Enaminosulfones from 3-Trifloxypropene Iminium Salts: A 1,5(O→C) Trifluoromethylsulfonyl Shift*

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Dedicated to Prof. Dr. Bärbel Schulze on the occasion of her 60th birthday

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Enamines, Iminium Salts, Rearrangement

Treatment of semicyclic 3-trifloxypropene iminium triflates **4a–c**,**e**,**f**, in which the iminium function is part of a six-membered ring, with a polymer-supported tertiary amine leads to 3-[(trifluoromethyl)sulfonyl]-1,4,5,6-tetrahydropyridines **7**. Related five- and seven-membered cyclic iminium salts do not react to give the corresponding enaminosulfones.

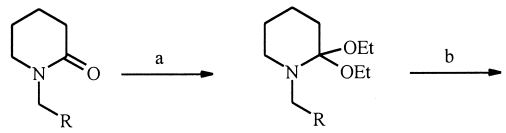
Introduction

Triflic anhydride (Tf_2O) is the reagent of choice for the introduction of the trifluoromethylsulfonyl (CF_3SO_2) group into a variety of organic substrates, and the resulting compounds often have a unique chemical reactivity [1]. A case in point is given by 3-trifloxypropene iminium triflates which are obtained by *O*-sulfonylation of enaminones with Tf_2O [2, 3] and which are suited for transformations that are not known for related [4] 3-chloropropene iminium salts. 3-Trifloxypropene iminium triflates are susceptible to nucleophilic substitution [2, 5], can be involved in intra- [6] und intermolecular [7] aromatic substitution reactions, and can be transformed into a wide range of propyne iminium triflates by β-elimination of triflic acid [6, 8, 9]. The latter transformation is either achieved with the help of a tertiary amine base or under purely thermal conditions.

In this communication, we report that certain semicyclic 3-trifloxypropene iminium triflates upon treatment with an amine base do not yield propyne iminium triflates but are converted into enaminosulfones.

Results and Discussion

The preparation of the semicyclic 3-trifloxypropene iminium triflates **4d–g** investigated in this study has already been reported by us [9]. The new salts **4a–c** were obtained in the same manner, *i.e.* by *O*-sulfonylation of enaminoketones **3a–c** with triflic anhydride. The enaminoketones were obtained in two steps, by analogy with published procedures [9, 10] from *N*-substituted lactams **1a**,**b** *via* the corresponding lactam acetals **2a**,**b** (Scheme 1). The NMR spectra of **4a–c** indicated the presence of only one isomer to which the *Z*, *s-trans* configuration of the propene iminium unit was assigned by analogy with related salts [3, 9].



1a: R = 3-thienyl
1b: R = Ph

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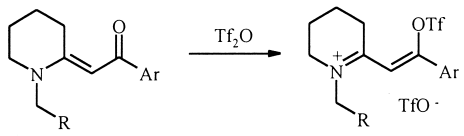

3 **4**

4	a	b	c
R	3-thienyl	Ph	3-thienyl
Ar	C_6H_4-4-Cl	3-thienyl	3-thienyl

Scheme 1. Conditions: a) $(MeO)_2SO_2$, 80 °C, then NaOEt (2 equiv.); b) H_3CCOAr, 80 °C. Tf = CF_3SO_2.

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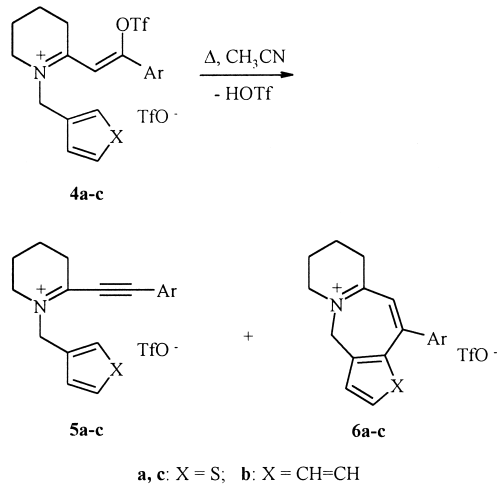
When iminium salts **4b**,**c** were kept in acetonitrile solution at 20 °C, elimination of triflic acid (HOTf) from the cation took place, and a mixture of propyne iminium triflates **5** and tricyclic azepinium salts **6** was obtained (Scheme 2). This transformation was complete within one day, and it was found that the ratio **5b**:**6b** remained unchanged after 77 days in solution. The analogous conversion of **4a** into a mixture of **5a** and **6a** required a higher activation energy; it was achieved by heating at 160 °C in acetonitrile solution in a closed pressure vessel. Only in this case, a separation of the two iminium salts **5** and **6** was undertaken.

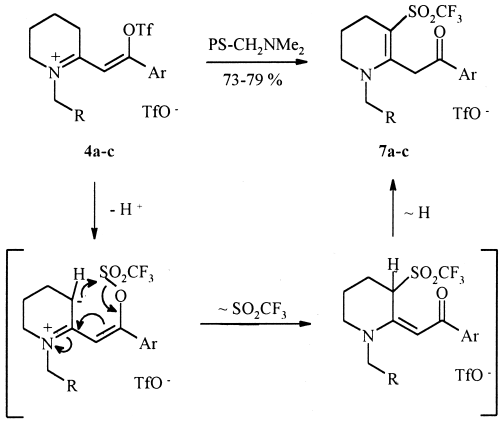


Scheme 2. See Table 1 for conditions and yields.

The smooth elimination of triflic acid from (3-thienyl)-substituted 3-trifloxypropene iminium salts **4b**,**c** with formation of a propyne iminium salt was not unexpected, since we have observed before that this transformation is facilitated when the trifloxy-substituted carbon atom of **4** bears an electron-donating (het)aryl substituent [3, 9]. On the other hand, the formation of azepinium salts **6a–c** is a novel feature of the reactivity of 3-trifloxypropene iminium salts [10]. The scope of this 1,7-cyclization reaction, which can be considered as an intramolecular aromatic substitution reaction, will be described elsewhere.

