reaction mixture, afforded 1-fluoro-4-phenylbicyclo[2.2.1]heptane (2, X = C_6H_5) as a white solid (0.08 g, 38% based on unreacted iodide). Recrystallization from hexane gave colorless prisms: mp 42–44 °C; mass spectrum, m/e 190 (M^+).

A vigorously stirred suspension of the phenyl derivative (2, X = C_6H_5; 0.107 g, 0.00056 mol) in acetic anhydride (1.5 mL) was treated with concentrated nitric acid (0.11 mL, sp gr 1.42) in the same manner as previously described for the corresponding BCO derivative.[69] A workup in the usual fashion afforded the nitro derivative (2, X = p-$NO_2C_6H_4$) as a cream solid (0.084 g, 64%) after sublimation. Recrystallization from methanol afforded colorless needles, mp 97–98 °C. Anal. Calcd for $C_{13}H_{14}FNO_2$: C, 66.37; H, 6.00. Found: C, 66.16; H, 5.84.

The amine (2, X = p-$NH_2C_6H_4$) was prepared by catalytic hydrogenation (H_2, 50 psi; 5% Pd/C) of the nitro compound (2, X = p-$NO_2C_6H_4$; 0.07 g, 0.0003 mol) in absolute ethaol (20 mL). A standard workup, followed by sublimation, afforded the amine (2, X = p-$NH_2C_6H_4$) as an off-white solid (0.035 g, 57%), mp 100–111 °C.

1-Fluoro-4-(trimethylstannyl)bicyclo[2.2.1]heptane [2, X = $Sn(CH_3)_3$]. A solution of the iodide (2, X = I; 0.51 g, 0.002 mol) in tetrahydrofuran (6 mL) was treated with trimethyltin lithium in tetrahydrofuran in a standard manner.[70] A workup in the usual fashion, followed by Kugelrohr distillation (2 times) of the crude product, afforded the tin compound [2, X = $Sn(CH_3)_3$] as a colorless liquid (0.22 g, 40%): bp 67–70 °C (2 mm); mass sectrum, m/e 274, 276, 278 (M^+).

1-Fluoro-4-methylbicyclo[2.2.1]heptane (2, X = CH_3). The carboxylic acid (2, X = COOH; 1.0 g, 0.0063 mol) was reduced with borane–methyl sulfide by following the procedure of Lane and co-workers.[71] A conventional workup, followed by distillation, afforded the hydroxymethyl derivative (2, X = CH_2OH) as a colorless oil (0.68 g, 75%), which solidified on standing: bp 105–110 °C (13 mm); mass spectrum, m/e 144 (M^+).

Treatment of the alcohol (2, X = CH_2OH; 0.65 g, 0.006 mol) in dry pyridine (1.5 mL) with p-toluenesulfonyl chloride (0.45 g)[72] afforded the tosylate (2, X = CH_2OTs; 1.20 g, 90%) as a white solid after a standard workup.

A solution of the tosylate (2, X = CH_2OTs; 1.20 g, 0.004 mol) in dry tetrahydrofuran (3.0 mL) was treated with lithium triethylborohydride in tetrahydrofuran (0.008 mol; 8.0 mL of 1 M solution) at 0 °C.[73] The resulting mixture was heated at 65 °C for 3 h and left to stir overnight at room temperature. After cooling, the reaction mixture was quenched with water, followed by 3 M NaOH (4 mL) and 30%, w/w, H_2O_2 (4 mL). The two phases were separated, and the aqueous layer was extracted several times with fluorotrichloromethane. The combined organic phase was then washed thoroughly with water to remove tetrahydrofuran. The organic layer was dried before distillation and afforded the volatile methyl derivative (2, X = CH_3) as a concentrate in fluorotrichloromethane. The solvent was finally removed by careful distillation through a short column packed with glass helices. A GLC analysis of the pale yellow residue revealed that the methyl compound was >95% pure: mass spectrum, m/e 128 (M^+).

1-Fluorobicyclo[2.2.1]heptane (2, X = H). 1-Norbornanol or bicyclo[2.2.1]heptan-1-ol (0.8 g, 0.007 mol)[74] was treated with a 3- to 4-fold excess of sulfur tetrafluoride as described above for the conversion of 13 to 2 (X = $COOCH_3$). After standing for 48 h, the excess sulfur tetrafluoride was carefully vented from the bomb, and the residue was extracted with fluorotrichloromethane. The extract was washed with aqueous sodium bicarbonate and dried, and the solvent was carefully removed through a short column packed with glass helices. Sublimation of the residue into a liquid-nitrogen cooled receive afforded 2 (X = H) as a colorless solid (0.6 g, 76%): mp 95–98 °C; mass spectrum, m/e 114 (M^+); ^1H NMR ($CDCl_3$) δ 1.26–1.93 (11 H, m). Anal. Calcd for $C_7H_{11}F$: C, 73.65; H, 9.71. Found: C, 73.61; H, 9.88.

Registry No. 2 (X = H), 78142-52-6; 2 (X = NO_2), 84553-37-7; 2 (X = CN), 84553-38-8; 2 (X = COOH), 84553-40-2; 2 (X = $CONH_2$), 88888-22-6; 2 (X = $COOCH_3$), 84553-41-3; 2 (X = $COCH_3$), 84553-39-9; 2 (X = OH), 84553-46-8; 2 (X = $OCOCH_3$), 84553-47-9; 2 (X = F), 84553-42-4; 2 (X = Cl), 84553-43-5; 2 (X = Br), 84553-44-6; 2 (X = I), 84553-45-7; 2 (X = NH_2), 84553-48-0; 2 (X = $NH_2{\cdot}CF_3CO_2H$), 88888-23-7; 2 (X = CH_3), 84553-50-4; 2 (X = CH_2OH), 88888-24-8; 2 (X = C_6H_5), 84553-49-1; 2 (X = p-$NO_2C_6H_4$), 88888-25-9; 2 (X = p-$NH_2C_6H_4$), 88888-26-0; 2 (X = p-$NH_2C_6H_4{\cdot}CF_3CO_2H$), 88888-27-1; 2 (X = $Sn(CH_3)_3$), 84010-89-9; 2 (X = CH_2OTs), 88888-32-8; 9, 81687-89-0; 10, 88888-28-2; 11, 88888-29-3; 12, 88888-30-6; 13, 88888-31-7; 1-norbornanol, 51566-98-4.

(69) Adcock, W.; Khor, T. C. *J. Org. Chem.* **1977**, *42*, 218.
(70) Tamborski, C.; Ford, F. E.; Soloski, E. J. *J. Org. Chem.* **1963**, *28*, 237.
(71) Lane, C. F.; Myatt, H. L.; Daniels, J.; Hopps, H. B. *J. Org. Chem.* **1974**, *39*, 3052.
(72) Vogel, A. I. "Practical Organic Chemistry"; Longmans: London, 1978; p 1103.
(73) Brown, H. C.; Krishnamurthy, S. *J. Org. Chem.* **1976**, *41*, 3064. *Ibid.* **1979**, *45*, 849.
(74) We thank Dr. E. W. Della for providing a sample of 1-norbornanol.

