Theses of doctoral (PhD) dissertation

Synthesis of potentially biologically active pterocarpan derivatives

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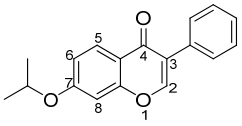
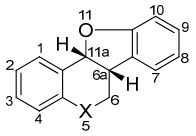
1. Introduction and objectives

Flavonoids are one of the largest and the most important group of naturally occurring *O*-heterocycles. According to the more general terminology, *O*-heterocyclic natural products possessing a diphenylpropane skeleton (C_6-C_3-C_6) and their related open chain derivatives are considered to belong to this family of organic compounds. In the past few decades, numerous and diverse pharmacological investigations were carried out which confirmed that flavonoids possess antibacterial, antiviral, antifungal, antiinflammatory, diuretic, anti-tumor and antiosteoporotic activity above their well-known antioxidant activity.

The aim of my dissertation was to synthetise 7-isopropyloxyisoflavone [Ipriflavone (**1a**)]'s analogues, such as pterocarpan (**1b**) and its related derivatives (**1c**,**d**) of potential antiosteoporotic activity in racemic and optically pure form and to study their stereochemistry.



Ipriflavone, or
7-isopropyloxyisoflavone (**1a**)



Pterocarpan (**1b–d**)
X= O, CH_2, N-R

As a continuation of our efforts on their enantioselective synthesis, the aim of my research was also to study of oxidative transformation of enol methyl ether and enol acetate of racemic flavanone [(±)-**189**, **205**] with thallium(III) nitrate (TTN), lead(IV) tetraacetate (LTA) and hypervalent phenyliodines (PIDA and HTIB) as well.

2. Applied methods

The macro-, semi-micro, and micro-methods of the modern preparative organic chemistry were used in the synthetic work. The purity of the

substances, the ratio of products were controlled and the reactions were monitored by thin-layer chromatography. Purification of the crude products and separation of the isomers were carried out either by crystallization, or by column chromatography. The characterisation and the structural elucidation of the compounds were obtained by determination of their melting point, one and two-dimensional (^{1}H-^{1}H-COSY, ^{13}C-^{1}H-HSQC, HMBC, NOESY) NMR spectroscopy, and MALDI/ESI-TOF mass spectrometry and by analytical RP-HPLC methods.

3. New scientific results of the dissertation

3.1. Synthesis of pterocarpan derivatives of potential antiosteoporotic activity

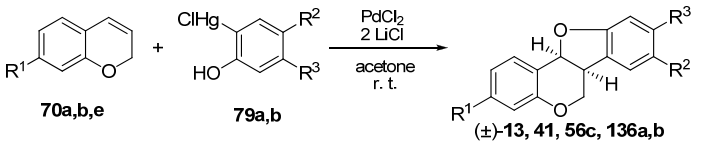
In order to study the antiosteoporotic activity of pterocarpans, the synthesis of a series of this type of compounds were achieved from appropriately substituted 2*H*-chromenes by Heck-type oxyarylation as well as from racemic 3-hydroxy-9-methoxy pterocarpan [(±)-**136c]** prepared from 7,2'-dihydroxy-4'-methoxyisoflavone (**140**) by the reduction of sodium tetrahydroborate followed, by a ring closure performed under acidic conditions at room temperature.

3.1.1. Synthesis of racemic pterocarpan [(±)-**13**], pterocarpin [(±)-**41**], 3-methoxypterocarpan [(±)-**56c**], 3-isopropyloxypterocarpan [(±)-**136a**] and 3-isopropyloxy-8,9-methylendioxypterocarpan [(±)-**136b**].

The Heck-oxyarylation of 2*H*-chromenes (**70a,b,e**) with *ortho*-mercuryphenol derivatives (**79a,b**) were prepared as described by Inoue *et al.* and the crude products have been purificated by column chromatography to give the corresponding racemic pterocarpan derivatives [(±)-**13**, **41**, **56c**,

136a, **136b**] in low and moderate yield (Scheme 1).

It should be noted that in good agreement with our previously results, the arylation of 2*H*-chromenes (**70a**,**b**,**e**) took place in a non-regioselective manner resulting in the bridged *O*-heterocycles [(±)-**137a-e**] due to cationic mechanism of this transformation besides racemic pterocarpan derivatives [(±)-**13**, **41**, **56c**, **136a**, **136b**].



