Summary of Ph.D. Thesis

SYNTHESIS OF FIVE-MEMBERED HETEROCYCLES CONDENSED TO THE STERANE CORE

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1. Introduction and aims

One of the most important molecules involved in the operation of living organisms are steroids, since they play a crucial role in the regulation of biological processes. The main driving force towards the preparation of steroidal compounds nowadays is the development of novel analogs with a biological target other than a hormone receptor, and therefore the reduction or elimination of unwanted hormonal effects. Experimental results achieved during the past few years have revealed that some steroidal derivatives play important roles in complex signal transduction mechanisms in a hormone receptor-independent manner by the upregulation of apoptotic pathways, and a number of synthetic steroidal heterocycles affect the proliferation of human cancer cells without influencing the division of intact cell.

Based on the previous results as mentioned above, the aim of our research was the synthesis of novel isoxazolines fused to different positions of androstane, estrane and pregnane skeletons. We also set out to prepare steroidal pyrazolines where the heteroring is condensed to ring A or D of the androstane or estone core. It was also our aim to study the regio- and stereoselectivity of the reactions and to purify the products by flash chromatography. The optimization of each reaction condition, in some cases using microwave (MW) heating techniques to increase the reaction yields was also planned. We set out the confirmation of the structures of all synthesized compounds by various analytical methods (NMR, MS), and furthermore we planned to subject all products to *in vitro* pharmacological studies in order to investigate their antiproliferative effects on different human gynecological cancer cell lines.

2. Experimental methods

Most of the reactions were carried out in millimolar scale, and monitored by thin-layer chromatography. The crude products were purified by flash chromatography. The structures of all synthesized compounds were confirmed by ^{1}H NMR, ^{13}C NMR and ESI MS measurements, and in some cases 2D NMR experiments (NOESY, COSY, HMBC and HSQC) were also performed for the structure determination.

3. Novel scientific results *

3.1. The intermolecular 1,3-dipolar cycloadditions of the steroidal unsaturated ketones, such as 17β-acetoxy-5α-androst-1-en-3-one (**5**), 3β-acetoxy-5α-androst-15-en-17-one (**7**) and pregnadienolone-acetate (**9**, PDA) with different aryl nitrile oxides (**4a**–**g**) under the optimized reaction conditions afforded the corresponding sterane-fused isoxazoline derivatives (**6a–g**, **8a–e**, **10a–e**) in the androstane and the pregnane series in moderate to excellent yields (*Scheme 1*). The yields of the heteroaromatic products (**6a–g**, **8a–e**, **10a–e**) were greatly influenced not only by the electronic features of the substituents on the aromatic ring of the 1,3-dipoles (**4a**–**g**), but by the mode of addition of *N*,*N*-diisopropylethylamine (DIPEA).

