Let us return to the initially posed question as to the structure of the $C_2H_2O^{\oplus\ominus}$ ions. Supplementing and supporting the results of the experiments, ab initio calculations (performed at the MP3/6-311++G(d,p)//6-31+G(d) level) yielded the following results:[10] **3a** (and several of its conformers), like the bent form of **5a**,[12] exist in potential minima (Fig. 2). **3a** is about 27.5 kcal/mol less stable than **5a**; the barrier for the isomerization **3a** → **5a** is 30.6 kcal/mol. Positive electron affinities are predicted for both species. The experimental observation that electron loss nonetheless occurs from **3a** must be due to the fact that **3a** is generated with excess energy upon electron attachment to vinylene carbonate **1**. If this amount of energy is large enough to overcome a barrier of about 30 kcal/mol (or less, if tunnel effects play a role), then the reaction **3a** → **B** → **5a** ⇄ **A** results necessarily in electron loss to form ketene **5b**; the latter is identified in the experiment. The radical anion of oxirene, **2a**, plays no role in the chemistry of the $C_2H_2O^{\oplus\ominus}$ species. **2a**, which is about 100 kcal/mol less stable than **3a**, corresponds, moreover, to a saddle point of second order (two imaginary frequencies).

Received: November 4, 1986;
revised: November 25, 1986 [Z 1980 IE]
German version: *Angew. Chem. 99* (1987) 153

[1] R. N. Compton, P. W. Reinhardt, H. C. Schweinler, *Int. J. Mass Spectrom. Ion Phys. 49* (1983) 113.
[2] Further discussions of C_2H_2O and, in particular, of oxirene: a) G. Maier, H. P. Reisenauer, T. Sayraç, *Chem. Ber. 115* (1982) 2192; b) W. J. Bouma, R. H. Nobes, L. Radom, C. E. Woodward, *J. Org. Chem. 47* (1982) 1869; c) E. G. Lewars, *Chem. Rev. 83* (1983) 519.
[3] To the best of our knowledge, neither theoretical nor other experimental results are available for the $C_2H_2O^{\oplus\ominus}$ species.
[4] J. L. Holmes, *Org. Mass Spectrom. 20* (1985) 169.
[5] W. J. Bouma, P. M. W. Gill, L. Radom, *Org. Mass Spectrom. 19* (1984) 610.
[6] F. W. McLafferty (Ed.): *Tandem Mass Spectrometry*, Wiley, New York 1983.
[7] Review: K. Levsen, H. Schwarz, *Mass Spectrom. Rev. 2* (1983) 77.
[8] Selected references: a) P. O. Danis, D. Wesdemiotis, F. W. McLafferty, *J. Am. Chem. Soc. 105* (1983) 7454; b) P. C. Burgers, J. L. Holmes, A. A. Mommers, J. K. Terlouw, *Chem. Phys. Lett. 102* (1983) 1.
[9] The CA spectra of **4c** and **5c** are found in B. van Baar, T. Weiske, J. K. Terlouw, H. Schwarz, *Angew. Chem. 98* (1986) 275; *Angew. Chem. Int. Ed. Engl. 25* (1986) 282.
[10] The notation MP3/6-311++G(d,p)//6-31+G(d) means that the calculation of individual points for the geometries optimized at a 6-31+G(d) level [11a] was carried out with the 6-311++G(d,p) basis set [11c], which is more than sufficient for anions. The effects of electron correlation were taken into consideration by perturbation calculations (according to Møller-Plesset [11d,e]) up to third order (MP3). The extended (+) basis sets are described in [11f]. Minima and maxima were unequivocally located by an analysis of the force-constant matrix. Complete data for geometries and energies of the structures reported here (and their conformers) are available on request.
[11] a) P. C. Hariharan, J. A. Pople, *Theor. Chim. Acta 28* (1973) 213; b) J. Chandrasekhar, J. G. Andrade, P. von R. Schleyer, *J. Am. Chem. Soc. 103* (1981) 5609, 5612; E. R. Davidson, D. Feller, *Chem. Rev. 86* (1986) 681; R. H. Nobes, D. Poppinger, W.-K. Li, L. Radom in E. Buncel, T. Durst (Eds.): *Comprehensive Carbanion Chemistry*, Part C, Elsevier, Amsterdam 1987; c) R. Krishnan, J. S. Binkley, R. Seeger, J. A. Pople, *J. Chem. Phys. 72* (1980) 650; d) C. Møller, M. S. Plesset, *Phys. Rev. 46* (1934) 618; e) R. Krishnan, M. J. Frisch, J. A. Pople, *J. Chem. Phys. 72* (1980) 4244; f) T. Clark, J. Chandrasekhar, G. W. Spitznagel, P. von R. Schleyer, *J. Comput. Chem. 4* (1983) 294.
[12] The fact that ketene has a negative electron affinity [Prof. E. Illenberger (Berlin), Prof. N. M. M. Nibbering (Amsterdam), private communication] does not contradict the ab initio results. Vertical electron attachment to **5b** yields the transition state **A**, corresponding to the topomerization of **5a**. In the process **A** → **5a** crossing with the hypersurface of the neutral C_2H_2O molecule (broken line in Fig. 2) occurs; this results in spontaneous electron loss with re-formation of **5b**.

