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THE STEREOCHEMISTRY OF SODIUM DITHIONITE REDUCTIONS OF CYCLIC KETONES

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Summary: The stereochemistry of reduction of several substituted cyclohexanones, norcamphor, and camphor by sodium dithionite (sodium hydrosulfite, $Na_2S_2O_4$) in aqueous DMF solution has been studied. The cyclohexanones yield mainly equatorial alcohols while the bicyclic ketones give mainly endo alcohols.

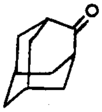
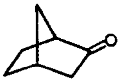
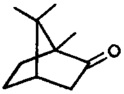
Sodium dithionite is an inexpensive reducing agent[1] and has been used for many years in the reductions of a variety of functional groups.[2] Recently several reports have appeared on the reduction of aldehydes and ketones[3,4] and one report deals with phase transfer reductions using sodium dithionite with several cyclic ketones.[5]

The stereochemical results of our reduction study of cyclic ketones using $Na_2S_2O_4$ in aqueous DMF are tabulated in Table I along with comparative data for $NaBH_4$ and Li-liquid ammonia-alcohol reductions of these same ketones. The general reduction procedure which was utilized in this study was to heat 70 ml of DMF under a nitrogen atmosphere and during the heating process to add 120 mmoles of $NaHCO_3$ and 30 mmoles of the ketone. When the internal temperature reached 110°C, 30 mmoles of $Na_2S_2O_4$ was added followed immediately by 30 ml of warm water. When the temperature reached 105°C, the mixture was heated at this temperature for 0.5 h, whereupon another 30 mmole portion of $Na_2S_2O_4$ was added and the mixture was heated for another 0.5 h. The mixture was then cooled and 150 ml of cold water was added. The products were extracted with CH_2Cl_2 (4 x 20 ml) and the extracts were washed with water (4 x 30 ml). The organic extract was dried over Na_2SO_4 and the solvent removed in vacuo. In the case of adamantanone the extraction process was omitted and the alcohol product merely filtered from the aqueous suspension.

It can be seen from the data in Table I that the dithionite reductions proceed fairly readily (camphor is sluggish and is also reduced slowly by $NaBH_4$). The stereoselectivity in all cases mirrors that found in the Li-liquid ammonia-alcohol reductions of the corresponding ketones. In fact, despite the obvious mechanistic difference between the reductions using $NaBH_4$ or $Na_2S_2O_4$, in three cases (camphor excluded) the stereochemistry results are similar. Since the reduction by $Na_2S_2O_4$ probably proceeds by an electron transfer mechanism[6] to the carbonyl group similar to the Li-ammonia-alcohol,[7] similarities in reduction stereochemistry might indeed be expected and the quantitative differences in stereoselectivities might merely be reflected in the temperature differential between these two reactions. The higher temperatures used in the dithionite reactions yield intermediates (anion-radicals and protonated radicals or anions) which probably would show less stereoselectivity on protonation at carbon).

TABLE I

STEREOCHEMICAL RESULTS OF REDUCTIONS OF CYCLIC KETONES

Ketone	% Reduction	$Na_2S_2O_4/DMF/H_2O$ [a] % trans or endo alcohol	$NaBH_4$ Redn [b] % trans or endo alcohol	$Li-NH_3$-Alcohol [c] % trans or endo alcohol
	100	-	-	-
	65	87	93	99
	60	71	71	99
	75	85	87	85
	20	65	24	90

[a] The percent recovery of products was greater than 70% in all cases. The crude reaction products were analyzed by glpc and the % of the epimeric alcohols calculated for the alcohol fraction (raw data). All analyses were performed on a 10% Carbowax 20M column on Chromosorb P except for entry 3 which was analyzed using 10% diglycerol on Chromosorb WHP.

[b] All reductions were quantitative except in the case of camphor which was reduced to the extent of 25%. Reductions were performed in isopropyl alcohol using the procedure described in Moore, J.A. and Dalrymple, D.L., Experimental Methods in Organic Chemistry, W.B. Saunders, 1976, pp 163-164.

[c] Huffman, J.W.; Charles, J.T. J. Am. Chem. Soc. 1968, 90, 6486-6492.

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