Diastereoface-Differentiating Synthesis of Substituted β-Lactams from Chiral Imines and/or Chiral α-Chloro Iminium Chlorides

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Received July 11, 1983

Reaction of imines carrying a chiral substituent at a nitrogen atom with symmetric or prochiral α-chloro iminium chlorides leads in a diastereoface-differentiating reaction to a mixture of diastereoisomeric or epimeric β-lactams. Attempts were made to determine the absolute configuration of obtained chiral β-lactams. Reaction of prochiral imines with chiral α-chloro iminium chlorides also provides mixtures of diastereoisomeric β-lactams or their enantiomers with a clear selectivity.

Chiral Imines

Reaction of α-chloro iminium chlorides with imines, as reported by Ghosez,[1] can be applied to asymmetric syntheses by the use of chiral imines, as was confirmed in our first communication.[2] In the present study, we extend this synthesis to new examples and determine the absolute configuration of the obtained substituted β-lactams.

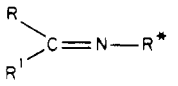
The substrates used are listed in Table I and Table II.

The reaction leads to β-lactams having two (type A) or one (type B) newly created chiral center, depending on

(1) Ghosez, L.; Haveaux, B.; Viehe, H. C. *Angew. Chem., Int. Ed. Engl.* **1969**, *6*, 454.
(2) Belzecki, C.; Rogalska, E. *J. Chem. Soc., Chem. Commun.* **1981**, 57.

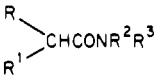
0022-3263/84/1949-1397$01.50/0

Table I. Chiral Imines



compd	R	R^1	R*
1	Ph	H	(*S*)-(+)-CH(Me)Ph
2	Ph	Me	(*S*)-(+)-CH(Me)Ph
3	Me	H	(*S*)-(+)-CH(Me)Ph
4	Ph	H	(*S*)-(+)-CH(Me)CH_2Ph

Table II. Amides



compd	R	R^1	$-NR^2R^3$
5	Me	H	NMe_2
6	Et	H	NMe_2
7	Ph	H	NMe_2
8	Me	H	morpholino
9	Me	Ph	NMe_2
10	Me	Me	NMe_2
11	H	H	NMe_2
12	H	H	morpholino

which amide is used (Scheme I).

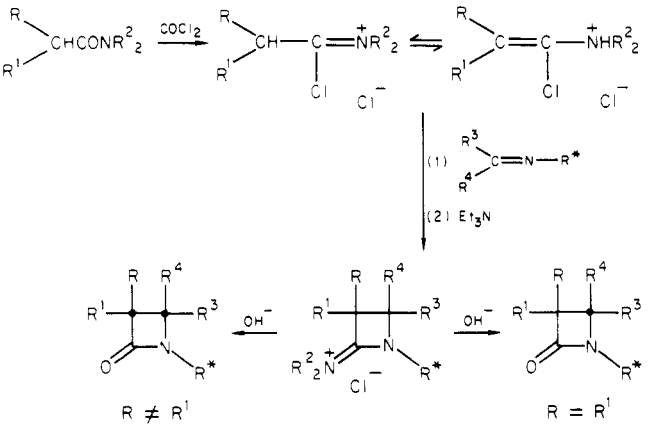
In type A syntheses, the reaction provides a mixture of diastereoisomeric β-lactams having two newly created chiral centers at C_3 and C_4. In type B syntheses, a mixture of epimeric β-lactams is obtained.

Since the 2-azetidylideneaminium salts were inconvenient both for separation and ^1H NMR analysis, they were hydrolyzed directly to β-lactams. After hydrolysis, the mixtures were separated from polar fractions, isolated, and analyzed (see Experimental Section). The quantitative ratio of the isomers was estimated by weighing the HPLC fractions or by integration of the ^1H NMR signals if the chromatographic separation was impossible or incomplete.

To make sure that hydrolysis of the iminium salts to β-lactams caused no change in the diastereoisomeric ratio, a gradual hydrolysis for a chosen mixture was done and the diastereoisomeric ratio was periodically determined. No change was observed and the yield of hydrolyzed material was quantitative. The results are collected in Table III.

In the first series of syntheses (type A) the use of the suitable substrates lets us come to the following conclusions. Product **13** was obtained from two different substituted amides. The morpholine amide gave a higher chemical yield and also a higher ratio of trans diastereoisomers.

Scheme I



Products **13–16** were obtained by using the imine **1** and *N,N*-dimethyl amides of several acids. An increase in the size of one of the substituents, R = Me or Ph, increases the ratio of trans diastereoisomers.

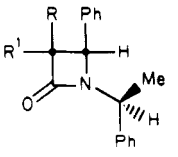
Increasing the size of the second substituent from R^1 = H to Me (compounds **15** and **16**) improves the chemical yield. Change of the chiral substituent in the imine to an α-benzylethyl group of the same configuration (*S*) changes drastically the stereochemistry of the reaction. In this case, only two diastereoisomers were isolated, *trans*- and *cis*-**17**, in the ratio of 78:22.

In the next group of syntheses (type B) imines **1–4** which are prochiral on C_1 and carry a chiral substituent on nitrogen were allowed to react with achiral amides such as **10–12** which are derivatives of acetic and isobutyric acid. The syntheses result in mixtures of epimeric β-lactams having a newly created chiral center at C_4. Mixtures of epimeric products were worked up and their quantitative ratio was estimated as described before. Complete separation by HPLC was not always possible. The results are collected in Table IV.

Chemical yields of these syntheses ranged from 53–90% and epimeric excesses ranged from 0–47%. The best result was achieved when chiral imine **1** and *N,N*-dimethylacetamide (**11**) were used.

The synthesis of epimeric mixtures of **21** and **22** has shown that just a small change of the chiral substituent in the imine clearly changes the stereochemistry of the reaction.

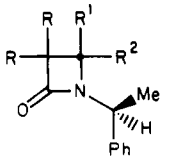
Table III. Diastereoisomeric Azetidinones with Two New Chiral Centers



compd	yield, %	imine + amide	R	R^1	% ratio of diastereoisomers given in sequence in HPLC separation/ optical rotation, deg; δ for H_α			
					trans		cis	
					3(*S*),4(*R*)	3(*R*),4(*S*)	3(*R*),4(*R*)	3(*S*),4(*S*)
13	68	1 + 5	Me	H	35/1; −8.8; 4.92	32/2; +0.87; 4.08	22/4; +121.8; 4.90	11/3; −112.2; 4.20
13	81	1 + 8	Me	H	40/1; −9.4; 4.92	28/2; +0.63; 4.08	20/4; +120.0; 4.90	12/3; −110.8; 4.20
14	65	1 + 6	Et	H	34/1; +10.6; 4.95	35/2; −10.8; 4.12	12/4; +106.6; 4.90	18/3; −105.7; 4.23
15	64	1 + 7	Ph	H	30/3; —;[b] 5.05	50/4; —;[b] 4.24	5/2; +113.0; 5.00	15/1; −216.7; 4.22
16[a]	92	1 + 9	Ph	Me	27/4; —;[c] 4.75	51/1; 27.6; 4.38	11/2; —;[b] 5.10	11/3; —;[b] 4.10

[a] The changing of the substituents at C_3 results in changing the priority for chirality at C_4 (e.g., trans 3(*R*),4(*R*) and 3(*S*),4(*S*) and cis 3(*R*),4(*S*) and 3(*S*),4(*R*)). [b] — indicates isomers were not separated and no optical rotation is available. [c] — indicates optical rotation was not reported.

