

Chimia 48 (1994) 560–564  
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 ISSN 0009–4293

# Synthetic Attempts towards Polymers with Pentafulvene Structural Units

Gengyi Zhang and Markus Neuenschwander\*

**Abstract.** Pentafulvenes with weakly electron-donating substituents at C(6) ( $X = \text{SMe}$ ) may be submitted to cationic polymerization which had been reported before only for 6-alkyl-, 6-aryl-, and 6,6-dialkylpentafulvenes. This procedure does not work for pentafulvenes like **1c** with strong electron-releasing substituents at C(6) ( $X = \text{Me}_2\text{N}$ ). Based on bromination-elimination experiments with model compound **6**, it has been shown that direct bromination of polyfulvene **2a**  $\rightarrow$  **10a** is very efficient. This result is important in view of the synthesis of polymers **3a** with pentafulvene structural elements. So far, only partial HBr elimination of polymer **10a** has been achieved, while  $\text{I}_2$  treatment of **10a** gives a insoluble charcoal-like black polymer absorbing in the whole UV/VIS range.

## Introduction

Pentafulvenes **1** are cyclic cross-conjugated molecules with a five-membered ring whose electronic properties are strongly varying with exocyclic substituents [1–3] influencing the extent of  $\pi$ -delocalization as well as the HOMO-LUMO gap. If these substituent effects would be operative in polymers containing pentafulvene structural units as well, then polymers with considerably varying electronic properties could, in principle, be available. In fact, semiempirical calculations [4] predict that some types of long-chain polyenes with fulvene or fulvalene structural units should be characterized by a relatively small energy difference between the HOMO and the LUMO. Therefore, they are very attractive in view of polymers with unique electrical and optical properties. Furthermore, polymers of this type, or their dihydro precursors (see *Scheme 1*), could be of interest in view of the synthesis of 'nonclassical non-alternant polymers' [5].

It is well-known that 6,6-dimethylpentafulvene (**1a**;  $R = X = \text{Me}$ ) reacts with traces of acid (like  $\text{CCl}_3\text{COOH}$ ) or *Lewis* acids (like  $\text{SnCl}_4$ ) to give nearly quantita-

$\text{Me}_2\text{N}$ ) with electron-donating substituents at C(6). Furthermore, we explored possible ways for the transformation **2**  $\rightarrow$  **3** (*Scheme 1*).

## Cationic Polymerization of Pentafulvenes 1a–c

We found, in agreement with earlier results [6], that 6,6-dimethylpentafulvene (**1a**) easily reacts with various protic acids and *Lewis* acids to give, after precipitation with MeOH and high vacuum drying, white polymer powders in a nearly quantitative yield. So, polymerization of 0.5 ml of **1a** by means of 0.5 mol-% of  $\text{CCl}_3\text{COOH}$  in 10 ml of  $\text{CH}_2\text{Cl}_2$  solution at  $0^\circ$  gave soluble (but  $\text{O}_2$ -sensitive) polymer **2a** with  $M_n = 38\,800$  and  $M_w = 53\,750$  and the spectral data typical for structure **2a** [6] [7].

Cationic polymerization of 6,6-bis(methylthio)pentafulvene (**1b**) turned out to be very slow under similar conditions with  $\text{CCl}_3\text{COOH}$ , but was fast enough with 1 mol-% of  $\text{SnCl}_4$  in a 10 vol-%  $\text{CH}_2\text{Cl}_2$  solution at  $0^\circ$ . A slightly yellowish polymer powder was isolated in a nearly quantitative yield which was soluble in usual organic solvents but easily cross-linking in the presence of  $\text{O}_2$ . GPC Measurements (*Fig. 1*) showed a similar molecular-weight

te yields of high-molecular-weight polymers **2a** [6] with interesting spectroscopic properties [7]. Therefore, we tried to apply the reaction **1**  $\rightarrow$  **2** to pentafulvenes **1b** ( $R = X = \text{SMe}$ ) and **1c** ( $R = \text{H}$ ,  $X =$

Scheme 1. Pathways to Polymers with Pentafulvene and Pentafulvalene Structural Units

