285. Intramolecular Thermal 2 + 2-Cycloadditions of Styrene-Derivatives

by **Wolfgang Oppolzer**[1]) and **Hans-Rudolf Loosli**

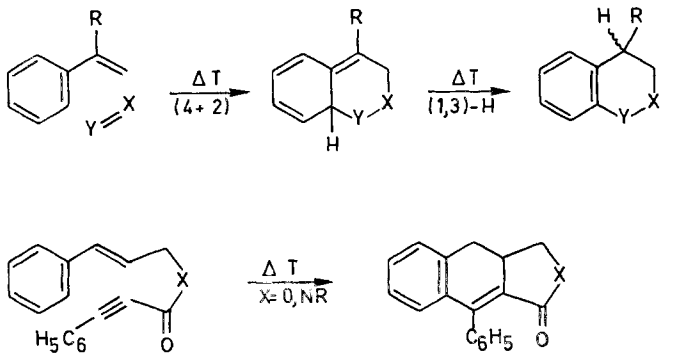
Sandoz Ltd, Pharmaceutical Division, Chemical Research, Basle, Switzerland

(28. X. 74)

Zusammenfassung. Beim Erhitzen des Bis-styryl Derivates **1** in siedendem *o*-Dichlorbenzol entstehen überraschenderweise in hoher Ausbeute die Aza[3.1.1]bicycloheptane **2** und **3**, deren Struktur durch ^{1}H- und ^{13}C—NMR.-Spektren unter Verwendung eines Computerprogrammes eindeutig bestimmt wurde. Auf analoge intramolekulare 2 + 2-Additionen **8** → **9** wird hingewiesen.

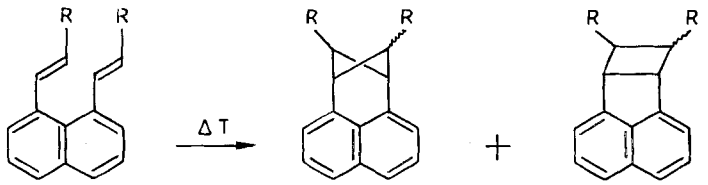
In connection with our studies on intramolecular pericyclic reactions [1] we were interested in cycloadditions of styrenes. Styrenes usually do not undergo 2 + 2-additions with simple olefins, but rather participate in inter- [2] and intra-molecular [3] 4 + 2-additions not only as dienophile but also as diene[2]) (*Scheme 1*).

Scheme 1



However, thermal intramolecular 2 + 2-additions of aryl conjugated olefins proceed readily in cases where the π-clouds of the reactants are forced into each

Scheme 2



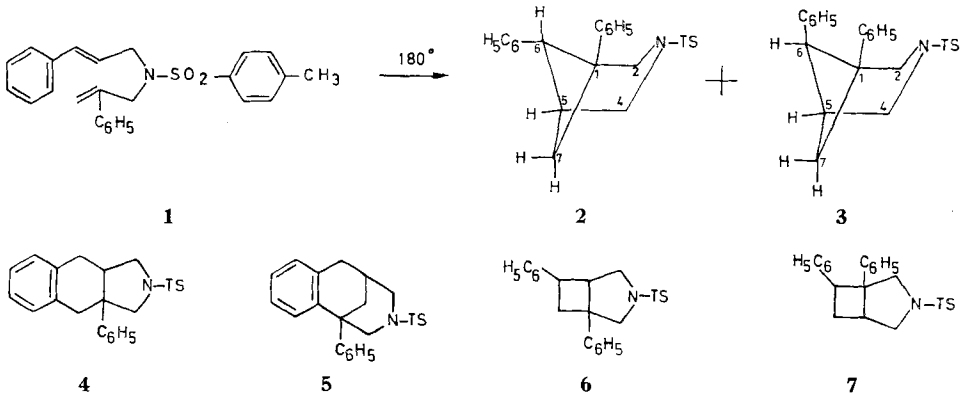
[1]) Present address: Département de Chimie Organique, Université de Genève, 30, quai Ernest Ansermet, 1211 Genève 4, Switzerland.

[2]) On thermolysis of styrene (neat or in benzene solution) 1-phenyltetralin and 1,2-diphenylcyclobutane (in the ratio 5:1 and 2:1, respectively) were obtained in minute yield [4].

other by steric reasons [5]. Thus the driving force of the isomerisation of 1,8-divinylnaphthalenes (*Scheme 2*) has been attributed to a considerable π-strain, caused by the *peri*-bridge [6].

