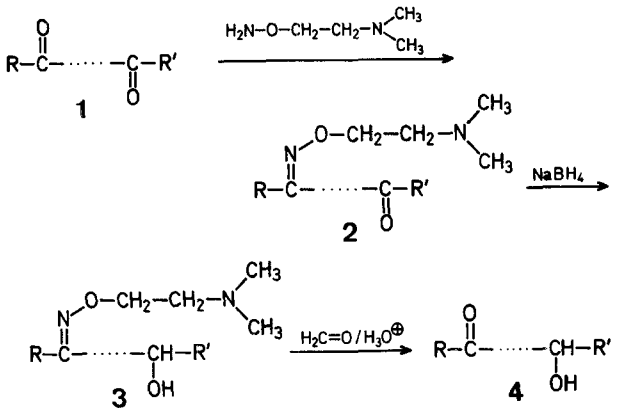
Partial Reduction of Diketones

Muhammad NAZIR*, Wolfgang KREISER, Hans Herloff INHOFFEN

Institut für Organische Chemie der Technischen Universität Braunschweig, D-33 Braunschweig

To achieve the partial reduction of a diketone, partial acetalization[1] or partial oximation[2] are generally applied to protect one of the carbonyl functions. The reaction product is resolved into the unreacted diketone, the monoketone, and the bis-acetal or dioxime by suitable chromatographic methods which are usually laborious. The monoketone is then subjected to reduction, and the bis-acetal or dioxime is hydrolysed and the hydrolysis product recycled together with the unreacted diketone. The partial reduction of diketones has also been achieved under special conditions[3,4].

We have found that under certain conditions *O*-(2-dimethylaminoethyl)-hydroxylamine dihydrochloride reacts with symmetrical diketones (**1**, R = R') forming mainly a mono-oxime (**2**). Furthermore, in the case of an unsymmetrical dione (**1**), the oxime formation occurs preferentially at one centre, e.g. in androstane-3,17-dione, the oxime formation occurs quantitatively at C-3. The oxime **2** by virtue of its second N-atom can be separated from the unreacted diketone **1** by extraction with dilute mineral acids; thus, the process of chromatographic resolution is eliminated. The monooxime **2** is reduced with sodium borohydride to give a mixture of the axial and equatorial/α- and β-oriented alcohols (**3**). The reduction product **3** is hydrolysed to regenerate the carbonyl function (**4**). The crude reaction mixture which is free from the diol is resolved by suitable chromatographic techniques.



All products obtained were identified by comparison of their spectral data with those of authentic samples and by their melting points and mixture melting points.

***threo*-3-(4-Hydroxycyclohexyl)-4-(4-oxocyclohexyl)-hexane (4a):**
A solution of *rac*.-3,4-bis[4-oxocyclohexyl]-hexane (**1a**; 2.8 g, 10 mmol) in ethanol (50 ml) and pyridine (1.25 ml) is placed in a round-bottom flask and *O*-(2-dimethylaminoethyl)-hydroxylamine hydrochloride (0.85 g, 2.5 mmol) is placed in the thimble of a Soxhlet extractor connected to the flask. The solution is heated for 3 h during which period the *O*-alkylhydroxylamine is gradually transferred into the reaction flask. As a result there is always a large excess of the diketone **1a** in the reaction mixture. At the end, the solvent is removed using a rotary evaporator and the residue is shaken with 0.05 normal sulfuric acid (200 ml). The unreacted **1a** (2.13 g) is recovered from this acidic layer by extraction with ether. Addition of potassium carbonate to the aqueous layer regenerates the oxime **2a** which is then extracted with ether. The ether is replaced by ethanol (20 ml) and the keto group reduced with sodium borohydride (100 mg). Ether (100 ml), hydrochloric acid (3 ml), and 40% aqueous formaldehyde (3 ml) are added to the reduced product **3a** and the mixture is stirred for a few hours at room temperature. The organic phase is washed neutral, dried with sodium sulfate, and evaporated. Preparative T.L.C. of the product on silica gel (cyclohexane/ethyl acetate, 1:1) gives pure **4a**; yield: 543 mg (82%). Separation of the product into **4a** with an axial hydroxy group (39 mg, 5.9%) and **4a** with an equatorial hydroxy group (504 mg, 76%) is carried out by preparative T.L.C. as above and developing the plate twice.

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* Present address to which correspondence should be sent: PCSIR Laboratories, Lahore, Pakistan.

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Table. Hydroxyketones (**4**) obtained from Diketones (**1**) via Reduction of the Diketone Monoximes (**2**)

	1	4	Yield[a] [%]	m.p.	Lit. m.p.
a	*rac*-3,4-Bis[4-oxocyclohexyl]-hexane	*threo*-3-(4-Hydroxycyclohexyl)-4-(4-oxocyclohexyl)-hexane	82	100°	Lit.[3], ax. oil eq. 100–101.5°
b	*trans*-3,4-Bis[4-oxocyclohexyl]-3-hexene	*trans*-3-(4-Hydroxycyclohexyl)-4-(4-oxocyclohexyl-3-hexene	81	125°	Lit.[5], ax. 146–150° eq. 127°
c	*trans*-2,3-Bis[1-methyl-4-oxocyclohexyl]-2-butene	*trans*-2-(1-Methyl-4-hydroxycyclohexyl)-3-(1-methyl-4-oxocyclohexyl)-2-butene	80	—	Lit.[4], ax. 118–119° eq. 89–90°
d	Androstane-3,17-dione[6]	17-Hydroxyandrostan-3-one	97	—	Lit.[6,7], 179–180°

[a] Based on 0.25 **1** (= 1.0 *O*-alkylhydroxylamine).