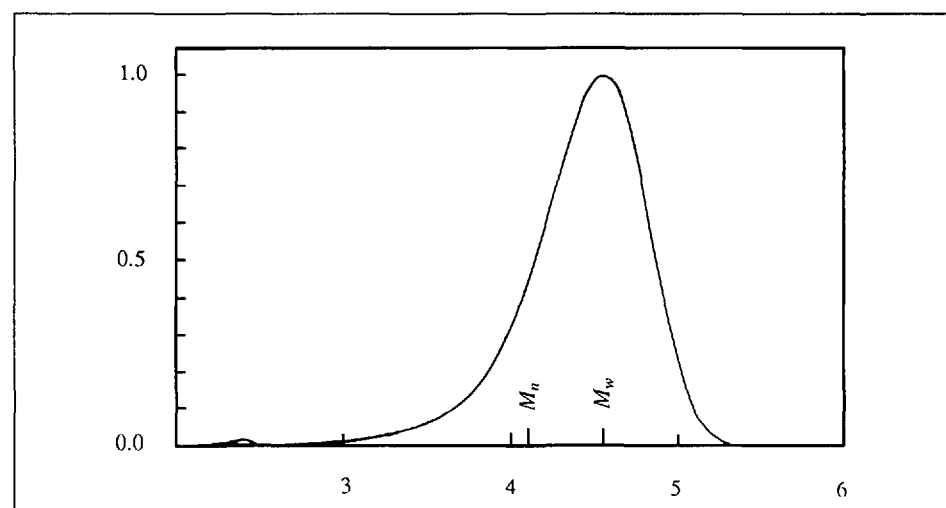
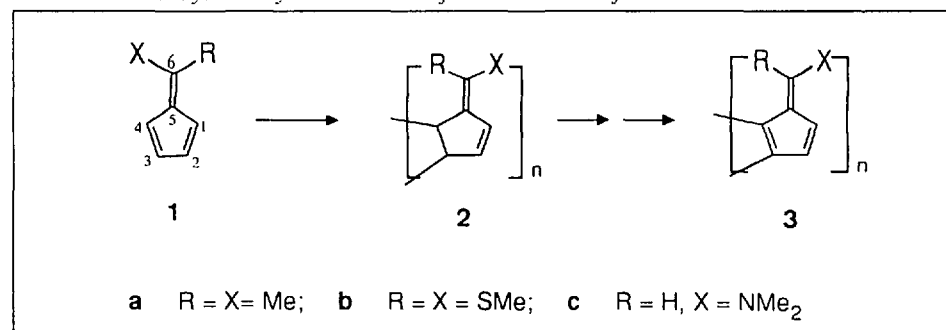


Fig. 1. Molecular-weight distribution of **2b** (GPC, Ultrastaygel, THF)

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distribution to that of **2a**, but with a smaller  $M_n = 12\,600$  and  $M_w = 35\,900$ .

All the spectroscopic data are consistent with structural elements **2b**: In the UV spectrum, the polymer shows a single maximum at 306 nm in dioxane ( $\epsilon = 11\,630$  per structural unit), the bathochromic shift compared with **2a** (248 nm in dioxane ( $\epsilon = 10\,130$ )) being compatible with the influence of the MeS units on the diene system of **2a** [8]. In the  $^1\text{H-NMR}$  spectrum, broad signals are observed at 6.7, 5.8, and 2.9 ppm together with the intense peak of the MeS units at 2.2 ppm. The  $^{13}\text{C-NMR}$  spectrum (Fig. 2) of **2b** is very similar to that of **2a** [6], which has been assigned by comparison with model compounds [7]: Quaternary vinylic C-atoms absorb at 156 and 122 ppm, proton-bearing vinylic C-atoms at 140 and 133 ppm, while the broad overlapping signals at 54 and 50 ppm are produced by alkyl C-atoms C(1) and C(2). Finally, the nearly equivalent MeS groups absorb at 17 ppm.

These results show that pentafulvenes with weakly electron-donating substituents like SMe (**1b**) are easily polymerized in the presence of Lewis acids like  $\text{SnCl}_4$  to give polymers of type **2b**. Compared with **1a** [7], the polymerization rate decreases and acids like  $\text{CCl}_3\text{COOH}$  are no more active enough to ensure a fast polymerization. According to Table 1, polymerization of pentafulvenes like **1c** with strong electron-donating groups fails even in the presence of strong Lewis acids, although one would expect ([1–3]) that the ease of attack of electrophiles increases within the series **1a** < **1b** < **1c**.

One major reason for that failure is the energy of pentadienyl cations **4** (see Scheme 2) resulting from electrophilic attack at pentafulvenes **1**. MNDO Calculations show that the energy of cations **4** strongly decreases in the series **4a** > **4b** > **4c** [9]. So highly delocalized pentadienyl cation **4c** has a comparably long lifetime and is prone to chain-transfer reactions of type **4c**  $\rightarrow$  **5c** (which are facilitated by the basic  $\text{Me}_2\text{N}$  groups), and which can easily restore fulvene structural elements of **1c** according to Scheme 2. In fact, pentafulvenes with amino groups at C(6) easily undergo electrophilic substitution instead of addition reactions [10][11].