We wish to report the efficient thermal isomerisation of the diene **1**, a bis-styryl derivative, which apparently does not exhibit any π-strain.

Scheme 3



Heating the diene **1** in boiling dichlorobenzene for 72 h gave in high yield two isomeric products, which were separated by chromatography. The less polar product, m.p. 162–164°, was assigned to structure **2**, whereas the more polar product, m.p. 118–119°, corresponds to structure **3** on the basis of NMR. evidence (*cf.* Tables 1–3).

Table 1. ^1H–*NMR. Data of the Azabicyclo[3.1.1]heptanes* **2** *and* **3**: *Chemical Shifts in* $CDCl_3$ (± 0.05 ppm)

Compound	H–C(2)eq	H–C(2)ax	H–C(4)eq	H–C(4)ax	H–C(5)	H–C(6)	H–C(7)eq[a])	H–C(7)ax[a])
2	3.8	3.5	3.8	3.7	2.65	3.2	2.85	1.65
3	3.85	3.7	3.7	3.5	2.9	3.7	2.1	1.95

[a]) Axial and equatorial position relative to the piperidine ring.

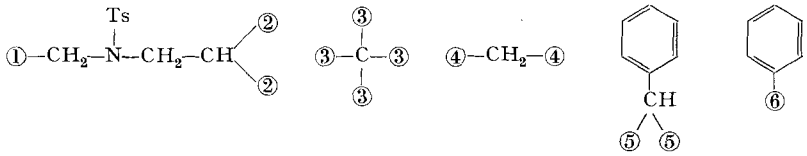
Table 2. ^1H–*NMR. Data of the Azabicyclo[3.1.1]heptanes* **2** *and* **3**: *Coupling Constants* (± 0,5 Hz)

Compound	2eq/2ax	2eq/7eq	4eq/4ax	4eq/5	4ax/5	5/6	5/7eq	5/7ax	6/7ax	7eq/ax
2	10	1	10	2.5	2.5	0	6.5	0	5.5	9.5
3	10	0	10	3	2	6.5	5.5	0	0	9.5

Table 3. ^{13}C–*NMR. Data of the Azabicyclo[3.1.1]heptanes* **2** *and* **3**: *Chemical Shifts in* $CDCl_3$ (± 0.1 ppm) *and Multiplicity*

Compound	C(1)	C(2)	C(4)	C(5)	C(6)	C(7)
2	48.0 *s*	59.0 *t*	51.6 *t*	33.3 *d*	52.8 *d*	31.3 *t*
3	47.8 *s*	50.2 *t*	44.8 *t*	32.7 *d*	45.6 *d*	36.6 *t*

Each product exhibits ^{1}H–NMR. signals of 14 aromatic protons, 1 methyl group and of 8 protons attached to sp^3-carbon atoms. These results are clearly incompatible with the structure of any 4 + 2-adduct such as **4** or **5**. The combined information from ^{1}H- and ^{13}C–NMR. spectra indicates that both products must be built up from the following five fragments:



In order to combine these fragments to arrive at a set of plausible molecular structures we made further use of the following data:

1) the chemical shifts of the hydrogen atoms (Table 1);

2) the ^{1}H–^{1}H coupling constants (Table 2);

3) the chemical shifts and the multiplicity of the carbon atoms (Table 3);

which imposed the following restrictions:

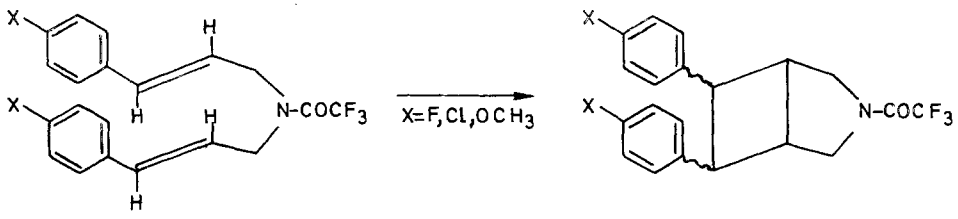
1) joining of the half-bonds (circled numbers in the diagram above) ① and ④, ① and ⑤, ① and ⑥, ④ and ⑥, as well as ⑤ and ⑥ is forbidden.

2) neither olefinic nor acetylenic bonds and no three membered rings are present.