We were surprised to find that the β-elimination of HOTf from propene iminium salts **4a–c** could not be achieved, as in other cases, with the help of an amine base. A polymer-supported base, dimethylaminomethyl-polystyrene, was used for this purpose, since the resulting ammonium salt can be removed conveniently by filtration from the product mixture. Treatment of **4a–c** with this base led to the formation of the cyclic enaminosulfones **7a–c** in good yields (Scheme 3). In the same manner, the *N*-allyl or *N*-homoallyl-substituted iminium salts **4e**,**f** were converted into **7e**,**f** (Scheme 4). The identity of these compounds was established by an X-ray crystal structure analysis of **7f** (Fig. 1). The ^{1}H and ^{13}C signals of the enaminosulfones could be fully assigned with the help of ^{1}H,^{13}C correlation spectra (gs-HMBC); the ^{13}C chemical shifts are given in Table 1. An interesting detail in the ^{1}H NMR spectra (500 MHz) of **7a–c** is the temperature-dependency of the signal for the exocyclic CH_2CO protons, which is very broad at 305 K but appears as a sharp singlet at 343 K. This dynamic behavior is probably associated with the heavy 1,2,3-trisubstitution of the tetrahydropyridine ring which slows down the free rotation around the $C_{ring}-C_{methylene}$ bond (C2–C3 in Fig. 1).

The formation of enaminosulfones **7** is likely to begin with deprotonation at the ring position C-3



Scheme 3. See Scheme 1 for R and Ar.

Table 1. Thermal elimination of triflic acid from **4a–c** (solvent: acetonitrile); conditions and products (see Scheme 2).

Compound	Conditions	Products
4a	160 °C/4 h	**5a** (71%), **6a** (18%)[a]
4b	20 °C/29 h	**5b** (44.5%), **6b** (55.5%)[b]
4c	20 °C/11 h	**4c** (7%), **5c** (55%), **6c** (38%)[b]

[a] Yields of isolated products;
[b] products not separated; relative yields are given.

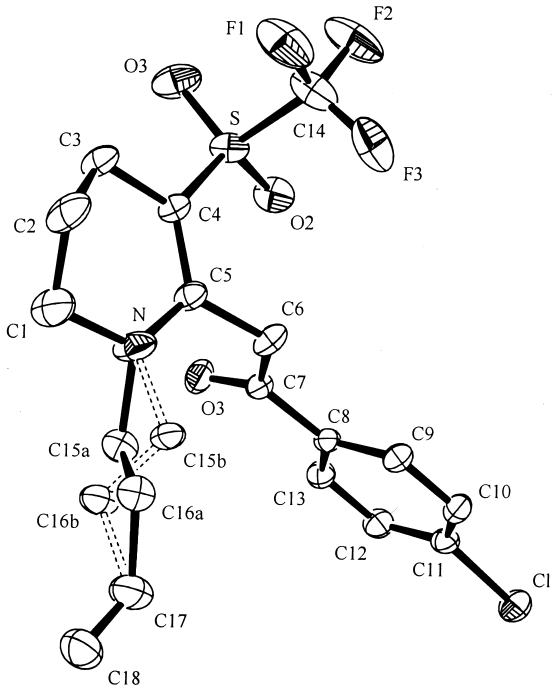
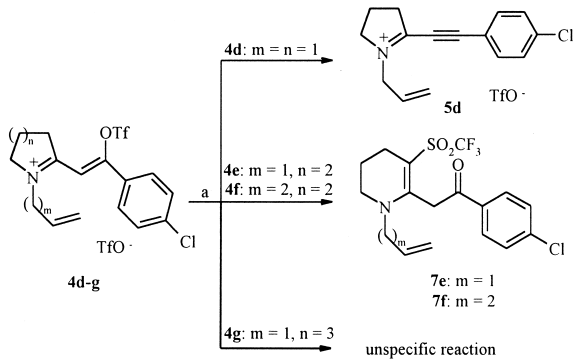


Fig. 1. Stereographic plot (ORTEP) of the structure of **7f** in the crystal. Hydrogen atoms are not shown. The *N*-homoallyl group occupies two positions, corresponding to a pseudoequatorial and pseudoaxial orientation with respect to the tetrahydropyridine ring which assumes a half-chair conformation. Dashed bonds mark the disorder of the homoallyl group. Selected bond lengths [Å]: S-O2 1.431(2), S-O3 1.431(3), S-C4 1.689(3), C4-C5 1.372(4), C5-N 1.330(4). Bond lengths [°]: S-C4-C5 123.4(2), C4-C5-C6 123.7(2), N-C5-C6 115.3(2), C5-N-C15a 125.9(3), C5-N-C15b 118.2(4). Torsion angles [°]: C3-C4-C5-N 8.2(4), C4-C5-N-C15a 151.9(4), C4-C5-N-C15b-159.6(4), N-C5-C6-C7 83.6(3).



Scheme 4. Conditions: a) Dimethylaminomethyl-polystyrene, CH_3CN, 1 h, rt.

of iminium salts **4** (Scheme 4). The facile deprotonation of iminium salts at this position is known [11, 12]. In the resulting enamine (shown as the dipolar resonance structure), 1,5(O→C) migration of the CF_3SO_2 group could occur, and a subsequent tautomerization would provide the final product.

The relevance of the six-membered cyclic iminium salt structure for this transformation was illustrated by some experiments with five- to seven-membered iminium salts **4d–g** which were all treated with dimethylaminomethyl-polystyrene (Scheme 4). From the five-membered ring system **4d**, only propyne iminium salt **5d** was obtained; however, the yield was considerably lower than in the thermally induced [9] elimination reaction (45 *vs.* 81%). The six-membered cyclic iminium salts **4e**,**f** afforded enaminosulfones **7e**,**f** in good yields. From the seven-membered system **4 g**, an undefined product mixture was obtained in which neither a propyne iminium salt nor an enaminosulfone could be detected by NMR spectroscopy; the broad NMR signals rather indicated the formation of oligomeric product. On the other hand, the exocyclic *N*-substituent appears to be important, too: Treatment of the iminium salt analogous to **4e**, but with *N*-Me instead of *N*-allyl, with the polymer-supported amine base gave again an unspecified product mixture rather than an enaminosulfone. These results show that the base treatment of semicyclic iminium salts **4** depends in a delicate manner on ring size and substituents at the propene iminium unit. Further experiments will show whether some of the present limitations of our enaminosulfone synthesis can be overcome by the use of a different base.