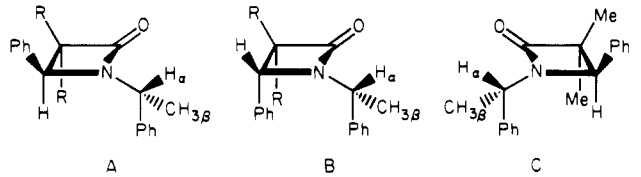
Table IV. Epimeric Azetidinones with a New Chiral Center at C_4



compd	imine + amide	yield, %	R,R	R^1	R^2	% ratio of epimers given in sequence by HPLC/ δ for H_α; $[\alpha]^{20}_D$, deg 4(*R*)	4(*S*)
18	1 + 10	81	Me	Ph	H	33/1; 4.88; +90.6	67/2; 4.20; −95.0
19[a]	3 + 11	90	H	Me	H	47/1; 4.82; −52.0	53/2; 4.58
20[b]	1 + 11	87	H	Ph	H	27/1; 4.15; −28.1	73/2; 4.95; +28.5
20[b]	1 + 12	58	H	Ph	H	40/1; 4.15; —[d]	60/2; 4.95; —[d]
21	2 + 10	63	Me	Ph	Me	49/1; 4.13; +43.5	51/2; 4.05; +10.2
22[c]	4 + 10	53	Me	Ph	H	67/1; 3.4; —[d]	33/2; 2.9; —[d]

[a] Epimer 4(*S*) contains 4(*R*). [b] Absolute configuration at C_4 has opposite sign as analogous compounds in this series. [c] A chiral N-substituent was used (*S*)-CH(Me)CH_2Ph. [d] — indicates epimers were not separated.

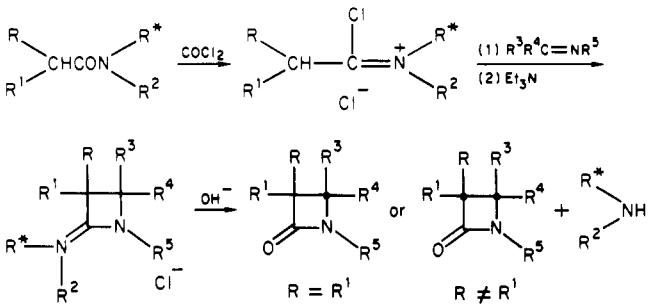
Scheme II[a]



A B C

[a] A: R = Me, epimer 4(*S*), H_α 4.9 ppm, H_β 1.5 ppm.[3] B: R = Me, epimer 4(*R*), H_α 4.2 ppm, H_β 1.9 ppm.[3] A and B: R = H, absolute configuration ref 4 and 5. C: our epimer 4(*R*)-**18**, H_α 4.88 ppm, H_β 1.52 ppm, enantiomeric with A (R = Me).

Scheme III



Comparison of **19** and **20** has shown that changing the substituent in the aldimine from Me to Ph favors an excess of epimer 4(*S*) (the absolute configuration at C_4 in **20** is opposite for the same geometry).

Finally, both examples of **20** envisage the role of the N-substituents in the amide (NMe_2 or morpholine).

The determination of the absolute configuration of epimers **18** (Scheme II) was based on the data reported by Furukawa[3] who determined the absolute configuration of (*S*)-2,2-dimethyl-3-phenyl-3-aminopropionic acid. This acid was obtained from a mixture of epimeric 4(*R*)- and 4(*S*)-*N*-((*R*)-α-phenylethyl)-3,3-dimethyl-4-phenylazetidin-2-one in which the 4(*S*) epimer was in excess. This epimer is enantiomeric with our **18** 4(*R*) epimer (see Scheme II).

The data presented, including the ^{1}H NMR spectra of the two epimeric mixtures, let us conclude that our epimer **18**, showing the signals H_α at 4.2 ppm and H_β at 1.9 ppm, represents epimer 4(*S*), and that the second epimer (H_α at 4.2 ppm and H_β at 1.52 ppm) has the 4(*R*) configuration.

The absolute configuration of epimer **19** was based on the ^{1}H NMR data reported by Kostyanovsky[4] for the identical compound. His assignment was based in turn on X-ray results reported earlier.[5]

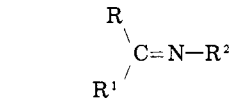
The comparison of the reported[3,4] ^{1}H NMR data and the data for our compounds lets us find certain regularities when considering H_α and H_β signals (Scheme II). We assumed that in the ^{1}H NMR spectra of the compounds carrying a proton and Ph group at C_4, signals of the methine proton, H_α, occur at lower field if the methine proton and the C_4 phenyl group are situated on the same side of the β-lactams ring. In such a conformation, depending on the configuration at C_4, the methine proton H_α and the H_β protons of the CH_3 group are shielded or deshielded by the C_4 phenyl substituent.

On this basis we proposed the absolute configurations for epimers **20**, **21**, and **22**.

The absolute configuration determination at C_3 for diastereoisomeric compounds **13**–**17** was based on the same rule and the characteristic values of the cis–trans coupling constants for the C_3 and C_4 protons.

This assumption was extended to compound **16**.

Table V. Imines



compd	R	R^1	R^2
23	Ph	H	Me
24	*t*-Bu	H	Me
25	Ph	Ph	Me

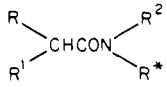
Chiral α-Chloro Iminium Chlorides

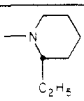
We have also examined the optical induction effects of chiral N-substituents in the starting amide. The advantage of this approach is that the chiral secondary amine can be recovered after the reaction is completed. The product of the reaction can be a mixture of diastereoisomers (two new chiral center at C_4 and C_3) or a mixture of enantiomers (Scheme III). Imines, prochiral on the C_1 carbon atom (aldimines), and chiral optically pure amides containing a chiral N-substituent were used for the syntheses. Substrates are shown in Tables V and VI.

In the first series of syntheses imine **23** and **24** and amides **26** and **30** were used. The quantitative ratio of

(3) Furukawa, M.; Okawara, T.; Noguchi, Y.; Terawaki, Y. *Chem. Pharm. Bull.* **1979**, *27*, 2795.
(4) Kostyanovsky, R. G.; Gella, I. M.; Markov, V. I.; Somojilova, Z. E. *Tetrahedron* **1974**, *30*, 39.
(5) Paulus, E. F.; Kobelt, D.; Jensen, H. *Angew. Chem.* **1969**, *81*, 1048.

