tion) and opening the possibility of alternative purification methods such as cationic exchange chromatography.

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Registry No. I, 116596-44-2; II, 116633-81-9; III, 116596-45-3; IV, 116596-46-4; BOC-Ser-OH, 3262-72-4; BOC-Thr-OH, 2592-18-9; (4-Pic)Cl, 10445-91-7; BOC-Ser(4-Pic)-OH, 116596-36-2; BOC-Thr(4-Pic)–OH, 116633-80-8; H-Ser(4-Pic)-OH, 116596-37-3; H-Ser-OH, 56-45-1; BOC-Asp-OH, 13726-67-5; BOC-Glu-OH, 2419-94-5; (3-Pic)OH, 100-55-0; BOC-Asp(O(3-Pic))-O(3-PIc), 116596-38-4; BOC-Glu(O(3-Pic))-O(3-Pic), 116596-39-5; BOC-Asp(O(3-Pic))-OH, 116596-40-8; Boc-Glu(O(3-Pic))-OH, 116596-41-9; BOC-Asp(1-piperidinyl)-OH, 116596-42-0; BOC-Glu(1-piperidinyl)-OH, 116596-43-1; BOC-Ser(Bzl)-OH, 23680-31-1; BOC-Asp(OBzl)-OH, 7536-58-5; BOC-Pro-OH, 15761-39-4; BOC-Gly-OH, 4530-20-5; BOC-Phe-OH, 13734-34-4; BOC-Val-OH, 13734-41-3; Fmoc-Ala-OH, 35661-39-3; H-Pro-Pro-Gly-Phe-Ser-Pro-OH, 23828-06-0; H-Ala-Gly-Asp-Val-OH, 99896-90-9; H-Asp-OH, 56-84-8; H-Glu-OH, 56-86-0; $(i\text{-Pr})_4N^+ \cdot ClO_4^-$, 116596-47-5.

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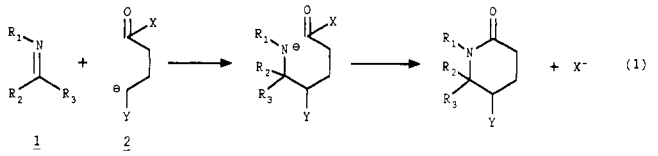
Remote Dianions. 3. Novel Synthesis of Substituted 2-Piperidones from Imines[1]

Summary: The dianion of 4-(phenylsulfonyl)butanoic acid reacts with imines activated by boron trifluoride etherate to afford, after cyclization, substituted 2-piperidones.

Sir: Imines have been relatively under utilized (yet easily prepared[2]) functional groups in the synthesis of heterocycles. Recently, certain derivatives of imines have been employed in cycloaddition chemistry,[3] and addition reactions to the imine moiety have been reported[4] (primarily via activation with Lewis acids), opening new opportunities for the construction of aza heterocyclic compounds. Indeed, an intramolecular extension of this latter process seemed particularly attractive to us since the second linkage, subsequent to addition of a nucleophile, could be formed by dehydration or acylation (eq 1; X = OR, OH, etc.).



1 2 (1)

Previously, we reported that the dianion of 4-(phenylsulfonyl)butanoic acid (4-PSBA) (**2**; X = O^-, Y = $PhSO_2$) reacts readily with a variety of carbonyl compounds to afford, after tandem cyclization assisted by trifluoroacetic anhydride (TFAA), pentanolides in good yield.[5] Application of this method to imines should provide rapid entry to the analogous nitrogen compounds (2-piperidones), assuming addition to the imine is successful. These derivatives would be of wide general interest owing to the number of piperidine natural products.[6] We now report that the reaction of imines activated with $BF_3 \cdot Et_2O$[7] with 4-PSBA dianion leads to 2-piperidones in high yields in a simple, one-pot process (eq 2, Table I).