### Bromination-Elimination Experiments with a Model Compound

In view of the desired conversion **2**  $\rightarrow$  **3** of cationic pentafulvene polymer **2** (Scheme 1), it seemed to be appropriate to explore the corresponding conversion of a

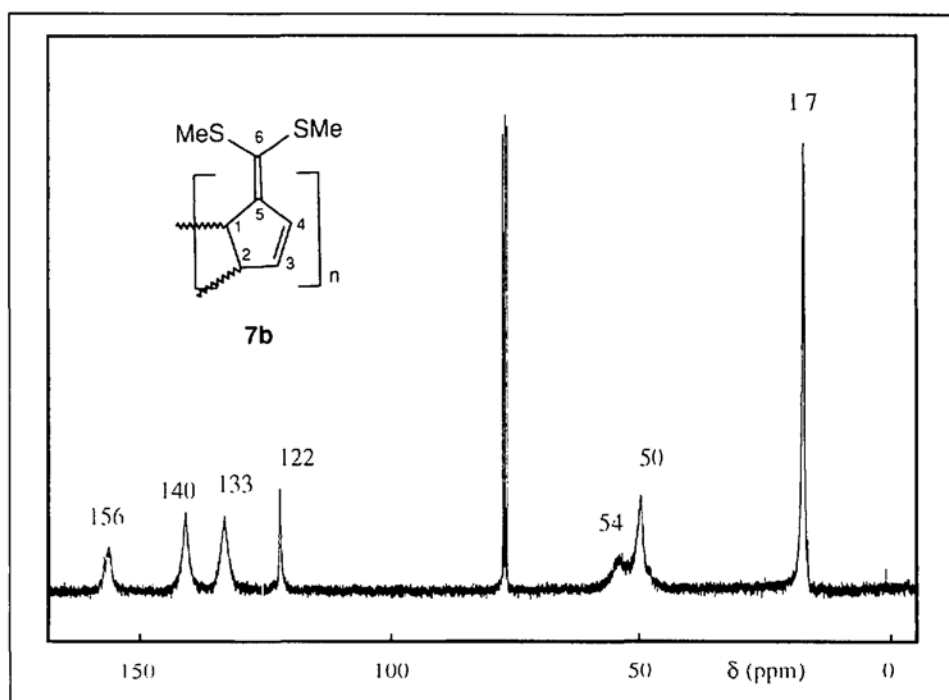
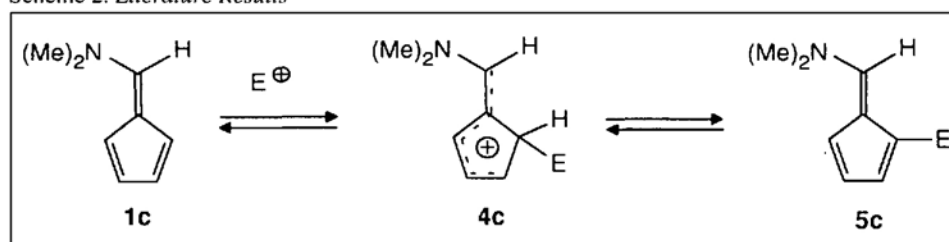


Fig. 2.  $^{13}\text{C-NMR}$  Spectrum ( $\text{CDCl}_3$ , 75 MHz) of **2b**

Table 1. Polymerization of Pentafulvenes **1a**, **1b**, **1c** with  $\text{SnCl}_4$  in  $\text{CH}_2\text{Cl}_2$  at  $0^\circ$

No.	$C_M$ [Vol.-%]	$C_I$ [mol.-%]	$t$ [min]	$\eta_{\text{red}}$ [ml/g]	Yield [%] after precipitation
<b>1a</b>	2.5	1	10	42	100
<b>1b</b>	10	1	60	18.6	97
<b>1c</b>	10	1	60	0	—