	R^1	R^2	R^3	Yield (%)
13	H	H	H	32
136a	OiPr	H	H	53
56c	OMe	H	H	31
41	OMe	O-CH_2-O		17
136b	OiPr	O-CH_2-O		38

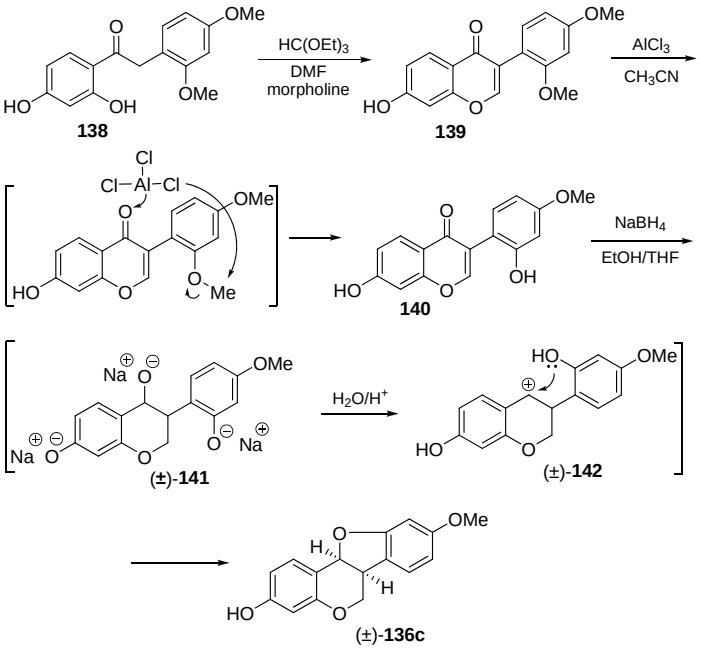
Scheme 1.: Synthesis of (±)-**13**, **41**, **56c**, **136a,b** pterocarpan derivatives.

3.1.2. Synthesis of racemic 3-hydroxy-9-methoxypterocarpan [(±)-**136c**], 3-isopropyloxy-9-methoxypterocarpan [(±)-**136d**], 3-ethoxy-9-methoxypterocarpan [(±)-**136e**] and 3-propyloxy-9-methoxypterocarpan [(±)-**136f**].

The synthesis of racemic 3-hydroxy-9-methoxypterocarpan [(±)-**136c]** has been carried out from 2,4-dihydroxyphenyl-2,4-dimethoxybenzyl-ketone (**138**) *via* 7-hydroxy-2',4'-dimethoxyisoflavone (**139)** in four steps (Scheme 2).

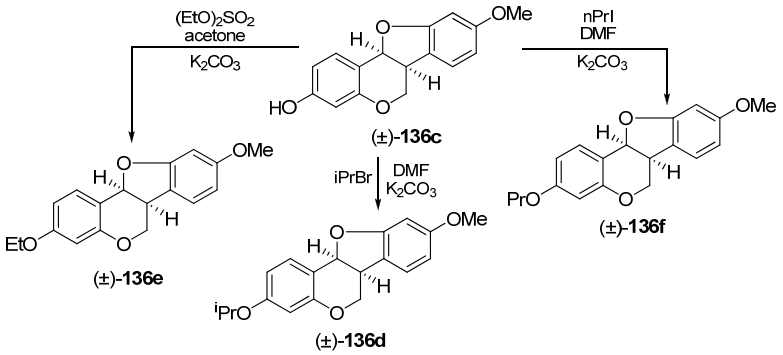
The critical step of this synthesis has been found to be the selective cleavage of 2'-methoxy group of isoflavone **139** with aluminum trichloride **(139→140**). Its success was strongly depended on the complexation of the reagent at the carbonyl group, which could be affected by the carefully

dried acetonitrile used as solvent in this reaction. In the next step, the reduction of **140** was performed by sodium-tetrahydroborate in the mixture of THF and EtOH at room temperature to result in the sodium salt of isoflavan-4-ol [(±)-**141**], which after removal of EtOH, was followed by its treatment with hydrochloric acid giving rise racemic 3-hydroxy-9-methoxypterocarpan [(±)-**136c**] in good yield.



Scheme 2.: Synthesis of (±)-**136c** pterocarpan derivative.

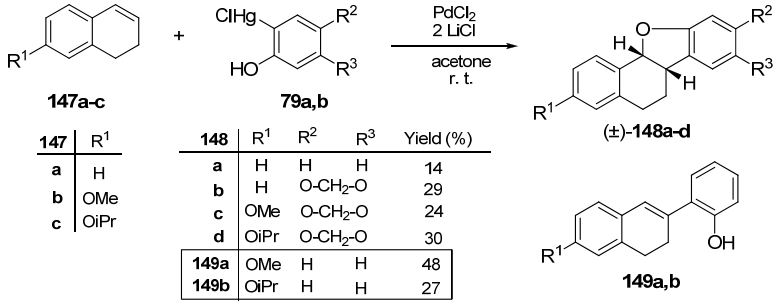
For the study of structure-oestrogen activity relationship of pterocarpans, the isopropyl-, ethyl- and n-propyl derivatives (±)-**136d-f** have been also prepared.



