Synthesis of 2-Azetidiniminium Salts. 1. Diastereoselectivity in Keteniminium Triflate/Imine Cycloadditions

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A systematic study of the synthesis of 2-azetidiniminium triflates, by annulation of aldimines with iminium salts derived from tertiary carboxamides and trifluoromethanesulfonic anhydride, has been carried out. The stereochemical output of a number of 2-azetidiniminium triflates is compared with that of the corresponding chloride salts synthesized by reaction of the same imines with α-chloro iminium chlorides. As a general rule, the stereochemical output of the reactions involving α-chloro iminium chlorides is in stark contrast to that of the corresponding triflates: while the chloride salts are *trans* stereoselective, the triflates show a preference for the *cis* products. The stereochemistry of the reactions involving the triflates has been examined in light of the structure of the reagents. Clear trends for a preferential formation of *cis* or *trans* products with the steric and electronic demand of the imine have been observed. By contrast, no correlation of the product distribution with the steric demand of the amide could be made. The transient formation of a keteniminium triflate intermediate has been suggested. According to this model, the annulation of the imine with the keteniminium triflates occurs with a mechanism closely similar to that observed in the Staudinger reaction. A comparison between the reactions involving the *bona fide* keteniminium triflates, and the corresponding isoelectronic ketenes with the same, or structurally closely related, imines has also been made. This comparison is performed in light of Georg's stereochemical rules that are used to explain, or predict, the stereochemical output of the Staudinger reaction.

Introduction

2-Azetidiniminium salts, whose synthesis and reactivity have been pioneered by Ghosez,[1a−f] are valuable synthetic intermediates that can be converted into a variety of useful heterocycles as β-lactams, 2-azetidinethiones, azetidinimines, oxazolidin-2-ones, and 2-amino-1-azetines or of highly functionalized alicyclic compounds, such as 1,2-amino alcohols and 1,2-amino acids. The literature reports on the synthesis of a number of 2-azetidiniminium salts by reaction, in the presence of Et_3N, of imines with α-chloro iminium chlorides, which were obtained by reaction of tertiary carboxamides with phosgene. The mechanism of the formation of these salts follows very closely that of the formation of β-lactams obtained *via* addition reaction of acid chlorides, imines, and Et_3N. In fact, several pathways can lead to a 2-azetidiniminium salt or to a β-lactam starting from an iminium salt or an acid chloride, respectively. As far as the formation of β-lactams is concerned, different electrophilic species, such as the acid chloride, the ketene, *N*-acylammonium, or *N*-acyliminium species may play a role in the reaction.[2a−g] In several cases it has been demonstrated that the type of electrophilic species depends on the sequence of the addition of the base, which more often causes an inversion of the stereochemical output (*cis*/*trans*) of the reaction.[3a−e] Similarly, the synthesis of 2-azetidiniminium salts involves the reaction of an imine with different electrophilic species derived from the tertiary carboxamide, such as the corresponding α-chloro iminium chloride (**A**, Scheme 1) or the α-chloro enamine (**B**), produced *in situ* by base-induced dehydrohalogenation of **A**, or the keteniminium salt (**C**), which is reversibly produced from the α-chloro enamine. Depending on the sequence of the base addition, the α-chloro iminium chloride (**A**) may be the partner in the aminoalkenylation of the Schiff base (step 2, method A) to give the intermediate **D**. Base-induced dehydrohalogenation of **D** produces the intermediate **E** (step 3), which can ionize to the *N*-enamino iminium derivative **F** (step 4). The formation of the 2-azetidiniminium chloride from intermediate **E** can occur *via* an S_N2 displacement (step 5) or *via* a [2 + 2] conrotatory cycloaddition of **F** (step 8). Alternatively, the α-chloro enamine **B** may be produced

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(1) (a) De Poortere, M.; Marchand-Brynaert, J.; Ghosez, L. *Angew. Chem., Int. Ed. Engl.* **1974**, *13*, 267−268. (b) Marchand-Brynaert, J.; Moya-Portuguez, M.; Lesuisse, D.; Ghosez, L. *J. Chem. Soc., Chem. Commun.* **1980**, 173−174. (c) Ghosez, L.; Bogdan, S.; Ceresiat, M.; Frydrych, C.; Marchand-Brynaert, J.; Moya-Portuguez, M.; Hubert, I. *Pure Appl. Chem.* **1987**, *59*, 393−398 and references therein. (d) Ghosez, L.; Marchand-Brynaert, J. *Adv. Org. Chem.* **1976**, *9*, 421−531. (e) Ghosez, L.; Marchand-Brynaert, J. Formation of Four-membered Heterocycles. In *Comprehensive Organic Synthesis;* Trost, B. M., Fleming, I., Paquette, L. A., Eds.; Pergamon Press: Oxford, 1991; Vol. 5, pp 85−122. (f) Marchand-Brynaert, J.; Moya-Portuguez, M.; Hubert, J.; Ghosez, L. *J. Chem. Soc., Chem. Commun.* **1983**, 818−819.

(2) For example, Linch has clearly shown, by FTIR spectroscopy, that β-lactam formation occurred in a number of cases exclusively through a ketene intermediate. Alternatively, Bose showed that the addition of the acyl chloride to the imine produces, with a reversible equilibrium, an intermediate that cyclizes to a β-lactam under the influence of the tertiary base. See, for example: (a) Linch, J. E.; Riseman, S. M.; Laswell, W. L.; Tschaen, D. M.; Volante, R. P.; Smith, G. B.; Shinkai, I. *J. Org. Chem.* **1989**, *54*, 3792−3796. (b) Bose, A. K.; Spiegelman, G.; Manhas, M. S. *Tetrahedron Lett.* **1971**, *34*, 3167−3170. (c) Bose, A. K.; Chiang, Y. H.; Manhas, M. S. *Tetrahedron Lett.* **1972**, *34*, 4091−4094. (d) Duran, F.; Ghosez, L. *Tetrahedron Lett.* **1970**, 245−248. (e) Decazes, J. M.; Luche, J. L.; Kagan, H. B. *Tetrahedron Lett.* **1972**, 3633−3636. (f) Bellus, D. *Helv. Chim. Acta* **1975**, *58*, 2509−2511. (g) Reference 4c.

(3) For a dependence of the stereochemical outcome on the sequence of the reagent addition, on the solvent, and on the base in the formation of β-lactams, see: (a) Bose, A. K.; Anjaneyulu, B.; Bhattacharaya, S. K.; Manhas, M. S. *Tetrahedron* **1967**, *23*, 4769−4776. (b) Wells, J. N.; Lee, R. E. *J. Org. Chem.* **1969**, *34*, 1477−1479. (c) Nelson, D. A. *J. Org. Chem.* **1972**, *37*, 1447−1449. (d) Arrieta, A.; Lecea, B.; Palomo, C. *J. Chem. Soc., Perkin Trans. 1* **1987**, 845−850. (e) See ref 2b,c.

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Scheme 1

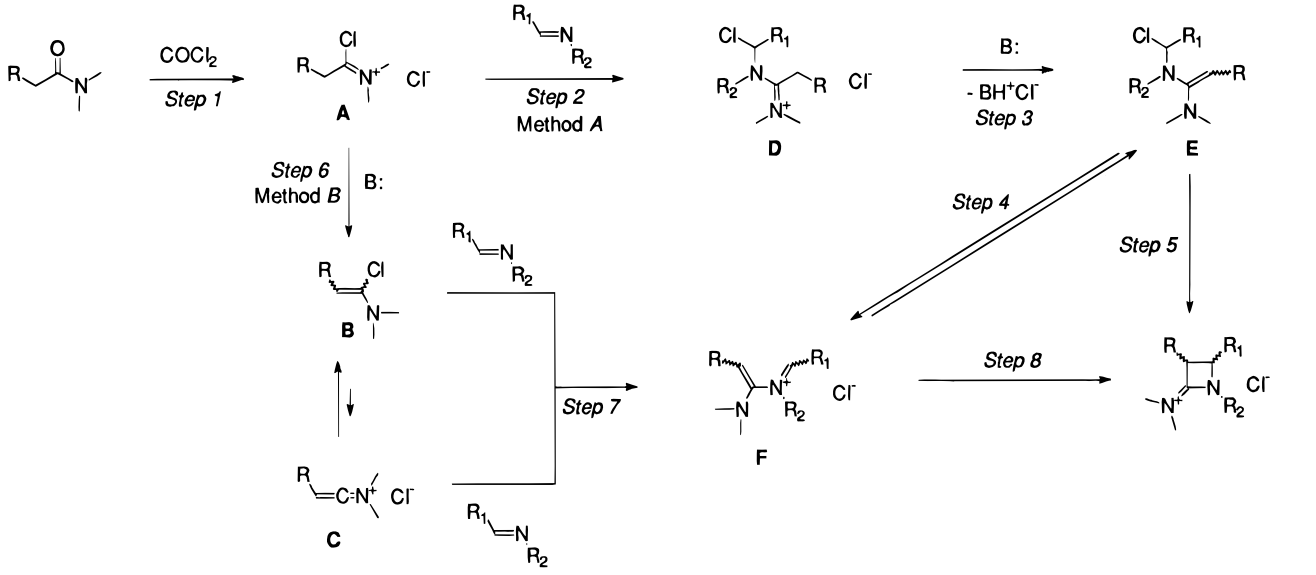
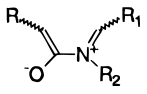


Chart 1

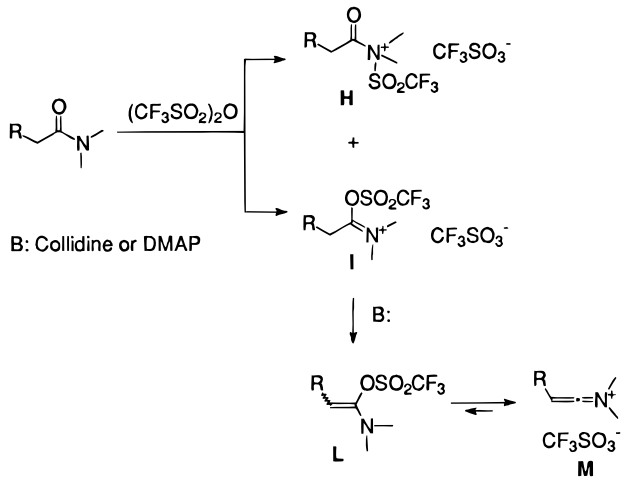


G

by base induced dehydrohalogenation of the α-chloro iminium chloride (**A**) (step 6, method B). According to Ghosez's suggestions:[1a] "the exceptional reactivity of α-chloroenamines toward nucleophilic reagents probably results from a fast pre-equilibrium of the α-chloroenamine with the corresponding keteniminium chloride." Whether the α-chloro enamine or the keteniminium chloride (**C**) are the partners in the aminoalkenylation of the Schiff base, such addition directly produces intermediate **F** (step 7).