Scheme 2. Literature Results



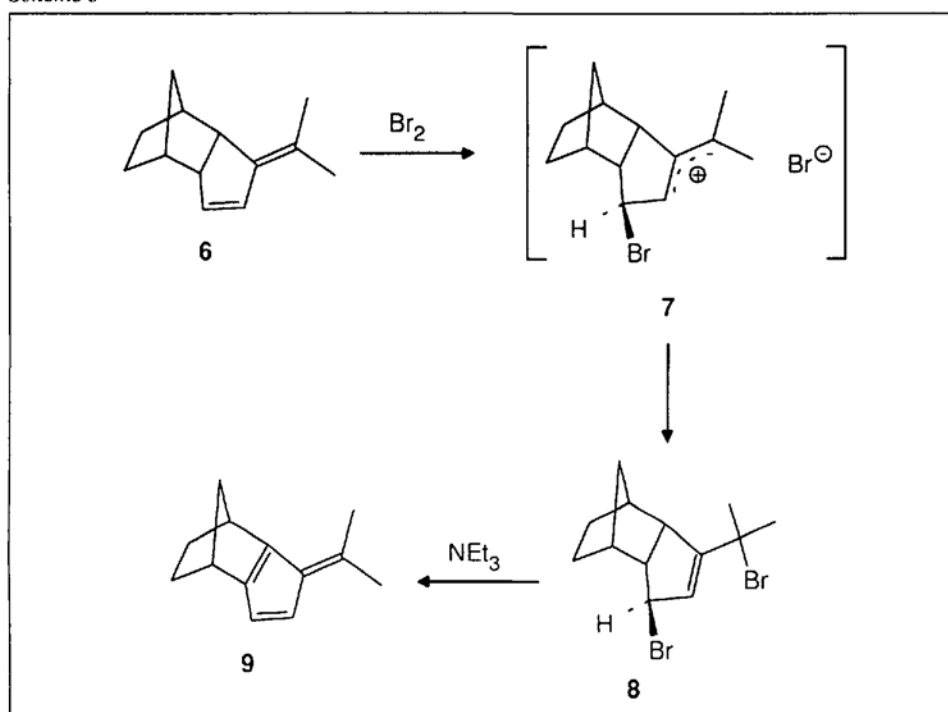
low-molecular-weight compound with the structural features of **2**. A reasonable model compound for that purpose is 5-isopropylidencyclopentadiene (**6**) which is available by Diels-Alder reaction of **1a** with cyclopentadiene (43% yield) followed by partial hydrogenation (92% yield) [7].

We investigated several procedures and showed that direct bromination of **6**, possibly proceeding over intermediate **7** and nearly quantitatively giving the dibromo compound **8** (Scheme 3), is much better than NBS bromination of **6**. As may be expected for a compound with two allylic Br-atoms, **8** is quite unstable at room temperature both in solution and in pure form which considerably hampers subsequent HBr elimination experiments.

In view of the planned conversion **8**  $\rightarrow$  **9**, we tried several bases like *t*-BuOK, DBU, and  $\text{Et}_3\text{N}/\text{AgBF}_4$  which did not produce the desired strained pentafulvene **9** in a high yield. Quite surprisingly, best results (51% yield of **9**) were obtained by reacting **8** with an excess of  $\text{Et}_3\text{N}$  in  $\text{CH}_2\text{Cl}_2$  at room temperature. The structures of both **8** and **9** convincingly follow from the spectroscopic data. Besides  $^{13}\text{C-NMR}$  data, most structural information follows from  $^1\text{H-NMR}$  spectra. In both cases, assignment is confirmed both by selective decoupling experiments and 1D and 2D experiments.

Our experiments with model compound **6** show that bromination/elimination is a feasible pathway for transforming 1,2-dihydro-pentafulvenes into pentafulvenes.

Scheme 3



Scheme 4

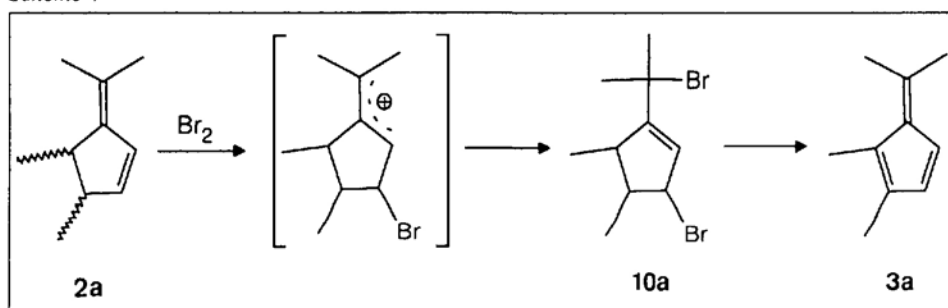


Table 2. Selected  $^1\text{H}$ - and  $^{13}\text{C}$ -NMR Spectral Data of Polymer **10a**<sup>a)</sup> and Model Compound **8**<sup>a)</sup>

