Reaction of 7-Fluorobenzo[c]phenanthrene-5,6-quinone with Acetophenone. The reaction of 2 (0.75 mg, 2.7 μmol), acetophenone (200 μL, 1.7 mmol), and H_2O (200 μL) in MeCN (1 mL) at 37 °C after a prolonged period of time (several days), yielded predominantly one product in quantity sufficient for characterization. Excess acetophenone was removed under a stream of argon followed by high vacuum. The product (8) was purified by HPLC (Zorbax SIL column (0.94 × 25 cm) eluted with 75/25 CH_2Cl_2/ethyl acetate at 4 mL/min): t_R (min) 17; HRMS (EI) m/z calcd for $C_{26}H_{17}O_3F$ 396.1162, found 396.1155; MS (EI) m/z 396 (M^+), 378 ($M^+ - H_2O$), 349 ($M^+ - H_2O - CHO$), 276 ($M^+ - C_6H_5COCH_3$), 248 ($M^+ - CO - C_6H_5COCH_3$); ^1H NMR ($CDCl_3$, 300 MHz) δ 3.36 (d, 1 H, J = 15.90 Hz, CH_aH_b), 4.01 (d, 1 H, CH_aH_b), 4.46 (s, 1 H, OH), 7.3-8.7 (14 H, aromatic); UV λ_{max} (90/10 MeOH/H_2O) 264.5 nm. The minor acetophenone adduct was not isolated in quantities sufficient for NMR but had a similar UV spectrum to the ether 4, UV λ_{max} (90/10 MeOH/H_2O) 228.5, 258.5 (shoulder) nm.

Conversion of the Ether 4 to Its Regioisomer 5. A small amount of the pure ether 4 dissolved in 4/1 acetone/H_2O (500 μL) containing 2-methylnaphthalene (125 μg, internal standard) was added to an amber screw-top vial, and the mixture was maintained at 25 °C. Samples (10 μL) were assayed by HPLC (Zorbax ODS column (0.46 × 25 cm) eluted with a linear gradient of 75/25 MeOH/H_2O to 100% MeOH at 1.1 mL/min over 15 min): t_R (min) 4, 5.6; 5, 6.0; 2-methylnaphthalene, 11.9.

Acknowledgment. We gratefully acknowledge the participation of Drs. Paul Ortiz de Montellano (University of California at San Francisco), Shimoga Prakash, Archie Sinhababu, Gerald Miwa, and Dan Sternbach (Glaxo Inc.) and Roland Lehr (University at Oklahoma) in many helpful discussions. We thank Mr. Douglas J. Minick (Burroughs Wellcome Co.) for his help in obtaining the FTIR spectra.

Supplementary Material Available: ^1H and ^{19}F spectra of the fluoroquinone 2 and the ethers 4 and 5 and results of ^{19}F-[^1H] heteronuclear decoupling experiments (4, 5) and of the NOE experiment (5) (6 pages). Ordering information is given on any current masthead page.

2(*S*),3-Pyridinediyl Thiocarbonate Reagent. Reactions with Amines

Daniel A. Laufer* and Emile Al-Farhan

Department of Chemistry, University of Massachusetts at Boston, Boston, Massachusetts 02125

