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An Efficient Synthesis of *anti*-(1R)-(+)-Camphorquinone 3-oxime.

Susmita Roy (née Bhattacharaya)[a] and Asit K. Chakraborti*[,a,b]

[a]Department of Chemistry, The University of Burdwan, Burdwan 713 104, India.

[b]Department of Medicinal Chemistry, National Institute of Pharmaceutical Education and Research, Sector 67, S. A. S. Nagar 160 062, India.

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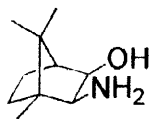
Abstract *: Nitrosation of camphor with iso-amylnitrite in presence of base leads to the title compound in high yields. Excellent stereoselectivity is observed leading to preferential formation of the anti-isomer.* © 1998 Elsevier Science Ltd. All rights reserved.

The camphor derived amino alcohol (**1**) is used as chiral auxiliary/reagent in various asymmetric transformations.[1] Reduction[1b,g,2] of camphorquinone 3-oxime (**2**) appears to be the most common synthetic strategy[1b,g,2] for **1**. However the poor yield for the preparation of **2** *via* the nitrosation[3] of camphor led to the alternative protocols[1b,d,2c] employing costly camphorquinone (**3**) as the starting material. Realising the poor yield during the reported nitrosation procedure[3] to be a result of concomitant reduction of camphor by Na in EtOH or Et_2O, we planned to use nonreducing bases.[4] Acid catalysed nitrosation procedures[5] were avoided due to the possibility of Beckmann rearrangement of the resultant α-oximino ketone.[3c,6] We report in this communication that **2** could be prepared in high yields (70-100 %) following the nitrosation route under various conditions. However, the *anti/syn* ratio was found to be dependent upon the base/solvent combinations[7] and in most of the cases the *anti*-isomer was formed almost exclusively.[8]



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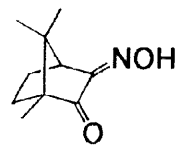

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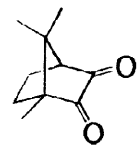

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In a typical experiment (1R)-(+)-camphor (7.61 g, 50 mmol) in dry THF (10 ml) was added dropwise to a magnetically stirred solution of ^{t}BuOK (1.73 g, 60 mmol) in dry THF (15 ml) at -30^{0}C under nitrogen. The mixture was stirred at -30^{0}C for 10 min., treated with ^{i}AmONO (7.03 g, 60 mmol), and left at room temperature under stirring for 12hr. The solvent was distilled off, the residue diluted with water and extracted with Et_2O to separate any neutral component. The aqueous part was acidified with cold HOAc and extracted with Et_2O to afford the crude oxime as light yellow solid which on crystallisation (hexane - EtOH) afforded the desired oxime[9] (7.7 g, 85 %).

References and Notes:

1. a. Colombo, L.; Giacomo, M. D.; Brusotti, G.; Milano, E. *Tetrahedron Lett.*, **1995**, 36, 2863; b. Bonner, M. P.; Thornton, E. R. *J. Am. Chem. Soc.*, **1991**, 113, 1299; c. Lowenthal, R. E.; Masamune, S. *Tetrahedron Lett.*, **1991**, 32, 7373; d. Kouklovsky, C.; Poulihes, A.; Langlois, Y. *J. Am. Chem. Soc.*, **1990**, 112, 6672; e. Itsuno, S.; Fréchet, J. M. J., *J. Org. Chem.*, **1987**, 52, 4140; f. Kitamura, M.; Suga, S.; Kawai, K.; Noyori, R. *J. Am. Chem. Soc.*, **1986**, 108, 6071; g. Ikota, N.; Sakai, H.; Shibata, H.; Koga, K. *Chem. Pharm. Bull.*, **1986**, 34, 1050; h. Kelly, T. R.; Arvanitis, A. *Tetrahedron Lett.*, **1984**, 25, 39.
2. a. Wilder, P. Jr.; Hsieh, W. C. *J. Org. Chem.*, **1971**, 36, 2552; b. Daniel, A.; Pavia, A. A. *Bull. Soc. Chim. Fr.*, **1971**, 1060. c. Chittenden, R. A.; Cooper, G. H.; *J. Chem. Soc. (C).*, **1970**, 49; d. Beckett, A. H.; Lan, N. T.; McDonough, G. R. *Tetrahedron*, **1969**, 25, 5689, 5693.
3. a. Smith, H. E.; Hicks, A. A. *J. Org. Chem.*, **1971**, 36, 3659; b. Cherry, P. C.; Cottrell, W. R. T.; Meakings, G. D.; Richards, E. E. *J. Chem. Soc. (C).*, **1968**, 459; c. Forster, M. O.; Rao, K. S. N. *J. Chem. Soc.*, **1926**, 2670.
4. Touster, O. *Org. React.*, **1967**, 7, 327.
5. a. Shamma. M.; Tomlinson, H. H. *J. Org. Chem.*, **1978**, 43, 2852; b. Cava, M. P.; Litle, R. L.; Napier, D. R. *J. Am. Chem. Soc.*, **1958**, 80, 2257.
6. a. Miljkovic, D.; Petrovic, J.; Stajic, M.; Miljkovic, M. *J. Org. Chem.*, **1973**, 38, 3585; b. Hassner, A.; Wentworth, W. A.; Pomerantz, I. H. *ibid*, **1963**, 28, 304.
7. Yield (%) and *anti/syn* ratio: $NaNH_2$/THF/-30^{0}C (90; 50:50); $NaNH_2/Et_2O$/-30^{0}C (85; 66:34); NaH/ Et_2O/-30^{0}C (85; 98:2); NaH/DMF/-30^{0}C (95; 100:0); KH/DMF/-30^{0}C (90; 100:0); KH/THF/-30^{0}C (70; 95:5); ^{t}BuOK/THF/-30^{0}C (85; 100:0); ^{t}BuOK/PhH/5^{0}C (100; 95:5); LDA/THF/-78^{0}C (90; 95:5).
8. *Anti/syn* ratios of 3:2 (ref. 3) and 5:1 (ref. 1b) were reported earlier. Pure *anti* oxime was obtained by boiling the mixture several hours in water(ref. 6a) or through repeated crystallisation (ref. 6b).
9. M.p. 150^{0}C; $[\alpha]^{25}_{D}$ +185^{0} (c 4.5, $CHCl_3$); IR (KBr): 3400, 1740, 1640 cm^{-1}; ^{1}H NMR(300 MHz, $CDCl_3$) δ 3.25(d, 1H, J = 4.4), 2.07-2.01(m, 1H), 1.82-1.77(m, 1H), 1.60-1.52(m, 2H), 1.03(s, 3H), 1.00(s, 3H), 0.88(s, 3H); CIMS(m/z): 182(100, MH^{+}).