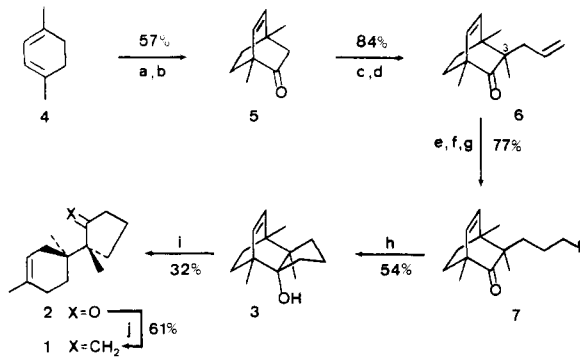
Scheme I[a]



[a] Reagents: (a) CH_2=C(CN)Cl, toluene, 90 °C; (b) $Na_2S \cdot 9H_2O$, EtOH, reflux, 24 h; (c) LDA, THF, −70 °C, then CH_3I, HMPA, −30 °C; (d) LDA, THF, −70 °C, then CH_2=$CHCH_2I$, HMPA, −60 °C; (e) 9-BBN, THF, then 30% aqueous H_2O_2, NaOH; (f) TsCl, C_5H_5N; (g) LiBr, acetone, reflux, 1.5 h; (h) Li, THF, 0 °C; (i) KH, HMPA, 140 °C, 1 h; (j) Ph_3P=CH_2, Me_2SO, 80 °C.

the reaction mechanism (eq 3) is believed to involve heterolytic cleavage of the allylic C(1)–C(2) bond in **3a** and rearrangement of the resultant allylic anion **2a** to the potassium enolate **2b**, which is subsequently protonated to afford **2**. Finally, Wittig methylenation as described[2c] furnished (±)-**1** in 61% yield.[14]

Registry No. (±)-**1**, 61505-17-7; (±)-**2**, 61375-52-8; (±)-**3**, 89398-34-5; **4**, 26120-52-5; (±)-**5**, 89398-35-6; (±)-**6**, 89398-36-7; (±)-**7**, 89398-37-8; CH_2=C(CN)Cl, 920-37-6; CH_2=$CHCH_2I$, 556-56-9.

(12) Spectroscopic data (IR, 360-MHz ^1H NMR, MS) of **2** are identical with those of an authentic sample provided by Professor R. H. Schlessinger. ^{13}C NMR ($CDCl_3$) δ 223.7 (s), 132.4 (s), 119.8 (d), 53.9 (s), 40.8 (t), 36.3 (s), 33.7 (t), 33.1 (t), 27.9 (t), 27.4 (t), 23.2 (q), 18.7 (t), 18.4 (q), 18.3 (q). For another stereoselective synthesis of **2**, see: Yamakawa, K.; Sakaguchi, R.; Nakanura, T.; Watanabe, K. *Chem. Lett.* **1976**, 991–992.

(13) The only moderate yield of **2** is believed to result in part from a competing alkoxide accelerated retro-Diels–Alder reaction of **3a**; isolation of 2-methyl-1-cyclopentanone from the reaction mixture supports this hypothesis. For a related precedent, see ref 4.

(14) ^1H and ^{13}C NMR spectra of (±)-**1** are identical with those of natural trichodiene provided by Professor D. E. Cane.

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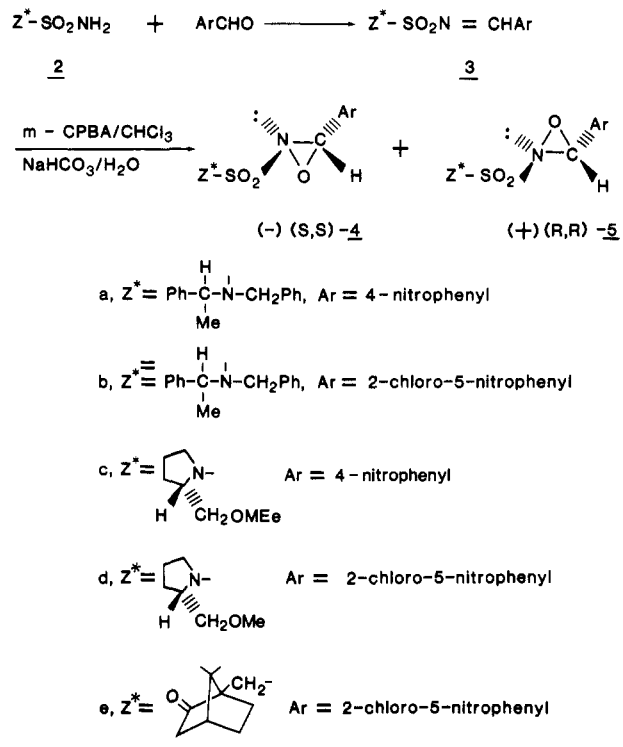
Chiral Sulfamides: Synthesis of Optically Active 2-Sulfamyloxaziridines. High Enantioselectivity in the Asymmetric Oxidation of Sulfides to Sulfoxides