Scheme 3.: Synthesis of (±)-**136d-f** pterocarpan derivatives.

3.1.3. Synthesis of 5-carba- [(±)-**148a-d**] and -azapterocarpans [(±)-**159a**,**b**].

Based on the examples published in the literature of medicinal chemistry, it is well-known that the similarity of the pterocarpans to the natural ligands of estrogen receptors can be increased by the replacement of their oxygen atom at position 5 with a methylene group. Therefore, (±)-**148a-d** 5-carbapterocarpans were also prepared from the appropriately substituted 1,2-dihydronaphthalene (**147a-c**) and *ortho*-mercuryphenol derivatives (**79a,b**) using Heck-oxyarylation reaction, respectively.



147	R^1
a	H
b	OMe
c	OiPr

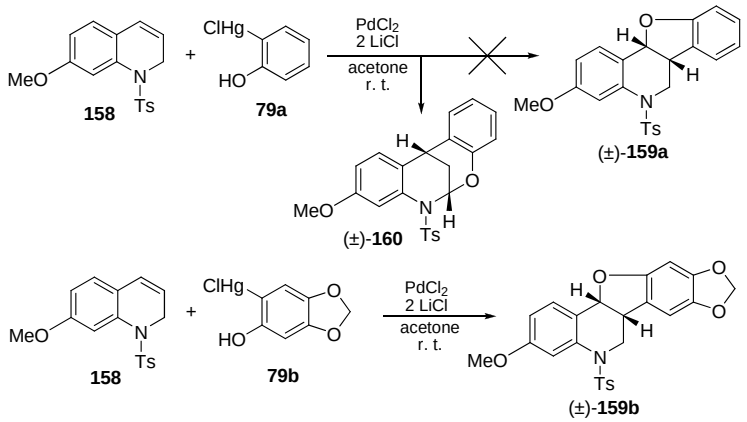
148	R^1	R^2	R^3	Yield (%)
a	H	H	H	14
b	H	O-CH_2-O		29
c	OMe	O-CH_2-O		24
d	OiPr	O-CH_2-O		30
149a	OMe	H	H	48
149b	OiPr	H	H	27

Scheme 4.: Synthesis of (±)-**148a-d** carba derivatives.

Interestingly, in the course of this reaction not only the ring closure leading to *rac*-**148a-d** and *rac*-**149a**,**b** took place, but in case of the **147b**,**c**

1,2-dihydronaphthalene derivatives, a β elimination (**147b,c**+**79a**→**149a,b**) could be also observed. Moreover, the fomation of the so-called *O*-bridged compounds (e.g **137a**, where O-5= CH_2) could not be detected at all. These facts have also clearly indicated, that the Heck-oxyarylation of **147b**,**c** naphtalene derivatives took place regioselectively with a cationic mechanism.

For the synthesis of 6-aza analogues [(±)-**159a,b**], the corresponding protected 1,2-dihydroquinoline derivative (**158**) has been prepared starting from *m*-anisidine and methyl-acrylate in 7 steps. Surprisingly, its coupling with *ortho*-mercuryphenol (**79a**) under the conditions of Heck-oxyarylation did not lead to the *rac*-**159a** aza-pterocarpan derivative but only the formation of the *O*-bridged compound [(±)-**160**] could be observed in 26% yield.

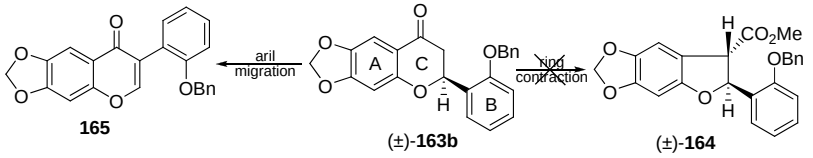


Scheme 5.: Synthesis of (±)-**159a,b** aza derivatives.

In the case of the **79b** mercuryphenol, only the formation of (±)-**159b** azapterocarpan derivative could be detected in low yield (20%).

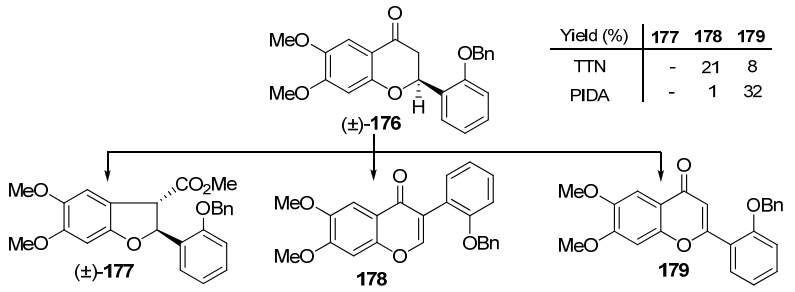
3.1.4. Attemps for enantioselective synthesis of pterocarpans.