Received April 24, 1990

Activated derivatives of carbonic acid may be regarded as bifunctional acylating reagents for the preparation of carbonate esters, ureas, carbamates, mixed carbonic anhydrides, carboxylic acids, esters, ketones, aldehydes, and other derivatives following two successive reactions with appropriate nucleophiles. Examples of such useful reagents include phosgene or triphosgene,[1] carbonyldiimidazole,[2] (alkyloxy)- or (aryloxy)carbonyl chlorides,[3,4] (α-haloalkyloxy)carbonyl chlorides,[5] dialkyl dicarbonates,[6] 2,2′-carbonylbis(3,5-dioxo-4-methyl-1,2,4-oxadiazolidine),[7] and others.[8] We also note that several diactivated ester derivatives of carbonic acid have been applied as acylating reagents in organic synthesis. Known carbonates of this type include bis(*p*-nitrophenyl),[9] 1,2,2,2-tetrachloroethyl *N*-succinimidyl,[10] and the di-2-pyridyl.[11] Comparable applications of cyclic carbonic acid esters such as the *o*-(4-nitrophenylene) carbonate,[12] 4,6-diphenylthieno[3,4-*d*]-1,3-dioxol-2-one 5,5-dioxide[13] or the 1,2(*S*)-pyridinediylium thiocarbonate[14] have not been often reported and merit further notice. Given the expected stability and convenient handling of such reagents, and in view of recent demand for more specific and less toxic chemicals[15] coupled with ongoing development of automated synthetic procedures,[16] we seek new cyclic diesters of carbonic acid as alternative diacylating reagents. In this paper we report the synthesis of a novel cyclic carbonate ester of 2(1*H*)-thioxo-3-pyridinol: 2(*S*),3-pyridinediyl thiocarbonate (2-oxo-1,3-oxathiolo[4,5-*b*]pyridine, 1, or PTC) and its regiospecific reactions with several primary and secondary amines.

Table I. Preparation of Disubstituted Ureas[a]

urea	N,N′-substituents	reaction solvent	isolated yield,[b] %
2a	dicyclohexyl	THF	93
2a	dicyclohexyl	H_2O	91
2b	diphenyl	C_6H_6	91
2c	dibenzyl	EtOAc	91
2d	diallyl	THF	90
2e	phenylallyl	THF	81

[a] Reaction 2. [b] Of ureas listed in ref 17.

Table II. Preparation of 2-Thioxopyrid-3-yl Carbamates[a]

carbamate	N-substit R	N-substit R′	react cond[b]	isol yield, %
3a	H	c-hexyl	A	81
3b	H	allyl	A	75
3c	*N*-piperidinyl		B	87
3d	*N*-pyrrolidinyl		B	91

[a] Reaction 3. [b] A: Dropwise addition of amine in THF at room temperature for 3 h. B: Rapid addition of amine in THF at room temperature for 3 h.

Results and Discussion

2(*S*),3-Pyridinediyl Thiocarbonate. Treatment of 2(1*H*)-thioxo-3-pyridinol (HOPyS) with carbonyldiimidazole (Im_2CO)[2] or 1,1′-carbonylbis(2-methylimidazole)

(1) (a) Hirschmann, R.; Schwam, H.; Strachan, R. G.; Schoenewaldt, E. F.; Barkemeyer, H.; Miller, S. M.; Conn, J. B.; Garsky, V.; Veber, D. F.; Denkewalter, R. G. *J. Am. Chem. Soc.* **1971**, *93*, 2746-2754. (b) Eckert, H.; Forster, B. *Angew. Chem., Int. Ed. Engl.* **1987**, *26*, 894-895.

(2) Staab, H. A. *Angew, Chem., Int. Ed. Engl.* **1962**, *1*, 351-367.

(3) (a) Vaughan, J. R., Jr.; Osato, R. L. *J. Am. Chem. Soc.* **1951**, *73*, 3547. (b) Anderson, G. W.; Zimmerman, J. E.; Callahan, F. M. *J. Am. Chem. Soc.* **1966**, *88*, 1338-1339.

(4) Anderson, G. W.; McGregor, A. C. *J. Am. Chem. Soc.* **1957**, *79*, 6180.

(5) Sennyey, G.; Barcelo, G.; Senet, J.-P.; Bensoam, J.; Loffet, A. *Synthesis* **1986**, *8*, 627.

(6) (a) Tarbell, D. S.; Yamamoto, Y.; Pope, B. M. *Proc. Natl. Acad. Sci. U.S.A.* **1972**, *69*, 730-732. (b) Moroder, L.; Hallett, A.; Wunsch, E.; Keller, O.; Wersin, G. *Hoppe-Seyler Z. Physiol. Chem.* **1976**, *357*, 1651-1653.

(7) Denarie, M.; Grenouillat, D.; Malfroot, T.; Senet, J.-P.; Sennyey, G.; Wolf, P. *Tetrahedron Lett.* **1987**, *28*, 5823-5826.

(8) (a) Anderson, G. W.; Zimmerman, J. E.; Callahan, F. M. *J. Am. Chem. Soc.* **1964**, *86*, 1839. (b) Nagasawa, T.; Narita, K.; Isowa, Y. *Bull. Chem. Soc. Jpn.* **1973**, *46*, 1269.

