tant for organic synthesis. Namely, [4 + 2] cycloaddition between furan and substituted 1,4-benzoquinones of type **2** cannot be expected to effectively proceed under thermal conditions. However, cycloadducts of furan and 1,4-benzoquinones can be synthesized by the high-pressure method according to our recently proposed procedure.[1]

Experimental Section

Melting points (uncorrected) were determined on a Kofler block. ^{1}H NMR spectra were recorded with a JEOL JNM-4H-100 spectrometer (δ scale, Me_4Si used as an internal standard). High-pressure experiments were performed in an apparatus of the piston-cylinder type, described in our earlier paper.[8]

***endo*-9,10-Dimethoxy-11-oxatricyclo[6.2.1.0^{2,7}]undeca-4,9-diene-3,6-dione (3a).** A sample (540 mg, 5 mmol) of **2a** and 640 mg (5 mmol) of **1** was dissolved in 5 mL of toluene. The mixture was placed in a Teflon brand ampule[9] which was inserted into a high-pressure vessel filled with ligroin as transmission medium, and it was closed with a mobile piston.[8] Then the high-pressure unit was placed between the pistons of a hydraulic press and the pressure was raised to 9.0 kbar at room temperature. The mixture was kept under these conditions for 20 h and decompressed. Subsequently crystalline **3a** which has precipitated under high pressure was immediately removed by filtration; 10 mL of ether were added to the filtrate, and this mixture was cooled to −10 °C to give the second crop of crystalline **3a**. The overall yield of analytically pure endo adduct **3a** was 1.02 g (86.5%): mp 89–90 °C; ^{1}H NMR spectrum cf. text.

Endo adduct 3b: obtained in the same manner, 89% yield; mp 86–87 °C; ^{1}H NMR δ 6.60 (q, J_{H-CH_3} = 2 Hz, 1 H), 5.18 (bs, 2 H_A), 3.68 (s, 6 H, OCH_3), 3.50 (bs, 2 H_B), 2.00 (d, J_{H-CH_3} = 2 Hz, 3 H, CH_3).

Endo adduct 3c: obtained in the same manner, 88.5% yield; dec over 50 °C; ^{1}H NMR δ 5.18 (bs, 2 H_A), 4.02 (s, 6 H, OCH_3), 3.72 (s, 6 H, OCH_3), 3.48 (bs, 2 H_B).

Kinetic Measurements. The experiments were carried out in a NMR tube (ϕ = 4 mm) in a chloroform-*d* solution (initial concentration 0.4 mmol/mL) at three temperatures: 26, 42, and 52 °C. Integration of the decreasing and increasing signals was measured at suitable time intervals between 0.5 and 2 min. The proton derived from $CHCl_3$ served as internal standard. The rate constants and activation energies were calculated by the least-squares method.

Acknowledgment. This work was supported by Polish Academy of Sciences Grant 03.10.

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Diphenylthiirene 1-Oxide. The Sulfoxide Functionality and Reactivity

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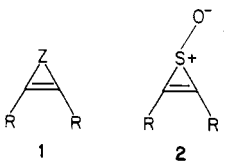
Systems of type **1** are unique: In cases of Z = O, S, NR, and PR they may be considered as "classically"antiaromatic as they have a cyclic array of 4nπ electrons predicted by theory to have little delocalization energy.[1]



On the other hand, on the basis of a naive analogy with cyclopropenones, the ground-state aromatic stabilization of which has been recently reconfirmed,[2] some kind of "aromaticity" can, in principle, be assigned to these systems when Z = SO or SO_2, assuming a possibility for transmission of electronic effects via π-conjugation.[3]

The thiirene oxide system **2** is of particular interest due to its being simultaneously both a potentially nonbenzenoid aromatic (4n + 2)π and antiaromatic 4nπ Hückel system.

The isolation and the characterization of the first diaryl-substituted members of this class of compounds (i.e., **2**, R = Ph)[4] enables one to carry out "bench scale" chemistry on this class of compounds under ordinary laboratory conditions.