In order to have a clear correlation between the structure and antiosteoporotic activity of pterocarpans discussed above, their synthesis in optically pure form has been also carried out. It seems to be quite obvious that they can be obtained from the corresponding substituted (+)-(2*R*)- or (2*S*)-2'-benzyloxyflavanone derivatives using the method recently developed by our research group. In the course of the synthesis of (+)-(6a*S*,11a*S*)-maackiain (**14c**) isolated from *Maackia amurensis*, and its 3-deoxy derivatives (**14a**), the oxidation of the racemic 2'-benzyloxy-6,7-methylenedioxyflavanone [(±)-**163b**] was performed with thallium(III) nitrate (TTN) or phenyl iodosonium diacetate (PIDA) under the conditions reported by Kapoor *et al.* and Prakash and Tanwar, respectively. Surprisingly, the reaction had an unexpected outcome and the predicted ring contraction [(±)-**163b**→(±)-**164**] did not occur, although it was believed that the electron-donatingmethylenedioxy group attached to C-6 and C-7 increased the migratory aptitude of this aryl group. Instead of the *trans*-2,3-dihydrobenzo[b]furan ester [(±)-**164**], the 2'-benzyloxy-6,7-methylenedioxy-isoflavone (**165**) could be isolated by repeated column chromatography in crystalline form with 47% yield as a sole product.



Scheme 6.: Transformation of (±)-**163b** flavanone derivative.

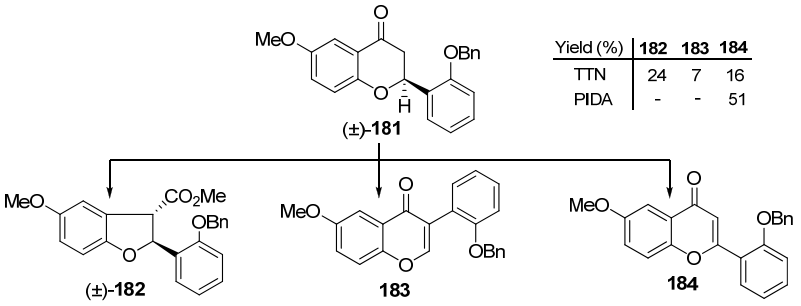
In order to get information about the reason of this unusual transformation the racemic 2'-benzyloxy-6,7-dimethoxyflavanone [(±)-**176**] and 6-methoxy-2'-benzyloxyflavanone [(±)-**181**] have been prepared and examined how these compounds will be reacted with TTN or PIDA.



Scheme 7.: Transformation of (±)-**176** flavanone derivative.

Similarly to 2'-benzyloxy-6,7-methylenedioxyflavanone [(±)-**163b**], the transformation of its 6,7-dimethoxy analogue [(±)-**176**] did not result in the ring-contracted product [(±)-**177**] either by TTN or by PIDA, but the corresponding isoflavone (**178**) and flavone (**179**) derivatives were formed in 21/1- and 1/32% yield, respectively.

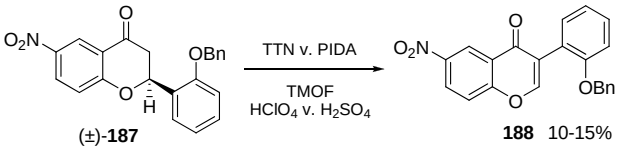
Moreover, the oxidation of 2'-benzyloxy-6-methoxy-flavanone [(±)-**181**], with TTN resulted in (±)-**182** *trans*-2,3-dihydrobenzo[b]furan ester as a major product besides the **183** isoflavone and **184** flavone derivatives. In the case of PIDA, only **184** flavone derivative could be isolated in 51% yield.



Scheme 8.: Transformation of (±)-**181** flavanone derivative.

Oxidation of 2'-benzyloxy-6-nitroflavanone [(±)-**187**] with TTN or PIDA resulted in 2'-benzyloxy-6-nitroisoflavone (**188**) in low yield (10-

15%).



(±)-**187** **188** 10-15%

Scheme 9.: Transformation of (±)-**187** flavanone derivative.

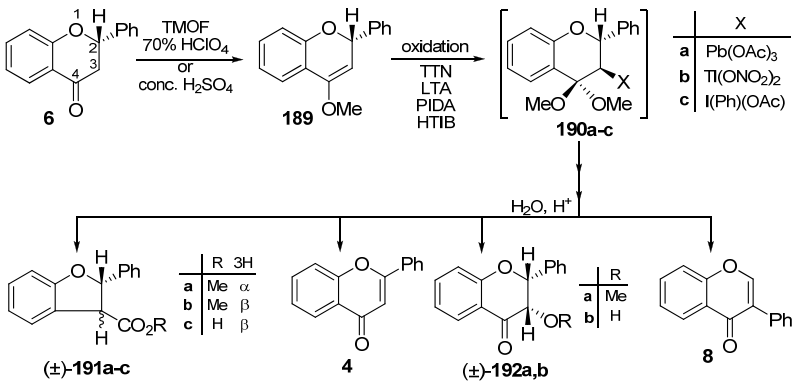
These results have clearly indicated that the pruduct's profile of the transformation of 2'-benzyloxyflavanones by TTN or PIDA was strongly dependent on their substitution of ring A and therefore this method was not suitable for the synthesis of naturally occurring pterocarpans possessing hydroxy, methoxy, or methlyenedioxy group at C-8 or/and C-9.