(9) (a) Wieland, T.; Heinke, B.; Vogeler, K. *Liebigs Ann. Chem.* **1962**, *655*, 189. (b) Glatthard, R.; Matter, M. *Helv. Chim. Acta* **1963**, *46*, 795.

(10) Jaouadi, M.; Martinez, J.; Castro, B.; Barcelo, G.; Sennyey, G.; Senet, J.-P. *J. Org. Chem.* **1987**, *52*, 2364-2367.

(11) Kim, S.; Ko, Y. K. *J. Chem. Soc., Chem. Commun.* **1985**, 473.

(12) (a) Fife, T. H.; McMahon, D. *J. Org. Chem.* **1970**, *35*, 3699-3704. (b) Laufer, D. A.; Doyle, K.; Zhang, X. *Org. Prep. Proced. Int.* **1989**, 771-776.

(13) Kirstgen, R.; Olbrich, A.; Rehwinkel, H.; Steglich, W. *Liebigs Ann. Chem.* **1988**, 437-440.

(14) Barton, D. H. R.; Crich, D.; Motherwell, W. B. *J. Chem. Soc., Chem. Commun.* **1983**, 939-941.

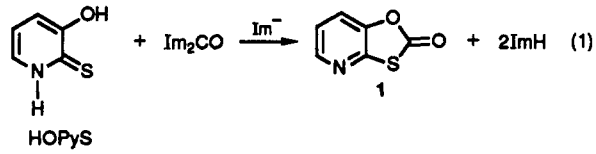
(15) Haffin, J. *Chem. Eng. News* **1987**, *65*, 26.

(16) (a) Frisbee, A. R.; Nantz, M. H.; Kramer, G. W.; Fuchs, P. L. *J. Am. Chem. Soc.* **1984**, *106*, 7143-7145. (b) Kramer, G. W.; Fuchs, P. L. *Chem. Tech.*, in press (and references cited therein).

(17) Weast, R. C., Astle, M. J., Eds. *CRC Handbook of Data on Organic Compounds*, Vol. 2; CRC Press: Boca Raton, 1985.

0022-3263/91/1956-0891$02.50/0

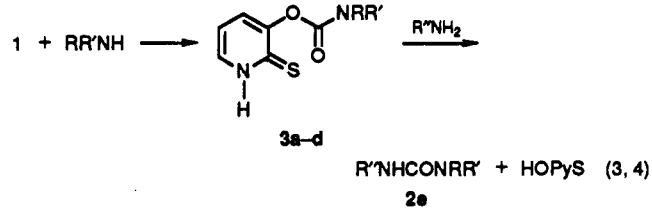
in combination with sodium imidazolide catalyst in tetrahydrofuran (THF) gave the pyridinediyl thiocarbonate (PTC) as white needles in 86–94% yields following crystallization from *n*-hexane. IR, NMR, UV, MS, and elemental analyses were consistent with structure 1 in reaction 1.



Reactions of PTC (1) with Amines. Preparation of Symmetrical Ureas. As indicated by reaction 2 and Table I, treatment of PTC with excess primary amines in THF, EtOAC, or benzene at room temperature led to symmetrically disubstituted ureas **2a–d** in 90–93% yields. Dicyclohexylurea (**2a**) was also prepared in water, suggesting potential biochemical applications in aqueous media.

$$1 + 2RNH_2 \rightarrow \underset{\textbf{2a–d}}{RNHCONHR} + HOPyS \qquad (2)$$

Stepwise Reactions of PTC with Amines. The path of these reactions was investigated by treating PTC with 1 equiv of amine to isolate the expected carbamate intermediate. We reasoned that since 3-pyridyl carboxylic esters[18] are aminolyzed more slowly than 2-pyridyl thioesters,[19] the 2-pyridyl thioxide leaving group of PTC might be displaced at a faster rate than the alternative 3-pyridoxide on attack by amine nucleophile. 2-Thioxopyrid-3-yl carbamates **3a–d** would thus be generated exclusively. As shown by reaction 3 and Table II, this was indeed the case.