To date, only the chemistry of 2,3-diphenylthiirene 1-oxide has been explored by Carpino et al.[4], whereas the first synthesis of alkyl-substituted thiirene sulfoxide was only very recently reported.[5] The possible preparation of the parent thiirene 1-oxide (i.e., **2**, R = H) is still under examination.[6]

On the basis of the available experimental data as well as extensive theoretical studies of the thiirene 1-oxide system,[7] the following conclusions concerning its structure, properties, and reactivity emerge: 1. Conjugative interactions and/or cyclic π-delocalizations are small compared with closely related systems.[7,8] 2. No significant antiaromatic destabilizing effects can be ascribed to the sulfur unshared pair of electrons. 3. The oxygen moiety in the sulfoxide function is not and probably should not be expected to be highly reactive. Thus, theoretical calculations predict[8] possible spiroconjugative-type[9] interaction between the $\pi^*_{C=C}$ orbital of the ring and the π orbitals of the SO (which leads to aromatic stabilization and a π charge transfer backwards from the SO to C=C). There exists, however, a rather strong destabilization of the $\pi^*_{SO}(d_{xz})$ orbital.[8] Experimentally, the ring carbon–carbon double bond rather than the sulfoxide function of thiirene 1-oxides was shown to be the primary active site of chemical attack.[4]

In order to study both the bonding in this Hückel molecule especially at sulfur—via an empirical carbon-13 NMR approach—and the chemical reactivity of the sulfoxide function as a result, we have gathered data on **1** (Z = SO and SO_2) and have investigated the reaction of the sulfoxide function of **2** with a variety of reagents.

We report here our results in this attempt to understand the relationship between bonding and chemical reactivity in molecules having this or similar structure.

Results and Discussion

The chemical shift of the vinylic carbon of 2,3-diphenylthiirene 1-oxide (**2a**) was found to be 137.3 ppm (downfield from Me_4Si) and those of the corresponding

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(2) Greenberg, A.; Tomkins, R. P. T.; Dobrovolny, M.; Liebman, J. F. *J. Am. Chem. Soc.* **1983**, *105*, 6855.
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(5) Ando, W.; Hanyu, Y.; Takata, T.; Ueno, K. *J. Am. Chem. Soc.* **1982**, *104*, 4981.
(6) Carpino, L. A. "The Petroleum Research Fund Reports on Research"; 1981, p 228.
(7) Ammon, H. L.; Faloon, L.; Plastas, L. A. *Acta Crystallogr., Sect. B* **1976**, *B32*, 2171.
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(9) (a) Simmons, H. E.; Fukunaga, T. *J. Am. Chem. Soc.* **1967**, *89*, 5208. (b) Schweig, A.; Weidner, U.; Hellwinkel, D.; Krapp, W. *Angew. Chem., Int. Ed. Engl.* **1973**, *12*, 310.

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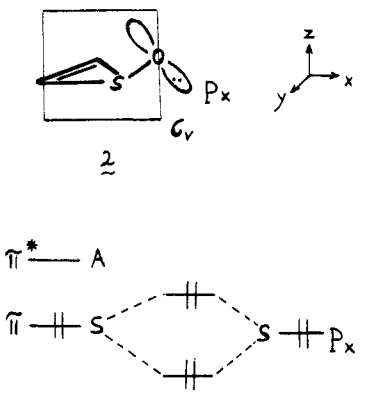
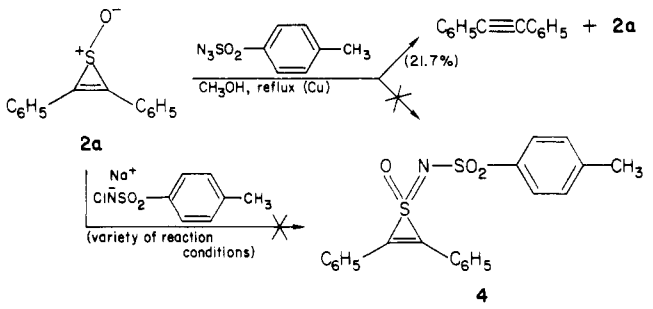


Figure 1.