It is worth noting that intermediate **F** is structurally similar to the zwitterionic intermediate (**G**, Chart 1) that is responsible for the preferential *cis*-selectivity in the formation of *β*-lactams *via* ketene/imine cycloadditions.[4a–d] In contrast, a preferential *trans* selectivity has been observed in the formation of 2-azetidiniminium chlorides irrespective of the sequence of the base addition. For this reason it is generally believed[1e] that the cycloadditions involving keteniminium salts are *trans* stereoselective. In our opinion, while the *trans* selectivity can be explained on steric grounds when the 2-azetidiniminium chlorides are formed *via* step 2, i.e., with the formation of the less congested and thermodinamically more stable stereoisomer, it is not clear why a *trans* selectivity should be observed when the 2-azetidiniminium salts are formed *via* step 6. In this case, in fact, if the aminoalkenylation of the Schiff base involves the keteniminium salt as the partner, the stereochemical output of the cycloaddition should be closely similar to that observed in the ketene/imine cycloadditions. At present, excellent theoretical studies have been reported on the mechanism of the *β*-lactam formation.[5a,b] These studies, involving a *bona fide* ketene intermediate as the electrophilic partner, are very useful tools in accounting for the observed stereochemical course of the reaction. In contrast, to our knowledge nothing has been reported in the literature regarding computational studies on the reactions involving the isoelectronic keteniminium salts as the partners of imines in concert with a systematic synthetic study.

Scheme 2



Interestingly, non-nucleophilic precursors of keteniminium salts, i.e., the (*N*,*N*-dialkylamino)alkenyl trifluoromethanesulfonates, have been synthesized from the sulfonylation of tertiary amides with trifluoromethanesulfonic anhydride.[6] The sulfonylation generally produces mixtures of *N*-sulfonylated (**H**, Scheme 2) and of *O*-sulfonylated products (**I**). When the sulfonylation is performed in the presence of a tertiary base, the *O*-sulfonylated derivatives are converted into (*N*,*N*-dialkyl-

(4) For a detailed discussion on the stereoselectivity problem in the ketene–imine cycloaddition, see, for example: (a) Hegedus, L. S.; Montgomery, J.; Narukawa, Y.; Snustad, D. C. *J. Am. Chem. Soc.* **1991**, *113*, 5784–5791 and references therein. (b) Brady, W. T.; Gu, Y. Q. *J. Org. Chem.* **1989**, *54*, 2838–2842. For a review of ketene–imine cycloaddition to produce *β*-lactams, see, for example: (c) Holden, K. G. Total Synthesis of Penicillins, Cephalosporins, and Their Nuclear Analogs. In *Chemistry and Biology of β-Lactam Antibiotics*; Morin, R. B., Gornan, M., Eds.; Academic Press: New York, 1982; Vol. 2, pp 114–131. (d) Georg, G. I.; Ravikumar, V. T. In *The Organic Chemistry of β-Lactams*; Georg, G. I., Ed.; VCH: New York, 1993; pp 295–368.

(5) For semiempirical theoretical studies on the formation of the *β*-lactams see: (a) Cooper, R. D. G.; Daugherty, B. W.; Boyd, D. B. *Pure Appl. Chem.* **1987**, *59*, 485–494. (b) Cossio, F. P.; Ugalde, J. M.; Lopez, X.; Lecea, B.; Palomo, C. *J. Am. Chem. Soc.* **1993**, *115*, 995–1004 and references therein.

(6) Falmagne, J. B.; Escudero, J.; Taleb-Saharaoui, S.; Ghosez, L. *Angew. Chem., Int. Ed. Engl.* **1981**, *20*, 879–880.

Table 1. *Cis/Trans* Product Distribution and Isolated Yields of 2-Azetidiniminium Perchlorates 5−18 and of β-Lactams 19 and 20

entry	compd	R	R_1	R_2	*cis/trans* (yield, %)
1	**19**	C_6H_5	C_6H_5	(*S*)-(+)-$CHMeC_6H_5$	0.12 (39)
2	**20**	Me	C_6H_5	(*S*)-(+)-$CHMeC_6H_5$	*cis* (38)
3	**5**	Me	C_6H_5	C_6H_4-*p*-OMe	16.0 (46)
4	**6**	C_6H_5	Me	$CH(C_6H_5)_2$	*cis* (37)
5	**7**	Me	C_6H_5	$CH(C_6H_5)_2$	*cis* (55)
6	**8**	Me	C_6H_4-*p*-OMe	C_6H_4-*p*-NO_2	2.0 (58)
7	**9**	Me	C_2H_5O	C_6H_5	0.62 (45)
8	**10**	Pht[a]	C_6H_5	C_6H_4-*p*-OMe	*cis* (70)
9	**11**	Pht[a]	C_2H_5O	C_6H_5	1.2 (30)
10	**12**	Pht[a]	CO_2Me	$CH(C_6H_5)_2$	*cis* (48)
11	**13**	Me	C_6H_5	CH_3	5.0 (11)
12	**14**	Cl	C_6H_5	C_6H_4-*p*-OMe	*cis* (64)
13	**15**	C_6H_5O	C_6H_5	C_6H_4-*p*-OMe	*cis* (23)
15	**16**	C_6H_5	C_2H_5O	C_6H_5	1.8 (41)
16	**17**	C_6H_5O	C_2H_5O	C_6H_5	1.1 (16)
17	**18**	Me	CO_2Me	$CH(C_6H_5)_2$	*cis* (15)

[a] Pht = phthalimido.

amino)alkenyl triflurometanesulfonates (**L**), which spontaneously ionize to the corresponding keteniminium triflates (**M**).

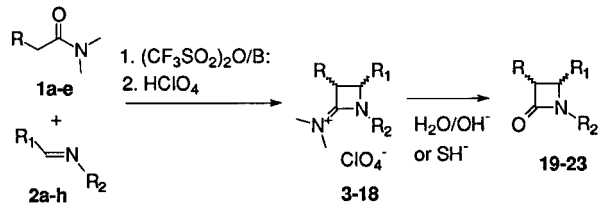
These observations sparked our interest in performing a systematic study of synthesis of *cis/trans* C_3,C_4-disubstituted 2-azetidiniminium salts *via* a protocol involving triflate salts of α-monosubstituted *N*,*N*′-dimethylamino-substituted carboxamides and aldimines. A comparison with the literature data regarding the chloride analogues, as well as the structurally related ketenes, will also be reported. The aim of the present study is to stimulate the interest of the researchers to perform computational studies on this subject which could be very useful in accounting for the observed stereochemical output of the above-mentioned reactions.[7,8]

Results and Discussion

For our study on diastereoselectivity a set of reactions between an array of monosubstituted (*N*,*N*-dimethylamino)alkenyl triflurometanesulfonates and an array of representative *N*-aryl- and *N*-alkyl-substituted imines was performed (Scheme 3 and Table 1).

The amides were selected based on the assumption that the formation of the 2-azetidiniminium triflates might proceed through a keteniminum intermediate. As a consequence, such selection was made according to the steric demand of the keteniminium salts, and thus, the amides were classified into three groups according to the size of their substituents. Such a classification follows the trend suggested by Georg,[4d] which allows for the prediction of the *cis/trans* stereochemistry of the Staudinger reaction involving imines and isoelectronic ketenes as the partners. As a general rule, the ketenes

Scheme 3



1a: R = C_6H_5; **1b**: R = Me; **1c**: R = Phtalimido; **1d**: R = Cl; **1e** = C_6H_5O
2a: R_1 = C_6H_5, R_2 = (*S*)-(+)-$CHMeC_6H_5$; **2b**: R_1 = C_6H_5, R_2 = C_6H_4-*p*-OMe;
2c: R_1 = Me, R_2 = $CH(C_6H_5)_2$; **2d**: R_1 = C_6H_5, R_2 = $CH(C_6H_5)_2$;
2e: R_1 = C_6H_4-*p*-OMe, R_2 = C_6H_4-*p*-NO_2; **2f**: R_1 = OC_2H_5, R_2 = C_6H_5;
2g: R_1 = CO_2Me, R_2: = $CH(C_6H_5)_2$; **2h**: R_1 = C_6H_5, R_2 = Me

3, 19: 1a+2a; **4, 20**: 1b+2a; **5, 21**: 1b+2b; **6, 22**: 1a+2c; **7, 23**: 1b+2d;
8: 1b+2e; **9**: 1b+2f; **10**: 1c+2b; **11**: 1c+2f; **12**: 1c+2g; **13**: 1b+2h;
14: 1d+2b; **15** = 1e+2b; **16** = 1a+2f; **17** = 1e+2f; **18** = 1b+2g

and the amides in the same group share similar preferences for the *cis* or the *trans* product formation with the same type of imines. The following amides were used: (a) the amide **1e** possessing the small sized substituent R = OC_6H_5 (group i); (b) the amide **1c** possessing the medium sized substituent phthalimido (group ii); and (c) the amides **1a**, **1b**, and **1d** possessing the large substituents C_6H_5, Me, and Cl (group iii). Similarly, the imines were also chosen according to Georg's classification. In particular, we used the imidate **2f**, which typically produces *trans*-configured products, the imine **2g** derived from glycolic acid that produces *cis*-configured products, and the *N*-arylimines **2b** and **2e** derived from amines of different basicity. A number of *C*-phenyl-substituted imines with different steric demand at nitrogen [(*S*)-**2a**, **2d**, and **2h**] and the C-methyl-substituted imine **2c** were also used. According to Hegedus' model[4a] for the Staudinger reaction we assume that these alicyclic aldimines exist predominantly as *trans* geometrical isomers.[9] In addition, we have confirmed the (*E*)-stereoconfiguration of imines **2a**, **2g**, and of **2h** by qualitative homonuclear NOE difference spectroscopy (see Experimental Section). The 2-azetidiniminium triflates were generated with a procedure similar to that used in the synthesis of cyclobutanones from olefins and tertiary amides; i.e., an equimolar solution of imine and 2,4,6-trimethylpyridine

(7) It is well known that a potentially interesting application of these heterocycles applies to the synthesis of β-lactams bearing stereogenic centers at C_3 and C_4 from the hydrolysis of chiral azetidiniminium salts derived from tertiary carboxamides with an asymmetric inductor at nitrogen, the inductor being recovered after the hydrolysis.[8] However, to achieve a good asymmetric induction in these reactions the following major problems must be solved, namely (i) A good control of the C_3, C_4-*trans*/*cis*-simple diastereoselection, which is the focus of the present study, (ii) A good control of the selectivity during the diastereoface-differentiating approach of the two reagents when one of them contains an asymmetric inductor, and (iii) the problem of the *cis* to *trans* isomerization of the azetidiniminium salts or of the β-lactams under the basic conditions used in both the cycloaddition and the hydrolysis step.