Structural formulas **3a–d** are assigned in accord with observed negative $FeCl_3$ tests for the 3-pyridinol functionality,[20] ^{13}C NMR chemical shifts and IR NH bands of **3c** and **3d**, in addition to IR carbamate CO bands at 1700–1720 cm^{-1} of **3a–d**. Since reaction 3 may be competitive with 4, precautionary measures such as maintaining the amine/PTC molar ratio at about 0.9, adding the less nucleophilic amine first and dropwise, keeping the reaction temperature near 0 °C, and selecting less polar solvents to promote carbamate precipitation should be undertaken for the more reactive primary amines. Such measures are not necessary for secondary amines because the corresponding carbamates do not react with the second secondary amine equivalent at room temperature. The smaller rate differential of reactions 3 and 4 for primary amines may stem from base-catalyzed formation of isocyanate intermediates (which is not possible for secondary amines).[21]

Finally, the conclusion that reaction 3 is regiospecific for primary as well as secondary amines was tested by reacting PTC with 1 equiv of aniline in *n*-hexane at room temperature, followed by in situ addition of allylamine. *N*-Phenyl-*N'*-allylurea (**2e**, Table I) precipitated immediately and was isolated in 81% yield. We conclude that PTC is a suitable and convenient reagent for the preparation of N,N'-disubstituted ureas. The reactivity and selectivity of PTC with amine nucleophiles is attributed to electron withdrawal by the pyridine nitrogen and to the emergent tautomeric thiolactim/thiolactam array in the carbamate intermediate and the HOPyS byproduct. Related carboxylic esters or thioesters of 2-thioxo-3-pyridinol,[22] 2-oxo-3-pyridinol,[22] 2-pyridinethiol,[19,23] or 2-pyridinol[24] exhibit rate or yield enhancements by conversion to the more stable tautomer,[25] by concerted proton transfer through tautomeric interconversion,[26] by intermolecular base catalysis[27] or by anchimeric assistance.[19] The reactions reported here are likewise characterized by relatively high rates in nonpolar solvents and by regiospecificity. This fact suggests that at least some of the above mechanisms are operative in this system. To the extent that PTC is so catalyzed in its reactions, it is distinguishable from known 1,3-benzoxathiol-2-one derivatives[28] which lack such tautomeric arrays.

Experimental Section

General Procedures. Melting points were determined on a capillary melting point apparatus without correction. Solid products were sampled in KBr disks for IR analysis. ^1H and ^{13}C NMR chemical shifts of samples in $CDCl_3$ were referenced to internal solvent peaks of $CHCl_3$ at 7.24 and $CDCl_3$ at 77.00 ppm, respectively. THF was distilled once from CaH_2. Other materials were used as supplied.

2(*S*),3-Pyridinediyl Thiocarbonate (1, PTC). A solution of HOPyS (1.27 g, 10 mmol) in dry THF (25 mL) was treated with ~5 mol % NaIm catalyst (freshly prepared by dissolving Na in an aliquot of 0.2 M ImH/THF stock solution equivalent to ~5 mol % PTC). The mixture was stirred for 10 min at room temperature, and a solution of Im_2CO (1.78 g, 11 mmol) in THF (30 mL) was dripped in under N_2 for ~2 h and left stirring overnight.[29] The solvent was evaporated to an oily residue, which was extracted with hot *n*-hexane (10 mL), swirled, and decanted into another flask. This extraction was repeated 5–8 times with decreasing volumes of hot *n*-hexane, the extracts were pooled, and PTC crystallized out on gradual cooling. Evaporation of the filtrate yielded a second crop of PTC. The PTC fractions were recrystallized from *n*-hexane, affording 1.37 g (90%) of white needles: mp 83–84 °C; IR 1750 (C=O), 1590 (C=C), and 1410 cm^{-1} (C=N); λ_{max} 281.5 nm (ϵ 8800); MS *m/z* 153; ^1H NMR 7.23–7.31 (H6), 7.46–7.52 (H4), and 8.31–8.34 ppm (H5); ^{13}C NMR 147.1, 144.2, 122.4, 118.1, 146.3 (py C2–C6), and 166.0 ppm (C=O). Anal. Calcd for $C_6H_3NO_2S$: C, 47.05; H, 1.98; N, 9.15; S, 20.93. Found: C, 47.20; H, 2.22; N, 9.10; S, 20.82. An alternative procedure substitutes 1,1'-carbonylbis(2-methylimidazole), i.e. $(MeIm)_2CO$, for Im_2CO to eliminate the multiple *n*-hexane extractions. HOPyS (2.54 g, 20 mmol) was dissolved in THF (100 mL) and treated with ~5 mol % NaIm prepared as above. Following 10 min of stirring, $(MeIm)_2CO$ (4.18 g, 22 mmol) was added to the solution, and the reaction flask was sealed for overnight stirring at room