Summary: The first synthesis of optically active 2-sulfamyloxaziridines **4a–d** and **5a–d**, which affords high enantioselectivity (38–68% ee) for asymmetric oxidations of sulfides to sulfoxides, is described.

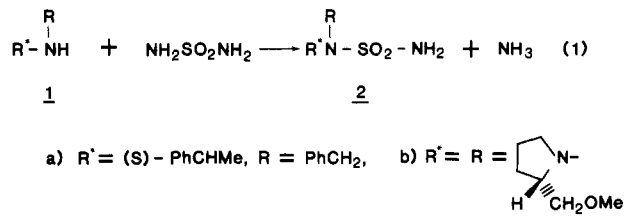
Sir: Although sulfamides ($R_2NSO_2NH_2$) have been known and studied for many years,[1] there are only a few synthetic procedures employing these reagents.[2] Furthermore, there

Scheme I



appear to be no optically active examples of these compounds. As part of a program to explore chiral sulfamides in organic synthesis we report the first examples of optically active sulfamides and their application to the synthesis of chiral 2-sulfamyloxaziridines **4a–d** and **5a–d** (Scheme I). Chiral 2-sulfamyloxaziridines are a new class of asymmetric oxidizing agents that afford the best enantioselectivity (38–68% ee) of any reagent for the oxidation of sulfides to sulfoxides.

Chiral sulfamide **2a**, 78% yield, mp 89–90 °C; $[\alpha]_D$ −22.0° (*c* 2.28, $CHCl_3$), was prepared by heating equivalent amounts of (−)-(*S*)-*N*-(α-methylbenzyl)-*N*-benzylamine (**1a**)[3] and sulfamide ($NH_2SO_2NH_2$) in dry dimethoxyethane for 3 days as described by McManus et al. (eq 1).[5] With



(+)-(*S*)-2-(methoxymethyl)pyrrolidine (**1b**)[6] this procedure gave only a 51% yield of sulfamide **2b**, mp 60–62 °C; $[\alpha]_D$ −3.46° (*c* 2.0, $CHCl_3$) after 5 days. However, the yield of **2b** was improved to 66% when the two reagents were heated in the absence of the solvent for 24 h (90 °C for

(1) For reviews on the chemistry of sulfamic acids that include discussions of sulfamides, see: (a) Spillane, W. J. *Int. J. Sulfur Chem.* **1973**, *8*, 469. (b) Benson, G. A.; Spillane, W. J. *Chem. Rev.* **1980**, *80*, 151. (c) Andersen, K. K. *Compr. Org. Chem.* **1979**, *3*, 363.

(2) Sulfamides have been primarily used in the synthesis of heterocyclic systems. In addition to the examples given in ref 1: (a) 1,2,6-Thiadiazirine 1,1-dioxides, Wright, J. B. *J. Org. Chem.* **1964**, *29*, 1905. Elguero, J.; Ochoa, C.; Stud, M.; Estaban-Calderon, C.; Martienz-Ripoll, M. *Ibid.* **1982**, *47*, 536. (b) Thiadiazine 1,1-dioxides, Timberlake, J. W.; Hodges, M. L. *J. Am. Chem. Soc.* **1973**, *95*, 634.

(3) This amine was prepared according to the procedure of Anderson and Santi[4] except that (−)-(*S*)-α-phenylethylamine (Hexcel) was used in the place of the racemic amine; $[\alpha]_D$ −39.9° (neat).

(4) Anderson, R. T., Jr.; Santi, D. V. *J. Med. Chem.* **1976**, *19*, 1270.

(5) McManus, J. M.; McFarland, J. W.; Gerber, C. F.; McLamore, W. M.; Laubach, G. D. *J. Med. Chem.* **1965**, *8*, 766.