The transformation **4**→**7** represents a novel approach to β-(trifluoromethylsulfonyl) enamines. Compounds of this type [13–17] as well as other enaminosulfones [18, 19] have been prepared by several different methods none of which would allow the synthesis of the cyclic enamines **7**. Cyclic β-tosyl enamines have recently been used as precursors to indolizidine alkaloids [20]. Due to their combination of different functional groups, tetrahydropyridines **7** should also be useful for further synthetic transformations.

Table 2. ^{13}C NMR data of enaminosulfones **7a–c**,**e**,**f** (in CD_3CN, δ/ppm).

Compound	$NCH_{2,ring}$	NCH_2CH_2	$N(CH_2)_2CH_2$	NC=*C*	N*C*=C	N*C*H_2R	CF_3 ($^1J_{C,F}$ [Hz])	*C*H_2CO	C=O	Other signals
7a	50.6	21.9	25.1	89.3	158.5	52.2	122.3 (328.5)	41.0	194.3	123.5 (C-2$_{Thie}$), 127.7 (C-4$_{Thie}$), 128.1 (C-5$_{Thie}$), 129.9 (C$_{Ar}$), 130.8 (C$_{Ar}$), 135.7 (C-Cl), 138.2 (C-3$_{Thie}$), 140.3 (C-1$_{Ar}$)
7b	50.7	21.9	25.2	89.7	158.8	56.2	122.4 (328.1)	42.0	189.4	127.6 (C-4$_{Thie}$), 127.7 (*o*-C$_{Ph}$), 128.1 (C-5$_{Thie}$), 128.7 (*p*-C$_{Ph}$), 129.9 (*m*-C$_{Ph}$), 134.3 (C-2$_{Thie}$), 137.2 (C-1$_{Ph}$), 141.9 (C-3$_{Thie}$)
7c	50.5	21.9	25.4	89.5	158.3	52.2	122.3 (328.2)	41.9	189.4	CH_2-Thienyl: 123.4 (C-2), 127.6 (C-4), 128.1 (C-5), 138.2 (C-3); CO-Thienyl: 127.6 (C-4), 128.1 (C-5), 134.3 (C-2), 141.9 (C-3)
7e	50.6	22.0	25.1	88.8	158.7	55.3	122.4 (328.3)	40.8	194.3	117.5 (=CH_2), 129.9 (*o*-C$_{Ar}$), 130.8 (*m*-C$_{Ar}$), 133.6 (*C*H=CH_2), 135.7 (C-1$_{Ar}$), 140.3 (C-Cl)
7f	50.5	21.9	25.2	88.4	158.4	52.6	122.4 (328.3)	40.8	194.2	33.2 (CH_2*C*H=CH_2), 118.2 (=CH_2), 130.0 (*o*-C$_{Ar}$), 130.8 (*m*-C$_{Ar}$), 135.5 (*C*H=CH_2), 135.7 (C-1$_{Ar}$), 140.3 (C-Cl)

Experimental Section

General remarks

Reactions were carried out in dry solvents and under an argon atmosphere. Dimethylaminomethyl-polystyrene was heated at 90 °C for 5 days to remove water. Triflic anhydride was distilled from phosphorus pentoxide prior to use.

NMR spectra were taken on Bruker AMX 500 and AC 200 instruments. As the internal reference, Me_4Si was used for the proton spectra and the solvent signal for the ^{13}C NMR spectra [$\delta(CDCl_3$ = 77.0 ppm, $\delta(CD_3CN)$ = 1.3 ppm]. Throughout the experimental section, signal assignments 2′-H–6′-H and C-2′–C-6′ are for the tetrahydropyridine ring. IR spectra were recorded on a Perkin Elmer IR 883 spectrometer. Microanalyses were carried out with an analyzer system Elementar Vario El at the Division of Analytical Chemistry of the University of Ulm. Column chromatography was performed under hydrostatic conditions (silica gel 60, Macherey-Nagel, 70–230 mesh).

1-(3-Thienylmethyl)piperidin-2-one (**1a**)

A suspension of sodium (2.30 g, 0.10 g-atom) in toluene (200 ml) was heated at reflux and a solution of piperidin-2-one (9.90 g, 0.10 mol) in toluene (40 ml) was added during 2 hours. The mixture was kept at reflux temperature for additional 4 h, during which time a white jelly-like solid formed, then cooled to rt. After addition of a solution of 3-(bromomethyl)thiophene (17.7 g, 0.10 mol) in toluene (20 ml) during 90 min, the mixture was heated at reflux for 2 h. The precipitate of NaBr was separated by centrifugation, the solvent was evaporated, and the residue was distilled at 125–132 °C/0.01 mbar to give 9.79 g (54%) of **1a** as a colorless liquid. – IR: ν = 1640, 1492, 1465, 1447, 1415, 1352, 1331, 1269 (all vs), 1230, 1176, 992, 959 (all s) cm^{-1}. – ^1H NMR ($CDCl_3$, 200.13 MHz): δ = 1.73–1.80 (m, 4H, 4-H, 5-H), 2.42 (m, 2 H, 3-H), 3.22 (m, 2 H, 6-H), 4.56 (s, 2 H, NC*H*$_2$Thie), 7.01 (dd, 1 H, 2-H$_{Thie}$), 7.12 (dd, 1 H, 4-H$_{Thie}$), 7.27 (dd, 1 H, 5-H$_{Thie}$). – ^{13}C NMR ($CDCl_3$, 50.3 MHz): δ = 21.5, 23.3, 32.5 (C-3), 45.5 (N*C*H$_2$Thie), 47.3 (C-6), 122.8, 126.1, 127.8, 138.2, 169.7 (C=O). – $C_{10}H_{13}NOS$ (195.28).