(18) Taschner, E.; Rzeszotarska, B. *Liebigs Ann. Chem.* **1965**, *690*, 177–181.
(19) Lloyd, K.; Young, G. T. *J. Chem. Soc. C* **1971**, 2890–2896.
(20) 2(1*H*)-Thioxo-3-pyridinol gives a positive $FeCl_3$ test.
(21) Bender, M. L.; Homer, R. B. *J. Org. Chem.* **1965**, *30*, 3975–3978.
(22) Laufer, D. A.; Setterlund, C., unpublished results from this laboratory.
(23) Corey, E. J.; Clark, D. A. *Tetrahedron Lett.* **1979**, 2875–2878 and references cited therein.
(24) Dutta, A. S.; Morley, J. S. *J. Chem. Soc. C* **1971**, 2896–2902.
(25) Carey, F. A.; Sundberg, R. J. *Advanced Organic Chemistry Part B*; Plenum Press: New York, 1983 (2nd ed); p 123.
(26) Rony, P. R. *J. Am. Chem. Soc.* **1969**, *91*, 6090–6096.
(27) Su, C.-W.; Watson, J. W. *J. Am. Chem. Soc.* **1974**, *96*, 1854–1857.
(28) (a) Greenwood, D.; Stevenson, H. *J. Chem. Soc.* **1953**, 1514–1519. (b) Pantlitschko, M.; Benger, H. *Monatsh. Chem.* **1950**, *59*, 1871. (c) Burton, H.; David, S. B. *J. Chem. Soc.* **1952**, 2193.
(29) Dispensing with the nitrogen atmosphere by simply sealing the reaction vessel following rapid rather than dropwise addition of Im_2CO appeared to reduce yields by only a few percent.

temperature. The THF solvent was evaporated to half volume, and the reaction mixture was cooled overnight at −10 °C to precipitate the 2-MeIm byproduct. The filtrate was evaporated to yield crude PTC, which upon crystallization from *n*-hexane yielded 2.78 g (91%) of PTC, mp 83–84 °C.

General Procedure for the Preparation of Symmetrical Ureas. The known symmetrical ureas[17] listed below were prepared in yields listed in Table I by adding the amine (11–15 mmol, 22 mmol for $C_6H_5NH_2$) to a solution of PTC (5 mmol) in THF or EtOAc (10–15 mL) and stirring at room temperature for 3–10 h. Except for **2d**, the precipitated products were isolated by suction filtration of the reaction suspension followed by crystallization from the indicated solvents.

***N,N'*-Dicyclohexylurea (2a)**: crystallized from $CHCl_3$, mp 231–232 °C (lit. mp 232–233 °C). In an alternative aqueous preparation, $C_6H_{11}NH_2$ (1.48 g, 15 mmol) was added to a suspension of PTC (0.765 g, 5 mmol) in water (50 mL) for an overnight reaction at room temperature. Filtration of the precipitate followed by crystallization from $CHCl_3$ yielded 1.14 g, mp 231–232 °C.