Table VI. Amides



compd	R	R^1	configuration
	$-NR^2R^*$ =		
27	Me	H	(S)-(+)
28	Me	Me	(S)-(+)
29	H	H	(S)-(+)
	$-NR^2R^*$ = -N(Me)-CH(Me)-CH_2Ph		
30	Me	H	(S)-(+)
31	H	H	(S)-(+)
32	Me	Me	(S)-(+)

enantiomers within the pairs of diastereoisomers was estimated by integration of the *N*-methyl signals of ^{1}H NMR spectra with Eu(tfc)$_2$ addition. Such an estimation could not be obtained for the cis enantiomeric pairs. The results are collected in Table VII.

The diastereoisomeric mixture **33** obtained from two different amides (**26** and **30**) shows that trans enantiomers are in excess. Enantiomeric excess within the trans pair is small (ca. 10% ee). Change of the substituent in the imine from Ph to *t*-Bu drastically alters the direction of the addition in favor of trans enantiomers and also differentiates their ratio to about 76% ee.

In the next series of syntheses the same imines were used as chiral amides derived from acetic and isobutyric acids. These syntheses yielded mixtures of β-lactam enantiomers with only one new chiral center on C_4. After workup as previously described, the enantiomeric excess was estimated by integrating the *N*-methyl signals in the ^{1}H NMR spectra with Eu(tfc)$_2$ addition. The results are shown in Table VIII.

The opposite sign of optical rotation in the same enantiomeric mixtures **35** and **36** obtained from amides with different chiral substituents indicates that the (*S*)-2-ethylpiperid-1-yl and (*S*)-2-(1-phenyl)propyl groups have opposite optical induction effects. Obviously switching from CH_3 to Me_2CH in the amide constituent improves the enantiomeric excess.

Addition of benzophenone ketimine **25** to amide **26** was done for comparison. An enantiomeric mixture of β-lactams chiral on C_3 was expected but the yield of the reaction was very low (ca. 15%) and the enantiomeric excess was undeterminable within experimental error (51:49).

The results demonstrate that the reaction of chiral α-chloro iminium chlorides with imines is useful in the diastereoface-differentiating synthesis of substituted chiral β-lactams. Mixtures **34** and **36** with high enantiomeric excess are of special interest. Additionally, product **34** contains only aliphatic substituents, a situation which is difficult to achieve in the classic "acid chloride" synthesis.

Experimental Section

Boiling points and melting points are uncorrected. IR spectra in thin film were determined with a Unicam 200 spectrometer. ^{1}H NMR spectra were measured on a JEOL-100 spectrometer. Optical rotations were measured on a Perkin-Elmer 141 spectro-polarimeter. The mixtures of diastereoisomers were separated by HPLC using three $^3/_4$ in. × 1 ft columns filled with 10 μ Lichosorb using hexane containing 15–40% of ethyl acetate as eluent and a refractive index detector. The ratio of diastereoisomers was also determined by ^{1}H NMR signal integration. For enantiomers an addition of Eu(tfc)$_3$ tris(3-(2,2,2-trifluoro-1-hydroxyethylidene)-(+)-camphorato)europium was employed. For all new compounds satisfactory elemental analysis were obtained. For representative β-lactams the elemental analysis is given.

Synthesis of the Substrates. Imines. Imines were obtained by the reaction of carbonyl compounds and primary amines with water absorbing agents (K_2CO_3, molecular sieves) or by azeotropic refluxing with addition of catalyst (BF_3·OEt_2). Crude products were distilled in vacuo.

(*S*)-(+)-1-Phenyl-*N*-benzylideneethylamine (1): yield 94%; bp 121–122 °C (0.2 mmHg); IR (film) cm^{-1} 1650 (C=N); ^{1}H NMR (CCl_4) δ 1.53 (d, 3 H, CH*CH*$_3$, *J* = 6.0 Hz), 4.44 (q, 1 H, NCH, *J* = 6.0 Hz), 8.25 (s, 1 H, PhC*H*); $[\alpha]^{20}_D$ +79.2 (*c* 2.6, CCl_4).

(*S*)-(+)-1-Phenyl-*N*-(1-phenylethylidene)ethylamine (2): yield 81%; bp 104–106 °C (0.1 mmHg); IR (film) cm^{-1} 1640 (C=N); ^{1}H NMR (CCl_4) δ 1.48 (d, 3 H, C*H*$_3$, *J* = 6.0 Hz), 2.1 (s, 3 H, CC*H*$_3$), 4.78 (q, 1 H, NCH, *J* = 6.0 Hz); $[\alpha]^{20}_D$ +97.7 (*c* 1.8, CCl_4).

(*S*)-(−)-1-Phenyl-*N*-ethylideneethylamine (3): yield 95%; bp 74–76 °C (6 mm Hg); IR (film) cm^{-1} 1660 (C=N); ^{1}H NMR (CCl_4) δ 1.36 (d, 3 H, NCHC*H*$_3$, *J* = 6.0 Hz), 1.88 (d, 3 H, =CHC*H*$_3$, *J* = 5.0 Hz), 4.13 (q, 1 H, PhC*H*, *J* = 6.0 Hz), 7.75 (q, 1 H, CH_3C*H*, *J* = 5.0 Hz); $[\alpha]^{20}_D$ −43.1 (*c* 1.7, CCl_4).

(*S*)-(+)-Methyl-2-phenyl-*N*-benzylideneethylamine (4): yield 87%, bp 122–123 °C (0.7 mmHg); IR (film) cm^{-1} 1640 (C=N); ^{1}H NMR (CCl_4) δ 1.2 (d, 3 H, CHC*H*$_3$, *J* = 6.0 Hz), 2.78 (d, 2 H, PhC*H*$_2$, *J* = 8.0 Hz), 3.40 (dq, 1 H, NCH, *J* = 8.0 Hz, *J* = 6.0 Hz), 7.94 (s, PhC*H*); $[\alpha]^{20}_D$ +241.0 (*c* 2.3, CCl_4).

Amides. Amides were obtained in the conventional way from acid chlorides and secondary amines with Et_3N in ethyl ether solution. Crude amides were purified by distillation in vacuo.

(*S*)-(+)-1-Acetyl-2-ethylpiperidine (29): yield 98%; bp 62–63 °C (0.05 mmHg); IR (film) cm^{-1} 1640 (C=O); ^{1}H NMR (CCl_4) δ 2.92 (s, 3 H, COC*H*$_3$); $[\alpha]^{20}_D$ +29.8 (*c* 1.35, CCl_4).

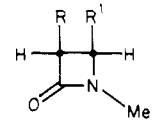
(*S*)-(+)-1-Propionyl-2-ethylpiperidine (27): yield 97%, bp 64–65 °C (0.05 mmHg); IR (film) cm^{-1} 1640 (C=O); ^{1}H NMR (CCl_4) δ 2.22 (q, 2 H, C*H*$_2$CH$_3$, *J* = 7.0 Hz), 1.02 (t, 3 H, C*H*$_3$CH$_2$, *J* = 7.0 Hz); $[\alpha]^{20}_D$ +31.6 (*c* 1.1, CCl_4).