1-(4-Chlorophenyl)-2-{1-[(thien-3-yl)methyl]-hexahydropyridin-2-ylidene}-1-ethanone (**3a**)

A two-phase mixture of **1a** (15.62 g, 0.08 mol) and of dimethyl sulfate (10.09 g, 0.08 mol) was heated at 80 °C for 12 h. After cooling, the homogeneous oil was washed with ether (50 ml), and residual solvent was removed *in vacuo*. The residue was slowly added to a solution of NaOEt [from sodium (3.68 g, 0.16 g-atom) in ethanol (80 ml)]. After 2 h, the precipitate was filtered off with suction under argon, the solvent was evaporated, and the residue was distilled at 130 °C/0.008 mbar to give 17.78 g of 2,2-diethoxy-1-[(thien-3-yl)-methyl]piperidine (**2a**) which was used immediately. A mixture of this acetal (17.78 g, 0.066 mol) and of 4-chloroacetophenone (10.20 g, 0.066 mol)

was heated at 80 °C for 10 h. The alcohol formed was removed *in vacuo*, and the remaining oil was converted into a solid by addition of ether and vigorous stirring. Recrystallization from EtOH–ether gave **3a** (15.29 g, 70%) as colorless flakes; m.p. 127–128 °C. – IR (KBr): ν = 1608 (s), 1586 (m), 1566 (m), 1535 (vs), 1518 (vs), 1473 (s) cm^{-1}. – ^1H NMR ($CDCl_3$, 500.14 MHz): δ = 1.70–1.75 (m, 2 H, 4′-CH_2), 1.79–1.84 (m, 2 H, 5′-CH_2), 3.38 (2 t, 4 H, 3′-CH_2, 6′-CH_2), 4.50 (s, 2 H, NCH_2Thie), 5.78 (s, 1 H, 2-H), 6.99 (dd, 1 H, J = 5.0, 1.4 Hz, 4-H_{Thie}), 7.10 (dd, 1 H, J = 3.0, 1.3 Hz, 2-H_{Thie}), 7.33 (dd, 1 H, J = 5.0, 3.0 Hz, 5-H_{Thie}), 7.26/7.62 (AA′BB′, 4 H_{Ar}). – ^{13}C NMR ($CDCl_3$, 125.8 MHz): δ = 19.1 (C-4′), 22.8 (C-5′), 28.3 (C-3′), 50.2 (C-6′), 51.8 (NCH_2Thie), 90.8 (NC=*C*), 121.6 (C-2_{Thie}), 126.3 (C-4_{Thie}), 126.7 (5-C_{Thie}), 127.9, 128.4, 135.8 (C–Cl), 136.2 (C-3_{Thie}), 141.2, 164.7 (N*C*=C), 185.9 (C=O). – $C_{18}H_{18}ClNOS$ (331.86): calcd. C 65.15, H 5.47, N 4.22; found C 64.93, H 5.59, N 4.19.

2-(1-Benzylhexahydropyridin-2-ylidene)-1-(3-thienyl)-1-ethanone (**3b**)

By analogy with the preceding procedure, 1-benzylpiperidin-2-one (**1b**) was converted into 1-benzyl-2,2-diethoxypiperidine (**2b**, b.p. 121 °C/0.009 mbar). Reaction of freshly distilled **2b** (97.5 g, 0.37 mol) with 3-acetylthiophene (46.7 g, 0.37 mol) and work-up as described above provided **3b** (89.1 g, 81%) as a yellow solid, m.p. 113–114 °C. – IR (KBr): ν = 1601 (m), 1529 (vs), 1480 (s), 1449 (m), 1353 (m), 1329 (m), 1228 (m), 1170 (s), 1074 (m) cm^{-1}. – ^1H NMR ($CDCl_3$, 500.14 MHz): δ = 1.67 (quin, 2 H, 4′-CH_2), 1.75 (quin, 2 H, 5′-CH_2), 3.23–3.39 (m, 4 H, 3′-CH_2, 6′-CH_2), 4.44 (s, 2 H, NCH_2Ph), 5.58 (s, 1 H, 2-H), 7.04 (dd, J = 5.0, 3.0 Hz, 1 H, 5-H_{Thie}), 7.13 (d, 2 H, o-H_{Ph}), 7.19 (dd, 1 H, 4-H_{Thie}), 7.20 (t, 1 H, p-H_{Ph}), 7.28 (t, 2 H, m-H_{Ph}), 7.46 (m, J = 3.0, 1.6 Hz, 1 H, 2-H_{Thie}). – ^{13}C NMR ($CDCl_3$, 125.8 MHz): δ = 19.3 (C-4′), 23.0 (C-5′), 28.1 (C-3′), 50.6 (C-6′), 55.9 (NCH_2Ph), 92.0 (N–C=*C*), 124.8 (C-5_{Thie}), 126.2 (*o*-C_{Ph}), 126.7 (C-2_{Thie}), 127.0 (C-4_{Thie}), 127.3 (*p*-C_{Ph}), 128.8 (m-C_{Ph}), 135.6 (C-1_{Ph}), 147.0 (C-3_{Thie}), 164.3 (C-2′), 181.9 (C=O). – $C_{18}H_{19}NOS$ (297.41): calcd. C 72.69, H 6.44, N 4.71; found C 71.49, H 6.46, N 4.79.