Scheme I



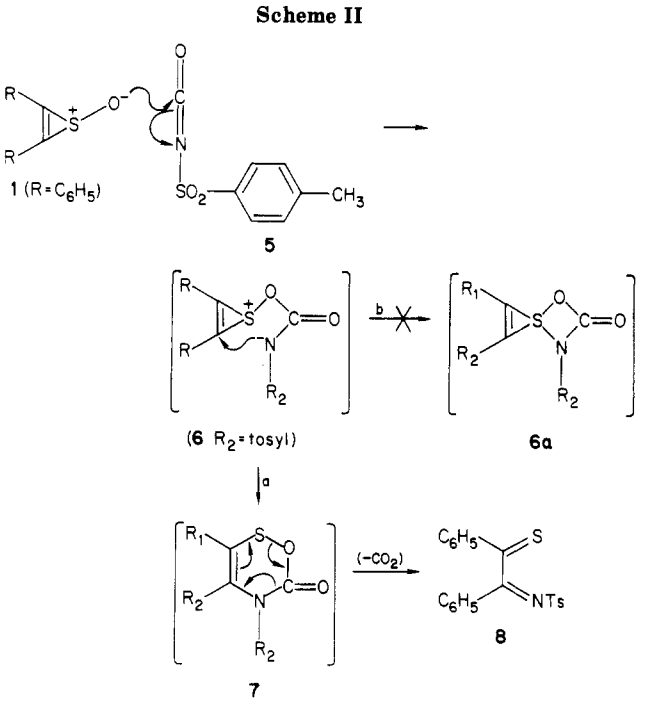
2,3-diphenyl- and 2,3-dimethylsulfone dioxides to be 158.9 and 167.4 ppm, respectively, compared with the reported values of 148.5 and 157.9 ppm for the 2,3-diphenyl- and 2,3-dimethylcyclopropenones, the analogous cycloketone Hückel systems. In comparing the degree of possible aromaticity (and therefore stability) of thiirene 1-oxides and thiirene 1-dioxides, we note that the degree of π-electron delocalization is expected to be proportional to the sulfur oxidation state, and the thiirene 1-dioxide **3** would have a higher C–S π-bond order than the thiirene 1-oxide **2**. The former molecule also has available spiroconjugative stabilization. On the other hand, the thiirene 1-oxide **2** suffers a homo-conjugative destabilization as is illustrated in the interaction diagram (Figure 1).

The ^{13}C chemical shift values found for the thiirene 1-oxide **2a** and the thiirene 1-dioxide **3a** corroborate these conclusions in suggesting a higher degree of aromaticity of the later compared with that of the sulfoxide **2a**. The need for particularly reactive reagents in order to facilitate reaction with the relatively low reactive sulfoxide function in the thiirene 1-oxide **2a**, (vide infra) is also in agreement with the bonding consequences of its unique structure.

Thus, numerous attempts to prepare the corresponding sulfilimine (or sulfoximine **4**) from the sulfoxide **2a** by using well-established methods applicable to other sulfoxides[10] failed. By using *p*-toluenesulfonyl azide, only diphenyl acetylene could be obtained in 21.7% yield apart from the recovered starting material **2a** (Scheme I).

In principle, the formation of the diphenylacetylene can be rationalized either in terms of oxidation of thiirene oxide **2a** to the corresponding sulfoximine **4** followed by hydrolysis to the sulfone and extrusion of sulfur dioxide under the reaction conditions or, alternatively, by assuming an extrusion of sulfur monoxide directly of the thiirene oxide under the catalytic influence of the zerovalent copper. The extrusion of sulfur dioxide of the analogous 2,3-diphenylthiirene dioxide has been shown to be catalytically affected by zero-valent transition-metal complexes.[11]

Scheme II



The sulfoxide function in the thiirene 1-oxide did react with the particularly electrophilic[12] *p*-toluenesulfonyl and chlorosulfonyl isocyanates. Hence, refluxing the sulfoxide **2a** with isocyanate **5** in methylene chloride for 24 h resulted in the isolation of the hitherto unknown deep blue "glassy" *N*-tosylmonothiobenzilimine **8** most probably due to the mechanism proposed in Scheme II.

The formation of **8** is in contrast to the formation of iminocyclopropenes in the reaction of activated isocyanates with cyclopropenones.[13]

Monothiobenzil was prepared about a decade ago by photolysis of the S-oxide of 2-benzoyl-2,4,5-triphenyl-1,3-oxathiole, by Dittmer et al., but could not be obtained in a pure form.[14] Interestingly, the physical characteristics of monothiobenzilimine **8** are quite similar to that of the monothiobenzil. Thus, both the UV and the fragmentation pattern of the two under electron impact conditions are remarkably alike.

Compound **8** resisted all attempts at crystalization and maintained its "glassy" appearance when not in solution. The analogous monothiobenzil in the solid state turns to a green polymeric glass and reverts after several hours to monomeric monothiobenzyl in inert solvents.[15]

Imine **8**, however, dimerizes in inert nonpolar solvents after standing at room temperature for several days. Heating the crude solid dimer **9** (which still contains some monomeric **8**) leads to the deep blue "glassy" monomer (eq 1).