***N,N'*-Diphenylurea (2b)**: crystallized from EtOAc, mp 238–239 °C (lit. mp 238 °C). ***N,N'*-Dibenzylurea (2c)**: crystallized from ethanol, mp 168–169 °C (lit. mp 168 °C). ***N,N'*-Diallylurea (2d).** This product was isolated by addition of *n*-hexane to the reaction solution and filtration of the resultant suspension, mp 92–94 °C (lit. mp 91–93 °C). ***N*-Phenyl-*N'*-allylurea (2e)** (in situ). A solution of PTC (1.53 g, 10 mmol) in THF (15 mL) was treated with aniline (0.93 g, 10 mmol) in *n*-hexane (200 mL) dropwise for 30 min at room temperature without observed precipitation. To this solution was added allylamine (0.57 g, 10 mmol), and the product precipitated immediately.[30] After stirring for 15 min, the urea was filtered and crystallized from benzene, affording 1.42 g, mp 115–116 °C (lit. mp 115–116 °C).

General Procedure for the Preparation of Secondary Carbamates 3a–b. Dropwise addition of the primary amine (10 mmol) either neat or in *n*-C_6H_{14} (150 mL) to a stirred solution of PTC (11 mmol) in THF (15 mL) and *n*-C_6H_{14} (40 mL) for 45–60 min at 0 to −10 °C precipitates the product. It is isolated by filtration and crystallization from the indicated solvent in the yields listed in Table II.

2-Thioxopyrid-3-yl cyclohexylcarbamate (3a): crystallized from C_6H_6; mp 145–146 °C; IR 3310 (NH), 1700–1720 cm^{-1} (C=O). Anal. Calcd for $C_{12}H_{16}N_2O_2S$: C, 57.12; H, 6.40; N, 11.10; S, 12.70. Found: C, 57.35; H, 6.54; N, 11.09; S, 12.50. **2-Thioxopyrid-3-yl allylcarbamate (3b)**: crystallized from $CHCl_3$; mp 110–111 °C; IR 3280 (NH), 1700 cm^{-1} (C=O). Anal. Calcd for $C_9H_{10}N_2O_2S$: C, 51.41; H, 4.80; N, 13.31; S, 15.25. Found: C, 51.58; H, 4.74; N, 13.10; S, 15.08.

General Procedure for the Preparation of Tertiary Carbamates 3c–d. A solution of PTC (10 mmol) in THF (25 mL) is mixed with the secondary amine (10 mmol), and the solution is stirred for 2–3 h at room temperature. The carbamate is isolated by solvent evaporation and crystallization from EtOAc.

2-Thioxopyrid-3-yl Piperidinylcarbamate (3c): mp 117–118 °C; IR 1715 cm^{-1} (C=O); GCMS *m/z* 238; ^{13}C NMR 171.9, 151.8, 129.9, 113.2, 133.9 (py C2–C6), 151.6 (C=O), 45.9, 45.4, 25.5, 24.2 ppm (pip C_α–C_γ). **2-Thioxopyrid-3-yl pyrrolidinylcarbamate (3d)**: mp 135–137 °C; IR 3320 (NH), 1720 cm^{-1} (C=O); MS *m/z* 224; ^{13}C NMR 171.8, 151.6, 130.1, 113.3, 133.9 (py C2–C6), 151.6 (C=O), 46.6, 46.5, 25.6, 24.9 ppm (pyrr C_α–C_β).

Acknowledgment. Carbon-13 NMR spectra were obtained at the NMR facilities of the Francis Bitter National Magnet Laboratory, Massachusetts Institute of Technology. The NMR facility is supported by Grant 00995 from the Division of Research of the National Institutes of Health and by the National Science Foundation under Contract C-76D. Assistance provided by Dr. David Ruben is appreciated.

(30) Since the *N*-allyl 2-thioxopyrid-3-yl carbamate (**3b**) was isolated in 75% yield, the sequence of amine addition may be reversed in this case.

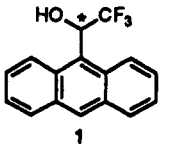
Enantioselective Reduction of Aryl Trifluoromethyl Ketones with BINAL-H. A Preparation of 2,2,2-Trifluoro-1-(9-anthryl)ethanol

J. Michael Chong* and Eduardo K. Mar

Guelph-Waterloo Centre for Graduate Work in Chemistry, Department of Chemistry, University of Waterloo, Waterloo, Ontario, Canada N2L 3G1

Received June 12, 1990

In connection with a study on the enantioselective synthesis of γ-lactones,[1] we required 2,2,2-trifluoro-1-(9-anthryl)ethanol [(*R*)- or (*S*)-**1**] for determination of optical purity by ^1H NMR spectroscopy.[2] Owing to the relatively high cost of this reagent[3] and the necessity of a severalfold (typically 3 mol equiv) excess of it to produce nonequivalence, we sought an alternative and economical route to this compound.