Stereoselective Alkylation of Aromatic Compounds with Threonine Trifluoromethanesulfonates**

By *Franz Effenberger** and *Thomas Weber*

Dedicated to Professor Rudolf Gompper on the occasion of his 60th birthday

Alkyl trifluoromethanesulfonates (alkyl triflates) have only been used in special cases for the alkylation of aromatic compounds.[1] We have now succeeded in synthesizing the *N*-protected triflates of (*S*)- and (*R*)-serine methyl ester as well as the *N*-protected triflates **1** of all diastereomeric threonine methyl esters in very good yields and with complete retention of configuration. This was accomplished by treating the *N*-phthaloyl-protected amino acid esters with trifluoromethanesulfonic anhydride in the presence of pyridine. With the triflates of the serine and threonine esters, it was possible to alkylate benzene and benzene derivatives to obtain phenylalanine and β-methylphenylalanine esters **2**, respectively.

These reactions proceed with retention of configuration at C-2 of the amino acid ester under all conditions employed. Of particular interest but difficult to predict was the stereochemistry at C-3 of the β-methylphenylalanine esters **2**. The Friedel-Crafts alkylation of aromatic compounds with optically active alkylating agents usually proceeds with extensive racemization.[2] However, *Suga* et al., in particular, have shown that alkylation with optically active compounds can also be carried out without significant racemization if special structural properties are fulfilled.[3] In general, these alkylations occur with inversion of confi-

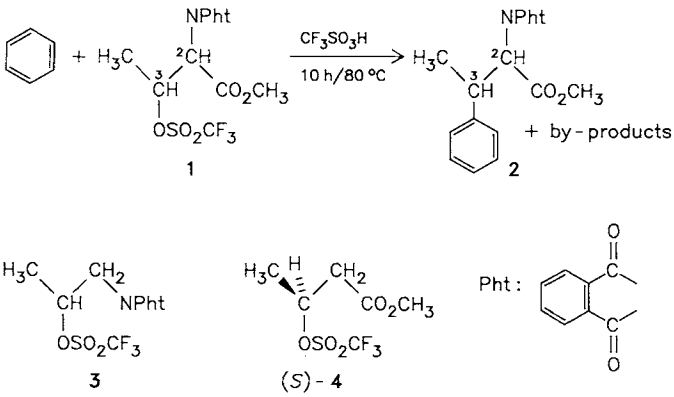


Table 1. Changes in configuration upon alkylation of benzene with the diastereomeric threonine derivatives **1** to give the phenylalanine derivatives **2** [a].

	Educt		Product		Relative amounts
1a	(2*S*,3*R*)	**2a**	(2*S*,3*S*)	+ **2c**	97 : 3
1b	(2*R*,3*S*)	**2b**	(2*R*,3*R*)	+ **2d**	98 : 2
1c	(2*S*,3*S*)	**2c**	(2*S*,3*R*)	+ **2a**	40 : 60
1d	(2*R*,3*R*)	**2d**	(2*R*,3*S*)	+ **2b**	40 : 60

[a] 3*R* in **1** and 3*S* in **2** correspond to the same configuration at C-3.

