

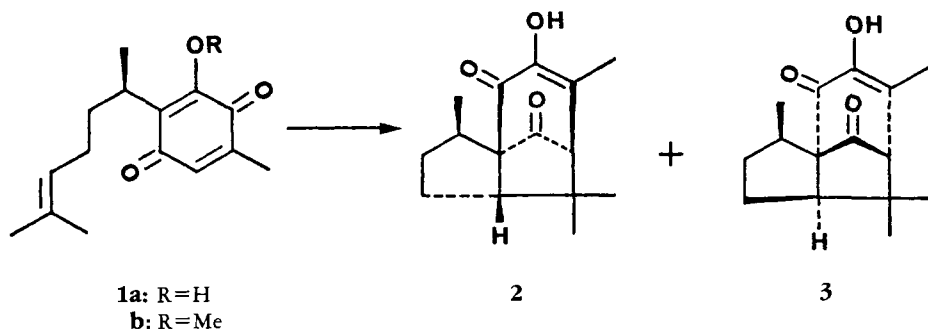
THE STEREOCONTROL OF THE PEREZONE TO
PIPITZOL TRANSFORMATIONI.H. SANCHEZ, F. BASURTO¹*Instituto de Química de la Universidad Nacional Autónoma de México,
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The remarkable transformation (1) of perezone (**1a**) into a mixture of α -pipitzol (**2**) and β -pipitzol (**3**) was rationalized (2, 3) and more recently proved (4) to occur through a concerted [$\pi^4s + \pi^2s$] cycloaddition (5) when the reaction is performed under thermal conditions that provide equal molar amounts of each tricyclic sesquiterpene (6).

Later on, it was found (7) that a highly stereoselective catalyzed-transformation, favoring the α -isomer (**2**) in a nine to one ratio, could be achieved by the boron trifluoride etherate treatment of perezone (**1a**).



In order to stereocontrol the transformation of the benzoquinone (**1a**) to any desired direction, it remained to find a set of reaction conditions under which the β -isomer (**3**) would be the predominant cycloaddition product. Thus, if one were able to alter drastically the stereochemical requirements of the reac-

tion intermediates using moderate temperature, such a stereocontrol could be plausible.

Along these lines, we now report that a stereocontrol in favor of the β -isomer (**3**) in a three to one ratio can be achieved under mild conditions by the AlCl_3 -diethyl sulfide treatment of *O*-methylperezone (**8**) (**1b**).

The change in the stereochemical outcome of the reaction of perezone (**1a**) with boron trifluoride against that of *O*-methylperezone (**1b**) with AlCl_3 -diethyl sulfide is due to transition state differences, since construction of Dreiding models clearly shows that for α -

pipitzol (**2**) there is (Figure 1A) a strong, nonbonded steric crowding between the secondary methyl and methoxyl groups. This situation is relieved for the case leading to β -pipitzol (**3**) as seen in Figure 1B. Furthermore, the *O*-methyl derivative (**1b**) with AlCl_3 gives rise to insoluble salts (9) that preclude further transformation. At the same time, the presence of a dialkyl sulfide is also required (10) since it helps to cleave any methoxyl-containing intermediates.

Achievement of stereocontrol for this

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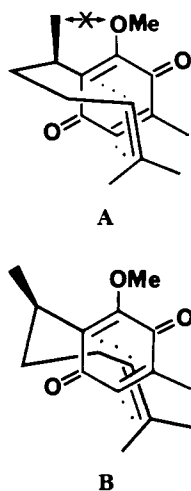


FIGURE 1. Molecular arrangements for the formation of α -pipitzol (A) and β -pipitzol (B) from *O*-methylperezone.

transformation in any desired direction should be of further utility because both syntheses of natural products (11, 12) and other transformations (13) have already been inspired by the perezone to pipitzol transformation.

EXPERIMENTAL

TRANSFORMATIONS OF *O*-METHYLPEREZONE (1b).—Solutions containing 130 mg (0.5 mmol) of *O*-methylperezone (8) (1b) and 200 mg (2.2 mmol) of diethylsulfide in anhydrous CH_2Cl_2 (10 ml) were cooled to 0° and treated portionwise with 15 mg (0.56 mmol) of AlCl_3 . After 90 min, the reaction mixtures were poured into ice H_2O and extracted with EtOAc. The organic layers were washed with diluted NaHCO_3 solutions and with H_2O , dried over anhydrous Na_2SO_4 , and evaporated to dryness under vacuum. The residues were separated by preparative tlc using GF-254 Merck silica-gel and a mixture of hexane- C_6H_6 - CHCl_3 -MeOH (20:20:1:1). The band showing R_f 0.53 was extracted with CHCl_3 , and the residues obtained after evaporation of the solvent under vacuum (44 mg, 36% yield) were subjected to pulse-FT pmr measurements at 80 MHz (FT-80A). The spectra displayed the familiar (7) signals owing to a mixture of α -pipitzol (2) and β -pipitzol (3) in a 1:3 ratio, as deduced from the integrated intensities (4) of the singlets at 2.83 and 2.76 ppm, respectively.

Further tlc separations, using hexane-EtOAc (9:1) as the mobile phase, provided pure specimens of 2 and 3, which were identical in all respects with authentic samples (14).

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