In a general procedure, the dianion of 4-PSBA (THF; 4.25 mmol, 0.075 M) was generated as previously described.[5] The dianion was maintained at −78 °C while in a separate flask the imine (4 mmol) was dissolved in 7 mL of THF and chilled to −78 °C. $BF_3 \cdot Et_2O$ (4 mmol) was added to the imine solution, occasionally giving a milky suspension (depending on imine). The activated imine was added to the yellow dianion solution via cannula or syringe. After the addition was complete, the mixture generally became colorless. The mixture was allowed to stir at −78 °C for 0.5 h to complete the addition. Then TFAA (8 mmol) was added at −78 °C, the cold bath was removed, and the mixture was stirred an additional 0.5 h. The reaction was diluted with an equal volume of diethyl ether and poured into saturated bicarbonate. Isolation of the crude product by crystallization ($CHCl_3/Et_2O$) or flash chromatography (100% ether) gave pure lactam.[8] The results of this sequence are presented in Table I.

It is evident that both aldimines and ketimines are amenable to addition–cyclization with 4-PSBA. Entry **3e**, which involved addition to the benzyl imine of cyclohexanone, is of particular interest since the 1-azaspiro[5.5]undecan-2-one, a model for histrionicotoxin and congeners,[9] is formed in good yield from inexpensive materials.

To extend the utility of this method would require effective desulfonylation of the intermediates **3a–f**.[10] At

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(7) The nature of this "activation" has not been established although the mechanism has been examined. See: Eis, M. J.; Wrobel, J. E.; Ganem, B. *J. Am. Chem. Soc.* **1984**, *106*, 3693.

(8) Compounds **3a–f** exhibited satisfactory analytical and spectral data.

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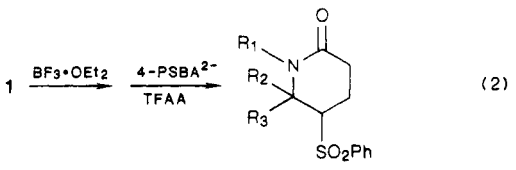
Table I. Boron Trifluoride Promoted Addition of 2 to Imines



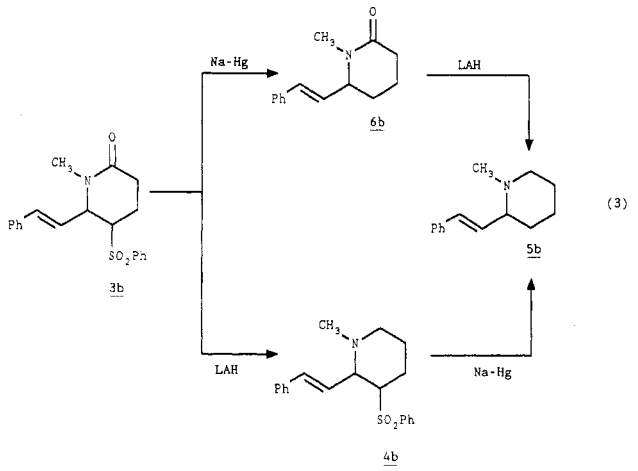
(2)

3a-f

entry	R_1	R_2	R_3	yield,[a] %	mp, °C
3a	*n*-Pr	*n*-Pr	H	70	150
3b	CH_3	PhCH=CH	H	82	116
3c	CH_3	Ph	H	90	155
3d	$PhCH_2$	*n*-Pr	H	66	124–5
3e	$PhCH_2$	$-(CH_2)_5-$		78	187
3f	CH_3	citryl[b]	H	85	136

[a] Isolated yields. [b] Citryl = $(CH_3)_2C{=}CHCH_2CH_2(CH_3)C{=}CH$.

present, there is scant information available on β-amido or β-amino sulfone eliminations, but it is reasonable to assume that lactams **3a–f** could be cleaved by this process. We examined both possibilities with the 6-cinnamyl lactam **3b** (eq 3) as this allylic system should be most sensitive



(3)

to the reaction conditions.[10d] Prior reduction of lactam **3b** to piperidine **4b** with LAH[11] and subsequent treatment with 6% sodium amalgam in methanol[12] afforded a 60% overall yield of desulfonylated product **5b**.[13] More interestingly, direct desulfonylation[10a] of the lactam **3b** yields 2-piperidone **6b** (93%). Treatment with LAH converted the lactam to piperidine **5b** (71%), suggesting this methodology will accommodate a wide variety of structural manipulation without ring scission.[14] The trans geometry of the olefin was preserved in all transformations. Further structural evidence was provided by conversion of lactam **3c** (Na–Hg then LAH; 55% overall) into the known 1-methyl-2-phenylpiperidine.[15]

The efficiency of this process and the ready availability of imines promises to provide a facile route to piperidine-containing natural products. We are currently examining this aspect and extension to chiral substrates.