The dimerization of thiobenzilimine **8** is not surprising: most thioketones are known to exist as dimers in solution,[16]

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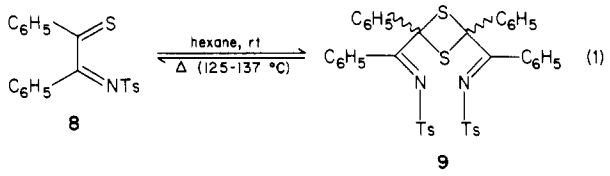
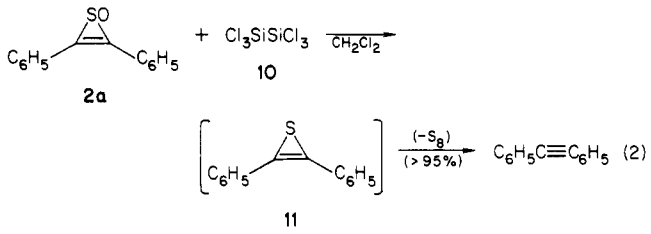
(15) Saville, B.; Steer, M. *J. Chem. Soc. Chem. Commun.* **1972**, 616.



including the closely related α-thio keto esters.[17]

The assigned structure of dimer **9** is based on physical and spectroscopic data (see Experimental Section) as well as on the comparison with the analogous monothiobenzil–monothiobenzil dimer pair.[18]

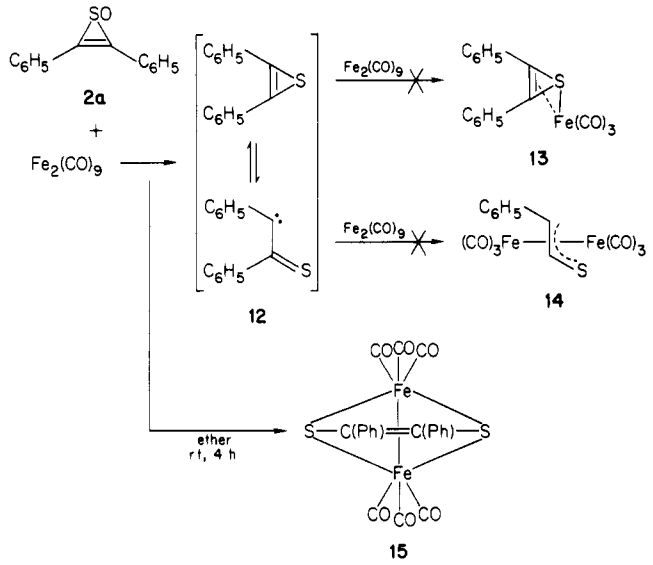
The deoxygenation of **2a** was readily affected under mild conditions by using hexachlorodisilane (**10**) as the reducing agent[19] to give diphenylacetylene as the isolated product (eq 2).



The intermediacy of thiirene **11** along the reaction coordinate has not been established as yet. Nevertheless, thiirenes were calculated to lie in a local energy minima,[20] implying that under appropriate reaction conditions they should be isolable or, at least, capable of being trapped.

Based on the well-known fact that certain reactive antiaromatic cyclodienes can be stabilized when complexed with a metal carbonyl moiety,[21] we anticipated the isolation of a stable thiirene–iron carbonyl complex **13** by reacting the sulfoxide **2a** with a diiron nonacarbonyl according to the deoxygenation[22]–complexation[21,23] route depicted in Scheme III. Unexpectedly, however, neither complex **13** nor the stable complex **14**—known to be formed in reactions where intermediate **12** is involved[24]—was isolated. Instead, the red organosulfur–iron complex **15**[25] was isolated in reasonable yield (see Experimental Section). This result is rather surprising since the formation of complex **15** requires the cleavage of three (1) carbon–sulfur bonds in the thiirene system. Although the mechanism of the formation of **15** from thiirene 1-oxide **2a** is as yet a matter of speculation, the formation of organosulfur–iron complexes of this type in the reaction of iron carbonyls with

Scheme III



various sulfur-containing compounds is quite common.[25]

Given the above experimental results (particularly those related to Schemes I and II), it can be fairly concluded that (1) the oxygen moiety in thiirene 1-oxides is not as nucleophilic (and consequently reactive) as the oxygen moieties of ordinary sulfoxides and (2) conjugative interactions which lead to both aromatic stabilization (although small compared with closely related systems)[7-9] and a strong destabilization of the $\pi^*_{SO}(d_{xz})$ orbital may account for the observed relatively low reactivity of the sulfoxide function in thiirene 1-oxides, compared with that of other acyclic and saturated cyclic sulfoxides. Any reaction with the sulfoxide function in thiirene 1-oxides should overcome a substantial energy barrier in order to be realized. Thus, there is a good correlation between theoretical predictions and experimental results in this case. Further studies of the thiirene 1-oxide system are currently being conducted.