1-(3-Thienyl)-2-[1-(3-thienylmethyl)hexahydropyridin-2-ylidene]-1-ethanone (**3c**)

A mixture of acetal **2a** (see above, 26.94 g, 0.10 mol) and of 3-acetylthiophene (12.62 g, 0.10 mol) was heated at 80 °C for 12 h. The alcohol formed was evaporated at 14 mbar, and the liquid residue was converted into a solid by addition of ether and vigorous stirring. Recrystallization from EtOH-ether provided **3c** (23.83 g, 79%) as a finely crystalline solid, m.p. 105 °C. – IR (KBr): ν = 1589 (s), 1529 (vs), 1483 (vs), 1354 (m), 1324 (m), 1299 (m), 1272 (m), 1260 (m), 1227 (m), 1175 (s), 1074 (m) cm^{-1}. – ^1H NMR ($CDCl_3$, 500.14 MHz): δ = 1.72 (quin, 2 H, 4′-CH_2), 1.81 (quin, 2 H, 5′-CH_2), 3.36–3.39 (m, 4 H, 3′-CH_2, 6′-CH_2), 4.50 (s, 2 H, NCH_2Thie), 5.76 (s, 1 H, 2-H), 7.01 (dd, J = 5.0, 1.3 Hz, 1 H), 7.12 (dd, J = 3.0, = 1.3 Hz, 1 H), 7.17 (dd, J = 5.0, 3.0 Hz, 1 H), 7.34 (dd, J = 5.0, = 3.0 Hz, 1 H), 7.35 (dd, J = 5.0, 1.3 Hz, 1 H), 7.63 (dd, J = 3.0, 1.3 Hz, 1 H). – ^{13}C NMR ($CDCl_3$, 125.8 MHz): δ = 19.2 (C-4′), 23.9 (C-5′), 28.1 (C-3′), 50.1 (C-6′), 51.7 (NCH_2Thie), 91.7 (N–C=*C*), 121.5, 124.8, 126.3, 126.5, 126.8, 127.0, 136.5, 146.9, 164.0 (C-2′), 181.7 (C=O) – $C_{16}H_{17}NOS_2$ (303.45): calcd. C 63.33, H 5.65, N 4.62; found C 62.94, H 5.70, N 4.57.

6-{(Z)-2-(4-Chlorophenyl)-2-[(trifluoromethyl)sulfonyloxy]ethenyl}-1-(3-thienylmethyl)-2,3,4,5-tetrahydropyridinium trifluoromethanesulfonate (**4a**)

A solution of enaminoketone **3a** (3.32 g, 10.0 mmol)) in CH_2Cl_2 (15 ml) was added dropwise to a cooled (–18 °C) solution of triflic anhydride (1.85 ml, 11.0 mmol) in CH_2Cl_2 (10 ml). After stirring for 30 min at –18 °C and for 30 min at 20 °C, most of the solvent was evaporated at 0.01 mbar. Ether was added until the solution remained turbid. Upon cooling at 0 °C, solid **4a** separated which was recrystallized from CH_2Cl_2-ether to give a colorless solid, m.p. 107–108 °C; yield: 4.50 g (74%). – IR (KBr): ν = 1667 (m), 1593 (w), 1534 (w), 1491 (w), 1415 (s), 1267 (vs), 1223 (sh), 1158 (s), 1135 (s), 1091 (m), 1031 (vs), 1015 (m) cm^{-1}. – ^1H NMR (CD_3CN, 500.14 MHz): δ = 1.86 (quin, 2 H, 4′-CH_2), 1.93 (m_c, 2 H, 3′-CH_2), 3.17 (t, 2 H, 5′-CH_2), 3.79 (t, 2 H, 2′-CH_2), 5.23 (s, 1 H, NCH_2Thie), 7.21 (dd, J = 5.1, 1.4 Hz, 1 H, 4-H_{Thie}), 7.22 (t, J = 1.7 Hz, 1 H, H_{olefin}), 7.52 (dd, J = 5.0, 3.0 Hz, 1 H, 5-H_{Thie}), 7.57/7.77 (AA′BB′, 4 H_{Ar}), 7.65 (dd, ^4J = 3.0, 1.3 Hz, 1 H, 2-H_{Thie}). – $^{13}C\{^1H\}$ NMR (CD_3CN, 125.8 MHz): δ = 17.4 (C-4′), 21.2 (C-3′), 33.9 (C-5′), 54.1 (C-2′), 58.1 (N-*C*H_2Thie), 114.9 (N=C-*C*), 119.1 (q, $^1J_{C,F}$ = 320.1 Hz, OTf_{cov}), 122.1 (q, $^1J_{C,F}$ = 320.4 Hz, TfO^-), 128.8 (C_{Thie}), 128.9 (C_{Thie}), 129.9 (m-C_{Ar}), 130.0 (C-1_{Ar}), 130.5 (o-C_{Ar}), 131.6 (C-3_{Thie}), 139.5 (C-Cl), 152.0 (*C*-OTf), 181.8 (C-6′). – $C_{22}H_{18}ClF_6NO_6S_3$ (613.99): calcd. C 39.12, H 2.95, N 2.28; found C 39.10, H 2.92, N 2.31.

1-Benzyl-6-{(Z)-2-(3-thienyl)-2-[(trifluoromethyl)-sulfonyloxy]ethenyl}-2,3,4,5-tetrahydopyridinium trifluoromethanesulfonate (**4b**)