In order to have further insight into this process and reveal the reasons of these surprising results, we examined the so-called „basic reaction" – the ring-contraction of enol ether of racemic flavanone [(±)-**189**] – to racemic methyl 2-phenyl-2,3-dihydrobenzo[b]furan-3-carboxylate [(±)-**191a**] by TTN monitored by HPLC. Thus, our research group have recently shown that this transformation took place stereoselectively resulting in the *trans*-[(±)-**191a**] and thus the carbonium ion **204** did not play a role as an intermediate of this procces.

3.2. Reinvestigation of the ring-contraction of flavanone [(±)-6]

3.2.1. Ring-contraction of enol methyl ether of racemic flavanone [(±)-**189**]

The transformation of racemic flavanone [(±)-**6**] has been perfomed with 1.1 mol equivalent TTN in TMOF in the presence of catalytic amount of 70% perchloric acid at room temperature monitored by HPLC. It has been clearly indicated that the conversion of (±)-**6** reached 98% in 30 minutes to result in a complex mixture.



Scheme 10.: Ring contraction of (±)-**6** flavanone.

Many components of this mixture could be nearly base-line separated and besides *rac*-flavanone [(±)-**6**, (2%)], *rac*-methyl 2,3-dihydro-2-phenylbenzo[b]furan-3-carboxylate [(±)-**191a** (76%)], flavone [**4** (3%)] and isoflavone [**8** (9%)] could be identified unequivocally by comparison with authentic samples (entry 1 in Table 1).

Entry	Reag.	Proced.	**6** *(7.26)*	**191a** *(7.90)*	**191b** *(7.20)*	**4** *(6.30)*	**192a** *(8.47)*	**192b** *(7.03)*	**8** *(6.70)*	**197** *(8.95)*	**202** *(8.14)*
1	TTN	A	2	76	-	3	<1	1	9	3	<1
2	TTN	B	15	40	-	28	-	1	2	9	<1
3	TTN	C	<1	45	-	3	3	<1	3	3	-
4	LTA	D	1	33	-	11	1	18	23	1	-
5	PIDA	E	4	66	-	10	<1	-	2	2	-
6	HTIB	E	3	49	-	6	2	-	1	5	-

Procedure A: TMOF/70% $HClO_4$/r. t./5 min TTN

Procedure B: TMOF/70% $HClO_4$/-10°C/5 min TTN

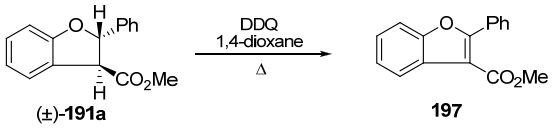
Procedure C: TMOF/70% $HClO_4$/r. t./30 min TTN

Procedure D: TMOF/conc. H_2SO_4/r. t./5 min LTA

Procedure E: TMOF/conc. H_2SO_4/r. t./5 min HTIB

Table 1.: Yields and retention times of the compounds of the transformation of flavanone [(±)-**6**].

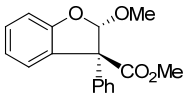
Moreover, the compound with t_R= 8,95 min could be also isolated by preparative TLC and it has been identified as methyl 2-phenylbenzo[b]furan-3-carboxylate (**197**) by its NMR and MS data. Its structure was also confirmed by chemical correlation with 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (DDQ) starting from (±)-**191a** derivative.



(±)-**191a** **197**

Scheme 11.: Synthesis of **197** derivative with DDQ.

In the reaction of (±)-**6** carried out at -10ºC, the transformation to the **189** enol ether took place slower as expected. The conversion of (±)-**6** reached only to 85% in 30 minutes, and a considerable change in the products's profile could be observed (entry 2 in Table 1). Moreover, the by-product at t_R= 8.14 min could be also isolated by preparative TLC. Its structure has been established by NMR and MS evidences as the methyl 2,3-dihydro-2-methoxy-3-phenylbenzo[b]furan-3-carboxylate with (2*S**,3*S**) relative configuration [(±)-**202**].