Atom	$^1\text{H}$ -NMR	$^{13}\text{C}$ -NMR <sup>b)</sup>	$^1\text{H}$ -NMR	$^{13}\text{C}$ -NMR
1	ca. 3.9 (br.)	50–60 <sup>c)</sup>	3.55	56.3
2	ca. 3.0 (br.)	50–60 <sup>c)</sup>	3.15	52.9
3	ca. 5.1 (br.)	50–60 <sup>c)</sup>	5.06	58.1
4	ca. 6.1 (br.)	132 (br)	5.90	129.1
5	–	155 (br.)	–	154.3
6	–	50–60 <sup>c)</sup>	–	6.3
$\text{CH}_3$	ca. 1.9 (br.)	36 (br.)	1.99	33.6
			1.90	

<sup>a)</sup> Identical numbering for relevant C-atoms of **8** and **10a**.

<sup>b)</sup> Additional small absorptions at 146, 140, 125 ppm as well as a broad absorption around 20 ppm could be due to a partial HBr elimination during recording of the  $^{13}\text{C}$ -NMR spectrum.

<sup>c)</sup> Broad absorption between 45 and 65 ppm, with maxima in the range of 50–60 ppm, due to several overlapping  $^{13}\text{C}$ -NMR signals.

In view of the planned synthesis of polymers with pentafulvene structural units, direct bromination of polyfulvenes **2** seems to be very attractive while HBr elimination still has to be improved.

**Bromination-Elimination Experiments with Poly(6,6-dimethylpentafulvene) (2a)**

Similarly to model-compound **6**, bromination of poly(6,6-dimethylpentafulvenes) proceeds very easily in  $\text{CCl}_4$  at room temperature. During the initial period of the reaction, the color of  $\text{Br}_2$  disappears immediately. Later on, brominated polymer starts to precipitate and, possibly because of the inhomogeneous reaction, the color change slows down. After filtration (under Ar) and high vacuum drying a colorless powder with a satisfying elemental analysis for  $(\text{C}_8\text{H}_{10}\text{Br}_2)_n$  is collected in a 87% yield.

The white powder is very sensitive to heat, air and moisture. It produces easily HBr either in solution or in pure form at room temperature and has to be stored at low temperature under Ar. Therefore, subsequent elimination experiments **10a**  $\rightarrow$  **3a** are best undertaken with freshly prepared brominated polyfulvene. GPC Measurements of the polymer (THF, *Ultrasyl*) give approximate values of  $M_n = 71\,300$  and  $M_w = 369\,500$ ; these values are not very accurate due to the fact that ca. 10% of the polymer with  $M_w > 10^6$  are beyond the exclusion limit of the gel. Considering the fact that virtually each structural element of a sample of polyfulvene **2a** with  $M_n = 38\,800$  and  $M_w = 53\,750$  was brominated (see **2a**  $\rightarrow$  **10a**) thus increasing in molecular weight from  $M = 106$  to  $M = 266$ , the obtained (inaccurate)  $M_n$  of **10a** is quite satisfactory in relation to a theoretical value of 97 300. The markedly increased  $M_w/M_n$  factor of 5.2 for brominated polymer **10a** compared with  $M_w/M_n = 1.39$  for the starting material **2a** hints at the conclusion that either a certain amount of chain-fission takes place during bromination, or that the polymer **10a** loses some HBr during the GPC measurement.

All the spectroscopic data of brominated poly(6,6-dimethylpentafulvene) are in agreement with the proposed structure **10a** and fit to the spectral characteristics of model compound **8**. So the UV spectra of the polymer ( $\lambda_{\text{max}} = 232$  nm in dioxane and  $\epsilon = 6\,600$  per structure unit) as well as of **8** (with  $\lambda_{\text{max}} = 230$  in dioxane and  $\epsilon = 8\,800$ ) are very similar. Furthermore, both  $^1\text{H}$ -NMR and  $^{13}\text{C}$ -NMR spectra of the brominated polymer show broad absorp-

tion in exactly the ranges in which appropriate  $^1\text{H}$ - and  $^{13}\text{C}$ -atoms of model compound **8** are absorbing (Table 2). Together with the analytical data we conclude that bromination of poly(6,6-dimethylpentafulvene) (**2a**) gives polymer **10a** with very high yields.

Attempts towards a complete HBr elimination of polymer **10a** to give polymer **3a** with pentafulvene structural units are not yet completely satisfactory and have to be continued. Similar to HBr elimination of model compound **8**  $\rightarrow$  **9**, HBr elimination of polymer **10a**  $\rightarrow$  **3a** was at first tried with  $\text{Et}_3\text{N}$  in refluxing  $\text{CH}_2\text{Cl}_2$  solution over 48 h. During reaction, the color of the solution changed from yellow to brown-red, and after 10 h, the polymer began to precipitate. However, elemental analysis of the precipitate as well as titration of inorganic salts showed that HBr elimination was not complete. The polymer is a dark-brown brittle solid, being insoluble (but swelling) in usual solvents. According to its UV spectrum (Fig. 3, left), the polymer is supposed to contain segments with conjugated pentafulvene structural elements.