Prepared as described for **4a** from enaminoketone **3b** (2.23 g, 7.5 mmol) in CH_2Cl_2 (25 ml) and Tf_2O (1.39 ml, 8.3 mmol) in CH_2Cl_2 (25 ml) at −18 °C. Colorless solid, m.p. 72 °C; yield: 3.30 g (76%). – IR (KBr): ν = 1661 (s), 1423 (s), 1282 (vs), 1264 (vs), 1232 (s), 1220 (s), 1202 (s), 1167 (s), 1155 (s), 1142 (s), 1029 (s) cm^{-1}. – ^1H NMR (CD_3CN, 500.14 MHz, 263 K): δ = 1.81–1.85 (m, 2 H, 4′-H), 1.88–1.92 (m, (2 H, 3′-H), 3.18 (s, br, 2 H, 5′-H), 3.73 (t, 2 H, 2′-H), 5.23 (s, 2 H, NCH_2Ph), 7.28 (s, 1 H, H_{olefin}), 7.44–7.50 (m, 5 H, H_{Ph}), 7.56 (dd, J = 5.1, 1.4 Hz, 1 H, 4-H_{Thie}), 7.63 (dd, J = 5.3, 3.1 Hz, 1 H, 5-H_{Thie}), 8.05 (dd, J = 2.8 Hz, 1.6 Hz, 1 H, 2-H_{Thie}). – $^{13}C\{^1H\}$ NMR (CD_3CN, 50.32 MHz, 263 K): δ = 17.3 (C-4′), 20.9 (C-3′), 33.6 (C-5′), 53.8 (C-2′), 62.6 (NCH_2Ph), 112.3 (N=C-CH), 118.9 (q, $^1J_{C,F}$ = 319.8 Hz, OTf_{cov}), 121.7 (q, $^1J_{C,F}$ = 320.3 Hz, TfO^-), 126.4 (C-4_{Thie}), 130.0 (C-5_{Thie}), 130.1 (C_{Ph}), 130.3 (C_{Ph}), 130.9, 131.0, 131.7 (C-1_{Ph}), 132.9 (C-3_{Thie}), 148.7 (C-OTf), 181.6 (s, C-6′). – $C_{20}H_{19}F_6NO_6S_3$ (579.56): calcd. C 41.45, H 3.30, N 2.42; found C 41.25, H 3.22, N 2.46.

1-(3-Thienylmethyl)-6-{(Z)-2-(3-thienyl)-2-[(trifluoromethyl)sulfonyloxy]ethenyl}-2,3,4,5-tetrahydropyridinium trifluoromethanesulfonate (**4c**)

Prepared as described for **4a** from enaminoketone **3c** (1.52 g, 5.0 mmol) in CH_2Cl_2 (15 ml) and Tf_2O (0.92 ml, 5.5 mmol) in CH_2Cl_2 (10 ml) at −16 °C. Bright-yellow solid, m.p. 105–106 °C; yield: 2.40 g (82%). – IR (KBr): ν = 1662 (s), 1422 (vs), 1264 (vs), 1248 (s), 1231 (s), 1222 (s), 1205 (s), 1161 (s), 1141 (s), 1031 (s) cm^{-1}. – ^1H NMR (CD_3CN, 500.14 MHz, 273 K): δ = 1.81 (m_c, 2 H, 4′-H), 1.89 (m_c, 2 H, 3′-H), 3.12 (t, 2 H, 5′-H), 3.73 (t, 2 H, 2′-H), 5.19 (s, 2 H, NCH_2Thie), 7.14 (t, 1 H, H_{olefin}); CH_2-thienyl: 7.18 (dd, J = 5.0, 1.3 Hz, 1 H, 4-H), 7.51 (dd, J = 5.0, 3.0 Hz, 1 H, 5-H), 7.63 (dd, J = 3.0, 1.3 Hz, 1 H, 2-H_{Thie}); C(OTf)-thienyl: 7.52 (dd, J = 5.1, 1.4 Hz, 1 H, 4-H), 7.61 (dd, J = 5.3, 2.9 Hz, 1 H, 5-H), 8.01 (dd, J = 3.0, 1.4 Hz, 1 H, 2-H). – $^{13}C\{^1H\}$ NMR (CD_3CN, 125.8 MHz, 273 K): δ = 17.3 (C-4′), 21.0 (C-3′), 33.6 (C-5′), 53.7 (C-2′), 57.6 (NCH_2Thie), 112.2 (N=C-CH), 118.9 (q, $^1J_{C,F}$ = 319.5 Hz, OTf_{cov}), 121.5 (q, $^1J_{C,F}$ = 320.0 Hz, TfO^-), 126.5, 128.7 (3 C_{Thie}), 130.0, 130.9, 131.6, 132.9, 148.7 (C-OTf), 181.3 (C-6′). – $C_{18}H_{17}F_6NO_6S_4$ (585.56): calcd. C 36.92, H 2.93, N 2.39; found C 36.60, H 3.21, N 2.31.

6-[2-(4-Chlorophenyl)ethynyl]-1-[(thien-3-yl)-methyl]-2,3,4,5-tetrahydropyridinium trifluoromethanesulfonate (**5a**) *and 11-(4-chlorophenyl)-4,5,8,9-tetrahydro-6H-pyrido[1,2-a]thieno[2,3-e]-azepinium trifluoromethanesulfonate* (**6a**)

A solution of **4a** (4.91 g, 8.0 mmol) in CH_3CN (10 ml) was heated at 160 °C for 4 h in a closed thick-walled Schlenk tube. After cooling, the solution was concentrated to half the volume and ether was added until an oil separated. The supernatant solution was removed with a pipette, the oil was dissolved in CH_3CN (10 ml), and ether was added until the cloudiness of the solution no longer disappeared immediately after addition. Upon cooling at −78 °C, a brownish solid separated which was isolated by filtration (the mother liquor was kept, *vide infra*) and recrystallized from CH_3CN-ether to yield **6a** as a yellow solid. To the mother liquor was added ether until the solution remained turbid. Vigorous stirring at 0 °C caused the separation of a brownish solid which was recrystallized from CH_2Cl_2-ether at −30 °C to furnish **5a** as a dark-yellow solid.

5a: Yield: 2.63 g (71%); m.p. 127–128 °C. – IR (KBr): ν = 2208 (vs, C≡C), 1640 (s), 1278, 1261, 1156, 1029 (all vs) cm^{-1}. – ^1H NMR (CD_3CN, 500.14 MHz): δ = 1.80–1.87 (m, 2 H, 4′-CH_2), 1.90–1.96 (m, 2 H, 3′-H), 3.11 (t, 2 H, 5′-H), 3.77 (m, 2 H, 2′-H), 5.32 (s, 2 H, NCH_2Thie), 7.21 (dd, J = 5.0, 1.4 Hz, 1 H, 4-H_{Thie}), 7.52 (dd, J = 5.0, 3.0 Hz, 1 H, 5-H_{Thie}), 7.63 (dd, J = 2.9, 1.4 Hz, 1 H, 2-H_{Thie}), 7.55/7.74 (AA′BB′, 4 H, H_{Ar}). – $^{13}C\{^1H\}$ NMR (CD_3CN, 125.8 MHz): δ = 17.4 (C-4′), 21.2 (C-3′), 35.1 (C-5′), 53.8 (C-2′), 59.0 (NCH_2Thie), 83.6 (C≡CAr), 114.0 (C≡CAr), 117.8 (C-1_{Ar}), 122.1 (q, $^1J_{C,F}$ = 320.8 Hz, TfO^-), 128.0, 128.5, 128.8 (3 C_{Thie}), 130.5 (C_{Ar}), 132.6 (C-3_{Thie}), 136.1 (o-C_{Ar}), 140.0 (C-Cl), 167.7 (C-6′). – $C_{19}H_{17}ClF_3NO_3S_2$ (463.92): calcd. C 49.19, H 3.69, N 3.02; found C 48.62, H 3.91, N 2.87.