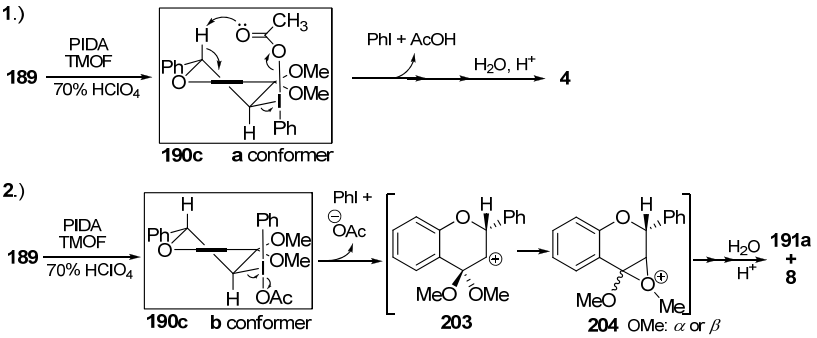


(±)-**202**

The HPLC monitoring of the transformation of racemic flavanone by LTA was also carried out. The conversion reached to 99% in 2 hours and the formation of (±)-**191a** (33%), **4** (11%), **192a** (1%), **192b** (18%), **8** (23%) és **197** (1%) could be detected. (entry 4 in Table 1). In contrast to the observation of Khanne, the formation of *cis*-(±)-**191b** could not be observed by at all.

The transformation of (±)-**6** flavanone by PIDA or HTIB in TMOF and

catalytic sulfuric acid was also studied at room temperature. Their HPLC monitoring has clearly shown that the transformations took place significantly slower in both cases than with TTN and their product's profiles were similar but significantly different from that obtained by TTN. The ring contraction of (±)-**6** by PIDA led to *trans*-(±)-**191a** (66%) as the main product and instead of the formation of isoflavone (**8**), the formation of flavone (**4**) was favoured as side-product (entry 5 in Table 1). This fact could be explained by quantum chemical calculations, which gave important informations about the structure of the (±)-**190c** intermedier (**190c/a** és **190c/b**).



Scheme 12.: Structure and reactivity of phenyliodosonium(III) intermediers [(±)-**190c/a** and **b**].

As shown in the Scheme 12. the flavone (**4**) was formed from the thermodinamically more stable phenyliodosonium(III)-intermedier [(±)-**190c/a**] and at the same time **190c/b**-one might be transformed *via* **204** carbonium or **204** epoxonium ion into *trans*-(±)-**191a** ester and isoflavone (**8**). Thus the HPLC monitoring of the transformation of *rac*-flavanone [(±)-**6**] has clearly shown that only the *trans*-(±)-**191a** ester was present in its crude product, the formation of the *cis*-one [(±)-**191b**] in traces could not be detected, therefore the heterolytic cleavage of C-3 and iodosonium(III) bond of (±)-**190c/a** or (±)-**190c/b** resulting in **203** carbonium ion could be

disclosed with certainly. Instead of this carbonium ion the **204** epoxonium ion was formed by a S_N2-type process, which has indicated the neigbouring group participation of C-4 methoxy group must play a determining role in this transformation.

3.2.2. Ring-contraction of enol acetate of racemic flavanone [(±)-**205**]

In order to examine of the role of neighbouring group participation in the ring-contraction, the transformation of enol acetate of racemic flavanone [(±)-**205**] prepared from (±)-**6** according to the literature was reacted with 1,1 mol equivalent TTN in TMOF in the presence of catalytic amount of 70% perchloric acid at room temperature. The HPLC monitoring of this reaction has clearly indicated that the conversion of (±)-**205** reached 99% in 30 minutes to result in a mixture of products shown in **Table 2** (entry 1).

All components of this mixture could be nearly base-line separated and besides *rac*-flavanone [(±)-**6** (1 %)], its enol-acetate [(±)-**205** (1 %)], isoflavone [**8** (78 %)], flavone [**4** (13 %)] could be identified. Surprisingly *rac*-methyl 2,3-dihydro-2-phenylbenzo[b]furan-3-carboxylate [(±)-**191a**], *cis-3*-methoxyflavanone (**192**), phenylbenzo[b]furan derivatives **197** and **202** did not formed at all. (entry 1 in Table 2).

