Pergamon

Tetrahedron Letters 39 (1998) 2411–2412

TETRAHEDRON LETTERS

A Short Synthesis of the Tricarbocyclic Framework of Oreodaphnenol

Tarun K. Sarkar* and Sandip K. Nandy

Department of Chemistry, Indian Institute of Technology, Kharagpur-721302, India

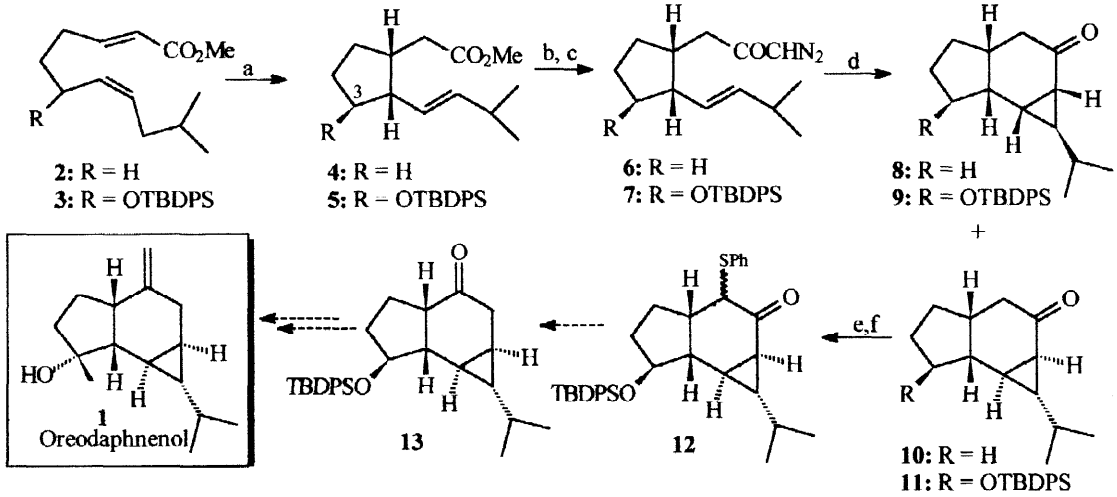
Received 25 November 1997; revised 16 January 1998; accepted 23 January 1998

In memory of Wolfgang Oppolzer

Abstract: A short synthesis of the carbon framework of oreodaphnenol, a recently isolated sesquiterpene alcohol is reported which entails two highly diastereoselective steps, e.g., a 5-(3,4) ene cyclization and a [Rh]-mediated cyclopropanation.

Oreodaphnenol (**1**) is a novel sesquiterpene alcohol isolated from Brazilizan tree, *Oreodaphnena Porosa* Mez[1] and contains an interesting 5-6-3 tricarbocyclic ring system. In connection with our on-going program to explore the potential of intramolecular ene reactions for organic synthesis,[2] we were interested in developing a flexible synthesis of **1**[1] which would also allow establishment of absolute configuration of this natural product which remains unsettled till to-day.[3] In this letter we report the synthesis of an advanced intermediate **12** for oreodaphnenol which entails two highly diastereoselective steps, e.g., a 5-(3,4) ene cyclization **3**→**5** and a $Rh_2(OAc)_4$ -mediated cyclopropanation **7**→**11** (Scheme 1).

Scheme 1



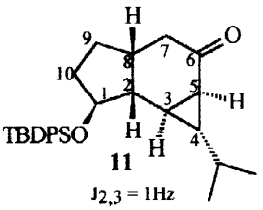
a) 235°C, toluene, 40h, 97%; b) KOH/MeOH, 90%; c) NaH/$(COCl)_2$, CH_2N_2, 90%; d) $Rh_2(OAc)_4/CH_2Cl_2$, r.t., 95%; e)TMSOTf/Et_3N, ether, 90%; f) PhSCl,-78°C, 90%.

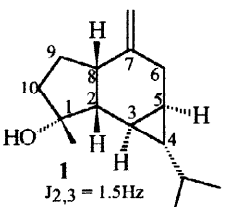
Our point of departure was the unsaturated ester **5**,[4] a high-yield synthesis of which was reported in a previous communication[2] from this laboratory by 5-(3,4) ene cyclization of a readily available 1,6-diene **3**. **5** was transformed into the α-diazo ketone **7** in the usual way in an overall yield of 81%. Since there was an element of uncertainty concerning the stereochemical outcome in the transition metal mediated cyclopropanation[5] **7**→**9/11**, it was deemed important to probe this point using a model compound, e.g., **6**.[6] The results of our initial attempts with either $CuSO_4$[7] or $Cu(TBS)_2$[8] were not encouraging as under these conditions **8** and **10** were formed in a ratio of 2:3, respectively. When the catalyst was changed to $Rh_2(OAc)_4$,[9]

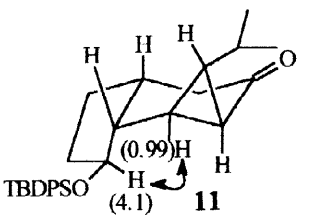
0040-4039/98/$19.00
PII: S0040-4039(98)00212-3

the diastereoselectivity in the cyclization improved thereby giving **10** as the preponderant product (**8/10** =1:4). Most interestingly, when **7** was exposed to 1 mol% $Rh_2(OAc)_4$ at room temperature, the diastereoselectivity in the cyclopropanation reaction took a dramatic turn and practically a single compound **11**[10] was obtained in very high yield (95%).