(8) For synthesis of chiral 2-azetidiniminium saltes, see: (a) Belzecki, C.; Rogalska, E. *J. Chem. Soc., Chem. Commun.* **1981**, 57−58. (b) Belzecki, C.; Rogalska, E. *J. Org. Chem.* **1984**, *49*, 1397−1402. (c) References 1c and 2e.

(9) This assumption is also the basis of the Georg stereochemical analysis.[4d] A preferential *trans*-configuration of the alicyclic aldimines is also assumed in the ester enolate−imine condensation route to β-lactams. See: Ha, D.-C.; Hart, D. J. Yang, T.-K. *J. Am. Chem. Soc.* **1984**, *106*, 4819−4825

(collidine) was added to a solution of a mixture of tertiary amide and trifluoromethanesulfonic anhydride.[10]

Since 2-azetidiniminium triflates **3** and **4** were inconvenient for both separation and ^{1}H NMR analysis, they were hydrolyzed directly to β-lactams **19** and **20** (Table 1, entries 1 and 2) according to the procedure used for the corresponding chlorides.[8b,11]

Instead, the 2-azetidiniminium triflates **5**−**18**, after their *cis*/*trans* isomer distribution was estimated directly for the crude reaction mixture by integration of the ^{1}H NMR signals, were rapidly converted and purified as perchlorate salts according to a general protocol (see Experimental Section). The samples of 2-azetidiniminium perchlorates **6**, **11**, and **13**−**17**, obtained after flash chromatographic workup, were still contaminated by variable amounts of the corresponding amides (Figures 2, 7, and 9−13, supporting information). The combustion analysis of compounds **5**, **7**−**10**, **12**, and **18**, not contaminated by the corresponding amides, was not feasible due to a presence of trace amounts of impurities such as the perchlorate salts of collidine and of the corresponding amides, which are barely detectable in their ^{1}H NMR spectra (see Figures 1, 3−6, 8, and 14, supporting information).[12] Nevertheless, the structures of the 2-azetidiniminium perchlorates were confidently assigned on the basis of their IR spectra, which showed an intense peak in the 1695−1720 cm^{-1} region, attributed to the exocyclic NC=N$^+$ function. HRMS spectra revealed the presence of two major peaks, one corresponding to m/z = M$^+$ − $HClO_4$, the other corresponding to the starting imine. Attached proton tests (APT) or distorsionless enhancement by polarization transfer (DEPT) experiments were performed to distinguish the different carbons. The stereochemistry at C_3 and C_4, when both *cis* and *trans* isomers were formed (compounds **5**, **8**, **9**, **11**, **13**, **16**, and **17**), was established by ^{1}H NMR analysis. The *cis* isomer gives a larger coupling constant than the *trans* isomer.[13] The assignment of *cis* stereochemistry to compounds **6** and **7** is evident just by examining the values of the coupling constants $J_{3,4}$ of the corresponding *cis*-β-lactams **22** and **23** (see Experimental Section), which are larger than 4.5 Hz[14] in all cases. Instead, the *cis* stereochemistry of **10**, **12**, **14**, and **15** was demonstrated by performing a *cis* to *trans* base-induced isomerization.[15,16] No variations in the *cis*/*trans* diastereoselection were observed when the reactions of entries 1−4 were performed in the presence of 2, 6-di-*tert*-butyl-4-methylpyridine (DMP) instead of collidine[17] or when the order of addition of the reagents was changed (see Experimental Section). Control experiments demonstrated that no epimerization occurred under the reaction conditions.[18]

Table 2. *Cis*/*trans* Product Distribution of Azetidiniminium Chlorides and Triflates Obtained from α-Chloro Iminium Chlorides (Method A or B) and from (*N*,*N*-Dimethylamino)alkenyl Trifluoromethanesulfonates

			cis/*trans* product distribution	
entry	amide	imine	chlorides	triflates
1	**1a**	**(*S*)-2a**	20/80[a] (A)	11/89
2	**1b**	**(*S*)-2a**	33/66[a] (A)	cis
3	**1b**	**2d**	25/75[b] (B)	cis
4	**1b**	**2g**	20/80[b] (B)	cis
5	**1c**	**2g**	3/97[c] (B)	cis
6	**1d**	**2b**		cis
7	**1d**	**PhCH=NPh**	*trans*[d] (B)	

[a] Reference 8b. The *cis*/*trans* product distribution is referred to the corresponding β-lactams. [b] Reference 1b. [c] Reference 1f. [d] Reference 1d.

The product distribution of reactions of amide chlorides and triflates generated from the same carboxamide is compared with the same imine (entries 1−5) or different imines with closely similar structures (**2b** of entry 6 and C_6H_5CH=NC_6H_5 of entry 7) in Table 2. As a general rule, the stereochemical output of the reactions of amide chlorides is in stark contrast to that of the corresponding triflates. In fact, only the reactions reported in entry 1 (Table 2) gave rise to similar product distributions. Instead, the reactions of entries 2−6 (Table 2), *via* triflate protocol, gave *cis* products stereoselectively, while the reactions of entries 2−5 and 7, *via* the chloride protocol, afforded the corresponding *trans*-2-azetidiniminium chlorides as the major isomers of variable *cis*/*trans* mixtures. These results suggest that the reactions performed via triflate protocol involve the formation of a keteniminium triflate intermediate as the electrophilic partner of the imine. The opposite trend observed in the reactions performed via chloride protocol suggests an alternative route involving the attack of a different electrophile such as the α-chloro iminium chloride or the α-chloro enamine. It is worth noting that the 2-azetidiniminium chlorides were obtained by two different methods (A and B, Scheme 1 and Table 2), which differ in the sequence of the base

(10) Schmit, C.; Falmagne, J. B.; Escudero, J.; Vanlierde, H.; Ghosez, L. *Org. Synth.* **1990**, *69*, 199−204.

(11) It has been demonstrated by Rogalska[8b] that the NaOH-induced hydrolysis of the chloride analogs of the triflate salts **3** and **4** to the corresponding β-lactams **19** and **20** caused no change in their diastereomeric ratio (3*R*,4*S*/3*S*,4*R*/3*R*,4*R*/3*S*,4*S*).

(12) A partial ClO_4^-/Cl^- ion exchange, which may occur during the extraction of the collidine perchlorate from the mixture of perchlorate salts with a 6 N aqueous solution of HCl (see Experimental Section), and/or an incomplete $CF_3SO_3^-$/ClO_4^- ion exchange cannot be excluded in principle. This may cause the presence of the corresponding triflate and chloride salts, as impurities, in the sample of 2-azetidiniminium perchlorates isolated after the chromatographic workup.

(13) Jackmann, L. M.; Sternhell, S. In *Applications of Nuclear Magnetic Resonance Spectroscopy in Organic Chemistry*; Barton, D. H. R., Doering, W., Eds.; Internetional Series of Monographs in Organic Chemistry; Pergamon: Oxford, 1969; Vol. 5, Chapters 3−8, p 234. Larger coupling constant values of the vicinal hydrogens and at C_3 and at C_4 in the *cis* isomers are observed in related small ring heterocycles as β-lactams, 2-iminooxetanes, oxetanes, and azetidines. See, for example: (a) Barbaro, G.; Battaglia, A.; Giorgianni, P. *J. Org. Chem.* **1988**, *53*, 5501−5506. (b) Aben, R. W. M.; Smit, R.; Schreen, J. W. *J. Org. Chem.* **1987**, *52*, 365−370. (c) Aben, R. W. M.; Ooms, P. H. J.; Nivard, R. J. F. *J. Org. Chem.* **1977**, *42*, 3128−3132.

(14) Alcaide, B.; Dominguez, B.; Escobar, G.; Parreno, U.; Plumet, J. *Heterocycles* **1986**, *24*, 1579−1583 and references therein.

(15) 2-Azetidiniminium salts behave similarly to the corresponding β-lactams. In fact, a base-induced isomerization of the C_3, C_4-disubstituted *cis*-β-lactams to the thermodynamically more stable *trans*-isomers is observed when acidic protons are present at C_3 or at C_4.[17] Similarly, we observed (Battaglia, A. Unpublished results) a competitive partial *cis* to *trans* $NaHS^-$-induced isomerization of the *cis*-2-azetidiniminium perchlorates **10**, **12**, **14**, and **15** when their conversion to the corresponding thiones was performed.[1f] Even if $NaHS^-$ is considered a weak base, the presence of a heteroatom (N, Cl, O) at the C_3 carbon atom of **10**, **12**, **14**, and **15** favors the isomerization. By contrast, no isomerization was observed when *cis*/*trans* mixtures of the chloride salts of **3**[8b] (20/80), **4**[8b] (33:66), and **7**[1f] (25/75) or of the triflates **5** (*cis*/*trans* = 16:1), *cis*-**6**, and *cis*-**7** (see Experimental Section) were hydrolyzed in the presence of the stronger base NaOH.

(16) Ogliaruso, M. A.; Wolfe J. F. In *Synthesis of Lactones and Lactams*; Patai, S., Rappoport, Z., Eds.; John Wiley & Sons: Chichester, 1993; Chapter 2, pp 880−883 and references therein.

(17) Instead, a substantial variation of the 3(*S*),4(*S*)/3(*R*),4(*R*) and of the 3(*S*),4(*R*)/3(*R*),4(*S*) with the type of the base was observed in the reactions of entries 1 and 2 (Table 1), see Experimental Section.