Taking into account the above mentioned fragments and restrictions a computer program after *Munk* [7] showed that only the structures **2**, **3**, **6**, and **7** come into consideration. It could be shown with the help of double-resonance experiments and the use of shift reagents that the coupling constants of the cyclobutane hydrogen-atoms do not agree with the structures **6** and **7** [8]; they are, however in full accord with the aza[3.1.1]bicycloheptane structures **2** and **3** [9]. Further examination of the coupling constants confirms, that both products differ from each only with respect to their configuration at C(6). Accordingly in the isomer **2** the axial position of H–C(6) follows from its long-range coupling $J_{6/7ax} = 5.5$ Hz and its vicinal coupling $J_{5/6} = 0$ Hz, whereas in the isomer **3** the constants $J_{6/7ax} = 0$ Hz and $J_{5/6} = 6.5$ Hz correspond to an equatorial H–C(6) [10].

Surprisingly no 4 + 2-adducts, such as illustrated by the formulas **4** and **5** could be detected in the reaction mixture. The reactions seem to be regiospecific since no 3-aza[3.2.0]bicycloheptane **6** was found, which agrees with the reaction mechanism discussed in the following communication [11].

Scheme 4



8 **9**

Thus it appears that simple styrenes can undergo efficient thermal intramolecular 2 + 2-cycloadditions even when favorable geometrical constraints, as exemplified by 1,8-divinylnaphthaline, are absent.

Similarly the recently observed thermal transformations **8** → **9** [12] suggest, that this type of reaction might be more general, than expected.

We thank Dr. *M. E. Munk* for providing the above mentioned program «STRUCTUR».

Experimental Part[4])

(in collaboration with *H. Fretz* and *A. Siegrist*)

N-(trans-1-Phenyl-2-propenyl)-trifluoroacetamide. To a stirred and cooled (ice/methanol) mixture of 58.1 g (0.64 mol) of cinnamylamine [13], 100 ml of pyridine and 600 ml of dichloromethane was added dropwise 162 g (0.77 mol) of trifluoroacetic anhydride. After 1 h at room temperature the reaction mixture was shaken three times with 10% aqueous citric acid, once with saturated $NaHCO_3$ sol., dried over Na_2SO_4, concentrated *in vacuo* and diluted with pentane to give 140.7 g (96% yield) of crystals: m.p. 108–110°. – IR. (CH_2Cl_2): 3420 m, 1723 s, 964 m. – ^{1}H–NMR. (60 MHz): 4.12 (2 H, *t*, J = 6 Hz); 6.2 (1 H, *d* × *t*, J = 15.5 Hz and 6 Hz); 6.6 (1 H, *d*, J = 15.5 Hz); 6.2–7.2 (1 H); 7.1–7.5 (5 H).

$C_{11}H_{10}F_3NO$ (229.5) Calc. C 57.6 H 4.4 N 6.1% Found C 57.4 H 4.2 N 5.8%

N-(2-Phenylallyl), N-(trans-3-phenylallyl)-toluenesulfonamide (**1**). To a stirred and cooled (ice/methanol) slurry of 9.2 g of 80% sodium hydride in 90 ml of freshly distilled hexamethylphosphoramide (under N_2) was added a solution of 70 g of N-(*trans*-1-phenyl-2-propenyl)-trifluoroacetamide in 150 ml of hexamethylphosphoramide. After the gas evolution had stopped a solution of 120 g of 3-bromo-2-phenylpropene [14] in 150 ml of hexamethylphosphoramide was slowly added to the stirred solution. Then the reaction mixture was kept at room temperature for 16 h, finally diluted with water and extracted with ether. Evaporation of the dried (Na_2SO_4) extracts, followed by chromatography of the oily residue on 1 kg of silica gel with benzene/petroleum ether 1:1 gave 64 g of N-(2-phenylallyl), N-(*trans*-3-phenylallyl)-trifluoroacetamide as a viscous oil, which was stirred with 1150 ml of 2N KOH in methanol for 1 h at room temperature. Evaporation of the mixture, shaking of the residue with water/ether, followed by evaporation of the dried ether extracts gave an oily residue which crystallized from petroleum ether to yield 40 g of crystalline N-(2-phenylallyl), N-(*trans*-3-phenylallyl)-amine, m.p. 32–35°, which was acylated in 320 ml of CH_2Cl_2 in the presence of 13.3 g of pyridine by dropwise addition of 32 g of *p*-toluenesulfonyl chloride in 90 ml of CH_2Cl_2 at 0°. The solution was kept at room temperature for 1 h, washed with 10% aqueous citric acid and saturated $NaHCO_3$ sol., dried and evaporated. The residue on crystallisation from CH_2Cl_2/petroleum ether furnished 55 g of pure N(2-phenylallyl), N-(*trans*-3-phenylallyl)-toluenesulfonamide (**1**), m.p.: 139–140°. – ^{1}H–NMR. (100 MHz): 2.4 (3 H, *s*); 3.9 (2 H, *d*, J = 6 Hz); 4.3 (2 H, *s*); 5.25 (1 H, *s*); 5.45 (1 H, *s*); 5.8 (1 H, *d* × *t*, J = 16 Hz and 6 Hz); 6.3 (1 H, *d*, J = 16 Hz); 7.0–7.5 (12 H); 7.7 (2 H, *d*, J = 8 Hz).