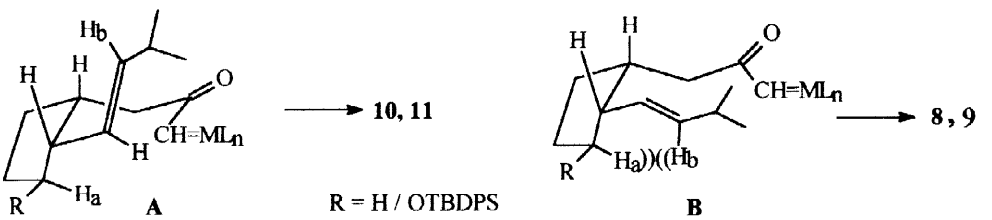
The structure and stereochemistry of tricyclic ketone **11** was determined by a combination of high-field (400 MHz) ^{1}H- & ^{13}C-NMR studies. Most importantly, the J values, e.g., $J_{2,3}$, $J_{3,4}$ and $J_{3,5}$ of **11** match nicely with the correspondig J values of oreodaphnenol (**1**).[1] In addition, in the 1D NOE experiment C1-H (δ 4.1) irradiation results in an enhancement of the signal due to C3-H at δ 0.99, thereby supporting the relative stereochemistry of **11**.







The formation of the tricyclic ketone **10** (major isomer) is accountable in terms of relevant transition state namely, **A**, which is favoured over **B** due to the absence of Ha and Hb interactions ($A^{1,3}$ - strain[11]). The much higher degree of diastereoselectivity in the case of **11** is probably due to the bulky TBDPS group which reduces Ha-Hb distance thus increasing steric crowding in **B**.



With **11** in hand, the stage was now set for the 1,2-carbonyl transposition[12] **11**→**13**, Wittig olefination, deprotection, oxidation and subsequent addition of MeLi from the *exo* face of the educt to deliver the natural product (Scheme 1). Although, paucity of **11** has not allowed us to complete the synthesis of **1**, we have found that further functionalization of **11** is possible *via* the corresponding enolsilane made with TMSOTf/Et_3N,[13] and exposure of the latter to PhSCl[14] to give **12** as a single product in very high yield (Scheme 1). Further transformation[12] of **12** to **13** and thence to the target molecule **1** is under vigorous investigation in this laboratory.

Acknowledgements: The support of CSIR, New Delhi [01(1368)/95-EMR-II] is gratefully acknowledged. The CSIR, New Delhi, is also thanked for the award of RA to SKN.

References and Notes:

1) Weyerstahl, P.; Marschall-Weyerstahl, H.; Wahlburg, H-C. *Liebigs Ann. Chem.* **1989**, 307. 2) Sarkar, T.K.; Ghorai, B.K.; Nandy, S.K.; Mukharjee, B.; Banerji, A. *J. Org. Chem.* **1997**, *62*, 6006 and references cited therein. 3) Private communication from Prof. P. Weyerstahl . 4). The C_3-diastereomer (~10%) present in **5**[2] was removed by fluoride induced O-Si bond cleavage, seperation of the corresponding alcohols and resilylation. 5) For a review see: McKervey, M.A.; Ye, T. *Chem. Rev.* **1994**, *94*, 1091. 6) **6** was prepared from **2** as described for **7**. 7) Srikrishna, A.; Krishnan, K. *J. Chem. Soc. Parkin Trans. 1* **1993**, 667. 8) Corey, E. J.; Myers, A. *Tetrahedron Lett.* **1984**, *25*, 3559. 9) Taber, D. F.; Hoerrner, R. S. *J. Org. Chem.* **1992**, *57*, 441. See also ref. 5. 10) 400 MHz ^{1}H-NMR shows the presence of a trace (~3%) of the other diastereomer, e.g., **9**. 11) For a review see: Hoffmann, R.W. *Chem. Rev.* **1989**, *89*, 1841. 12) For a review see: Kane, V. V.; Singh, V.; Martin, A.; Doyle, D. L. *Tetrahedron* **1983**, *39*, 345. 13) Frick, U.; Simchen, G. *Synthesis* **1984**, 929. 14) Trost, B.M.; Curan, D.P. *J. Am. Chem. Soc.* **1989**, *102*, 5699.