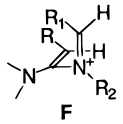
(18) An In principle possible partial *cis* to *trans* isomerization of the azetidinium triflates **8**, **9**, **11**, **16**, and **17** may occur during their formation. Such isomerization causes some interpretative problems of the stereochemical output of these reactions. However, in our opinion, it is quite probable that these salts will not epimerize since compounds *cis*-**10**, *cis*-**12**, *cis*-**14**, and *cis*-**15**, which slowly epimerize in the presence of $NaHS^-$ (see ref 15), are stable under the reaction conditions.

addition. However, as the monosubstituted enamines are prepared *in situ* due to their thermal instability, the presence of the α-chloro iminium chloride as a competitive reagent cannot be excluded *in principio*. A quite similar behavior has been observed by Bose[2b,c,3a] when C_3,C_4-disubstituted *β*-lactams were synthesized according to two methods (A, B) that differ in the sequence of the base addition. In procedure A the acyl chloride and the imine were admixed before the base was added. Formation of the *β*-lactam probably occurs via direct attack of the imine to the acyl chloride with the formation of an acyl ammonium intermediate. In procedure B the acyl chloride was added to a solution of the imine and base. As an alternative, procedure B may involve the ketene pathway. Procedure A usually gave a larger amount of *trans β*-lactams than procedure B.

The 2-azetidiniminium salts synthesized *via* the α-cloro iminium chloride protocol were usually obtained in higher yields with respect to the corresponding triflates. Similarly, *β*-lactams were usually obtained in higher yields when prepared *via* procedure A. In several cases we have also observed that the yields of 2-azetidiniminium perchlorates are higher or comparable with the yields of the corresponding *β*-lactams when the keteniminium triflates and the corresponding ketenes are involved as the possible intermediates.[19] For example, the imidate **2f** afforded only trace amounts of *β*-lactam with $C_6H_5CH{=}C{=}O$ and $MeCH{=}C{=}O$ and afforded 31% and 42% yields with $C_6H_5OCH{=}C{=}O$ and $PhtCH{=}C{=}O$, while the corresponding 2-azetidiniminium perchlorates were obtained in 41% (entry 15, Table 1), 45% (entry 7), 16% (entry 16), and 30% yield (entry 9), respectively. Similarly, benzylidene-*N*-phenylimine gave the *β*-lactam in 30% with $PhtCH{=}C{=}O$, 19% with $ClCH{=}C{=}O$, and 50% with $MeCH{=}C{=}O$, while the structurally closely related imine **2b** afforded the corresponding 2-azetidiniminium perchlorates in 70% (entry 8, Table 1), 64% (entry 12), and 46% (entry 3) yields. Only in one case was the 2-azetidiniminium perchlorate obtained in substantial lower yields (23%, entry 13, Table 1) with respect to that observed (89%) in the reaction involving benzylidene-*N*-phenylimine and $C_6H_5OCH{=}C{=}O$.

The hypothesis that keteniminium triflates are involved as the transient intermediates has stimulated our interest to probe specific substituents in the amide and in the imine in order to introduce a controlled range of both steric bulk and electronic effects. This may provide further information on the mechanism of these reactions, especially if we compare the stereochemical output of the reactions in Table 1 with those observed in the annulation of imines to the structurally related isoelectronic ketenes. In fact, a useful model for the keteniminium salt/imine cycloadditions could be the one described by Hegedus[4a] for the Staudinger reaction. According to this model, the addition of imine to the keteniminium salt takes place *via* an attack of the nonbonding electrons of the nitrogen atom of the imine to the LUMO of the keteniminium C=N group, which is coplanar to the substituent R. The approach of the imine occurs from the less hindered side of the keteniminum triflate so that steric interactions are minimized. In other words, the hydrogen atom of the heterocumulene is *endo* oriented and the R group is *exo* oriented. Such an attack gives

Chart 2



F

rise to the intermediate **F** of Scheme 1 with the plane of the imine portion perpendicular to that of the enamine portion (Chart 2). Electrocyclic conrotatory ring closure produces the thermodynamically less stable *cis*-2-azetidiniminium salt. The formation of *cis*−*trans* product mixtures can be explained with this mechanism provided that structure **F** is an intermediate prior to the cyclization process. Thus, the substituent of the iminium fragment stabilizes the positive charge at the carbon atom favoring the rotation around the C−N bond and leading to the formation of the thermodynamically more stable *trans* isomer. Due to the similarity of this model with the one suggested for the Staudinger reaction, the rules for ketenes and imines suggested by Georg to explain, or predict, the stereochemical output of the Staudinger reactions, which are substantiated by the experimental findings of several researchers, may constitute a powerful tool for a comparison of the reactions of Table 1 with those of structurally related ketenes and imines.

(A) Stereoelectronic Effects of the Substituents of the Imines on the *Cis*/*Trans* Product Distribution. We already examined the *cis* selectivity of the reactions of the electrophilically activated imine **2g** with carboxamides **1b** and **1c**, which bear a large and a medium sized substituent, respectively. According to Georg's stereochemical rules, this type of imine produces exclusively *cis* products regardless of the partner since the α-carbonyl group prevents the stabilization of intermediate **F**. Similar results have also been reported for the Staudinger reaction. For example, in the literature[20] *cis* products have been reported to be stereoselectively formed in the reaction of $MeCH{=}C{=}O$ with MeO_2-$CCH{=}NC_6H_4$-*p*-OMe. In contrast, preferential *trans* product formation has been observed in the reactions of imidate **2f** regardless of the type of ketene[2c] ($RCH{=}C{=}O$: R = Me, Pht, C_6H_5, C_6H_5O). In our hands the imidate **2f** gave variable *cis*/*trans* mixtures with the structurally related keteniminium salts (Table 1). The *trans* selectivity can be explained by the ability of the imidate to stabilize the positive charge at the carbon atom of the iminium fragment of **F**.[21] It is worth noting, however, the greater *cis* selectivity of the reaction of the keteniminum triflates with respect to the related ketenes. Following the considerations above, we examined the stereochemical behavior of the diarylimine **2b**. According to Georg, the diarylimines possess a borderline behavior since they form *cis* products with ketenes with small substituents and *trans* products with ketenes with large substituents. For example, $C_6H_5CH{=}NC_6H_5$ was reported to give a *cis*/*trans* = 6:1 mixture of *β*-lactams with $C_6H_5OCH{=}C{=}O$ and the *trans* isomer with $MeCH{=}C{=}O$,

(19) The yields on *β*-lactams here reported are taken from ref 2c, and they refer to a typical protocol (method A) that involves the formation of the ketene as the possible intermediate. According to this method the acyl chloride was added to a mixture of imine and Et_3N.

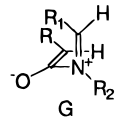
(20) (a) Palomo, C.; Ontoria, J. M.; Odriozola, J. M.; Aizpurua, J. M.; Ganboa, I. *J. Chem. Soc., Chem. Commun.* **1990**, 248−249.

(21) According to Cossio, theoretical studies of the Staudinger reaction between methoxyketene and a simple imidate provide an explanation for the *trans* selectivity observed. The key step responsible for this stereochemical outcome is a facile interconversion between two zwitterionic intermediates through a biradical transition state. These studies use the AM1 semiempirical Hamiltonian and unrestricted Hartree−Fock (UHF) calculations. See: Arieta, A.; Ugalde, J. M.; Cossio, F. P. *Tetrahedron Lett.* **1994**, *35*, 4465−4468.

PhtCH=C=O, and ClCH=C=O.[2c] In our hands, **2b** gave *cis* products regardless of the size of the substituent of the amides (**1b**, **1c**, **1d**, and **1e**), once more proving the greater aptitude of the amide triflates to give *cis*-configured products with respect to the corresponding ketenes. Another interesting electronic effect on the stereochemical output of these reactions is the basicity of the imines derived from *N*-arylamines. In the Staudinger reaction the relative amount of *trans* isomer increases when the basicity of the imine decreases. For example, when the C-aryl substituent of diaryl imines is a better cation-stabilizing group than that of the *N*-aryl substituent, the positive charge at the carbon atom of the iminium fragment is stabilized, thus allowing for bond rotation. This effect has been noticed in the synthesis of 3-phenoxy,[22] 3- azido,[23] and 3-*N*-methyl-*N*-phenyl-2-azetidinones.[4b] We observed a similar behavior when **1b** was reacted with the imines **2b** and **2e**. The less basic imine **2e** gave a *cis*/*trans* mixture of products while **2b** was *cis*-diastereoselective. As far as the steric effects are concerned, the *cis*/*trans* product distribution should be influenced by the steric bulk of the *N*-substituent. That is, as the *N*-substituent becomes smaller, its steric interaction with the adjacent substituent at the carbon atom of the iminium fragment decreases, hence favoring the isomerization. This effect has been observed in the reaction of ketenes with cinnamylidene imines[24] and $(Me_3Si)_2CH$-*N*-substituted imines.[25] We probed this effect by reacting the triflate of amide **1b** with benzylidene imines with increasing steric demand at the nitrogen atom, in the order: *N*-Me (**2h**), *N*-C_6H_4-*p*-OMe (**2b**), *N*-$CHMeC_6H_5$ (**2a**), *N*-$CH(C_6H_5)_2$ (**2c**) (Table 1, entries 11, 3, 2, and 4, respectively). Not surprisingly, the imine **2h** gave the higher relative amount of *trans* isomer (*cis*/*trans* = 5.0) while **2b** gave a *cis*/*trans* ratio of 16.0 and the sterically hindered imines **2a** and **2c** gave the *cis* isomer, exclusively. In our opinion, these results also suggest that the steric bulk of the substituent on the nitrogen atom plays a minor role, with respect to electronic effects, in the stereochemical output of these reactions.

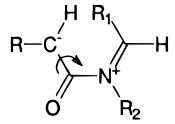
(B) Stereoelectronic Effects of the Substituents at the Carbon Atom of the *N*-Dimethyl-Substituted Carboxamides on the *Cis/Trans* Product Distribution. According to Georg the trends for preferential *cis*/*trans* product formation in the Staudinger reactions can be correlated with the steric demand of the ketenes. Structurally related ketenes belonging to the groups i and iii show a strong preference for *cis* and *trans* products, respectively, while the ketenes belonging to the groups ii typically give *cis* products with alkylarylimines and *trans* products with diarylimines. In contrast, no correlation between the stereochemical results and the steric effects of the substituents of the keteniminum triflates was found. For instance, the diarylimine **2b** gave only *cis* products with amides **1e** (group i), **1c** (group ii), **1d** (group iii), and a 16:1 *cis*/*trans* mixture with **1b** (group iii), while the imidate **2f** gave the following *cis*/*trans* mixtures: 1.1 with amide **1e**, 1.2 with amide **1c**, 1.8 with amide **1a** (group iii), and 0.60 with amide **1b**. In particular, no clear trend with the type of substituent of the amide was observed in the reactions involving the imidate **2f**, even if substantial amounts of *trans* products were always formed. These results clearly indicate that the substituent in the amide plays a minor role in the stereochemistry of the formation of the 2-azetidiniminium triflates with respect to that of the corresponding ketenes in the Staudinger reaction.