Experimental Section

^{13}C NMR spectra were recorded on Varian XL-100 and JOEL PF-100 spectrometers in $CDCl_3$, with Me_4Si as internal reference. ^1H NMR spectra were recorded on a Varian T-60 instrument, and the IR with a Beckman 4240 high-resolution spectrometer. MS were obtained with a Hitachi MAT 112S.

Reaction of Thiirene 1-Oxide with *p*-Toluenesulfonyl Isocyanate: *N*-Tosylmonothiobenzilimine (8). 2,3-Diphenylthiirene 1-oxide (**2a**) (0.6395 g, 2.83 mmol) and isocyanate **5** (0.6131 g, 3.11 mmol) were refluxed in anhydrous methylene chloride (7 mL) under argon for 24 h. The blue reaction mixture was chromatographed on a column packed with silica gel (Fisher, 100–200 mesh) to yield a deep blue "glass" (300 mg, 27.8%), the spectroscopic and physical data of which were in full agreement with the assigned structure **8**. The remaining material eluted from the column was the recovered unreacted sulfoxide **2a**. Compound **8** could not be recrystallized from any solvent and/or a mixture of solvents. Solutions of **8** in nonpolar organic solvents (hexane, etc.) gave after several days the colorless dimer of **8** (i.e., **9**). Imine **8** has the following spectral data: IR ($CHCl_3$) 1584, 1553 (s, C=N), 1447, 1325 (s, NSO_2), 1271, 1159 (vs, NSO_2), 1089, 683 cm^{-1}; UV (95% EtOH) λ_{max} 607 nm (ϵ 26); ^1H NMR ($CDCl_3$) δ 8.13–7.64 (m, 6 H, Ar), 7.64–7.09 (m, 8 H, Ar), 2.43 (s, 3 H, CH_3); MS, *m/e* 379 (M^+), 331 (M – SO), 313, 258 (M – PhCS), 155 (CH_3 – Ph – SO_2), 121 (PhCS), 105 (base peak); ^{13}C NMR δ 196.69 (C=S), 175.0 (C=N), 143.55–127.22 (C Ar), 21.5 (CH_3). Anal. Calcd for $C_{21}H_{17}NO_2S_2$: C, 66.46; N, 3.68; S, 16.92. Found: C, 66.46; N, 3.68; S, 16.90.

Dimerization of Thiobenzilimine 8. An off-yellow solid is separated out from solutions of compound **8** in either hexane or hexane–ehter which was left to stand at room temperature for

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several days. The dimer **9**—separated by filtration—is not pure (contains trace amounts of the "glassy" blue monomer). On heating, the crude dimer **9** turns into the "glassy" deep blue monomer at 125–137 °C. The IR spectrum of the colorless crude dimer **9** is quite similar to that of the monomer **8**, and its methyl group gives a singlet at δ 2.40 (downfield from Me_4Si) in the ^1H NMR spectrum.

Deoxygenation of 2,3-Diphenylthiirene 1-Oxide (2a) with Hexachlorodisilane (10). The sulfoxide **2a** (0.155 g, 0.685 mmol) and the deoxygenation agent **10** (0.1882 g, 0.7 mmol) were mixed together in dry CH_2Cl_2 (5 mL) for 1 h. Workup according to the procedure of Mislow et al.[19] afforded diphenylacetylene in essentially quantitative yield (0.125 g). The spectrophotometric data of the product were identical with those of an authentic sample.

Reaction of Thiirene 1-Oxide 2a with Diiron Nonacarbonyl: Synthesis of the Organosulfur–Iron Complex (μ,μ'-(*cis*-Stilbene-α,β-dithiolato))bis(tricarbonyliron) (15). 2,3-Diphenylthiirene 1-oxide (**2a**) (1.215 g, 5.37 mmol) and diiron nonacarbonyl (1.953 g, 5.37 mmol) were stirred in anhydrous ether (150 mL) at room temperature over a period of 4 h. The dark red etheral solution was filtered through a Celite filter aid (to remove unreacted iron carbonyls), and then it was chromatographed on a column packed with silica gel to yield 0.969 g (34.6%) of a red viscuous oil. A second chromatography using benzene as an eluant afforded the pure complex **15** (0.785 g, 28%) as a viscous dark red oil which solidified in the refrigerator (no optimization of the yield was attempted). The spectral data and the elemental analysis of the product **15** were in full agreement with that of the known **15**,[25] including the single-crystal X-ray analysis:[26] ^{13}NMR δ 207.8 (CO), 131.7–123.4 (C Ar), 89.4 (C=C).