(6) Enders, D.; Eichenauer, H. *Chem. Ber.* **1979**, *112*, 2933.

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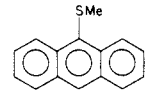
Table I. Properties of Chiral 2-Sulfamyloxaziridines 4 and 5

entry	config[a]	mp, °C (dec)	$[\alpha]_D$,[b] deg	asymmetric oxidations, % ee (config)[g,h] temp, °C	p-Tol-S-CHMe$_2$	
1	(−)-(S,S)-**4a**[c]	122–124	−110.0 (c 3.45, $CHCl_3$)	25	16.5 (S)	23.2 (S)
2	(+)-(R,R)-**5a**[c]	124–126	+2.5 (c 2.87, $CHCl_3$)	25	11.0 (R)	18.7 (R)
3	(−)-(S,S)-**4b**[d]	121–123	−109.0 (c 1.60, $CHCl_3$)	25	37.6 (S)	50.0 (S)
4	(+)-(R,R)-**5b**[d]	137–138	+42.7 (c 1.76, $CHCl_3$)	25	38.0 (R)	53.1 (R)
5				−42	65.0 (R)	68.4 (R)
6	(−)-(S,S)-**4c**[e]	102–104	−198.0 (c 2.0, $CHCl_3$)	25	10.5 (S)	23.2 (S)
7	(+)-(R,R)-**5c**[e]	73–74	+61.0 (c 2.0, $CHCl_3$)	25	10.8 (R)	24.9 (R)
8	(−)-(S,S)-**4e**[f]			25	22.5 (S)[i]	45.5 (S)[i]

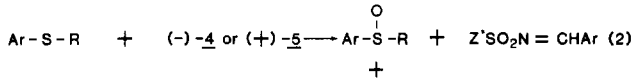
[a] Proposed configuration based on chiral recognition mechanism. See text. [b] Rotations measured at 20 °C in a 1-dm cell. [c] **4a/5a** (47:53) (92% yield); separated on a Varian MCH-10 reverse-phase C_{18} column (0.8 × 50 cm) eluting with methanol/water (70:30) at a flow rate of 3.0 mL/min, 320 nm; (−)-**4a** is the first to be eluted. [d] **4b/5b** (53:47) (86% yield); separated on a Varian Si-10 column (0.8 × 50 cm) eluting with n-hexane/methylene chloride (60:40) at a flow rate of 2.5 mL/min, 320 nm; (+)-**5b** is the first to be eluted. [e] **4c/5c** (72:28) (78% yield); isolated by crystallization, see text. [f] Reference 9. [g] Sulfoxide enantiomers were separated on a Regis Pirkle covalent phenyl glycine HPLC column; isopropyl p-tolyl sulfoxide: elution with n-hexane/2-propanol (95:5) at a flow rate of 1.0 mL/min, 254 nm; methyl 9-anthryl sulfoxide: elution with n-hexane/2-propanol (90:10) at a flow rate of 1.0 mL/min, 254 nm. [h] See ref 12. [i] Corrected for purity of (−)-(S,S)-**4e**, which was 60% optically pure. Oxidation of isopropyl p-tolyl sulfide using optically pure (−)-(S,S)-**4e** affords the (−)-(S)-sulfoxide in 20.8% ee; ref 9.

1 h, 120 °C 4 h, and then 90 °C for 18 h) until the evolution of ammonia gas had ceased.

Sulfamylimines **3a–c**[7] were prepared in 94–95% yield by heating equivalent amounts **2a,b**, p-nitrobenzaldehyde, or 2-chloro-5-nitrobenzaldehyde with Aerocat Triple A/5-Å molecular sieves in benzene.[8] Preparation of **3d**[7] in a similar manner failed but was accomplished, in 75% yield, by heating **2b**, 2-chloro-5-nitrobenzaldehyde diethyl acetal, and $AlCl_3 \cdot 6H_2O$ at 115 °C until ethanol had ceased to distill.[8] In addition to satisfactory elemental analysis the ^1H NMR spectra of sulfamylimines **3a–d** are characterized by a downfield singlet at δ 8.6–9.0 ascribed to the imino proton.