Chart 3



G

Chart 4



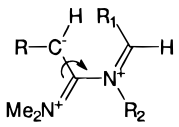
G'

Conclusions

We have shown that the iminium triflate salt/imine protocol for the synthesis of 2-azetidiniminium salts is complementary to the one employed for the chloride analogs since it is possible to modulate the *cis*/*trans* diastereoselection using the same partners. On the whole, these two protocols may constitute attractive alternative routes to that of the Staudinger reaction for the synthesis of β-lactams. The stereochemistry of the reactions involving amide triflates shows trends closely similar to those observed in the Staudinger reaction depending on the structural effects of the imine partner. Consequently, keteniminium triflates and isoelectronic ketenes share similar preferences for the *cis*/*trans* product formation with the same type of imines. These preferences can be explained by the fact that intermediates **F** and **G** display similar features for the iminium fragment of the molecule. On the other hand, while clear trends in the stereochemical output of the Staudinger reactions with the steric demand of the ketenes are observed, the substituent of the amide does not seem to play a similarly pivotal role in the iminium triflate salt/imine protocol. The different stereochemical results obtained in the reactions of ketenes and of the corresponding keteniminium triflates with the same imines probably derive from the different electronic effects of the heteroatom (O^-, $:NMe_2$) in the enolate and in the enamino fragments of **G** and **F**, exclusively, since the steric demand of both intermediates is identical. These electronic effects may be tentatively explained provided that in both reactions the cyclization does not proceed directly from the initially formed intermediates, as depicted in Charts 2 and 3, rendering rotation around the enolate and the enamine portion of **G** and **F** possible. In the Staudinger reaction, such isomerization is favored by good anion stabilizing groups that stabilize the resonance structure **G′** (Chart 4), thus favoring the rotation around the enolate portion of the molecule (prior to cyclization) leading to the formation of the more stable *trans* isomer. In contrast, the effect of the anion-stabilizing group in the enamino portion of **F** is far less important since the contribution of the structure **F′**

(22) Sharma, S. D.; Kaur, S.; Mehra, U. *Indian J. Chem. Sect. B* **1986**, *25*, 141−144.
(23) Just, G.; Ugolini, A.; Zamboni, R. *Synth. Commun.* **1979**, *9*, 117−121.
(24) Moore, H. W.; Hughes, G.; Srinavasachar, K.; Fernandez, M.; Nyugen, N. W.; Shoon, D.; Tranne, A. *J. Org. Chem.* **1985**, *50*, 4231−4238.
(25) Palomo, C.; Aizpurua, J. M.; Iturburu, M.; Urchegui, R. *J. Org. Chem.* **1994**, *59*, 240−244.

Chart 5



F'

(Chart 5) to the resonance hybrid is negligible. Put in another way, the π bond order of the enamino fragment of **F** is greater than that of the corresponding enolates **G**, so that rotation around the C_2-C_3 bond in **F** is unfavored.[26] From the comparison so far reported it appears that, as opposed to that reported by Georg, not only the steric demand but also the electronic effects of the substituents of the ketenes play a pivotal role in the stereochemical output of the Staudinger reaction.[27]

Experimental Section

General Procedures. ^{1}H and ^{13}C NMR spectra were recorded at 200 and 50 MHz, respectively, in $CDCl_3$ solvent. Chemical shifts are in δ ppm downfield from TMS; signal multiplicities were established by DEPT or APT experiments. Coupling constants *J* are given in Hz. For ^{13}C NMR spectra only relevant resonances are given. All reactions were run under a dry nitrogen atmosphere. All the solvents were dried and distilled by standard procedures. The tertiary amides and the aldimines were prepared according to standard procedures and were characterized by their satisfactory spectroscopic data. The (*E*)-configuration of **2a**, **2g**, and **2h** was confirmed by qualitative homonuclear NOE difference spectroscopy. **2a**: ^{1}H NMR ($CDCl_3$) δ 1.67 (d, 3 H, Me of NCH*Me*C_6H_5, $J = 7.5$ Hz), 4.61 (q, 1 H, CH of NC*H*MeC_6H_5), 5.65 (d, 1 H, $J = 5.1$ Hz), 7.30−7.90 (m, 10 H, arom), 8.43 (s, 1 H of *H*-C=N). The irradiation of the signal centered at δ 8.43 ppm showed a large enhancement (14%) of the neighboring proton centred at 4.61 ppm. **2g**: ^{1}H NMR ($CDCl_3$) δ 3.88 (s, 3 H, Me of CO_2*Me*), 5.69 (d, 1 H, CH of NC*H*(C_6H_5)$_2$), 7.20−7.40 (m, 10 H, arom), 7.80 (d, 1 H, of *H*C=N, $J = 1.0$ Hz). The irradiation of the signal centered at δ 7.80 ppm showed a large enhancement (10%) of the neighboring proton centered at 5.69 ppm. **2h**: ^{1}H NMR ($CDCl_3$) δ 3.40 (d, 3 H, Me of N*Me*, $J = 1.7$ Hz), 7.35−7.45 (m, 3 H, arom), 7.65−7.75 (m, 2 H, arom), 8.25 (d, 1 H of *H*C=N, $J = 1.7$ Hz). The irradiation of the signal centered at δ 3.40 ppm showed a large enhancement (7%) of the neighboring proton centered at 8.25 ppm.

Synthesis of 2-Azetidiniminium Perchlorates. General Procedure. Unless otherwise stated, an equimolar mixture of imine and collidine in CH_2ClCH_2Cl was added at −20 °C to a solution of the amide and triflic anhydride. The progress of the reaction was monitored by IR following the formation of the peak of the 2-azetidiniminium triflate at 1695−1720 cm^{-1}. The solvent was evaporated, and the *cis*/*trans* product distribution of the 2-azetidiniminium triflates was determined by ^{1}H NMR. Unless otherwise stated, the oily residue was repeatedly extracted with Et_2O and dissolved in CH_2Cl_2. The mixture of the *cis*/*trans* 2-azetidiniminium triflates was converted into the corresponding perchlorate salts. The collidine perchlorate was extracted from the reaction mixture by washing with a 6 N aqueous solution of HCl and with H_2O. The organic layer was dried over Na_2SO_4. After evaporation of the solvent the 2-azetidiniminium perchlorates were purified by flash chromatography (SiO_2, CH_2Cl_2/CH_3CN).

Synthesis of *β*-Lactams. General Procedure. Unless otherwise stated, the conversion of 2-azetidiniminium salts to the corresponding β-lactams was performed with a 1 N aqueous solution of NaOH in a 1:2 mixture of acetone/H_2O. A specific example describing the hydrolysis of *cis*-**6** follows. A 1 N aqueous solution of NaOH (10 mL) was added to an acetone/H_2O solution (10 mL) of azetidinium perchlorate *cis*-**6** (0.41 g, 0.9 mmol). The solution was left at 25 °C for 1 h. The solvent was concentrated under vacuo and extracted with CH_2Cl_2. The organic layer was dried over Na_2SO_4. After evaporation of the solvent, chromatography (*n*-pentane/EtOAc, 13:2) afforded 0.22 g (76%) of ***cis*-3-phenyl-4-methyl-1-benzydryl-azetidin-2-one (*cis*-22)**: oil; ^{1}H NMR ($CDCl_3$): δ 0.75 (d, 3 H, $J = 7.4$ Hz), 3.97 (m, 1 H), 4.55 (d, 1 H, $J = 4.7$ Hz), 6.18 (s, 1 H), 7.10−7.40 (m, 15 H); ^{13}C NMR ($CDCl_3$) δ 16.4, 53.2, 57.7, 60.4, 127.4, 127.6, 127.9, 128.1, 128.5, 128.6, 128.7, 128.8, 129.0, 133.6, 138.5, 139.3, 168.1; IR 1744 cm^{-1}. Anal. Calcd for $C_{23}H_{21}NO$: C, 84.37; H, 6.46; N, 4.28. Found: C, 84.40; H, 6.50; N, 4.25.

Reaction of (*S*)-(+)-1-Phenyl-*N*-benzylideneethylamine [(*S*)-2a] and *N*,*N*-Dimethyl-2-phenylacetamide (1a). (i) A solution (5 mL) of imine (*S*)-**2a** (0.5 g, 2.40 mmol) and collidine (0.37 mL) was added over 20 min to a solution (6 mL) of amide **1a** (0.4 g, 2.45 mol) and triflic anhydride (0.41 mL). The solution was left at −20 °C for 5 h and then at 25 °C for 12 h. After the conversion of the diastereomeric 2-azetidiniminium triflates (3*R*,4*S*)-*trans*-**3**, (3*S*,4*R*)-*trans*-**3**, (3*R*,4*R*)-*cis*-**3**, and (3*S*,4*S*)-*cis*-**3** into the corresponding β-lactams according to the procedure described in ref 8b, the chromatography of the crude reaction mixture (SiO_2, C_6H_6/EtOAC, 10:1) gave 0.31 g (39%) of a 1:8.5 *cis*/*trans* mixture of β-lactams **19** (*RR*:*SS*:*RS*:*SR* = 4.0:4.0:33.0:35.0). (ii) A solution (5 mL) of **2a** (g, 0.42, 2.00 mmol) and DMP (0.41 g) was added over 20 min to a solution (6 mL) of **1a** (0.33 g, 2.02 mmol) and triflic anhydride (0.34 mL). The solution was left at -20 °C for 30 min then at 25 °C for 1 h. After hydrolysis of the 2-azetidiniminium salts, chromatography of the reaction mixture gave 0.18 g (28%) of a 1.0:8.0 *cis*/*trans* mixture of β-lactams **19** (*RR*:*SS*:*RS*:*SR* = 3.8:1.0:14.2:24.0). The spectroscopic data of (3*R*,4*S*)-*trans*-**19**, (3*S*,4*R*)-*trans*-**19**, (3*R*,4*R*)-*cis*-**19**, and (3*S*,4*S*)-*cis*-**19** are identical to those reported in the literature.[8b]