$C_{25}H_{25}NO_2S$ (403.5) Calc. C 74.4 H 6.2 N 3.5 S 7.9% Found C 74.3 H 6.2 N 3.5 S 7.7%

Attempts to obtain the crystalline toluenesulfonamide **1** by analogous alkylation of N-(*trans*-3-phenylallyl)-toluenesulfonamide with 1-bromo-2-phenyl-2-propene were unsuccessful.

Thermolysis of N-(2-phenylallyl), N-(trans-3-phenylallyl)-toluenesulfonamide (**1**). 9.4 g of the diene **1** was heated under N_2 in 200 ml of boiling *o*-dichlorobenzene (purified by distillation over K_2CO_3) for 72 h. Then the solution was stirred at room temperature with 20 g of silica gel, filtered and evaporated. Crystallisation of the residue from ether furnished 2.4 g of crystalline *cis*-1,6-diphenyl-3-azabicyclo[3.1.1]heptane-3-toluenesulfonamide (**2**), m.p.: 162–164°. – ^{1}H–NMR. (100 MHz): see Tables 1 and 2; additional signals: 2.4 (3 H, *s*); 6.7–7.2 (10 H); 7.3 (2 H, *d*, J = 8 Hz);

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[4]) All m.p. are incorrected. IR. spectra: *Perkin-Elmer* 21, max in cm^{-1}. NMR. spectra: *Varian* A60, *Varian* HA-100 and *Bruker* HX 90E in $CDCl_3$ internal standard: tetramethylsilane, δ = 0 ppm, abbreviations: *s* = singulett, *d* = doublet, *t* = triplet, *q* = quartet, *m* = multiplet, J = spin-spin coupling constant (Hz).

7.7 (2H, *d*, J = 8 Hz). – ^{13}C–NMR. (22.63 MHz): see Table 3; additional signals: 21.4 (*q*); 125.7 (*d*); 126.0 (*d*); 126.8 (*d*); 127.5 (*d*); 127.8 (*d*) 129.2 (*d*) 134.2 (*s*); 138.6 (*s*); 140.7 (*s*) 142.7 (*s*).

$C_{25}H_{25}NO_2S$ (403.5) Calc. C 74.4 H 6.2 N 3.5% Found C 74.1 H 6.4 N 3.6%

The mother liquor was chromatographed on 150 g of silica gel: elution with toluene/pentane 3:1 gave further 0.46 g of recrystallised isomer **2**, m.p. 163–164° (total yield: 30%), whereas elution with toluene furnished the more polar isomer **3** (2.4 g = 26% yield after crystallisation from ether): m.p.: 118–119°. – ^{1}H–NMR. (100 MHz): see Tables 1 and 2; additional signals: 2.4 (3 H, *s*); 6.7–7.5 (14 H). – ^{13}C–NMR. (22.63 MHz): see Table 3. additional signals: 21.3 (*q*) 125.1 (*d*); 125.5 (*d*); 126.4 (*d*); 126.6 (*d*); 127.8 (*d*); 128.0 (*d*); 128.9 (*d*); 134.1 (*s*); 137.0 (*s*); 142.1 (*s*); 143.7 (*s*).

$C_{25}H_{25}NO_2S$ (403.5) Calc. C 74.4 H 6.2 N 3.5% Found C 74.5 H 6.1 N 3.5%

In order to check the uniformity of the thermolysis 0.25 g of N-(2-phenylallyl), N-(*trans*-3-phenylallyl)-toluenesulfonamide (**1**) was heated in 5 ml of refluxing *o*-dichlorobenzene for 72 h to give after evaporation and chromatographic removal of apolar and strongly polar impurities 0.23 g (92%) of an oil, which by ^{1}H–NMR. analysis appeared to be exclusively a 1:1 mixture of the isomers **2** and **3** containing ~4% of the starting diene **1**.

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