Biphasic oxidation (m-CPBA–$CHCl_3$/$NaHCO_2 \cdot H_2O$) of **3a–d**[9] affords diastereomeric (E)-2-sulfamyloxaziridines **4** and **5** in good isolated yields (78–92%) (Scheme I, Table I).[10] Crystallization of **4c/5c** (72:28) from methanol gave the major diastereomer (−)-**4c** (50%) optically pure, while crystallization from ethanol gave (+)-**5c** (12%). Separation of **4a,b,d/5a,b,d** by crystallization was unsuccessful but was accomplished for **4a,b/5a,b** by using semipreparative HPLC (Table I). Separation of the diastereomers of **4d/5d** has been unsuccessful to date.

Asymmetric oxidations were accomplished by reacting **4** or **5**, in $CHCl_3$ with equimolar amounts of the sulfide (ArSR) at 25 or −42 °C for 4 or 48 h (eq 2). The optically



active sulfoxides were isolated by preparative TLC (silica gel G) in greater than 90% yield. Sulfoxide enantiomeric purity (% ee) and absolute configuration were determined on a Regis Pirkle covalent phenylglycine HPLC column.[11,12] These results are summarized in Table I.

Chiral 2-sulfamyloxaziridines **4b** and **5b** exhibit the best asymmetric bias to date for the oxidation of a sulfide to a sulfoxide, i.e., 38% and 53% ee, respectively, for oxidation of isopropyl p-tolyl sulfide and methyl 9-anthryl sulfides at 25 °C (Table I, entries 3–5). Significantly, the asymmetric bias increases from 38% to 65.0% ee for oxidation of isopropyl p-tolyl sulfide and from 53.1% to 68.4% ee for oxidation of methyl 9-anthryl sulfide on lowering the temperature from 25 °C to −42 °C (Table I). Indeed the asymmetric bias shown by **4b,5b** is similar to that displayed by enzymatic systems.[9,13]

The fundamental processes controlling asymmetric induction which enables the realization of high enantioselectivitey remain unclear, despite impressive achievements in the asymmetric epoxidation of allylic alcohols[14] and the asymmetric formation of C–C and C–H bonds.[15] This lack of understanding is illustrated by the asymmetric oxidation of unfunctionalized alkenes and sulfides with chiral peracids and hydroperoxides where the asymmetric bias is only 0–8 % ee.[9,16]

Recently we demonstrated that chiral 2-sulfonyloxaziridines **4e** and **5e** are useful reagents for probing the origins of asymmetric induction in oxygen-transfer reactions because of their well-defined active sites.[9,16] It was established that the product stereochemistry was determined by the configuration of the oxaziridine three-mem-

(7) **3a** (92%), mp 157–158 °C, $[\alpha]_D$ −93.0° (c 2.45, $CHCl_3$); **3b** (95%), mp 97–98 °C, $[\alpha]_D$ −98.0° (c 2.04, $CHCl_3$); **3c** (73%), mp 118–120 °C, $[\alpha]_D$ −113.5° (c 2.0, $CHCl_3$); **3d** (79%), mp 58–60 °C, $[\alpha]_D$ −31.2 (c 2.00, $CHCl_3$).

(8) Details of the synthesis of sulfamylimines and sulfonimines (ZSO_2N=CHAr; Z = NR_2, R) will be described elsewhere.

(9) Davis, F. A.; Jenkins, R. H., Jr.; Awad, S. B.; Stringer, O. D.; Watson, W. H.; Galloy, J. *J. Am. Chem. Soc.* **1982**, *104*, 5412.

(10) Oxidation of rapidly equilibrating E–Z mixtures of sulfonimines affords only (E)-oxaziridines. See ref 9 and: Buciarelli, M.; Forni, A.; Moretti, I.; Torre, G. *J. Chem. Soc., Perkin Trans. 2* **1983**, 923.

(11) Pirkle, W. H.; Finn, J. M.; Hamper, B. C.; Schreiner, J.; Pribish, J. R. *ACS Symp. Ser.* **1982**, *185*, 245.

(12) The report by Pirkle et al.[11] that the R sulfoxides of isopropyl p-tolyl sulfoxide and methyl 9-anthryl sulfoxide are the most retained (last eluted) enantiomer on the Regis Pirkle covalent phenylglycine HPLC column was confirmed by using enriched optically active sulfoxides of known configuration.

(13) For leading references to enzymatic oxidations of sulfides to sulfoxides, see: Mikolajczyk, M.; Drabowicz, J. In *Top. Stereochem.* **1982**, *13*, 333. Takata, T.; Yamazaki, M.; Fujimori, K.; Kim, Y. H.; Iyanagi, T.; Oae, S. *Bull. Chem. Soc. Jpn.* **1983**, *56*, 2300.