Reaction of (*S*)-(+)-1-Phenyl-*N*-benzylideneethylamine ((*S*)-2a) and *N*,*N*-Dimethyl-2-methylacetamide (1b). (i) A solution (6 mL) of imine (*S*)-**2a** (0.83 g, 3.97 mmol) and DMP (0.80 g) was added over 20 min at −20 °C to a solution (10 mL) of amide **1b** (0.40 g, 3.96 mmol) and triflic anhydride (0.68 mL). The reaction temperature was left at −20 °C for 15 min then at 25 °C for 2 h. After the conversion of the diastereomeric 2-azetidiniminium triflates (3*R*,4*S*)-*trans*-**4**, (3*S*,4*R*)-*trans*-**4**, (3*R*,4*R*)-*cis*-**4**, (3*S*,4*S*)-*cis*-**4** into the corresponding β-lactams according to the procedure described in ref 8b, the chromatography (*n*-pentane/EtOAc, 10:2) gave 0.40 g (38%) of a mixture of *cis*-β-lactams **20** (*RR*:*SS* = 1.4:1.0). (ii) A solution (6 mL) of **2a** (g, 0.62 g, 2.97 mmol) and collidine (0.40 mL) was added over 20 min at −20 °C to a solution (6 mL) of **1b** (0.30 g, 2.97 mmol) and triflic anhydride (0.51 mL). After the solution was stirred for 1 day at 25 °C, the workup of the reaction mixture as described above gave 0.27 g (34%) of a mixture of *cis*-β-lactams **20** (*RR*:*SS* = 0.9:1.0). (iii) A solution (6 mL) of (*S*)-**2a** (0.52 g, 2.49 mmol) and collidine (0.26 mL) was added over 30 min at 0 °C to a solution (8 mL) of **1b** (0.30 g, 2.97 mmol) and triflic anhydride (0.36 mL). After the solution was stirred for 12 h at 25 °C, the reaction mixture was worked up as described above. Chromatography gave 0.12 g (18%) of a 4.0:1.0 *cis*/*trans* mixture of β-lactams **20** (*RR*:*SS*:*RS*:*SR* = 1.0:7.0:1.0:1.0). The spectroscopic data of (3*R*,4*S*)-*trans*-**20**, (3*S*,4*R*)-*trans*-**20**, (3*R*,4*R*)-*cis*-**20**, and (3*S*,4*S*)-*cis*-**20** are identical to those reported in the literature.[8b]

***trans*- and *cis*-3-Methyl-4-phenyl-1-(4-methoxyphenyl)azetidine-2-(*N*-dimethyliminium perchlorate) (*trans*-**

(26) This hypothesis seems to fit into a framework of the mechanism suggested by Cossio.[5b] According to Cossio, MO calculations suggest a two-step nonconcerted mechanism for the Staudinger reaction. The first step consists of an attack of the nonbonding electrons of the nitrogen atom of the imine to the LUMO of the ketene with the formation of a zwitterionic transoid intermediate, which can rotate about N−C2 before the ring closure step. The stereochemistry depends on the geometry of the initial approach of the reagents. When an *E* imine is used, the substituent at the C4 position is inward with respect to the β-lactam ring. The formation of *cis*- and *trans*-β-lactams depends upon the *endo*/*exo* approach between the iminic nitrogen atom and the carbonyl group of the ketene and the relative in/out relationship between the C_3 and the C_4 substituents. Detailed computational studies are required to account for the differences in the stereochemical output observed when the type of heteroatom is changed.

(27) Nevertheless, the classification done by Georg is still very useful for a qualitative prediction of the stereochemical output of the Staudinger reaction.

and *cis*-5). (i) A solution (6 mL) of imine **2b** (0.52 g, 2.47 mmol) and DMP (0.5 mL) was added in 20 min at −20 °C to a solution (6 mL) of amide **1b** (0.25 g, 2.47 mmol) and triflic anhydride (0.41 mL). The reaction mixture was left at −20 °C for 20 min then at 25 °C for 12 h. After hydrolysis of the 2-azetidiniminium salts, chromatography of the reaction mixture (SiO_2, *n*-pentane/EtOAC, 5:1) gave 0.24 g (36%) of the corresponding *β*-lactams **21** (*cis*/*trans* = 16:1). (ii) To a cooled (−20 °C) solution (12 mL) of **2b** (0.52 g, 2.47 mmol), collidine (0.32 mL), and **1b** (0.25 g, 2.47 mmol) was added a solution (6 mL) of triflic anhydride (0.41 mL) in 2 h. The reaction mixture was left at 25 °C for 48 h. Workup of the reaction mixture as described above gave 0.26 g (40%) of *β*-lactams **21** (*cis*/*trans* = 16:1). (iii) To a cooled (−20 °C) solution (12 mL) of **2b** (0.52 g, 2.47 mmol) and collidine (0.32 mL) was added a solution (6 mL) of triflic anhydride (0.41 mL) and **1b** (0.25 g, 2,47 mmol) over 60 min. The reaction mixture was left at 25 °C for 48 h. The mixture of 2-azetidiniminium triflates was converted to the corresponding perchlorate salts. Chromatography (SiO_2, CH_2Cl_2/CH_3CN, 4:1) gave 0.45 g (46%) of a 16:1 *cis*/*trans* mixture of **5**. *cis*-**5**: ^{1}H NMR ($CDCl_3$) δ 1.13 (d, 3 H, J = 7.5 Hz), 2.97 (s, 3 H), 3.30 (s, 3 H), 3.72 (s, 3 H), 4.28 (m, 1 H), 5.65 (d, 1 H, J = 5.1 Hz), 6.70−7.50 (m, 10 H); ^{13}C NMR ($CDCl_3$): δ 10.5, 38.9, 40.6, 41.8, 55.4, 68.7, 114.7, 128.0, 128.3, 128.7, 129.2, 132.0, 160.1, 167.2; IR (CCl_4) 1700 cm^{-1}; HRMS *m*/*z* ($M^+ - HClO_4^-$) calcd for $C_{19}H_{22}N_2O$ 294.1732, found 294.1739. *trans*-**5**: ^{1}H NMR relevant resonances ($CDCl_3$) δ 1.69 (d, 3 H, J = 7.5 Hz), 4.97 (d, 1 H, J = 1.5 Hz). After hydrolysis of *cis*- and *trans*-**5**, chromatography (SiO_2, *n*-pentane/EtOAC, 5:1) gave 0.23 g (35%) of the corresponding *β*-lactams **21** (*cis*/*trans* = 16:1). The spectroscopic data of *cis*/*trans*-**21** are identical to those reported in the literature.[28]

***cis*-3-Phenyl-4-methyl-1-benzhydrylazetidine-2-(*N*-dimethyliminium perchlorate) (*cis*-6).** (i) A solution (6 mL) of imine **2c** (0.5 g, 2.44 mmol) and DMP (0.50 g) was added in 30 min to a solution (6 mL) of amide **1a** (0.40 g, 2.45 mmol) and triflic anhydride (0.41 mL). The solution was left at −20 °C for 1 h then at 25 °C for 2 h. After conversion of the azetidiniminium triflate to the corresponding perchlorate, chromatography (SiO_2, CH_2Cl_2/CH_3CN, 5:1) gave 0.41 g (37%) of *cis*-**6**: ^{1}H NMR ($CDCl_3$) δ 0.56 (d, 3 H, J = 6.8 Hz), 2.95 (s, 3 H), 3.13 (s, 3 H), 4.35 (m, 1 H), 4.98 (d, 1 H, J = 5.6 Hz), 6.67 (s, 1 H), 7.10−7.50 (m, 15 H); IR (CCl_4) 1705 cm^{-1}; ^{13}C NMR ($CDCl_3$) δ 15.9, 38.7, 41.7, 48.9, 60.2, 65.3, 127.7, 128.7, 128.9, 129.1, 129.2, 129.3, 129.7, 129.8, 130.2, 130.7, 135.5, 138.3, 166.0; HRMS *m*/*z* ($M^+ - HClO_4^-$) calcd for $C_{25}H_{26}N_2$ 354.2096, found 354.2110.

***cis*-3-Methyl-4-phenyl-1-benzhydrylazetidin-2-(*N*-dimethyliminium perchlorate) (*cis*-7).** (i) A solution (12 mL) of imine **2d** (1.88 g, 6.93 mmol) and collidine (1.06 mL) was added over 4 h at 25 °C to a solution (6 mL) of **1b** (0.70 g, 6.93 mmol) and triflic anhydride (1.25 mL). After conversion of the azetidiniminium triflate to the corresponding perchlorate, chromatography (SiO_2, CH_2Cl_2/CH_3CN, 5:1) gave 1.73 g (0.38 mmol, 55%) of *cis*-**7**: ^{1}H NMR ($CDCl_3$) δ 1.09 (d, 3 H, J = 7.6 Hz), 3.07 (s, 3 H), 3.26 (s, 3 H), 4.13 (m, 1 H), 5.04 (d, 1 H, J = 5.5 Hz), 6.53 (s, 1 H), 6.90−7.30 (m, 15 H); ^{13}C NMR ($CDCl_3$) δ 10.8, 39.3, 40.1, 41.3, 65.6, 66.1, 128.0, 128.2, 128.4, 128.6, 128.7, 128.8, 128.9, 132.7, 136.7, 137.2, 169.7; IR (CH_2Cl_2) 1699 cm^{-1}; HRMS *m*/*z* ($M^+ - HClO_4^-$) calcd for $C_{25}H_{26}N_2$ 354.2096, found 354.2092. After the hydrolysis of *cis*-**7**, chromatography (SiO_2, *n*-pentane/EtOAC, 6:1) gave 0.75 g (41%) of ***cis*-3-methyl-4-phenyl-1-benzhydrylazetidin-2-one (*cis*-23)**: mp 111−112 °C (from benzene/*n*-pentane); ^{1}H NMR ($CDCl_3$) δ 0.87 (d, 3 H, J = 7.6 Hz), 3.56 (m, 1 H), 4.80 (d, 1 H, J = 5.7 Hz), 5.64 (s, 1 H), 7.00−7.40 (m, 15 H); ^{13}C NMR ($CDCl_3$) δ 9.8, 49.1, 59.8, 62.7, 127.5, 127.6, 127.8, 128.2, 128.3, 128.4, 128.5, 135.9, 138.8, 139.5, 171.4; IR 1744 cm^{-1}. Anal. Calcd for $C_{23}H_{21}NO$: C, 84.37; H, 6.46; N, 4.28. Found: C, 84.33; H, 6.49; N, 4.24.