6a: Yield: 0.66 g (18%); m.p. 194 °C. – IR (KBr): ν = 1640 (m), 1554 (s), 1514 (m), 1491 (m), 1441 (s), 1385 (m), 1263 (vs), 1225 (s), 1152 (s), 1031 (vs) cm^{-1}. – ^1H NMR (CD_3CN, 500.14 MHz): δ = 1.77–1.86 (m, 4 H, 7-H, 8-H), 2.96 (t, 2 H, 9-H), 3.96 (t, 2 H, 6-H), 4.73 (s, 2 H, 4-H), 6.75 (s, 1 H, 10-H), 7.34 (d, J = 5.1 Hz, 1 H, 3-H), 7.54/7.62 (AA′BB′, 4 H_{Ar}), 7.97 (d, J = 5.1 Hz, 1 H, 2-H). – $^{13}C\{^1H\}$ NMR (CD_3CN, 125.8 MHz): δ = 17.8 (C-8), 21.7 (C-7), 32.3 (C-9), 55.6 (C-4), 55.6 (C-6), 121.5 (C-10), 128.7 (C-3), 129.9 (C_{Ar}), 132.6 (C_{Ar}), 136.1

(C-2), 136.6 (C-3a), 137.8 (C-Cl), 138.8 (C-11a), 141.2 (C-1_{Ar}), 150.9 (C-11), 175.2 (C-9a). – $C_{19}H_{17}ClF_3NO_3S_2$ (463.92): calcd. C 49.19, H 3.69, N 3.02; found C 48.60, H 3.76, N 2.93.

Preparation of enaminosulfones **7a–c,e,f**
General procedure

Dimethylaminomethyl-polystyrene (257 mg, 1.06 mmol) was added at 20 °C in several portions to a solution of iminium triflate **4** (1.0 mmol) in CH_3CN (10 ml). A color change from yellow to red was observed after a few minutes. After 1 h, the polymer was removed by filtration and washed twice with CH_3CN (2 × 10 ml). The combined organic phases were concentrated to leave a dark-red oil. In the case of **4a–c**, trituration with ether gave enaminosulfones **7a–c** as solids which were recrystallized from CH_2Cl_2-ether. In the case of **4e**,**f**, the oily residue was subjected to column chromatography (silica gel, CH_3CN as eluent) to give enaminosulfones **7e**,**f** which were recrystallized from CH_3CN-ether.

1-(4-Chlorophenyl)-2-{1-[(thien-3-yl)methyl]-3-[(trifluoromethyl)sulfonyl]}-1,4,5,6-tetrahydropyridin-2-yl]ethan-1-one (**7a**)

Yield: 73%; m.p. 134 °C. – IR (KBr): ν = 1690 (s), 1589 (m), 1552 (vs), 1330 (vs), 1212 (s), 1199 (s), 1176 (vs), 1128 (s), 1092 (s), 1031 (m) cm^{-1}. – ^1H NMR (CD_3CN, 500.14 MHz): δ = 1.88 (quin, 2 H, 5′-H), 2.52 (t, 2 H, 4′-H), 3.34 (t, 2 H, 6′-H), 4.45 (s, 2 H, NCH_2Thie), 4.58 (s, br, 2 H, CH_2CO), 6.99 (dd, J = 5.1, 1.2 Hz, 1 H, 4-H_{Thie}), 7.20 (dd, J = 2.8, 1.2 Hz, 1 H, 2-H_{Thie}), 7.41 (dd, J = 5.0, 2.9 Hz, 1 H, 5-H_{Thie}), 7.49/7.91 (AA′BB′, 4 H_{Ar}). – $C_{19}H_{17}ClF_3NO_3S_2$ (463.92): calcd. C 49.19, H 3.69, N 3.02; found C 48.67, H 3.80, N 2.93.

2-{1-Benzyl-3-[(trifluoromethyl)sulfonyl]-1,4,5,6-tetrahydropyridin-2-yl}-1-[(thien-3-yl)methyl]-ethan-1-one (**7b**)

Yield: 74%; m.p. 145–147 °C. – IR (KBr): ν = 1676 (s), 1547 (vs), 1358 (m), 1332 (s), 1262 (m), 1204 (s), 1186 (s), 1171 (s), 1131 (s), 1092 (s), 1030 (s) cm^{-1}. – ^1H NMR (CD_3CN, 500.14 MHz): δ = 1.90 (quin, 2 H, 5′-H), 2.55 (t, 2 H, 4′-H), 3.34 (t, 2 H, 6′-H), 4.48 (s, 2 H, NCH_2Ph), 4.40–4.70 (s, br, 2 H, CH_2CO), 7.19 (2 H_{Ar}), 7.30 (1 H_{Ar}), 7.37 (2 H_{Ar}), 7.43 (dd, J = 5.2, 2.8 Hz, 1 H, 5-H_{Thie}), 7.49 (dd, J = 5.1, 1.4 Hz, 1 H, 4-H_{Thie}), 8.18 (dd, J = 2.8, 1.3 Hz, 1 H, 2-H_{Thie}). – $C_{19}H_{18}F_3NO_3S_2$ (429.47): calcd. C 53.14, H 4.22, N 3.26; found C 53.16, H 4.41, N 3.14.