This unsatisfactory result prompted us to test a procedure by which a polymer containing structural elements **12A** and **12B** – which is obtained by  $\text{TiCl}_4$ -induced polymerization of spiro[2,4]hepta-4,6-diene (**11**) – had been partially transformed into conjugated segments **13A** and **13B** by treatment with  $\text{I}_2$  [12]. When  $\text{I}_2$  was added to the solution of poly(6,6-dimethylpentafulvene) (**2a**) in  $\text{CCl}_4$  at room temperature, the intense color of  $\text{I}_2$  did not disappear, but a violet-black precipitate started to be formed after a short time. If the mixture was boiled under reflux for 24 h, more and more black polymer was precipitating. The polymer was collected by filtration, washed with  $\text{CCl}_4$  and  $\text{CH}_2\text{Cl}_2$ , until the color of  $\text{I}_2$  had vanished, and vacuum dried.

The polymer had the appearance of charcoal; it is insoluble in all the usual solvents. The result of the elemental analysis of 'iodine-treated poly(6,6-dimethylpentafulvene)' was fitting to the formula  $\text{C}_8\text{H}_{9.2}\text{I}_{0.66}$  and showed that a substantial amount of  $\text{I}_2$  had been incorporated. So far, conductivity measurements failed, because it was not possible to prepare adequate sample pellets. The UV spectrum (Fig. 3, right) of the polymer is very surprising insofar that the polymer has approximately the same absorption throughout the whole range from 200 to 800 nm, the absorption range obviously extending far beyond 800 nm. A more detailed investigation of 'iodine-treated poly-DMF' is in progress.

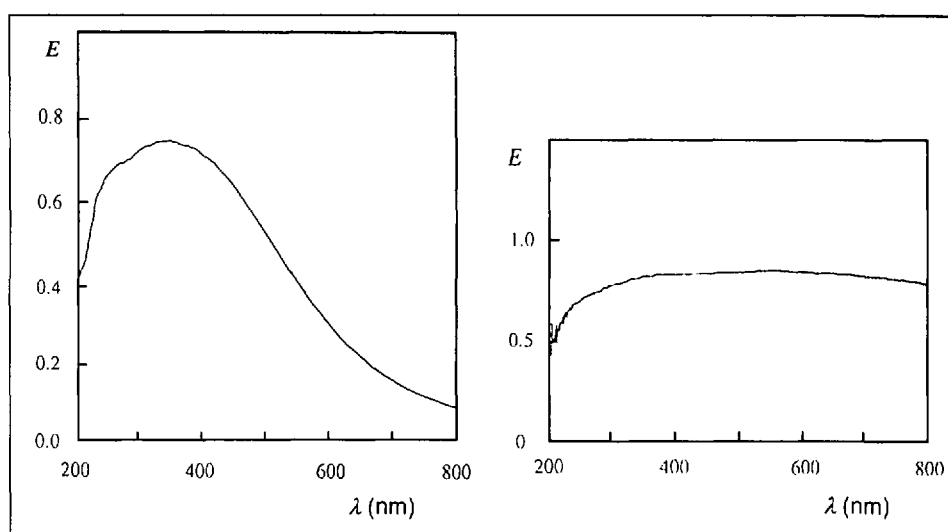
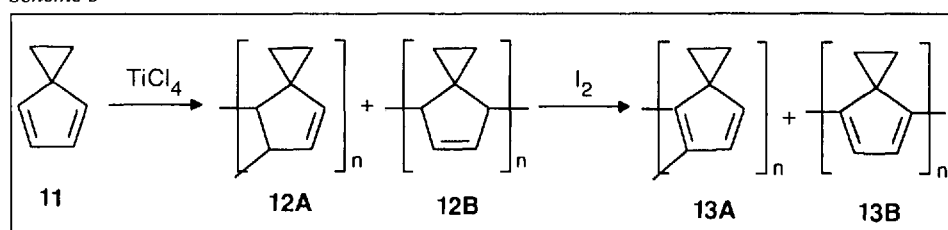


Fig. 3. UV Spectra of polymer samples containing structure elements of the type **3a**. Left: Product after treatment of polymer **10a** with an excess of  $\text{Et}_3\text{N}$  in boiling  $\text{CH}_2\text{Cl}_2$ . Right: Product after treatment of polymer **10a** with  $\text{I}_2$  in  $\text{CCl}_4$ .