1

One possible route to **1** is the asymmetric reduction of 9-anthryl trifluoromethyl ketone (**2a**). In 1977, Pirkle reported the asymmetric reduction of **2a** with a reducing agent derived from lithium aluminum hydride and a chiral oxazoline, providing (*R*)-**1** in 51% ee.[2] Since that time, however, numerous asymmetric reducing agents have been developed,[4] and it was our expectation that one could be found to reduce **2a** with much better selectivity. Furthermore, we were interested in the effect of the trifluoromethyl group on the enantioselectivity of some asymmetric reductions since, in contrast to the voluminous literature on the reduction of alkyl aryl ketones, there were very few reports of the asymmetric reduction of trifluoromethyl ketones.[5-7]

A brief survey of the reagents most commonly used for the asymmetric reduction of alkyl aryl ketones revealed that Noyori's BINAL-H reagent[8] reduces **2a** and other "hindered" aryl trifluoromethyl ketones in good to excellent enantioselectivities.[9] Other asymmetric reducing agents were ineffectual. For example, reduction of **2a** with Itsuno's reagent[10a] [derived from BH_3 and (*S*)-2-amino-3-

(1) Chong, J. M.; Mar, E. K. *Tetrahedron Lett.* **1990**, *31*, 1981.
(2) Pirkle, W. H.; Sikkenga, D. L.; Pavlin, M. S. *J. Org. Chem.* **1977**, *42*, 384.
(3) The price of (*R*)- or (*S*)-**1** is $24.30/100 mg (Aldrich).
(4) For a comparison of various asymmetric reducing agents for the reduction of different classes of ketones, see: Brown, H. C.; Park, W. S.; Cho, B. T.; Ramachandran, P. V. *J. Org. Chem.* **1987**, *52*, 5406.
(5) (a) BINAL-H reduction of fluoroalkyl alkynyl ketones: Hanzawa, Y.; Kawagoe, K.; Kobayashi, Y. *Chem. Pharm. Bull.* **1987**, *35*, 2609. (b) Yeast reduction of aryl trifluoromethyl ketones: Bucciarelli, M.; Forni, A.; Moretti, I.; Torre, G. *Synthesis* **1983**, 897.
(6) There are several scattered reports on the asymmetric reduction of 2,2,2-trifluoroacetophenone. Enantioselectivities ranged from 0.7 to 77% ee. (a) Brown, H. C.; Pai, G. G. *J. Org. Chem.* **1985**, *50*, 1384. (b) Midland, M. M.; Kazubski, A. *J. Org. Chem.* **1982**, *47*, 2495. (c) Baba, N.; Matsumura, Y.; Sugimoto, T. *Tetrahedron Lett.* **1978**, 4281. (d) Nasipuri, D.; Bhattacharya, P. K. *J. Chem. Soc., Perkin Trans. 1* **1977**, 576. (e) Morrison, J. D.; Tomaszewski, J. E.; Mosher, H. S.; Dale, J.; Miller, D.; Elsenbaumer, R. L. *J. Am. Chem. Soc.* **1977**, *99*, 3167. (f) Seebach, D.; Daum, H. *Chem. Ber.* **1974**, *107*, 1748.
(7) After this work was completed, Corey reported the reduction of **2a** with a modified "CBS" reducing agent consisting of a chiral *B*-*n*-butyloxazaborolidine as catalyst and catecholborane. (*R*)-**1** was obtained in 94% ee and >95% yield. Corey, E. J.; Bakshi, R. K. *Tetrahedron Lett.* **1990**, *31*, 611.
(8) Noyori, R.; Tomino, I.; Tanimoto, Y.; Nishizawa, M. *J. Am. Chem. Soc.* **1984**, *106*, 6709.
(9) For all reductions described in this work, the BINAL-H reagent with EtOH as coligand was used.

0022-3263/91/1956-0893$02.50/0