(*S*)-(+)-1-Isobutyryl-2-ethylpiperidine (28): yield 93%, bp 69–70 °C (0.05 mmHg); IR (film) cm^{-1} 1640 (C=O); ^{1}H NMR (CCl_4) δ 2.74 (septet, 1 H, C*H*Me$_2$, *J* = 7.0 Hz), 1.00 (d, 6 H, CH*Me*$_2$, *J* = 7.0 Hz), 1.55 (m, protons of cycle); $[\alpha]^{20}_D$ +23.2 (*c* 1.7, CCl_4).

(*S*)-(+)-*N*-Acetyl-*N*-methylamphetamine (31): yield 90%, bp 87–88 °C (0.1 mmHg); IR (film) cm^{-1} 1640 (C=O); $[\alpha]^{20}_D$ +52.7 (*c* 1.7, CCl_4).

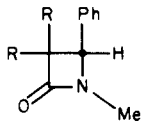
(*S*)-(+)-*N*-Propionyl-*N*-methylamphetamine (30): yield 90%, bp 90–91 °C (0.1 mmHg); IR (film) cm^{-1} 1640 (C=O); $[\alpha]^{20}_D$ +33.1 (*c* 1.1, CCl_4).

Table VII



compd	imine + amide	yield, %	R	R^1	% diastereoisomers ratio trans	cis	% ratio of trans enantiomers
33	**23** + **27**	57	Me	Ph	68	32	57:43
33	**23** + **30**	69	Me	Ph	69	31	64:36
34	**24** + **27**	54	Me	*t*-Bu	100		88:12

Table VIII



compd	imine + amide	yield, %	R	% ratio of enantiomers		$[\alpha]^{20}_D$ of enantiomers, deg
35	27 + 29	82	H	53	47	−6.9
35	27 + 31	50	H	57	43	+19.0
36	27 + 28	60	Me	88	12	+118.0
36	27 + 32	30	Me	86	14	−67.3

(*S*)-(+)-*N*-Isobutyryl-*N*-methylamphetamine (32): yield 91%, bp 98–99 °C (0.1 mmHg); IR (film) cm^{-1} 1640 (C=O); $[\alpha]^{20}_D$ +51.6 (*c* 1.0, CCl_4).

General Method for the Synthesis of β-Lactams. To a solution of 5 mmol of amide in 5 mL of dry methylene chloride was added dropwise 2.5 g of cooled phosgene and the solution was left for 48 h in a sealed flask at room temperature. After this time the reaction mixture was evaporated to dryness, 5 mmol of imine in 5 mL of dry methylene chloride was added, and the mixture was stirred for 3 h in a sealed flask. 10 mmol of Et_3N was added and the mixture stirred for another 2 h. The solvent was evaporated, 10 mL of aqueous 0.5 N NaOH was added, and the reaction was left stirring for 1 h at room temperature. After the C=N peak (1700 cm^{-1}) in the IR disappeared (in the case it was still present, the hydrolysis was repeated with aqueous 1.0 N NaOH), the product was extracted with methylene chloride, dried, and purified by rapid short column chromatography to remove polar side products. The mixture of diastereoisomers was resolved by HPLC with hexane/ethyl acetate as eluent.

***N*-((*S*)-α-Phenylethyl)-3-methyl-4-phenylazetidin-2-one (13) from 1 and 5**: yield 68.5%, IR (film) cm^{-1} 1740 (C=O); M^+ 265. Anal. Calcd for $C_{18}H_{19}NO$: C, 81.58; H, 7.17; N, 5.28. Found: C, 81.58, H, 7.21; N, 5.33.

3(*R*),4(*S*)-*trans*-**13**: $[\alpha]^{20}_D$ +0.87; ^1H NMR (CCl_4) δ 1.32 (d, 3 H, Me C_3, *J* = 7.5 Hz), 1.82 (d, 3 H, −NCHCH_3, *J* = 7.0 Hz), 2.88 (dq, 1 H C_3, *J* = 7.5 Hz, *J* = 2.5 Hz), 3.75 (d, 1 H, C_4, *J* = 2.5 Hz), 4.08 (q, 1 H, NCH, *J* = 7.0 Hz).

3(*S*),4(*R*)-*trans*-**13**: $[\alpha]^{20}_D$ −8.8; ^1H NMR (CCl_4) δ 1.24 (d, 3 H, Me C_3, *J* = 7.5 Hz), 1.34 (d, 3 H, NCHCH_3, *J* = 7.0 Hz), 2.90 (dq, 1 H C_3, *J* = 7.5 Hz, *J* = 2.5 Hz), 3.67 (d, 1 H C_4, *J* = 2.5 Hz), 4.92 (q, 1 H, −NC*H*, *J* = 7.0 Hz).

3(*S*),4(*S*)-*cis*-**13**: $[\alpha]^{20}_D$ +112.2; ^1H NMR (CCl_4) δ 0.80 (d, 3 H, Me C_3, *J* = 7.5 Hz), 1.88 (d, 3 H, NCHCH_3, *J* = 7.5 Hz), 3.30 (dq, 1 H, C_3, *J* = 7.5 Hz, *J* = 5.0 Hz), 4.20 (q, 1 H NCH, *J* = 7.5 Hz), 4.40 (d, 1 H C_4, *J* = 5.0 Hz).

3(*R*),4(*R*)-*cis*-**13**: $[\alpha]^{20}_D$ +121.8; ^1H NMR (CCl_4) δ 0.82 (d, 3 H Me C_3, *J* = 7.5 Hz), 1.50 (d, 3 H NCHCH_3, *J* = 7.5 Hz), 3.28 (dq, 1 H C_3, *J* = 7.5 Hz, *J* = 5.0 Hz), 4.43 (d, 1 H C_4, *J* = 5.0 Hz), 4.90 (q, 1 H NCH, *J* = 7.5 Hz).

13 from 1 and 8: yield 81.6%; ^1H NMR data as above. 3-(*S*),4(*R*)-*trans*-**13**: $[\alpha]^{20}_D$ −9.4. 3(*R*),4(*S*)-*trans*-**13**: $[\alpha]^{20}_D$ +0.83. 3(*R*),4(*R*)-*cis*-**13**: $[\alpha]^{20}_D$ +120.0. 3(*S*),4(*S*)-*cis*-**13**: $[\alpha]^{20}_D$ −110.8.

***N*-((*S*)-α-Phenylethyl)-3-ethyl-4-phenylazetidin-2-one (14) from 1 and 6**: yield 65.0%; IR (film) cm^{-1} 1740 (C=O); M − 2, 277. Anal. Calcd for $C_{19}H_{21}NO$: C, 81.72; H, 7.53; N, 5.02. Found: C, 81.82; H, 7.58; N, 5.08.

3(*R*),4(*S*)-*trans*-**14**: $[\alpha]^{20}_D$ −10.8; ^1H NMR (CCl_4) δ 1.02 (t, 3 H CH_2CH_3, *J* = 7.5 Hz), 1.78 (dq, 2 H CH_2CH_3, *J* = 2.5 Hz, *J* = 7.5 Hz), 1.85 (d, 3 H NCHCH_3, *J* = 7.5 Hz), 3.82 (dt, 1 H C_3, *J* = 2.5 Hz, *J* = 7.5 Hz), 3.87 (d, 1 H C_4, *J* = 2.5 Hz), 4.12 (q, 1 H NCH, *J* = 7.5 Hz).