#### Scheme 5



#### Experimental Part [13]

All the reactions were run under Ar. Prior to the introduction of the reagents, the reaction vessel was thoroughly flame-dried while being flushed with Ar.

**Bromination of Cationic Poly(6,6-dimethylpentafulvene) (**2a**)  $\rightarrow$  **10a**.** A 100-ml two-necked flask equipped with septum, Ar-bubbler and magnetic stirrer was flame-dried and flushed with Ar. The flask was charged with 852 mg (8.0 mmol per monomer unit) of **2a** [6] in 30 ml of  $\text{CCl}_4$ . After dissolving the polymer, a soln. of 1286 mg (8.0 mmol) of  $\text{Br}_2$  in 4 ml of  $\text{CCl}_4$  was dropwise added at r.t. by means of a syringe. During the addition the color of  $\text{Br}_2$  disappeared, and the polymer began to precipitate towards the end of the addition. The white precipitate was filtered (through a funnel) under Ar and purified by washing it 3 times with  $\text{CCl}_4$ , twice with  $\text{Et}_2\text{O}$ , and 3 times with pentane. The combined  $\text{CCl}_4$  filtrates were dropwise added to 150 ml of pentane under Ar, and the white precipitate was filtered and washed twice with  $\text{Et}_2\text{O}$  and 3 times with pentane. The combined precipitates were dried under vacuum ( $10^{-3}$  Torr) at  $-20^\circ$  to give 1870 mg (87.5%) of a white powder of polymer **10a**. Anal. calc. for  $(\text{C}_8\text{H}_{10}\text{Br}_2)_n$  ( $(256.95)_n$ ): C 36.28, H 3.87, Br 60.50; found C 36.13, H 3.79, Br 60.08. GPC Measurements:  $M_n = 71324$ ,  $M_w = 369504$ ,  $M_w/M_n = 5.18$ .

**Treatment of Polymer **2a** with  $\text{I}_2$ .** A 100-ml two-necked flask equipped with dropping funnel, reflux condenser,  $\text{N}_2$ -bubbler and magnetic stirrer was flame-dried and flushed with Ar. The flask was charged with 262 mg **2a** (2.6 mmol per monomer unit) in 10 ml of  $\text{CCl}_4$ . After the polymer had dissolved, a soln. of 658 mg (2.6 mmol)

of  $\text{I}_2$  in 30 ml of  $\text{CCl}_4$  was dropwise added under stirring at r.t. A violet-black precipitate was formed within min. After the addition was complete, the mixture boiled under reflux for 24 h, cooled and the precipitate was filtered through a funnel under Ar. The precipitate was washed 3 times with 5 ml of  $\text{CCl}_4$ , then several times with  $\text{CH}_2\text{Cl}_2$  in order to remove traces of  $\text{I}_2$ . After drying under high vacuum ( $10^{-3}$  Torr), 253 mg of a black powder were isolated. Anal. calc. for  $(\text{C}_8\text{H}_8)_n$  ( $(104.144)_n$ ): C 92.26, H 7.74; found C 50.36, H 4.88, I 43.73 [15].

Received: July 29, 1994

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- [13] For detailed experimental procedures, analytical and spectroscopic data as well as for reproductions of spectra see [14]. Procedures of the reactions **1b** → **7b** and **6** → **8** → **9** as well as spectroscopic data will be published in a full paper.
- [14] G. Zhang, Ph. D. thesis, University of Bern, 1993.
- [15] Corresponding to the average formula  $C_8H_{9,2}I_{0,66}$ .

*Chimia* 48 (1994) 564–569  
© Neue Schweizerische Chemische Gesellschaft  
ISSN 0009-4293

## Isolierung, HPLC-Trennung und Quantifizierung der Sesquiterpenfraktion von *Petasites hybridus* (L.) G. M. et SCH. [1]

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**Abstract.** A simple and easily reproducible HPLC procedure allows to separate total extracts of *Petasites hybridus* (L.) G. M. et SCH. and to detect numerous sesquiterpenes (in most cases sesquiterpene esters) of the general formula **1** (isopetasols), **2** (neopetasols), **3** (petasols), **4** (13-substituted isopetasols), and **5** (13-substituted neopetasols). Four so far unknown sesquiterpene esters **2f** (neo-S-petasin), **2g** ((*E*)-3-(methylthio)acryloyl-neopetasol), **3g** ((*E*)-3-(methylthio)acryloyl-petasol), and **5b** (3-desoxy-13-(angeloyloxy)-neopetasol) have been isolated and the contents of the pharmacologically most interesting compounds isopetasin (**1b**), neopetasin (**2b**), and petasin (**3b**), have been quantitatively determined. Additionally two of the basic alcohols petasol and isopetasol have been detected for the first time in small amounts in roots of *P. hybridus*.