1-(Thien-3-yl)-2-{1-[(thien-3-yl)methyl]-3-[(trifluoromethyl)sulfonyl]-1,4,5,6-tetrahydropyridin-2-yl}ethan-1-one (**7c**)

Yield: 79%; m.p. 124–125 °C. – IR (KBr): ν = 1671 (s), 1552 (vs), 1510 (m), 1413 (m), 1359 (m), 1332 (m), 1318 (m), 1235 (m), 1212 (s), 1188 (vs), 1172 (vs), 1131 (vs), 1091 (vs), 1029 (m), 1011 (m) cm^{-1}. – ^1H NMR (CD_3CN, 500.14 MHz): δ = 1.88 (quin, 2 H, 5′-H), 2.52 (t, 2 H, 4′-H), 3.37 (t, 2 H, 6′-H), 4.44 (s, 2 H, NCH_2Thie), 4.58 (s, br, 2 H, CH_2CO); CH_2-Thienyl: 6.99 (dd, J = 5.0, 1.3 Hz, 1 H, 4-H), 7.19 (dd, J = 2.9, 1.3 Hz, 1 H, 2-H), 7.41 (dd, J = 5.0, 2.9 Hz, 1 H, 5-H); CO-Thienyl: 7.44 (dd, J = 5.1, 2.8 Hz, 1 H, 5-H), 7.50 (dd, J = 5.1, 1.3 Hz, 1 H, 4-H), 8.21 (dd, J = 2.9, 1.3 Hz, 1 H, 2-H). – $C_{17}H_{16}F_3NO_3S_2$ (435.49): calcd. C 46.89, H 3.70, N 3.22; found C 46.73, H 3.79, N 3.17.

2-{1-Allyl-3-[(trifluoromethyl)sulfonyl]-1,4,5,6-tetrahydropyridin-2-yl}-1-(4-chlorophenyl)ethan-1-one (**7e**)

Synthesis starting from salt **4e** [9]; yield: 79%; m.p. 103 °C. – IR (KBr): ν = 1694 (s), 1591 (m), 1369 (m), 1331 (vs), 1211 (s), 1187 (vs), 1150 (m), 1022 (m) cm^{-1}. – ^1H NMR (CD_3CN, 500.14 MHz): δ = 1.85–1.96 (m, 2 H, 5′-H), 2.52 (t, 2 H, 4′-H), 3.38 (t, 2 H, 6′-H), 3.85 (d, 2 H, NC$H_{2,allyl}$), 4.54 (br s, 2 H, CH_2CO), 5.14 (d, J = 17.3 Hz, 1 H, =CH_2), 5.21 (d, J = 10.9 Hz, 1 H, =CH_2), 5.78 (m_c, 1H, CH=CH_2), 7.52/7.93 (AA′BB′, 4 H_{Ar}). – $C_{17}H_{17}ClF_3NO_3S$ (407.84): calcd. C 50.07, H 4.20, N 3.43; found C 49.79, H 4.23, N 3.28.

2-{1-(But-3-en-1-yl)-3-[(trifluoromethyl)sulfonyl]-1,4,5,6-tetrahydropyridin-2-yl}-1-(4-chlorophenyl)ethan-1-one (**7f**)

Synthesis starting from salt **4f** [9]; yield: 77%; m.p. 93 °C. – IR (KBr): ν = 1693 (s), 1589 (m), 1546 (s), 1333 (s), 1210 (m), 1191 (vs), 1167 (s), 1091 (m) cm^{-1}. – ^1H NMR (CD_3CN, 500.14 MHz): δ = 1.94 (m_c, 2 H, 5′-CH_2), 2.32 (q, 2 H, CH_2CH=CH_2), 2.50 (t, 2 H, 4′-CH_2), 3.26 (t, 2 H, NCH_2CH_2CH=), 3.42 (t, 2 H, 6′-CH_2), 4.58 (br s, 2 H, CH_2CO), 5.03 (dd, J = 10.2, 1.9 Hz, 1 H, =CH_2), 5.08 (dd, J = 17.1, 1.8 Hz, 1 H, =CH_2), 5.76 (m_c, 1H, CH=CH_2), 7.53/7.95 (AA′BB′, 4 H_{Ar}). – $C_{17}H_{17}ClF_3NO_3S$ (407.84): calcd. C 50.07, H 4.20, N 3.43; found C 49.79, H 4.23, N 3.28.

X-ray crystal structure determination of **7f**

Crystal data: $C_{18}H_{19}ClF_3NO_3S$, triclinic space group $P\bar{1}$; a = 5.602(1), b = 8.859(1), c = 19.788(2) Å, α = 84.11(1), β = 87.26(1), γ = 82.59(1)°; D_{calc} =

1.447 g·cm^{-3}; Z = 2. Data collection: crystal size 1.10 × 0.64 × 0.38 mm; Stoe IPDS instrument, monochromatized Mo$K\alpha$ radiation; T = 295(2) K, 13606 reflections collected, 3472 unique reflections (R_{int} = 0.0258). Structure solution and refinement was achieved with the program system SHELX-97 [21]. Full-matrix least-squares refinement of 264 parameters (18 restraints) against F^2 values gave the following R values: R = 0.0651 and R_w = 0.1495 for all data, and R = 0.0522, R_w = 0.1413 for 2690 observed reflections [$I > 2\sigma(I)$]. The residual electron density was between 0.40 and −0.33 e·Å^{-3}. Two orientations of the *N*-homoallyl moiety were found in the solid sate which affected the methylene groups C15 and C16 (Fig. 1) and consequently also the hydrogen atom positions at the olefinic bond. This disorder was treated appropriately, and the occupancy factors for the two positions were refined to give values of 0.58 and 0.42.

Crystallographic data (excluding structure factors) for the structure reported in this paper have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication no. CCDC-178456. Copies of the data can be obtained free of charge on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK [Fax: Int. Code +(1223)336-033; E-mail: deposit@ccdc.cam.ac.uk].

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