3(*S*),4(*R*)-*trans*-**14**: $[\alpha]^{20}_D$ +10.6; ^1H NMR (CCl_4) δ 0.97 (t, 3 H CH_2CH_3, *J* = 7.5 Hz), 1.35 (d, 3 H NCHCH_3, *J* = 7.5 Hz), 1.65 (dq, 2 H CH_2CH_3, *J* = 7.5 Hz), 2.85 (dt, 1 H C_3, *J* = 2.5 Hz, *J* = 7.5 Hz), 3.80 (d, 1 H C_4, *J* = 2.5 Hz), 4.95 (q, 1 H NCH, *J* = 7.5 Hz).

3(*S*),4(*S*)-*cis*-**14**: $[\alpha]^{20}_D$ −105.7; ^1H NMR (CCl_4) δ 0.75 (t, 3 H CH_2CH_3, *J* = 7.5 Hz), 1.42 (dq, 2 H CH_2CH_3, *J* = 2.5 Hz, *J* = 7.5 Hz), 1.90 (d, 3 H NCNCH$_3$, *J* = 7.5 Hz), 3.13 (dt, 1 H C_3, *J* = 2.5 Hz, *J* = 7.5 Hz), 4.23 (d, 1 H C_4, *J* = 5.0 Hz), 4.43 (q, 1 H NCH, *J* = 7.5 Hz).

3(*R*),4(*R*)-*cis*-**14**: $[\alpha]^{20}_D$ +100.6; ^1H NMR (CCl_4) δ 0.72 (t, 3 H CH_2CH_3, *J* = 7.5 Hz), 1.35 (dq, 2 H CH_2CH_3, *J* = 2.5 Hz, *J* = 7.5 Hz), 1.48 (d, 3 H NCHCH_3, *J* = 7.5 Hz), 4.35 (d, 1 H C_4, *J* = 5.0 Hz), 3.08 (dt, 1 H C_3, *J* = 2.5 Hz, *J* = 7.5 Hz), 4.90 (q, 1 H NCH, *J* = 7.5 Hz).

***N*-((*S*)-α-Phenylethyl)-3,4-diphenylazetidin-2-one (15) from 1 and 7**: yield 64%; IR (film) cm^{-1} 1740 (C=O); M^+, 327. Anal. Calcd for $C_{23}H_{21}NO$: C, 84.40; H, 6.42; N, 4.28. Found: C, 84.33; H, 6.41; N, 4.33.

3(*R*),4(*S*)-*trans*-**15**: ^1H NMR (CCl_4) δ 1.95 (d, 3 H, NCHCH_3, *J* = 7.5 Hz), 4.24 (q, 1 H NCH, *J* = 7.5 Hz), 4.60 (s, 1 H C_3, *J* = 0.0 Hz), 4.65 (s, 1 H C_4, *J* = 0.0 Hz).

3(*S*),4(*R*)-*trans*-**15**: ^1H NMR (CCl_4) δ 1.42 (d, 3 H, NCHCH_3, *J* = 7.5 Hz), 4.60 (s, 1 H C_3, *J* = 0.0 Hz), 4.65 (s, 1 H C_4, *J* = 0.0 Hz), 5.05 (q, 1 H NCH, *J* = 7.5 Hz).

3(*S*),4(*S*)-*cis*-**15**: $[\alpha]^{20}_D$ −216.7; ^1H NMR (CCl_4) δ 1.97 (d, 3 H NHCH_3, *J* = 7.5 Hz), 4.05 (d, 1 H C_4, *J* = 2.5 Hz), 4.13 (d, 1 H C_3, *J* = 2.5 Hz), 4.22 (q, 1 H, NCH, *J* = 7.5 Hz).

3(*R*),4(*R*)-*cis*-**15**: $[\alpha]^{20}_D$ +113.0; ^1H NMR (CCl_4) δ 1.45 (d, 3 H NCHCH_3, *J* = 7.5 Hz), 4.02 (d, 1 H C_4, *J* = 2.5 Hz), 4.17 (d, 1 H C_3, *J* = 2.5 Hz), 5.00 (q, 1 H NCH, *J* = 7.5 Hz).

***N*-((*S*)-α-Phenylethyl)-3-methyl-3,4-diphenylazetidin-2-one (16) from 1 and 9**: yield 92%; IR (film) cm^{-1} 1740 (C=O); M^+, 341. This azetidinone which carries Ph and Me substituents at C_3 has according to Prelog's rule the opposite sign of configuration at C_4 as analogues compounds of this series. Anal. Calcd for $C_{24}H_{23}NO$: C, 84.46; H, 6.74; N, 4.11. Found: C, 84.66; H, 6.68; N, 4.15.

3(*R*),4(*R*)-*trans*-**16**: $[\alpha]^{20}_D$ −27.6; ^1H NMR (CCl_4) δ 1.15 (s, 3 H, Me C_3), 1.90 (d, 3 H NCHCH_3, *J* = 7.5 Hz), 4.38 (q, 1 H NC*H*, *J* = 7.5 Hz), 4.48 (s, 1 H C_4).

3(*S*),4(*S*)-*trans*-**16** (isolated, not pure): ^1H NMR (CCl_4) δ 1.12 (s, 3 H Me C_3), 1.60 (d, 3 H NCHCH_3), 4.48 (s, 1 H C_4), 4.75 (q, 1 H, NC*H*CH$_3$, *J* = 7.5 Hz).

3(*S*),4(*R*)-*cis*-**16** (isolated, not pure): ^1H NMR (CCl_4) δ 1.55 (s, Me C_3), 1.92 (d, 3 H, NCHCH_3, *J* = 7.7 Hz), 4.10 (s, 1 H C_4), 4.20 (q, 1 H, NC*H*CH$_3$, *J* = 7.5 Hz).

3(*R*),4(*S*)-*cis*-**16** (isolated, not pure): ^1H NMR (CCl_4) δ 1.38 (d, 3 H, NCHCH_3, *J* = 7.5 Hz), 1.55 (s, 3 H, Me C_3), 1.62 (s, 1 H C_4), 5.10 (q, 1 H, NC*H*CH$_3$, *J* = 7.5 Hz).

***N*-((*S*)-1-Phenyl-2-propyl)-3-methyl-4-phenylazetidin-2-one (17) from 4 and 5**: yield 54%; IR (film) cm^{-1} 1740 (C=O); M^+, 341. Anal. Calcd for $C_{19}H_{21}NO$: C, 81.72; H, 7.53; N, 5.02. Found: C, 81.83; H, 7.61; N, 5.12. Only two diastereoisomers were separated. The ^1H NMR spectra of the mixture of isomers consists of a series of overlapping signals and did not allow for the differentiation of the isomers. However, the number and ratio of isomers was determined by integration of only 2 signals corresponding to the proton at C_4. The isomers were separated by HPLC. *trans*-**17**: ^1H NMR (CCl_4) δ 3.70 (d, 1 H C_4, *J* = 2.5 Hz); $[\alpha]^{20}_D$ +78.6. *cis*-**17**: ^1H NMR (CCl_4) δ 4.40 (d, 1 H C_4, *J* = 5.0 Hz); $[\alpha]^{20}_D$ +26.3.

