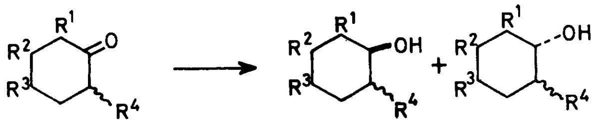
Stereochemistry of Methylcyclohexanones Reduction by Sodium Dithionite under Conventional and Phase Transfer Conditions

By Francisco Camps, José Coll, and Magín Riba
(*Instituto de Química Bioorgánica, C.S.I.C., c/Jorge Girona Salgado, Barcelona-34, Spain*)

Summary Reduction of methylcyclohexanones by sodium dithionite in benzene–water using Adogen as the phase transfer agent affords good yields of isomeric mixtures of the corresponding methylcyclohexanols with stereoselectivities comparable to those exhibited by conventional hydride reagents.

Recently two reports[1,2] have indicated the possible application of sodium dithionite as an advantageous alternative to metal hydrides in the reduction of aldehydes and ketones. In this context, we describe here the results of the reduction of methylcyclohexanones (**1**)—(**4**) by this reagent in basic medium under conventional and phase transfer (PT) conditions. Although PT has received wide acceptance in organic synthesis, its applicability in reduction reactions has been so far limited, due, in part, to the nature of the usual reducing agents.[3] However, its application seemed appropriate in the present case, because one



(1); R^1 = Me, R^2 = R^3 = R^4 = H
(2); R^2 = Me, R^1 = R^3 = R^4 = H
(3); R^3 = Me, R^1 = R^2 = R^4 = H
(4); R^1 = R^4 = Me, R^2 = R^3 = H

of the problems of the above procedure is derived from the insolubility of the organic substrates to be reduced in aqueous sodium dithionite solution. This has been circumvented by addition of dioxan or dimethylformamide as cosolvents.[2]

Using conventional methods sodium dithionite was added to a stirred aqueous solution of methylcyclohexanone (2%) and sodium bicarbonate at 80 °C over a period of 8 h at regular intervals. (Longer reaction times did not improve substantially the yields of alcohols obtained). The aqueous layer was extracted with diethyl ether while the organic layer, after the usual treatment, afforded a residue that was distilled (bulb-to-bulb) at reduced pressure. Yields of alcohols were estimated by g.l.c. analysis of the distillate (2·5 m × 3 mm packed column of 10% Carbowax on Chromosorb W at 80 °C). Isomeric ratios were determined by the relative integration of *H*–C–O- and CF_3CO_2-signals in the ^{1}H and ^{19}F n.m.r. spectra of the corresponding trifluoroacetates.[4] The molar ratios used and results obtained are summarised in the Table.

After several unsuccessful attempts to transfer sodium dithionite from the aqueous layer into benzene with classical transfer agents, Adogen 464, a liquid commercial mixture of methyl trialkyl (C_8–C_{10}) ammonium chlorides, recently recommended for the solubilization of other dianions in organic solvents,[5] proved to be satisfactory.

The PT procedure was carried out as above using a 1:1 benzene: water mixture as solvent, with a reaction time of 20 h and molar ratios as shown in the Table. After decantation, the organic layer was filtered through a silica gel column, whence Adogen could be recovered by elution with methanol and reused.

As depicted in the Table, the PT procedure afforded higher yields of alcohols than the conventional procedure, the most remarkable being the yield increase observed in the reduction of sterically hindered 2,6-dimethylcyclohexanone (**4**). Likewise, the stereoselectivities obtained using the PT procedure were also somewhat higher, and were comparable to those reported with classical hydride reagents such as sodium borohydride.[6]

TABLE. Methylcyclohexanones reduction by sodium dithionite

Compound	Molar ratios Ketone : $Na_2S_2O_4$: $NaHCO_3$: Adogen	Yield/%	Alcohol	Isomer ratio ^{1}H n.m.r.	Isomer ratio ^{19}F n.m.r.
(**1**)	1:8:6:-	63	*cis*:*trans*	1:2	1:1·75
(**1**)	1:8:6:8	76	*cis*:*trans*	1:2·5	1:2
(**2**)	1:8:6:-	67	*cis*:*trans*	3:1	3:1
(**2**)	1:8:6:8	81	*cis*:*trans*	4:1	3·75:1
(**3**)	1:8:6:-	68	*cis*:*trans*	1:2	1:2:25
(**3**)	1:6:4:6	82	*cis*:*trans*	1:3·3	1:3·5
(**4**)[a]	1:8:6:-	15	*c,c*:*t,t*:*t,c*	—	—
(**4**)	1:12:8:6	70	*c,c*:*t,t*:*t,c*	—	1·6:2:1

[a] A 85:15 *cis*:*trans* mixture (F. Johnson and L. G. Duquette, *Chem. Comm.*, 1969, 1448) of this ketone was used in the reduction. [b] *c,c* = *c*-2,*c*-6-dimethylcyclohexan-*r*-1-ol; *t,t* = *t*-2,*t*-6-dimethylcyclohexan-*r*-1-ol; *t,c* = *t*-2,*c*-6-dimethylcyclohexan-*r*-1-ol.

We thank Ugimica S.A. for a predoctoral fellowship (to M.R.).

(*Received*, 6*th August* 1979; *Com.* 853.)

---

[1] H. Minato, S. Fujie, K. Okuma, and M. Kobayashi, *Chem. Letters*, 1977, 1091.
[2] J. G. de Vries, T. J. van Bergen, and R. M. Kellogg, *Synthesis*, 1977, 246.
[3] W. P. Weber and G. W. Gokel, in 'Phase Transfer Catalysis in Organic Synthesis,' Springer Verlag, New York, 1977, p. 215.
[4] H. J. Schneider, G. Jung, E. Breitmaier, and W. Voelter, *Tetrahedron*, 1970, **26**, 5369.
[5] R. O. Hutchins, N. R. Natale, and W. J. Cook, *Tetrahedron Letters*, 1977, 4167.
[6] H. C. Brown and S. Krishnamurthy, *Tetrahedron*, 1979, **35**, 567.