Entry	Reag.	Proced.	**6** *(7.20)*	**4** *(6.10)*	**8** *(6.65)*	**205** *(7.76)*
1	TTN	A	2	18	77	1
2	PIDA	B	7	13	78	-
3	PIDA	C	4	65	1	15

Procedure A: TMOF/70%-os $HClO_4$/r. t./5 min TTN

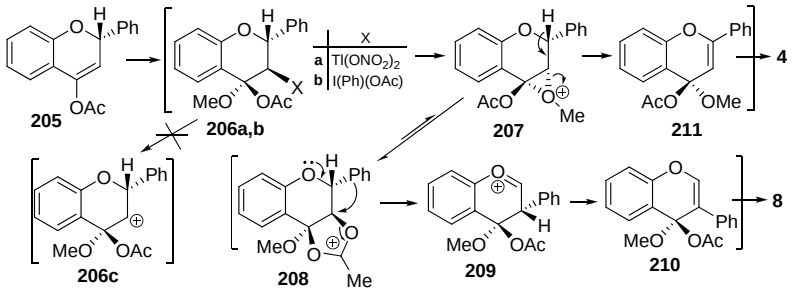
Procedure B: TMOF/conc. H_2SO_4/r. t./5 min PIDA

Procedure C: Glacial acetic acid/5 min PIDA

Table 2.: Yields and retention times of the compounds of the transformation of enol acetate [(±)-**205**].

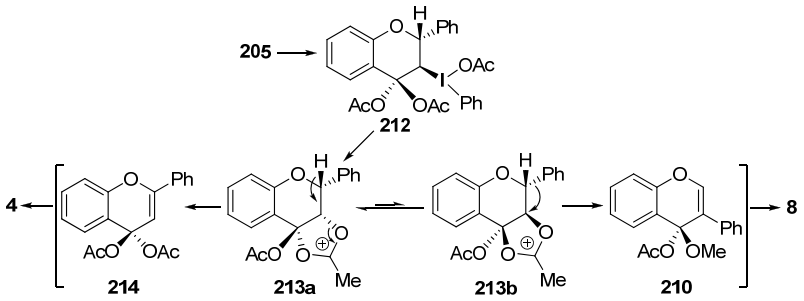
Very similar product's profile could be observed when PIDA was used as oxidizing agent. Besides racemic flavanon [(±)-**6**] and flavone (**4**), isoflavone (**8**) could be detected as a main product (entry 2 in Table 2).

These results have very clearly indicated that the substitution of the methyl group of (±)-**189** with the acetyl one has prevented the ring-contraction (±)-**205** to (±)-**191a**, but the formation of isoflavone (**8**) was strongly preferred in both cases. This observation could be explained by the neighboring group participation of acetoxy and methoxy groups at C-4 of (±)-**206a,b** intermediers formed from (±)-**205** by TTN or PIDA, as depicted in Scheme 13.



Scheme 13.: The transformation of (±)-**205** enol acetate in TMOF by PIDA.

The HPLC monitoring of the transformation of (±)-**205** by PIDA in glacial acetic acid at room temperature gives also some interesting information about the feature of this reaction. The conversion of (±)-**205** reached 85 % in 2 hours and the flavone (**4**) as a main product was obtained in 65% yield, besides traces of isoflavone [**8** (1%)], flavanone [(±)-**6** (4%)] and enol acetate [(±)-**205** (15%)] shown in Table 2 and in Scheme 14.



Scheme 14.: The transformation of (±)-**205** enol acetate in glacial acetic acid by PIDA.

In the absence of methanol, the triacetoxy-phenyliodosonium intermediate (**212**) formed in the course of the stereo-controlled addition of the electrophilic reagent (PIDA) to (±)-**205**. In the next step, its transformation by the neighboring participation of its acetoxy group of *α* configuration in S_N2-type manner gave **213a** 1,3-dioxolanium ion in equilibium **213b**. The deprotonation of **213a** resulted in 4,4-diacetoxy-4*H*-flavene (**214**) whose hydrolysis afforded flavone (**4**) as a main product (65%) during the workup of reaction mixture. Although this equilibrium of **213a-213b** is strongly shifted towards **213a** the small amount of isoflavone (**7**) could be also formed by 2→3 phenyl migration followed by a deprotonation and hydrolysis (**213b→210→8**). This has been observed experimentally indeed (entry 3 in Table 2).

It is noteworthy that the transformation of flavanone enol acetate (**205**) by TTN or PIDA in TMOF in the presence of catalytic amount of 70% perchloric acid has revealed a convenient and new approach to the synthesis of isoflavone (**8**). While the transformation of **205** by PIDA in glacial acetic acid has discovered a new simple route to flavone (**4**).