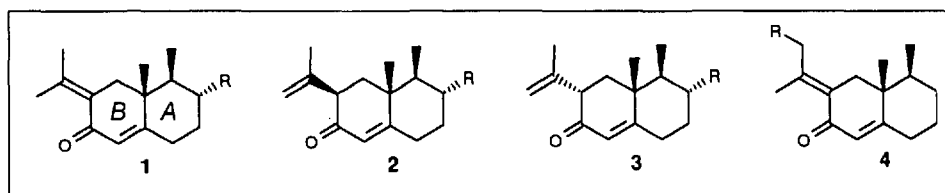
### 1. Einleitung

*Petasites hybridus* (L.) G. M. et SCH. (Familie: Compositae) ist eine ausdauernde, häufig in dichten Beständen auftretende Pflanze mit kräftigem Wurzelstock und meterlangen Ausläufern. Sie stellt in Europa die am weitesten verbreitete Art der Gattung *Petasites* MILLER dar und wächst im Flachland und seltener im Gebirge auf sickernassen, zeitweise überfluteten, nährstoffreichen, tonigen Böden an Bach- und Flussufern. Bereits im 1. Jahrhundert n. Chr. wurde die gemeine Pestwurz von

*Pedanius Dioskurides*, dem Legionärsarzt unter *Claudius* und *Nero*, in seinem Werk 'De materia medica', welches bis ins 17. Jh. als unumstössliche Grundlage der Arzneimittellehre und Botanik galt, als Heilpflanze erwähnt. Der pharmakologische Nachweis der antispastischen Wirkung [3] erfolgte mit einem methanolischen Rohextrakt aus frisch gegrabenen *P. hybridus*-Wurzeln am isolierten Meerschweinchendarm. Daraus ergaben sich die neuzeitlichen Anwendungsgebiete, welche sowohl die spasmolytische Wirkung als auch eine analgetische Wirkung des Pflanzenextrak-

tes mit einem spezifischen Effekt im Sinne eines Tranquilizers ausnutzen. Heute werden die Pflanzendroge und ihre Zubereitungen zunehmend als 'Spasmo-Analgetikum mit beruhigender und vegetativ regulierender Wirkung' eingesetzt. Die biologische Aktivität von Inhaltsstoffen aus volksmedizinisch verwendeten Pflanzen ist ein wichtiges Bindeglied zwischen Chemie und Medizin, und die Suche nach aktiven Verbindungen ist auch heutzutage aktuell. So zeigen neueste Untersuchungen zur Antitumor-Wirkung des *P. hybridus*-Gesamtextraktes eine *in vitro* antiproliferative Wirkung für humane T24-Blasenkarzinom-Zellen bei einer Verdünnung von 1:200 000 ( $\cong$  5 µg/ml). Die  $IC_{50}$ -Werte ( $\cong$  50% Wachstumshemmung) der Petasin- bzw. S-Petasin-Zone lagen bei 0,17 resp. 0,12 µg/ml [4]. Bekannte als Antitumor-Mittel in Frage kommende Substanzen weisen ähnliche Werte auf.

Bei den ersten phytochemischen Untersuchungen [5–9] konnten vier Verbindungen (Isopetasin (**1b**), Iso-S-petasin (**1f**), Petasin (**3b**), S-Petasin (**3f**)) des Eremophilantyps isoliert und in ihrer Struktur bis auf sterische Details aufgeklärt werden. Als aktivstes und genuines antispastisches Prinzip von *P. hybridus* wurde Petasin (**3b**) erkannt. Später gelang es [10][11], 16 Sesquiterpen-Inhaltsstoffe zu isolieren und in ihrer Struktur aufzuklären, die sich in drei Hauptgruppen einteilen lassen: Isopetasol- (**1**), Neopetasol- (**2**) und Petasol-Gruppe (**3**), welche sich voneinander durch Isomerie im Ring *B* des Decalin-Gerüsts unterscheiden. Ring *B* liegt bei der Petasol- und Isopetasol-Gruppe als Sessel, im Falle der Neopetasol-Gruppe dagegen als Wanne vor. Ring *A* nimmt überall die Sessel-Form ein. Von einer vierten Gruppe konnte nur ein Vertreter gefunden wer-



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