[*] Prof. Dr. F. Effenberger, Dipl.-Chem. T. Weber
Institut für Organische Chemie der Universität
Pfaffenwaldring 55, D-7000 Stuttgart 80 (FRG)

[**] Electrophilic Aromatic Substitution, Part 32. This work was supported by the Deutsche Forschungsgemeinschaft and the Fonds der Chemischen Industrie. *T. W.* thanks the Fonds der Chemischen Industrie for a doctoral fellowship.—Part 31: F. Effenberger, F. Reisinger, K. H. Schönwälder, P. Bäuerle, J. J. Stezowski, K. H. Jogun, K. Schöllkopf, W. D. Stohrer, *J. Am. Chem. Soc.*, in press.

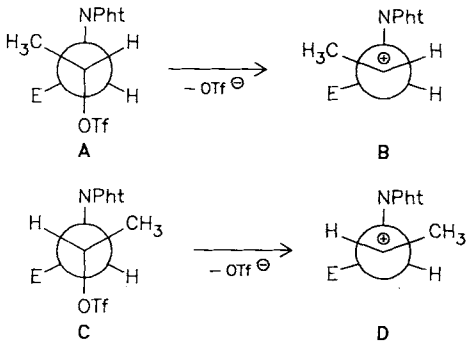
guration of the attacking C atom of the alkylating agent. Retention was observed for alkylation with β-phenylalkyl halides: in the first step, intramolecular alkylation with inversion results in the formation of a cyclohexadienylium intermediate, which, in the second step, again with inversion, reacts with the aromatic compound.[4]

In the alkylation of benzene with the triflates of the *N*-phthaloylthreonines **1a,b** and the *N*-phthaloylallothreonine methyl esters **1c,d**, we obtained in every case the β-methyl-*N*-phthaloyl phenylalanine methyl esters **2**. The overall yields of **2** are between 20 and 40%, because, in addition to the substitution of **1** to give **2**, substantial elimination occurs to give α,β- (25–30%) and β,γ-dehydroamino acid esters (35–40%).

Whereas the configuration at C-2—as previously mentioned—is maintained upon the reactions of **1a–d** to give **2**, the threonine (**1a,b**) and allothreonine (**1c,d**) derivatives show diverse behavior upon alkylation with respect to the stereochemistry at C-3.

The threonine derivatives **1a,b** react largely with retention at C-3, whereas the allothreonine derivatives **1c,d** afford diastereomeric mixtures in the ratio of 2:3. The characterization and structural assignments of the four diastereomers **2a–d** were determined by comparison of their optical rotations and ^{1}H-NMR data with literature values.[5] For **2a**, we confirmed the configuration by carrying out an X-ray structure analysis.[6] Furthermore, we were able to show that the product obtained by acid hydrolysis of **2a**, removal of the phthaloyl protecting group, and acetylation is identical with the reported (2*S*,3*S*)-*N*-acetyl-β-methylphenylalanine.[7]

The high stereoselectivity observed in the alkylation of benzene with **1a, b** and the different behavior of **1c, d** can be explained in terms of the different conformations of the carbenium ions **B** and **D**, which are formed as intermediates in the alkylation.



E = CO_2CH_3; Tf = SO_2CF_3

Alkylation of benzene with (*S*)- and (*R*)-1-methyl-2-phthaloylaminomethyl triflate **3** results in partial retention, whereas with methyl (*S*)-3-trifluoromethanesulfonyloxybutyrate, (*S*)-**4**, complete racemization is observed. We conclude from this that, in the dissociation step, the threonine derivatives **1a,b** prefer conformation **A**, whereas the allothreonine derivatives **1c,d** prefer conformation **C**. In the carbenium ion **B** formed from **A**, rotation is rendered difficult by the two large neighboring substituents (CH_3, CO_2CH_3); moreover, the aromatic compound can react only from the bottom side with **B**, because the cationic center is blocked from above by the *N*-phthaloyl group. This explains the retention observed in the reactions of **1a,b**. For the cationic intermediate **D**, on the other hand, no or at most only a small hindrance to rotation is expected, which is confirmed by the results of the reactions of **1c,d**.

In analogy to the reactions of benzene, alkyl- and alkoxybenzenes can also undergo reaction with the triflates **1** of the threonine ester. In a one-pot procedure, it is also possible to synthesize phenylalanines and β-methylphenylalanines such as **2** from the corresponding aromatic compounds, the *N*-protected esters of serine and threonine, and trifluoromethanesulfonic anhydride (without isolation of the triflates of type **1**). Trifluoromethanesulfonic acid can be precipitated as its barium salt and thus recovered.