(14) Katsuki, T.; Sharpless, K. B. *J. Am. Chem. Soc.* **1980**, *102*, 5974. Sharpless, K. B.; Behrens, C. H.; Ktsuki, T.; Lee, A. W. M.; Martin, V. S.; Takatani, M.; Viti, S. M.; Walker, F. J.; Woodard, S. S. *Pure Appl. Chem.* **1983**, *55*, 589.

(15) For leading references on asymmetric synthesis, see: (a) Morrison, J. D.; Mosher, H. S. "Asymmetric Organic Reactions"; American Chemical Society: Washington, DC, 1976. (b) Apsimon, J. W.; Seguin, R. P. *Tetrahedron* **1979**, *35*, 3797. (c) Kagan, H. B.; Fiaud, J. C. *Top. Stereochem.* **1979**, *10*, 1975. (d) Valentine, D., Jr.; Scott, J. W. *Synthesis* **1978**, 329. (e) Meyers, A. I. *Acc. Chem. Res.* **1978**, *11*, 375.

(16) Davis, F. A.; Harakal, M. E.; Awad, S. B. *J. Am. Chem. Soc.* **1983**, *105*, 3121.

bered ring and that nonbonded steric interactions in the transition state were responsible for the chiral recognition. Thus, oxidations of sulfides to sulfoxides using (−)-(*S*,*S*)-2-sulfonyloxaziridine, **4e**, afforded in every case the (−)-*S* sulfoxides.[9] Since the mechanism of chiral recognition for asymmetric oxidations using 2-sulfamyloxaziridines (eq 2) and 2-sulfonyloxaziridines is likely to be similar, the *S*,*S* and *R*,*R* configurations are tentatively assigned to the oxaziridine three-membered rings in (−)-**4a–d** and (+)-**5a–d**, respectively.[17] Note that like 2-sulfonyloxaziridines, the absolute configuration of the oxaziridine three-membered ring in **4** and **5** determines the product stereochemistry; i.e., (−)-**4a–d** and (+)-**5a–d** give the opposite sense of asymmetric induction, respectively (Table I).

The increased enantioselectivity exhibited by 2-sulfonyl- and 2-sulfamoyloxaziridines is likely a manifestation of the closer proximity of the oxaziridine substituents to the active site in comparison to peracids or hydroperoxides. In oxaziridines the active site oxygen is located in a rigid three-membered ring one bond removed from the carbon and nitrogen chiral centers. The group size difference (GSD) effect may be responsible for the higher asymmetric bias observed for oxidation of methyl 9-anthryl sulfide compared to isopropyl *p*-tolyl sulfide (53.0% vs. 38.0% ee at 25 °C).[9,16] As the GSD in the substrate increases, the asymmetric bias increases because attack of one of the enantiotopic sulfur electron pairs on the electrophilic oxaziridine oxygen is increasingly favored from the direction where there are the fewest nonbonding steric interactions.

Since the mechanism of chiral recognition is controlled by nonbonded steric interaction it is perhaps not surprising that the sulfamyl group in **4a–d** and **5a–d** has relatively little influence on the asymmetric bias because of its distance from the active site.[18] What is surprising is the effect of changing the aryl group from *p*-nitrophenyl to 2-chloro-5-nitrophenyl, nearly tripling the asymmetric bias (Table I, compare for example entries 1 and 2 with 3 and 4). While a definitive explanation of this effect is, at present, not possible, it may be related to greater system rigidity caused by the ortho substituent.[19] Rigidity in the oxaziridine would also be expected to increase on lowering the temperature. More conformational degrees of freedom available to isopropyl *p*-tolyl sulfide compared to methyl 9-anthryl sulfide may be reflected in the greater change in % ee on lowering the temperature of oxidation. System rigidity, caused by internal ligand chelation and/or rigid ring systems, is frequently associated with high stereoselectivities.[15,21] The relationship of the asymmetric bias to oxaziridine rigidity is currently under study.

In summary, chiral 2-sulfamyloxaziridines give the best results to date for the asymmetric oxidation of sulfides to sulfoxides. The great structural diversity conceivable for 2-sulfamyloxaziridines makes possible not only synthesis of more efficient asymmetric oxidizing reagents but also an increased understanding of the origins of asymmetric induction.