***N*-((*S*)-α-Phenylethyl)-3,3-dimethyl-4-phenylazetidin-2-one (18) from 1 and 10**: yield 81%; IR (film) cm^{-1} 1740 (C=O); M^+, 279. Anal. Calcd for $C_{19}H_{21}NO$: C, 81.72; H, 7.53; N, 5.02. Found: C, 81.60; H, 7.59; N, 5.07.

18 (epimer 4(*R*)): $[\alpha]^{20}_D$ +90.6; ^1H NMR (CCl_4) δ 0.75 (s, 3 H, Me C_3), 1.20 (s, 3 H, Me C_3), 1.52 (d, 3 H, NCHCH_3, *J* = 7.5 Hz), 3.92 (s, 1 H, C_4), 4.88 (q, 1 H, NC*H*CH$_3$, *J* = 7.5 Hz).

18 (epimer 4(*S*)): $[\alpha]^{20}_D$ −95.6; ^1H NMR (CCl_4) δ 0.72 (s, 3 H, Me C_3), 1.28 (s, 3 H, Me C_3), 1.90 (d, 3 H, NCHCH_3, *J* = 7.5 Hz), 3.98 (s, 1 H, C_4), 4.20 (q, 1 H, NC*H*CH$_3$, *J* = 7.5 Hz).

***N*-((*S*)-α-Phenylethyl)-4-methylazetidin-2-one (19) from 3 and 11**: yield 90%; IR (film) cm^{-1} 1740 (C=O); M^+, 189. Anal. Calcd for $C_{12}H_{15}NO$: C, 76.19; H, 7.94; N, 7.41. Found: C, 76.03; H, 7.88; N, 7.48.

19 (epimer 4(*R*)): $[\alpha]^{20}_D$ −52.0; ^1H NMR (CCl_4) δ 1.28 (d, 3 H, C_4, *J* = 6.0 Hz), 1.75 (d, 3 H, NCHCH_3, *J* = 7.5 Hz), 2.38 (dd, 1 H, C_3, *J* = 2.5 Hz, *J* = 15.0 Hz), 3.93 (dd, 1 H, C_3, *J* = 5.0 Hz, *J* = 15.0 Hz), 4.48 (m, 1 H, C_4, *J* = 6.0 Hz, *J* = 5.0 Hz, *J* = 2.5 Hz), 4.82 (q, 1 H, NC*H*CH$_3$, *J* = 7.0 Hz).

19 (epimer 4(*S*)) (contains epimer 4(*R*)): ^1H NMR (CCl_4) δ 1.12 (d, 3 H, Me C_4, *J* = 6.0 Hz), 1.70 (d, 3 H, NCHCH_3, *J* = 7.5 Hz), 2.35 (dd, 1 H, C_3, *J* = 2.5 Hz, *J* = 15.0 Hz), 2.94 (dd, 1 H, C_3, *J* = 5.0 Hz, *J* = 15.0 Hz), 3.52 (m, 1 H, C_4, *J* = 6.0 Hz, *J* = 5.0 Hz, *J* = 2.5 Hz), 4.58 (q, 1 H, NC*H*CH$_3$, *J* = 7.0 Hz).

N-((S)-α-Phenylethyl)-4-phenylazetidin-2-one (20) from 1 and 11: yield 74.0%; IR (film) cm^{-1} 1740 (C=O); M^+, 251. Anal. Calcd for $C_{17}H_{17}NO$: C, 81.27; H, 6.77; N, 5.58. Found: C, 81.38; H, 6.68; N, 5.52. In this case the absolute configuration has the opposite sign at C_4.

20 (epimer 4(R)): $[\alpha]^{20}_D$ 28.1; ^1H NMR (CCl_4) δ 1.82 (d, 3 H, NCHCH_3 J = 7.5 Hz), 2.72 (d, d 1 H, C_3, J = 2.5 Hz, J = 15 Hz), 3.23 (dd, 1 H, C_3, J = 5.0 Hz, J = 15 Hz), 4.15 (q, 1 H, NC*H*CH_3, J = 7.5 Hz), 4.25 (dd, 1 H, C_4, J = 2.5 Hz, J = 5.0 Hz).

20 (epimer 4(S)): $[\alpha]^{20}_D$ +28.5; ^1H NMR (CCl_4) δ 1.35 (d, 3 H, NCHCH_3, J = 7.5 Hz), 2.72 (dd, 1 H, C_3, J = 2.5 Hz, J = 15.0 Hz), 3.18 (dd, 1 H, C_3, J = 5.0 Hz, 15.0 Hz), 4.22 (dd, 1 H, C_4, J = 2.5 Hz, J = 5.0 Hz), 4.95 (q, 1 H, NC*H*CH_3, J = 7.5 Hz).

N-((S)-α-Phenylethyl)-3,3,4-trimethyl-4-phenylazetidin-2-one (21) from 2 and 10: yield 63.0%; mp 116-118 °C; IR (KBr) cm^{-1} 1740 (C=O); M^+, 293. Anal. Calcd for $C_{20}H_{23}NO$: C, 81.91; H, 7.85; N, 4.78. Found: C, 81.82; H, 7.80; N, 4.71.

21 (epimer 4(S)): $[\alpha]^{20}_D$ +10.2; ^1H NMR (CCl_4) δ 0.65 (s, 3 H, Me C_3), 1.18 (s, 3 H, Me C_3), 1.25 (s, 3 H, Me C_4), 1.99 (d, 3 H, NCHCH_3, J = 7.5 Hz), 4.05 (q, 1 H, NC*H*CH_3, J = 7.5 Hz).

21 (epimer 4(R)): $[\alpha]^{20}_D$ +43.5; ^1H NMR (CCl_4) δ 0.65 (s, 3 H, Me C_3), 1.30 (s, 3 H, Me C_3), 1.75 (d, 3 H, NCHCH_3, J = 7.5 Hz), 1.85 (s, 3 H, Me C_4), 4.13 (q, 1 H, NC*H*CH_3, J = 7.5 Hz).

N-((S)-1-Phenyl-2-propyl)-3,3-dimethyl-4-phenylazetidin-2-one (22) from 4 and 10: yield 53.0%; IR (film) cm^{-1} 1740 (C=O); M^+, 293; $[\alpha]^{20}_D$ +74.8. The mixture of epimers was not separated by HPLC. Anal. Calcd for $C_{20}H_{23}NO$: C, 81.91; H, 7.85; N, 4.78. Found: C, 81.28; H, 7.78, N, 4.70. The ^1H NMR spectrum of the mixture of epimers consisted of a series of overlapping signals and did not allow for full differentiation of isomers. However, the ratio of epimers was determined by integration of the signals for H at C_4: **22** epimer (ca. 65%), ^1H NMR (CCl_4) δ 3.98 (s, 1 H, C_4). **22** epimer (ca. 35%), ^1H NMR (CCl_4) δ 3.82 (s, 1 H, C_4).