***trans*- and *cis*-3-Methyl-4-(methoxyphenyl)-1-(4-nitrophenyl)azetidine-2-(*N*-dimethyliminium perchlorate) (*trans*- and *cis*-8).** A solution (6 mL) of imine **2e** (0.7 g, 2.73 mmol) and collidine (0.32 mL) was added over 30 min at 0 °C to a solution (6 mL) of **1b** (0.25 g, 2.47 mmol) and triflic anhydride (0.41 mL). The reaction mixture was left at 25 °C for 24 h. The mixture of 2-azetidiniminium triflates was converted into the corresponding perchlorate salts. Chromatography (SiO_2, CH_2Cl_2/CH_3CN, 4:1) gave 0.63 g (58%) of *cis*- and *trans*-**8** (*cis*/*trans* = 2:1): IR 1710 cm^{-1}; HRMS *m*/*z* ($M^+ - HClO_4^-$) calcd for $C_{19}H_{21}N_3O_3$ 339.1583, found 339.1569. *cis*-**8**: ^{1}H NMR ($CDCl_3$) δ 1.21 (d, 3 H, J = 7.5 Hz), 3.09 (s, 3 H), 3.38 (s, 3 H), 3.73 (s, 3 H), 4.28 (m, 1 H), 5.77 (d, 1 H, J = 5.2 Hz), 6.80−8.20 (m, 8 H); ^{13}C NMR ($CDCl_3$) δ 10.6, 40.3, 41.3, 43.0, 55.3, 68.4, 114.6, 122.7, 125.0, 127.2, 130.0, 140.7, 147.5, 160.8, 167.1. *trans*-**8**: ^{1}H NMR ($CDCl_3$) δ 1.72 (d, 3 H, J = 7.2 Hz), 3.09 (s, 3 H), 3.43 (s, 3 H), 3.68 (s, 3 H), 3.90 (dq, 1 H), 5.20 (d, 1 H, J = 2.0 Hz), 6.80−8.20 (m, 8 H); ^{13}C NMR ($CDCl_3$) δ 12.6, 40.5, 41.1, 47.5, 55.3, 71.7, 114.8, 124.1, 124.9, 126.9, 129.8, 139.7, 147.4, 161.1, 166.1.

***trans*- and *cis*-3-Methyl-4-ethoxy-1-phenylazetidin-2-(*N*-dimethyliminium perchlorate) (*trans*- and *cis*-9).** A solution (6 mL) of imine **2f** (0.29 g, 1.94 mmol) and collidine (0.32 mL) was added over 30 min at 0 °C to a solution (6 mL) of **1b** (0.20 g, 1.94 mmol) and triflic anhydride (0.41 mL). The reaction mixture was left at 25 °C for 2 h. The 2-azetidiniminium triflates were converted into the corresponding perchlorates. Chromatography (SiO_2, CH_2Cl_2/CH_3CN, 4:1) gave 0.29 g (45%) of a 38:62 mixture of *cis*/*trans*-**9**: IR 1715 cm^{-1}; HRMS *m*/*z* ($M^+ - HClO_4^-$) calcd for $C_{14}H_{20}N_2O$ 232.1576, found 232.1584; ^{1}H NMR ($CDCl_3$) of the mixture of *cis*-**9** and *trans*-**9** δ 1.03 (t, 3 H, J = 7.5 Hz), 1.06 (t, 3 H, J = 7.5 Hz), 1.43 (d, 3 H, J = 7.6 Hz), 1.63 (d, 3 H, J = 7.6 Hz), 2.80 (s, 3 H), 2.88 (s, 3 H), 3.26 (s, 3 H), 3.23 (s, 3 H), 3.35-3.67 (m, 3 H, 1 H of C_3H of *trans* and 2 H of OCH_2 of *cis* and *trans*), 4.09 (m, 1 H), 5.33 (d, 1 H, J = 1.1 Hz), 5.58 (d, 1 H, J = 5.6 Hz), 7.30−7.60 (m, 5 H); ^{13}C NMR ($CDCl_3$) of the mixture of *cis*-**9** and *trans*-**9** δ 9.1, 11.2, 14.9, 15.0, 38.6, 39.3, 40.5, 41.0, 43.4, 46.0, 65.8, 67.6, 91.1, 94.2, 126.7, 127.0, 129.7, 130.0, 134.2, 134.9, 163.8, 165.9.

***cis*-3-Phthaloyl-4-phenyl-1-(4-methoxyphenyl)azetidine-2-(*N*-dimethyliminium perchlorate) (*cis*-10).** A solution (6 mL) of imine **2b** (0.81 g, 3.84 mmol) and collidine (0.48 mL) was added over 30 min at −20 °C to a solution (6 mL) of **1c** (0.90 g, 3.88 mmol) and triflic anhydride (0.66 mL). The reaction mixture was left at 25 °C for 1 h. The 2-azetidiniminium triflate was converted into the corresponding perchlorate. Chromatography (SiO_2, CH_2Cl_2/CH_3CN, 4:1) gave 1.41 g (70%) of *cis*-**10**: ^{1}H NMR ($CDCl_3$) δ 3.07 (s, 3 H), 3.19 (s, 3 H), 3.79 (s, 3 H), 6.01 (d, 1 H), 6.35 (d, 1 H, J = 4.7 Hz), 6.90−7.80 (m, 13 H); ^{13}C NMR ($CDCl_3$) δ 39.0, 41.2, 53.5, 55.5, 72.3, 115.0, 123.8, 127.7, 128.7, 129.6, 130.0, 130.8, 131.0, 134.9, 160.7, 161.9, 165.5, 167.6; IR 1727 cm^{-1}; HRMS *m*/*z* ($M^+ - HClO_4^-$) calcd for $C_{26}H_{23}N_3O_3$ 425.1739, found 425.1743.

***trans*- and *cis*-3-Phthaloyl-4-ethoxy-1-phenylazetidine-2-(*N*-dimethyliminium perchlorate) (*trans*- and *cis*-11).** A solution (6 mL) of imine **2f** (0.19 g, 1.27 mmol) and collidine (0.16 mL) was added over 30 min at −20 °C to a solution (6 mL) of **1c** (0.30 g, 1.30 mmol) and triflic anhydride (0.22 mL). The reaction mixture was left at 25 °C for 1 h. The 2-azetidiniminium triflates were converted into the corresponding perchlorates. Chromatography (SiO_2, CH_2Cl_2/CH_3CN, 3:1) gave 0.18 g (30%) of a 54:46 mixture of *cis*- and *trans*-**11**: IR 1720 cm^{-1}; HRMS *m*/*z* ($M^+ - HClO_4^-$) calcd for $C_{21}H_{21}N_3O_3$ 363.1583, found 363.1571. *cis*-**11**: ^{1}H NMR ($CDCl_3$) δ 0.86 (t, 3 H, J = 7.1 Hz), 2.93 (s, 3 H), 3.18 (s, 3 H), 3.51 (m, 2 H), 5.85 (d, 1 H), 6.21 (d, 1 H, J = 3.6 Hz), 6.80−7.90 (m, 9 H). *trans*-**11**: ^{1}H NMR ($CDCl_3$) δ 1.08 (t, 3 H, J = 7.1 Hz), 2.98 (s, 3 H), 3.16 (s, 3 H), 3.80 (m, 2 H), 5.98 (d, 1 H), 6.03 (d, 1 H, J = 1.0 Hz), 6.80−7.90 (m, 9 H); ^{13}C NMR ($CDCl_3$) of the mixture of *cis*-**11** and *trans*-**11** δ 14.9, 15.0, 38.7, 39.4, 40.5, 41.3, 53.1, 54.2, 65.0, 68.1, 92.4, 92.5, 123.3, 123.7, 124.0, 124.2, 124.4, 126.3, 126.9, 129.9, 130.1, 130.3, 130.5, 130.9, 131.1, 131.2, 133.3, 133.9, 135.1, 135.2, 135.5, 158.7, 160.8, 166.0, 165.2, 166.3, 167.6.

***cis*-3-Phthaloyl-4-carbomethoxy-1-benzhydrylazetidine-2-(*N*-dimethyliminium perchlorate) (*cis*-12).** A solution (6 mL) of imine **2g** (0.32 g, 1.30 mmol) and collidine (0.16 mL) was added over 30 min at −20 °C to a solution (14 mL) of **1c**

(28) Barbaro, G.; Battaglia, A.; Giorgianni, P. *J. Org. Chem.* **1994**, *59*, 906−913.

(0.30 g, 1.30 mmol) and triflic anhydride (0.22 mL). The reaction mixture was left at 25 °C for 1 h. The 2-azetidiniminium triflate was converted into the corresponding perchlorate. Chromatography (SiO_2, CH_2Cl_2/CH_3CN, 3:1) gave 0.30 g (48%) of *cis*-**12**: ^{1}H NMR (CD_2Cl_2) δ 3.07 (s, 3 H), 3.12 (s, 3 H), 3.30 (s, 3 H), 4.59 (d, 1 H), 6.04 (d, 1 H, J = 5.6 Hz), 6.67 (s, 1 H), 7.30−8.00 (m, 14 H); ^{13}C NMR ($CDCl_3$) δ 39.6, 41.6, 48.2, 53.0, 63.5, 66.9, 124.7, 128.1, 128.9, 129.2, 129.6, 130.1, 131.7, 134.9, 135.8, 139.2, 159.0, 164.0, 166.4, 176.7; IR 1700, 1755 cm^{-1}; HRMS m/z ($M^+ - HClO_4^-$) calcd for $C_{21}H_{19}N_3O_4$ 377.1376, found 377.1372.