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An Efficient Synthesis of *N*-Bromoperhalo-1-alkanimines

Summary: Certain perhalogenated nitriles have been found to react readily with bromine and active cesium fluoride to afford high yields of *N*-bromoperhalo-1-alkanimines ($R_xFC{=}NBr$; R_x = CF_3, C_2F_5, n-C_3F_7, CF_2Cl, CCl_3). Photolysis of the perfluorinated *N*-bromo compounds affords the novel perfluoroazines $R_fFC{=}NN{=}CFR_f$.

Sir: A number of *N*-bromoperhalo-1-alkanimines ($R_xFC{=}NBr$) have long been known, but their chemistry has remained unexplored due to the inefficiency of the reported syntheses.[1] Here we report a simple, high-yield synthesis of five of these compounds by reaction of the corresponding perhalogenated nitriles with bromine and active cesium fluoride. These reactions probably proceed by initial formation of $R_xFC{=}N^-$, followed by oxidation of the intermediate anion by bromine to afford $R_xFC{=}NBr$. This postulate is supported by mechanistically similar chemistry reported for other unsaturated perfluorinated systems.[2]

The preparation of $CF_3FC{=}NBr$ (**1**) is described as a typical example. (*CAUTION*! Many *N*-halo compounds are known to be powerful explosives. We have experienced no explosions during the preparation and handling of the *N*-bromoperhalo-1-alkanimines, but the potential instability of these compounds and certain of their derivatives should be kept in mind. We advise that preparations and reactions of these materials be done on a small scale.) Trifluoroacetonitrile (15 mmol) and then bromine (30 mmol)[3] were condensed into a 100-mL Pyrex flask containing active cesium fluoride (35 mmol)[4] and fitted with

(17) Suitable crystals of **4** and **5** satisfactory for X-ray analysis have proven to be elusive to date.

(18) Note that replacement of the sulfamyl group by a camphorsulfonyl group has a major influence on the asymmetric bias particularly for oxidation of isopropyl *p*-tolyl sulfide (Table I: compare entries 3 and 4 with 8).

(19) An X-ray structure of (−)-(*S*,*S*)-2-[(*d*-α-bromo-π-camphoryl)-sulfonyl]-2-chloro-5-nitrophenyl)oxaziridine (**4e**, Z* = *d*-α-bromo-π-camphoryl)[9] reveals, that in the solid state, the oxaziridine aryl and C–N bonds are nearly coplanar and that there is some interaction between the nitrogen lone pair and an aromatic ortho proton.[9] In 2-sulfonyloxaziridines lacking an ortho substituent the aryl groups are slightly twisted out of coplanarity with the oxaziridine C–N bond.[20] The *o*-chloro substituent may inhibit rotation about the C-aryl oxaziridine bond resulting in greater system rigidity.

(20) Chen, J. S.; Watson, W. H.; Davis, F. A.; Lamendola, J. F., Jr.; Nadir, U. K. *Acta Crystallogr., Sect. B* **1978**, *B34*, 2861. Kimura, M.; Watson, W. H.; Davis, F. A.; Lamendola, J. F., Jr.; Nadir, U. K. *Ibid.* **1979**, *B35*, 234.

(21) (a) Heathcock, C. H. *ACS Symp. Ser.* **1982**, *185*, 55. (b) Evans, D. A. *Aldrichimica Acta* **1982**, *15*, 23. (c) Meyers, A. I.; Williams, D. R.; Erickson, G. W.; White, S.; Druelinger, M. *J. Am. Chem. Soc.* **1981**, *103*, 3081.

(1) (a) Tullock, C. W. Brit. Pat. 870328, 1968. See also: *Chem. Abstr.* **1962**, *56*, 8561*f*. (b) Chambers, W. J.; Coffman, D. D. U.S. Pat. 3023208, 1962. See also: *Chem. Abstr.* **1962**, *57*, 11215. (c) Tullock, C. W. U.S. Pat. 3057849, 1962. See also: *Chem. Abstr.* **1963**, *58*, 3315*b*. (d) Chambers, W. J.; Tullock, C. W.; Coffman, D. D. *J. Am. Chem. Soc.* **1962**, *84*, 2337.

(2) Chambers, R. D. "Fluorine in Organic Chemistry"; Wiley: New York, 1973.

(3) The excess bromine is eventually absorbed by the solid phase. Presumably, $CsBr_3$ and higher cesium polybromides are formed.

(4) The cesium fluoride was activated by fusion in a platinum dish, followed by grinding to a fine powder in a ball mill under dry nitrogen.

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