) was refluxed with zinc-copper couple (30 g of zinc dust) in methanol–water for 4 h. After usual work-up, the 2-benzoylpropionitrile was obtained as an oily product (0.99 g, 98%) which did not crystallize. δ (CDCl₃) 2.30 (3 H, s, ArCH₃), 3.50 (1 H, d, Ph₂CHCH), 4.1 (1 H, d, Ph₂CHCH), and 6.90–7.80 (14 H, m, Ar).

Dihydro-3-ethoxycarbonylcoumarin.—3-Ethoxycarbonylcoumarin^{9c} (17) (0.8 g, 0.0036 mol) was refluxed with zinc-copper couple (30 g of zinc dust) in methanol–water for 6 h.

Usual work-up gave a crude product which was passed through a silica-gel column to afford an oil (0.76 g, 94%) (Found: C, 65.45; H, 5.45; O, 29.1 $C_{12}H_{12}O_4$ requires C, 65.44; H, 5.49; O, 29.06%). $\delta(CDCl_3)$ 1.23 (3 H, t, CH_2CH_3), 2.10–2.40 (4 H, m, methylene H), 3.60–4.40 (1 H, m, 3-H), and 7.10 (3 H, m, Ar).

Ethyl 3-Phenylpropionate.—Ethyl cinnamate¹⁰ (10) (1 g, 0.0056 mol) was refluxed with zinc–copper couple in methanol for 5 h. After work-up, the product was distilled under reduced pressure. An oily colourless liquid was collected between 120 and 124 °C 25 mmHg (0.85 g, 84%), n_D 1.4960 (lit.,¹¹ n_D 1.4954).

5-Phenylpentanoic Acid.—5-Phenylpenta-2,4-dienoic acid¹⁰ (9) (1 g, 0.0057 mol) was refluxed with zinc–copper couple in methanol–water (3 : 1) for 6 h. The isolated oily crude product (0.98 g, 96%) did not crystallize from any available solvent. $\delta(\text{acetone})$ 1.10–1.60 (4 H, m, $ArCH_2CH_2CH_2CH_2CO_2H$), 2.20–2.80 (4 H, m, $ArCH_2CH_2CH_2CH_2CO_2H$), and 7.30 (6 H, d, Ar and OH which disappeared on deuteration).

Dihydrofagaramide.—Fagaramide (*N*-isobutyl-3,4-methylenedioxy-cinnamamide) (11) (1 g, 0.004 mol) was refluxed with zinc–copper couple in methanol–water (3 : 1) for 5 h. Usual work-up gave a crude product (0.98 g, 97%) which was recrystallized from acetone to give dihydrofagaramide, m.p. 102–104 °C. $\delta(CDCl_3)$ 0.83 (3 H, s, Me), 0.93 (3 H, s, Me), 1.40–1.96 (1 H, m, CH), 2.28–2.60 (2 H, m, CH_2), 2.80–3.18 (4 H, t, $ArCH_2CH_2$), 5.90 (2 H, s, OCH_2O), and 6.80 (3 H, s, Ar).

Dihydroveprisine.—Veprisine¹² (2,6-dihydro-7,8-dimethoxy-2,2,6-trimethylpyrano[3,2-*c*]quinolin-5-one) (18) (1 g, 0.003 mol) was refluxed with zinc–copper couple in methanol (100 ml) for 96 h. Usual work-up gave an oily crude product (0.96 g) which was passed through a silica-gel column to give a solid compound which was recrystallized from ethyl acetate–*n*-pentane to give *dihydroveprisine* (0.85 g, 85%), m.p. 154–156 °C (Found: C, 67.3; H, 6.9; N, 4.65; O, 22.2. $C_{17}H_{21}O_4N$ requires C, 67.31; H, 6.98; N, 4.0; O, 21.10%). $\delta(CDCl_3)$ 0.90 (6 H, d, Me \times 2), 1.45 (3 H, t,

CH_2), 2.8 (2 H, t, CH_2), 3.86 (3 H, s, NMe), 3.95 (6 H, s, $OMe_3 \times 2$), 6.87 (1 H, d, Ar), and 7.82 (1 H, d, Ar).

Methyl Isovalerate.—Methyl 3,3-dimethylacrylate (13) (1 g, 0.008 mol) was refluxed for 24 h with zinc–copper couple in methanol (200 ml). Usual work-up gave methyl isovalerate (0.90 g, 88%); n_D 0.8800 (lit.,¹¹ n_D 0.8808).

Attempted Reduction of Coumarin (17a).—Coumarin (1 g, 0.007 mol) was treated with zinc–copper couple in boiling methanol for 24 h. Work-up gave starting material (0.95 g) as shown by the spectral data and m.p.

Attempted Reduction of Isoeugenol (2-Methoxy-4-prop-1-enylphenol) (17b).—Isoeugenol (1 g, 0.006 mol) was treated with zinc–copper in boiling methanol for 120 h. Work-up gave starting material (0.96 g).

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