4. Publikációk jegyzéke/List of Publications

4.1. Az értekezés alapjául szolgáló közlemények

1. **Németh, I.**; Gulácsi, K.; Antus, S.; Kéki, S.; Zsuga, M.; "New Insight into the Ring Contraction of 2'-Benzyloxyflavanones", *Nat. Prod. Commun.*, **2007**, *1*(11), 991-996.
2. Gulácsi, K.; **Németh, I.**; Szappanos, Á.; Csillag, K.; Illyés, T.Z.; Kurtán, T.; Antus, S.; "Heck-oxyarylation of 2-phenyl-2*H*-chromenes and 1,2-dihydronaphthalenes", *Croat. Chem. Acta*, **2012**, *85(0)*, 000-000, ISSN 0011-1643
3. **Németh, I.**; Kiss-Szikszai, A.; Illyés, T.Z.; Mándi, A.; Komáromi, I.; Kurtán, T.; Antus, S.; "Oxidative Rearrangement of Flavanones with Thallium(III) nitrate, Lead Tetraacetate and Hypervalent Iodines in Trimethylortoformate and Perchloric or Sulfuric Acid", *Z. Naturforsch.*, **2012**, *67b*, 1-8.
4. **Németh, I.**; Kiss-Szikszai, A.; Mándi, A.; Komáromi, I.; Kurtán, T.; Antus, S.; "Oxidation of Enol-acetate of Flavanone with Thallium(III) nitrate or Phenyliodosonium Diacetate: Convenient Routes to Isoflavone or Flavone", (beküldve)

4.2. Konferencia előadások a dolgozat témájában

1. **Németh István**, Antus Sándor, Gulácsi Katalin, Kéki Sándor, Zsuga Miklós: Észrevételek a 2'-benziloxiflavanonok gyűrűszűkítési átalakításáról, Flavonoid Munkabizottsági Ülés, 2006. december 1, Budapest
2. **Németh István**, Antus Sándor, Gulácsi Katalin: 2'-Benziloxiflaanonok gyűrűszűkítési átalakításának vizsgálata, Flavonoid Munkabizottsági Ülés, 2008. okt. 20, Debrecen

3. **I. Németh**, K. Gulácsi, S. Antus: Investigation of Ring-Contraction of 2'-Benzyloxyflavanones, Third German-Hungarian Workshop, May 14-18, 2008, Paderborn
4. **Németh István**, Gulácsi Katalin, Antus Sándor: 2'-Benziloxiflavanonok gyűrűszűkítési átalakításának vizsgálata, Kisfaludy Előadóülés, 2009. március 9, Budapest
5. **Németh István**, Gulácsi Katalin, Antus Sándor: 2'-Benziloxiflavanonok gyűrűszűkítési átalakításának vizsgálata, Heterociklusos Munkabizottsági Ülés, 2009. május 20-22, Balatonszemes.
6. **Németh István**, Gulácsi Katalin, Antus Sándor: 2'-Benziloxiflavanonok gyűrűszűkítési átalakításának vizsgálata, Flavanoid Munkabizottsági Ülés, 2009. december 7, Budapest.
7. Mándi A., Komáromi I., **Németh I.**, Kiss-Szikszai A., Kurtán T., Antus S.: Flavanon származékok PIDA-val végrehajtott gyűrűszűkülési reakcióinak tanulmányozása elméleti módszerekkel, KeMoMo-QSAR konferencia, 2010, Szeged
8. **I. Németh**, T. Kurtán, S. Antus: Synthesis of potentially bioactive pterocarpan derivatives, Fourth German-Hungarian Workshop, June 14-16, 2011, Debrecen
9. **Németh István**, Szabados Nikolett, Papp Tamás, Kurtán Tibor, Antus Sándor: Potenciálisan biológiailag aktív pterokarpán származékok előállítása, Heterociklusos Kémiai Munkabizottsági Ülés, 2011. szeptember 26-28, Balatonszemes
10. **Németh István**, Kurtán Tibor, Antus Sándor: Potenciálisan biológiailag aktív pterokarpánok előállítása, MTA Alkaloid- és Flavonoidkémiai Munkabizottsági Ülés, 2012. május 14-15, Balatonalmádi

4.3. Konferencia poszterek az értekezés témájában

1. **I. Németh**, K. Gulácsi, S. Antus: A New into the Synthesis of Pterocarpans, Second German- Hungarian Workshop, April 4-9, 2006, Debrecen
2. **I. Németh**, K. Gulácsi, S. Antus: Investigation of Ring-Contraction of 2'-Benzyloxyflavanones, Third German-Hungarian Workshop, May 14-18, 2008, Paderborn
3. **Németh István**, Antus Sándor: 2'-Benziloxiflavanonok gyűrűszűkítési reakciójának tanulmányozása, Országos Vegyészkonferencia, 2008. jún. 19-21, Hajdúszoboszló
4. **Németh István**, Kiss Attila, Mándi Attila, Antus Sándor: Flavanon gyűrűszűkülési reakciójának felülvizsgálata, Országos Vegyészkonferencia, 2010. jún. 30- júl. 2., Hajdúszoboszló
5. **Németh István**, Gulácsi Katalin, Kurtán Tibor, Antus Sándor: Potenciálisan biológiailag aktív pterokarpán származékok előállítása, MKE 1. Nemzeti Konferencia, 2011. máj. 22-25., Sopron
6. **I. Németh**, T. Kurtán, S. Antus: Synthesis of potentially bioactive pterocarpan derivatives, Fourth German-Hungarian Workshop, June 14-16, 2011, Debrecen