N,3-Dimethyl-4-phenylazetidin-2-one (33) from 27 and 23: yield 57.0%; IR (film) cm^{-1} 1750 (C=O); M^+, 175. Anal. Calcd for $C_{11}H_{13}NO$: C, 75.42; H, 7.42; N, 8.00. Found: C, 75.31; H, 7.38; N, 8.08.

***cis*-10**: $[\alpha]^{20}_D$ +2.2 (*c* 2.4, CCl_4); ^1H NMR (CCl_4) δ 0.83 (d, 3 H, Me C_3, J = 7.5 Hz), 2.88 (s, 3 H, NMe), 3.55 (dq, 1 H, C_3, J = 5.0 Hz, J = 7.5 Hz), 4.62 (d, 1 H, C_4, J = 5.0 Hz).

***trans*-33**: $[\alpha]^{20}_D$ +9.2 (*c* 2.6, CCl_4); ^1H NMR (CCl_4) δ 1.47 (d, 3 H, Me C_3), 2.80 (s, 3 H, NMe), 3.02 (dq, 1 H, C_3, J = 2.0 Hz, J = 7.5 Hz), 4.02 (d, 1 H, C_4, J = 2.0 Hz).

33 from 30 and 23: yield 69.0%; cis isomer, $[\alpha]^{20}_D$ +9.2 (*c* 2.6, CCl_4); trans isomer, $[\alpha]^{20}_D$ +7.2 (*c* 2.0, CCl_4); ^1H NMR data as above.

N,3-Dimethyl-4-*tert*-butylazetidin-2-one (34) from 24 and 27: yield 50.0%; IR (film) cm^{-1} 1750 (C=O); M^+, 155. Anal. Calcd for $C_9H_{17}NO$: C, 69.68; H, 10.97; N, 9.03. Found: C, 69.57; H, 10.85; N, 9.13.

***trans*-11**: $[\alpha]^{20}_D$ +11.0; ^1H NMR (CCl_4) δ 1.00 (s, 9 H, *t*-Bu), 1.25 (d, 3 H, Me C_3, J = 7.5 Hz), 2.8 (s, 3 H, NMe), 2.85 (dq, 1 H, C_3, J = 2.5 Hz, J = 7.5 Hz), 2.95 (d, 1 H, C_4, J = 2.5 Hz).

N-Methyl-4-phenylazetidin-2-one (35) from 29 and 23: yield 82.0%; IR (film) cm^{-1} 1750 (C=O); M^+, 161; $[\alpha]^{20}_D$ -6.0 (*c* 1.9, CCl_4). Anal. Calcd for $C_{10}H_{11}NO$: C, 74.53; H, 6.83; N, 8.69. Found: C, 74.41; H, 6.78; N, 8.76. ^1H NMR (CCl_4) δ 2.78 (s, 3 H, NMe), 3.40 (dd, 1 H, C_3, J = 5.0 Hz, J = 12.5 Hz), 4.50 (dd, 1 H, C_4, J = 2.5 Hz, J = 5.0 Hz).

35 from 8 and 1: yield 50%; $[\alpha]^{20}_D$ +19.0 (*c* 1.9, CCl_4); spectral data as above.

N,3,3-Trimethyl-4-phenylazetidin-2-one (36) from 28 and 23: yield 60.0%; IR (film) cm^{-1} 1750 (C=O); M^+, 189; $[\alpha]^{20}_D$ +118.0 (*c* 2.6, CCl_4). Anal. Calcd for $C_{12}H_{15}NO$: C, 76.19; H, 7.94; N, 7.41. Found: C, 76.27; H, 7.86; N, 7.57. ^1H NMR (CCl_4) δ 0.77 (s, 3 H, C_3 Me), 1.43 (s, 3 H, Me C_3), 2.85 (s, 3 H, NMe), 4.25 (s, 1 H, C_4).

36 from 32 and 23: yield 30.0%; $[\alpha]^{20}_D$ -63.3 (*c* 2.2, CCl_4); spectral data as above.

Reactions of (Aryloxy)oxosulfonium Ylides with Carbonyl Compounds

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Reactions of (aryloxy)oxosulfonium salts with alkyllithium followed by the addition of carbonyl compounds gave β-aryloxy sulfones, β-aroyloxy sulfones, and α,β-unsaturated or β,γ-unsaturated sulfones in 1.4-17.9%, 1.2-7.2%, and 4.5-13.5% yields, respectively. Ylides obtained by treatment of these sulfonium salts with *n*-BuLi reacted with carbonyl compounds to give betaines, which formed unusual four-membered cyclic alkoxyoxosulfonium salts. The aryloxy anions thus formed attacked β-carbons of these salts to afford β-aryloxy sulfones. The aroyloxy anion that might be formed by autoxidation also attacked β-carbons of these salts to afford β-aroyloxy sulfones. When these anions attacked the α- or γ-protons of these satls, unsaturated sulfones were obtained. This is the first example that the reaction of ylide with carbonyl compounds gave sulfone derivatives via four-membered cyclic alkoxyoxosulfonium salts that were produced by the intramolecular S_N2 mechanism. The yields of unsaturated sulfones were raised up to 35-60% by a one-pot reaction.

It is well-known that sulfonium and oxosulfonium salts react with bases to give the corresponding ylides, which act as methylene transfer reagents toward carbonyl compounds.[1] However, there is no report that sulfur ylides react with carbonyl compounds to give unsaturated sulfones via four-membered cyclic intermediates. Whiting et al., Still et al., and Oishi et al. reported that the reactions of (aryloxy)oxosulfonium salts **1** with nucleophiles gave not only the corresponding ylides but also the corresponding sulfoxides.[2] We are interested in this anomalous reactivity. If ylides are formed by the reaction of these salts with bases, betaines derived from carbonyl compounds may afford the S^+-attacked products (i.e., sulfurane oxides

(1) Corey, E. J.; Chaykovsky, M. *J. Am. Chem. Soc.* **1965**, *87*, 1353. For reviews, see: Trost, B. M.; Melvin, L. S., Jr. "Sulfur Ylides"; Academic Press: New York, 1975. Block, E. "Reactions of Organosulfur Compounds"; Academic Press: New York, 1978. Stirling, C. J. M., Ed. "The Chemistry of The Sulphonium Group"; Wiley: New York, 1981.

(2) (a) Chalkley, G. R.; Snodin, D. J.; Stevens, G.; Whiting, M. C. *J. Chem. Soc. C* **1970**, 682. Chalkley, G. R.; Snodin, D. J.; Stevens, G.; Whiting, M. C. *J. Chem. Soc., Perkin Trans. 1* **1978**, 1580. (b) Shimagaki, M.; Tsuchiya, H.; Ban, Y.; Oishi, T. *Tetrahedron Lett.* **1978**, *3435*. (c) Still, I. W. J.; Szilagyi, S. *Synth. Commun.* **1979**, *9*, 923. Still, I. W. J.; Ablenas, F. J. *J. Org. Chem.* **1983**, *48*, 1617.

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