Acknowledgment. We wish to thank Loyola University of Chicago for the purchase of the Varian 300-MHz NMR instrument used in this study. D.L.C.G. wishes to thank the Graduate School and R.K. wishes to thank Baxter Healthcare Corporation for financial support.

Supplementary Material Available: NMR spectral data for compounds **3a–f**, **4**, **5**, and **6** are available (10 pages). Ordering information is given on any current masthead page.

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(13) (a) Compound **5b**: bp 92 °C (0.3 mmHg); ^1H NMR ($CDCl_3$, 300 MHz) δ 1.25–1.3 (m, 1 H), 1.48 (dq, *J* = 3.5, 1 H), 1.56–1.65 (m, 3 H), 1.70–1.75 (m, 1 H), 1.99 (dt, *J* = 4 and 11.3, 1 H), 2.21 (s, 3 H), 2.44 (dt, *J* = 3 and 8, 1 H), 2.88 (d, *J* = 8, 1 H), 6.12 (dd, *J* = 16 and 9, 1 H), 6.45 (d, *J* = 16, 1 H), 7.15–7.35 (m, 5 H); ^{13}C NMR ($CDCl_3$, 300 MHz) δ 23.9, 26.0, 33.5, 44.6, 56.5, 68.0, 126.2, 127.2, 128.5, 130.5, 133.7, 137.2. Anal. Calcd for $C_{14}H_{19}N$: C, 83.53; H, 9.51; N, 6.96. Found: C, 83.43; H, 9.69; N, 6.89. (b) Hasiak, B. *Bull. Soc. Chim. Fr.* **1976**, *9–10*, 1526.

(14) 5-Phenylsulfonyl lactam **3b** (1 mmol) was dissolved in 5 mL of dry methanol and chilled to 0 °C; 6% Na–Hg amalgam (finely crushed) was added portionwise with vigorous stirring over 0.25 h. After an additional 0.25 h of mixing, the reaction mixture was filtered through Celite, diluted with ether, extracted, and dried. Compound **6b**: bp 166 °C (0.3 mmHg); ^1H NMR ($CDCl_3$, 300 MHz) δ 1.78–2.04 (m, 4 H), 2.40 (q, *J* = 8 and 13.6, 2 H), 2.91 (s, 3 H), 4.01 (q, *J* = 11.2 and 5.4, 1 H), 6.07 (dd, *J* = 15.8 and 7, 1 H), 6.42 (d, *J* = 16, 1 H), 7.21–7.37 (m, 5 H); ^{13}C NMR ($CDCl_3$, 300 MHz) δ 17.8, 29.2, 32.1, 33.4, 61.3, 126.3, 127.8, 128.5, 129.0, 131.6, 170.3.

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Isobraunicene, Wolficene, and Isowolficene. New Cyclic 1′–3 Fused Isoprenoids from *Botryococcus braunii*

Summary: Three new isoprenoid hydrocarbons, isobraunicene (**2**), wolficene (**3**), and isowolficene (**4**), were isolated from the Berkeley strain of *Botryococcus braunii*. ^1H NMR and mass spectra indicate the compounds contain terminal methylenecyclohexane rings like that in braunicene (**1**). Isobraunicene is a C_{32} regioisomer of **1** with the ring at the opposite end of the isoprenoid chain. Wolficene and isowolficene are C_{31} regioisomers with methylenecyclohexane rings at the same ends of the chain as **1** and **2**, respectively.

Sir: The B form of *Botryococcus braunii*, a fresh water colonial green alga, produces and accumulates a family of 1′–3 linked isoprenoid hydrocarbons, which constitute up to 75% of its biomass.[1–3] Pulse-chase experiments indicate that a parent C_{30} triterpene formed by condensation of two farnesyl residues is successively methylated by *S*-adenosyl

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