Acknowledgment. This research was supported by a grant from the United States–Israel Binational Science Foundation (BSF), Jerusalem, Israel, and is gratefully acknowledged. Also, the author wishes to thank the NIH for support.

Registry No. **2a**, 31247-21-9; **5**, 4083-64-1; **8**, 94731-68-7; **9**, 94731-69-8; **10**, 13465-77-5; **15**, 14406-62-3; diphenylacetylene, 501-65-5; diiron nonacarbonyl, 15321-51-4.

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Chiral Synthesis of Doxpicomine

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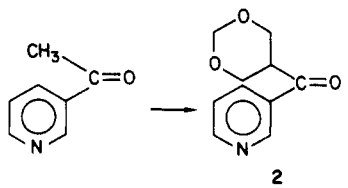
Received August 21, 1984

The syntheses and novel analgesic activities of a variety of 1,3-dioxanylamines were described by Booher.[1] One compound from this group, (*R*)-α-(1,3-dioxan-5-yl)-*N*,*N*-dimethyl-3-pyridinemethanamine hydrochloride (**1**),[2] was selected for further biological study. Recently, the analgesic activity of **1**, doxpicomine, in humans was reported.[3] In support of such studies, a more efficient synthesis of this compound was needed.

While examining other approaches to doxpicomine a procedure was devised to prepare conveniently the 1,3-dioxan-5-yl 3-pyridyl ketone (**2**) in one step in 57% yield by condensation of 3-acetylpyridine with paraformaldehyde and boron trifluoride etherate in acetic acid.



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Various routes were examined to utilize this ketone in a chiral synthesis. The successful route followed the work of Nichols,[4] who reduced imines prepared from (S)-(−)-α-methylbenzylamine and various phenylacetones. A similar procedure was also used by Pirkle[5] for the synthesis of (*S*)-(+)-2,2,2-trifluoro-1-phenylethylamine. The route devised is depicted in Scheme I.

The ketone **2** reacted sluggishly with (*S*)-(−)-α-methylbenzylamine in the preparation of the imine. With acid catalyst in a hydrocarbon solvent with removal of water, yields of 70% were obtained. Yields of greater than 90% were obtained by using titanium tetrachloride[6] in methylene chloride. Slightly more than 1 equiv of the α-methylbenzylamine was used and 6 equiv of triethylamine were added as the acid scavenger.

Although the imine was not crystalline and could not be purified, spectral data confirmed its structural assignment as **3**. Both the ^{13}C and ^{1}H NMR spectra indicate that the imine is present principally as a single geometric isomer. Comparison of the ^{13}C spectrum of the imine with that of the ketone as described by Bunnell and Fuchs[7] shows an upfield shift of the 2 and 4 carbons of the pyridine ring of 7.14 and 1.71 ppm. The carbons of the dioxane portion show only a small downfield shift. Thus the pyridyl and α-methylbenzylamine groups are assigned syn geometry. In a recent report[8] a 4:1 ratio of *E* and *Z* isomers was found for the imine base prepared from 2-norbornanone and (*R*)-α-methylbenzylamine.

Initially, catalytic hydrogenation was used in reduction studies and the product was evaluated by HPLC.[9] Using 10% Pd–C, modest diastereomeric selection was found at room temperature: 72% of the desired ***R*,*S*** diastereomer and 28% of the *S*,*S* diastereomer (44% de). Hydrogenation at 0–5 °C gave only a slight improvement in this ratio (56% de). Nichols[4] found high diastereoselection in his series of compounds using these conditions. Reduction with sodium cyanoborohydride and acid gave similar results, 50% de, with **3**. Again these conditions were similar to those of Pirkle where reduction of some fluoroalkylated imines gave good diastereoselection.

Surprisingly, the diastereoselection on reduction of **3** was markedly improved by using sodium borohydride in methanol. With 1 molar equiv of borohydride at room temperature an 80% de was obtained. The best diastereoselection was found at −45 to −40 °C where 88% de was obtained routinely.

The diastereomeric ratio obtained reflects the presence of a single geometric isomer as seen by ^{13}C NMR. The product obtained is best explained by the Felken[10] model

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