Experimental Procedure

2a: *N*-phthaloyl-*O*-(trifluoromethanesulfonyl)-(2*S*,3*R*)-threonine methyl ester **1a** (1.58 g, 4 mmol) and trifluoromethanesulfonic acid (0.61 g, 4 mmol) were stirred in 8 mL of benzene for 10 h at 80°C under dry atmosphere. The excess benzene was then removed in vacuo. After addition of water to the residue, the mixture was extracted with chloroform. The combined organic phases were dried over $MgSO_4$ and evaporated; the residue was chromatographed on silica gel with petroleum ether/ethyl acetate (9:1). Yield 300 mg (24%) **2a**, m.p. = 107°C (petroleum ether), $[\alpha]_D^{20}$ = −139.1° (*c* = 1, $CHCl_3$) and 10 mg (0.77%) **2c**, oil, $[\alpha]_D^{20}$ = −120.5° (*c* = 0.6, $CHCl_3$).

One-pot procedure: *N*-phthaloyl-(2*S*,3*R*)-threonine methyl ester (0.53 g, 2 mmol) and trifluoromethanesulfonic anhydride (0.56 g, 2 mmol) were allowed to react as described above. Yield 0.15 g (23%) **2a**, $[\alpha]_D^{20}$ = −138.3° (*c* = 1, $CHCl_3$).

Received: October 6, 1986;
revised: November 17, 1986 [Z 1947 IE]
German version: *Angew. Chem. 99* (1987) 146

[1] a) F. Effenberger, *Angew. Chem. 92* (1980) 147; *Angew. Chem. Int. Ed. Engl. 19* (1980) 151, and references cited therein; b) B. L. Booth, R. N. Haszeldine, K. Laali, *J. Chem. Soc. Perkin Trans. 1 1980*, 2887.
[2] a) C. C. Price, M. Lund, *J. Am. Chem. Soc. 62* (1940) 310; b) A. Streitwieser, Jr., P. J. Stang, *ibid. 87* (1965) 4953.
[3] a) T. Nakajima, S. Suga, T. Sugita, K. Ichikawa, *Bull. Chem. Soc. Jpn. 40* (1967) 2980; b) T. Nakajima, S. Masuda, S. Nakashima, T. Kondo, Y. Nakamoto, S. Suga, *ibid. 52* (1979) 2377; c) O. Piccolo, F. Spreafico, G. Visentin, E. Valoti, *J. Org. Chem. 50* (1985) 3945.
[4] M. Shinji, T. Nakajima, S. Suga, *Bull. Chem. Soc. Jpn. 56* (1983) 1089.
[5] Y. Kataoka, Y. Seto, M. Yamamoto, T. Yamada, S. Kuwata, H. Watanabe, *Bull. Chem. Soc. Jpn. 49* (1976) 1081.
[6] We thank Prof. Dr. *John J. Stezowski* for the X-ray structure analysis.
[7] a) H. Arold, M. Eule, S. Reissmann, *Z. Chem. 9* (1969) 447; b) G. I. Tsuchihashi, S. Mitamura, K. Ogura, *Bull. Chem. Soc. Jpn. 52* (1979) 2167.

Asymmetric Synthesis of Cyclic α-Amino Acids by the Bislactim Ether Method**

By *Ulrich Schöllkopf,** *Rolf Hinrichs,* and *Ralph Lonsky*

Dedicated to Professor G. Quinkert on the occasion of his 60th birthday

Optically active α-methylproline **10a** and its analogues **10b** and **11** are of interest because of their potential biological activity as competitive enzyme inhibitors.[2] (*S*)-α-Methylproline (*ent*-**10a**) was prepared by *Seebach* et al.[3] from naturally occurring L-proline in an asymmetric synthesis. This synthesis, although elegant, has the disadvantage that it cannot be applied to ring homologues without modification, because homologues of proline do not exist in the "chiral pool" of nature. We report here a very flexible asymmetric synthesis of 2-methyl-1-azacycloalkane-2-

[*] Prof. Dr. U. Schöllkopf, Dipl.-Chem. R. Hinrichs, Dr. R. Lonsky
Institut für Organische Chemie der Universität
Tammannstrasse 2, D-3400 Göttingen (FRG)

[**] Asymmetric Syntheses via Heterocyclic Intermediates. Part 32.—Part 31: [1].