***cis*-3-Methyl-4-phenyl-1-methylazetidine-2-(*N*-dimethyliminium perchlorate) (*cis*-13).** A solution (6 mL) of imine **2h** (0.29 g, 2.43 mmol) and collidine (0.32 mL) was added over 1 h at −20 °C to a solution (6 mL) of **1b** (0.25 g, 2.50 mmol) and triflic anhydride (0.42 mL). The reaction mixture was left at −25 °C for 3 h then at 25 °C for 3 h. The solvent was evaporated, and the *cis*/*trans* product distribution of the 2-azetidiniminium triflates was determined by ^{1}H NMR (*cis*/*trans* = 5.0). No variation in the *cis*/*trans* isomer ratio was observed after the triflates were converted into the corresponding perchlorates. Chromatography (SiO_2, CH_2Cl_2/CH_3CN, 3:1) gave a mixture of 0.08 g (11%) of *cis*- and *trans*-**13**: IR 1718 cm^{-1}; HRMS m/z ($M^+ - HClO_4^-$) calcd for $C_{13}H_{18}N_2$ 202.1470, found 202.1462. *cis*-**13**: ^{1}H NMR ($CDCl_3$) δ 0.91 (d, 3 H, J = 7.6 Hz), 3.16 (s, 3 H), 3.26 (s, 3 H), 3.40 (s, 3 H), 3.91 (m, 1 H), 5.19 (d, 1 H, J = 5.1 Hz), 7.20−7.40 (m, 5 H); ^{13}C NMR ($CDCl_3$) δ 10.1, 33.6, 38.1, 40.4, 41.7, 65.9, 127.6, 129.1, 129.2, 131.8, 168.2. *trans*-**13**: ^{1}H NMR relevant resonances ($CDCl_3$) δ 1.55 (d, 3 H, J = 7.5 Hz), 3.15 (s, 3 H), 3.20 (s, 3 H), 4.54 (d, 1 H, J = 1.5 Hz); ^{13}C NMR relevant resonances ($CDCl_3$) δ 12.5, 32.9, 38.3, 40.2, 46.9, 69.4, 166.8.

***cis*-3-Chloro-4-phenyl-1-(4-methoxyphenyl)azetidine-2-(*N*-dimethyliminium perchlorate) (*cis*-14).** A solution (6 mL) of imine **2b** (0.43 g, 2.04 mmol) and collidine (0.27 mL) was added over 30 min at −20 °C to a solution (6 mL) of **1d** (0.25 g, 2.06 mmol) and triflic anhydride (0.34 mL). The reaction mixture was left at 25 °C for 1 h. The 2-azetidiniminium triflate was converted into the corresponding perchlorate. *cis*-**14** (0.53 g, 64%) was obtained: ^{1}H NMR ($CDCl_3$) δ 3.00 (s, 3 H), 3.41 (s, 3 H), 3.75 (s, 3 H), 5.85 (d, 1 H), 6.06 (d, 1 H, J = 4.7 Hz), 6.80−7.50 (m, 9 H); ^{13}C NMR ($CDCl_3$) δ 39.1, 41.1, 54.4, 55.6, 71.9, 115.0, 127.0, 128.1, 128.7, 129.2, 130.0, 130.4, 160.8, 162.7; IR 1724 cm^{-1}; HRMS m/z ($M^+ - HClO_4^-$) calcd for $C_{18}H_{19}N_2OCl$ 314.1186, found 314.1172.

***cis*-3-(Benzyloxy)-4-phenyl-1-(4-methoxyphenyl)azetidine-2-(*N*-dimethyliminium perchlorate) (*cis*-15).** A solution (6 mL) of imine **2b** (0.35 g, 1.70 mmol) and collidine (0.22 mL) was added over 30 min at −10 °C to a solution (6 mL) of **1e** (0.30 g, 1.70 mmol) and triflic anhydride (0.28 mL). The reaction mixture was left at 25 °C for 3.0 h. The 2-azetidiniminium triflate was converted into the corresponding perchlorate. Chromatography (SiO_2, CH_2Cl_2/CH_3CN, 3:1) gave 0.18 g (23%) of *cis*-**15**: ^{1}H NMR ($CDCl_3$) δ 3.02 (s, 3 H), 3.43 (s, 3 H), 3.74 (s, 3 H), 5.75 (d, 1 H, J = 4.2 Hz), 6.50 (d, 1 H), 6.60−7.50 (m, 14 H); ^{13}C NMR ($CDCl_3$) δ 38.7, 40.9, 55.4, 74.0, 114.8, 115.2, 122.8, 127.0, 127.8, 128.4, 129.3, 129.4, 129.8, 155.1, 160.5, 162.2; IR 1715 cm^{-1}; HRMS m/z ($M^+ - HClO_4^-$) calcd for $C_{24}H_{24}N_2O_2$ 372.1838, found 372.1849.

***trans*- and *cis*-3-Phenyl-4-ethoxy-1-phenylazetidine-2-(*N*-dimethyliminium perchlorate) (*trans*- and *cis*-16).** A solution (6 mL) of imine **2f** (0.32 g, 2.15 mmol) and collidine (0.27 mL) was added over 30 min at −20 °C to a solution (6 mL) of **1a** (0.35 g, 2.15 mmol) and triflic anhydride (0.34 mL). The solvent was evaporated, and the *cis*/*trans* product distribution of the 2-azetidiniminium triflates was determined by ^{1}H NMR (*cis*/*trans* = 1.8:1). No variation in the *cis*/*trans* isomer ratio was observed after the triflates were converted into the corresponding perchlorates. Chromatography (SiO_2, CH_2Cl_2/CH_3CN, 4:1) gave 0.35 g (41%) of *trans*- and *cis*-**16**: IR 1718 cm^{-1}; HRMS m/z ($M^+ - HClO_4^-$) calcd for $C_{19}H_{22}N_2O$ 294.1732, found 294.1728. *cis*-**16**: ^{1}H NMR ($CDCl_3$) δ 0.78 (t, 3 H, J = 7.2 Hz), 2.91 (s, 3 H), 2.98 (s, 3 H), 3.22 (dq, 1 H, J = 9.5 Hz), 3.37 (dq, 1 H), 5.26 (d, 1 H), 5.75 (d, 1 H, J = 4.0 Hz), 7.30−7.70 (m, 10 H). *trans*-**16**: ^{1}H NMR ($CDCl_3$) δ 1.00 (t, 3 H, J = 7.2 Hz), 2.97 (b, 6 H), 3.62 (m, 2 H), 4.78 (d, 1 H), 5.51 (d, 1 H, J = 0.5 Hz), 7.30−7.70 (m, 10 H); ^{13}C NMR ($CDCl_3$) of the mixture of *cis*-**16** and *trans*-**16** δ 14.7, 15.0, 38.9, 39.7, 41.0, 41.3, 54.2, 55.5, 65.8, 66.4, 92.0, 95.7, 126.9, 127.2, 128.1, 128.5, 128.7, 129.0, 129.1, 129.4, 129.5, 129.9, 130.0, 130.1, 130.3, 133.9, 134.7, 162.4, 163.8.

***trans*- and *cis*-3-(Benzyloxy)-4-ethoxy-1-phenylazetidine-2-(*N*-dimethyliminium perchlorate) (*trans*- and *cis*-17).** A solution (8 mL) of imine **2f** (0.25 g, 1.69 mmol) and collidine (0.22 mL) was added over 30 min at −15 °C to a solution (6 mL) of **1e** (0.30 g, 1.67 mmol) and triflic anhydride (0.28 mL). The solvent was evaporated, and the *cis*/*trans* product distribution of the 2-azetidiniminium triflates was determined by ^{1}H NMR (*cis*/*trans* = 1.1). No variation of the *cis*/*trans* isomer ratio was observed after the triflates were converted to the corresponding perchlorates. Chromatography (SiO_2, CH_2Cl_2/CH_3CN, 4:1) gave 0.11 g (16%) of *trans*- and *cis*-**17**: IR 1715 cm^{-1}; HRMS m/z ($M^+ - HClO_4^-$) calcd for $C_{19}H_{22}N_2O_2$ 310.1681, found 310.1693. *cis*-**17**: ^{1}H NMR ($CDCl_3$) δ 0.96 (t, 3 H, J = 7.1 Hz), 2.89 (s, 3 H), 3.35 (s, 3 H), 3.51 (dq, 1 H, J = 9.5 Hz), 3.61 (dq, 1 H), 5.86 (d, 1 H), 6.32 (d, 1 H, J = 3.2 Hz), 6.80−7.60 (m, 10 H). *trans*-**17**: ^{1}H NMR ($CDCl_3$) δ 1.04 (t, 3 H, J = 7.1 Hz), 2.99 (s, 3 H), 3.42 (s, 3 H), 3.70 (m, 2 H), 5.68 (s, 1 H), 5.80 (d, 1 H, J = 0.0 Hz), 6.80−7.60 (m, 10 H); ^{13}C NMR ($CDCl_3$) of the mixture of *cis*-**17** and *trans*-**17** δ 14.9, 38.6, 39.6, 41.1, 41.4, 66.8, 67.8, 75.1, 77.2, 94.7, 94.8, 115.0, 115.2, 123.0, 123.4, 126.2, 126.6, 128.2, 129.8, 129.9, 130.0, 130.5, 132.8, 134.0, 155.4, 156.0, 158.2, 161.7.

***cis*-3-Methyl-4-carbomethoxy-1-benzhydrylazetidine-2-(*N*-dimethyliminium perchlorate) (*cis*-18).** A solution (8 mL) of imine **2g** (0.51 g, 2.0 mmol) and collidine (0.26 mL) was added over 30 min at −20 °C to a solution (10 mL) of **2b** (0.20 g, 2.0 mmol) and triflic anhydride (0.33 mL). The reaction mixture was left at 0 °C for 1 h. After the 2-azetidiniminium triflate was converted to the corresponding perchlorate, chromatography (SiO_2, CH_2Cl_2/CH_3CN, 4:1) gave 0.13 g (15%) of *cis*-**18**: ^{1}H NMR ($CDCl_3$) δ 1.33 (d, 3 H, J = 7.4 Hz), 2.99 (s, 3 H), 3.19 (s, 3 H), 3.52 (s, 3 H), 3.99 (m, 1 H), 4.34 (d, 1 H, J = 5.7 Hz), 6.49 (s, 1 H), 7.30−7.60 (m, 10 H); ^{13}C NMR ($CDCl_3$) δ 10.5, 37.5, 39.1, 41.1, 52.3, 60.1, 66.1, 127.5, 128.7, 128.8, 129.3, 129.4, 131.0, 134.5, 138.8, 168.1, 169.1; IR 1705, 1750 cm^{-1}; HRMS m/z ($M^+ - HClO_4^-$) calcd for $C_{21}H_{24}N_2O_2$ 336.1838, found 336.1847.

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Supporting Information Available: 200-MHz ^{1}H spectra of new compounds (**5**−**18**) lacking combustion data and a listing of ^{1}H and relevant ^{13}C NMR data, accompanied by subjective peak assignments of compounds **5**−**18** (16 pages). This material is contained in libraries on microfiche, immediate follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

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