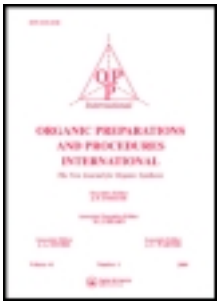

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A FACILE PREPARATION OF BUSPIRONE N-OXIDE USING DAVIS' REAGENT

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Collect. Vol. VIII, p. 486. This report describes a modification of the procedure reported in ref. 1 which uses 1:1 LDA:DMPU as the base for the deconjugative alkylation.

3. For safety reasons, DMPU was substituted for the HMPA used in the original procedure. When the deconjugative alkylations were run on the same scale in HMPA, products **5** and **6** were produced in 62% and 85% purified yields (unoptimized). Our lower yield of **5** in both solvents, compared with the earlier report of 90% by Schlessinger, likely results from mixing and localized heating problems associated with the larger scale used in the current reactions.

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7. This reaction also proceeded in HMPA but, for safety reasons, DMPU was used. The yield was essentially the same in both solvents.

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A FACILE PREPARATION OF BUSPIRONE N-OXIDE USING DAVIS' REAGENT

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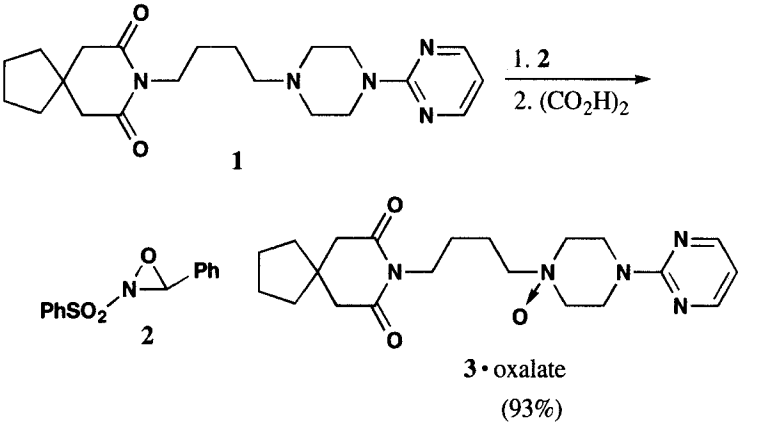
The heterocyclic compound 8-{4-[4-(2-pyrimidinyl)-1-piperazinyl]butyl}-8-azaspiro[4,5]-decane-7,9-dione (*buspirone*, **1**) is a novel, effective antianxiety drug.[1] It is equipotent with benzodiazepines but does not cause habituation and side-effects such as sedation, muscle relaxation, motor impairment and anticonvulsion that are associated with benzodiazepine therapy.[2] In a project related to the metabolism of *buspirone* (**1**), we required efficient access to buspirone N-oxide (**3**). Conversion of trialkylamines to the corresponding amine N-oxides by oxidation with hydrogen peroxide and peracids is well documented.[3] However, these reagents are also known to oxidize pyrimidines to pyrimidine N-oxides.[4] Indeed, when *buspirone* (**1**) was treated with one equivalent of the commercially available *m*-chloroperbenzoic acid in methylene chloride at 0°, a mixture of products was obtained which consisted of the buspirone N-oxide (**3**) and the other pyrimidine N-oxide in a ratio of 90:10. Attempts to purify this crude product by recrystallization were unsuccessful. The formation of the pyrimidine N-oxide by-product was due, at least in part, to the protonation of the most basic piperazine nitrogen by the resulting *m*-chlorobenzoic acid which resulted in the turnover of the oxidation

site to the pyrimidine nitrogen atoms.

Recently, Zajac and coworkers reported a highly selective oxidation of quinine with Davis' N-sulfonyloxaziridine **2**.[5] Because of the electrophilic and aprotic nature of N-sulfonyloxaziridines,[6] the oxidation of quinine with **2** took place at the quinuclidine nitrogen in the presence of the quinoline nitrogen atom and the chemoselectivity was >95%; the N-oxide was isolated by chromatography in 94% yield. The differentiation among trialkyl, dialkyl aryl and pyrimidinyl nitrogen atoms all in one molecule has not been reported previously. We now describe here a facile preparation of buspirone N-oxide (**3**) by using Davis' N-sulfonyloxaziridine without the involvement of chromatographic separation of products.



Thus, buspirone (**1**) was treated with 1.05 equivalent of 2-phenylsulfonyl-3-phenyloxaziridine (**2**)[7] in methylene chloride at room temperature. The oxidation was complete in one hour without to formation of even a trace amount of the undesired pyrimidine N-oxide, as evidenced by HPLC and ^{1}H NMR. The piperazine N-oxide was readily isolated in 93% yield as its oxalic acid salt **3**. No chromatographic separation of product was required.

EXPERIMENTAL SECTION

Melting points were determined on Mel-Temp apparatus and are uncorrected. ^{1}H NMR spectra were recorded in $CDCl_3$ and referenced to TMS (0.00 ppm) on a Bruker AC-P 300 FT NMR spectrometer. Buspirone was obtained from Bristol-Myers Squibb Co. 2-Phenylsulfonyl-3-phenyloxaziridine (**2**) was prepared according to literature procedure.[7]

Buspirone N-Oxide Oxalic Acid Salt (3).- In a 500 mL round bottom flask were placed buspirone (**1**, 11.57g, 30mmol) and methylene chloride (100 mL). The mixture was stirred at 25° to give a solution. Davis' N-sulfonyloxaziridine (**2**, 8.23g, 31.5mmol) was added as solid in one portion and the reaction was stirred for 1 hr. Oxalic acid (2.70g, 30mmol) then was added and the resulting mixture was stirred for 0.5 hr to give a solution. The solvent was then removed using a rotary evaporator and replaced by

ethyl acetate (250 mL). The resulting mixture was heated to reflux for 10 minutes. After cooling to room temperature, the white solid was collected, washed with ethyl acetate (3 x 50 mL) and dried to give 13.7 g (93%) of buspirone N-oxide oxalic acid salt (**3**), mp 114-116°C. ^{1}H NMR ($CDCl_3$): δ 8.37 (d, J = 4.2Hz, 2H), 6.62 (t, J = 4.2Hz, 1H), 4.79 (m, 2H), 3.98 (m, 2H), 3.80 (m, 6H), 3.23 (m, 2H), 2.59 (s, 4H), 1.90 (m, 2H), 1.65 (m, 6H), 1.47 (m, 4H).

Anal. Calcd. for $C_{23}H_{33}N_5O_7$: C, 56.20; H, 6.77; N, 14.25. Found: C, 56.12; H, 6.75; N, 14.20

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A FACILE METHOD FOR DEBROMINATION OF *vic*-DIBROMIDES

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Dehalogenation of organic halides is an important and widely utilized reaction in organic chemistry.[1] Although there have been reports on the application of organotellurium reagents to the dehalogenation of *vic*-dihalides,[2-5] the debromination of *vic*-dibromides by dibutyl telluride has never