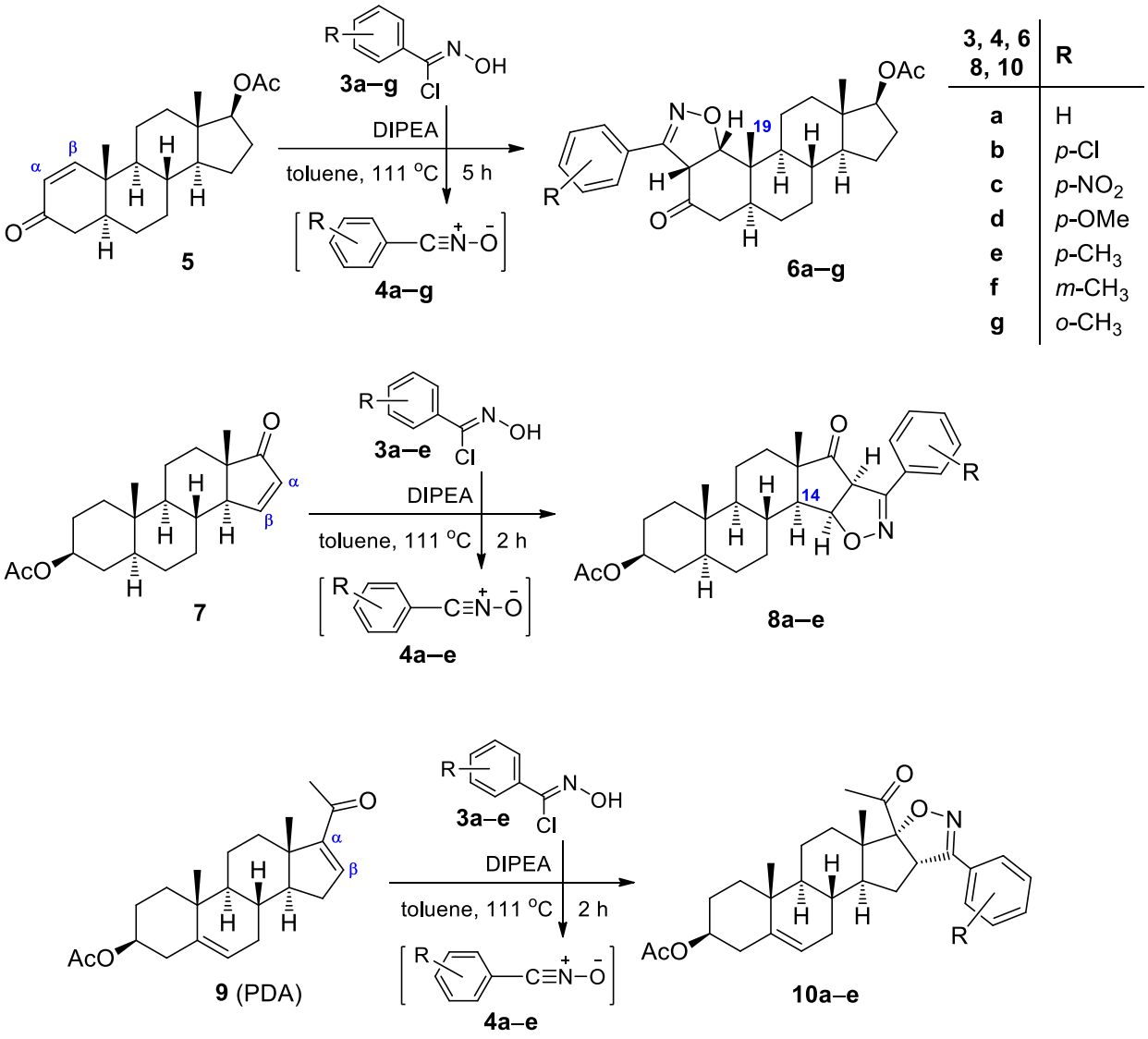
3.2. Most of the aryl nitrile oxides possessed relatively long half-lives at room temperature. The presence of an electron-withdrawing substituent on the aromatic ring (**4b**, **4b**) facilitates dimerization, while the resistance to furoxane formation is enhanced by electron-donating groups (**4d–f**) and sterically by *ortho* substituents (**4g**).

3.3. The cyclic enone moiety of the six-membered ring A (**5**) proved to be less reactive than that of the five-membered ring D (**7** or **10**), but all the reactions were affected significantly by the substitution pattern of the nitrile oxide dipole. A similar difference in reactivity was earlier observed for the reactions of cyclopentene and cyclohexene, the former being more reactive due to ring strain and conformational effects.

3.4. The ring-closures proved to occur in a regio- and stereoselective manner to furnish a single isomer in all cases (**6a–g**, **8a–e**, **10a–e**). After purification by flash chromatography, the structures of all the synthesized compounds were confirmed by ^{1}H, ^{13}C NMR and 2D NMR measurements.

** The numbering of the compounds accords with that in the Ph.D. Thesis*

3.5. During the ring-closures of the 5α-androstane precursor (**5**), regioisomer in which the *O* terminus of the nitrile oxide dipoles is attached to the β-carbon of the dipolarophile was formed in a stereoselective manner to furnish exclusively 1α,2α-condensed isoxazolines (**6a**–**g**). The attack of the dipole from above the general plane of the sterane framework (the β side) is unlikely in **5** in consequence of the same spatial orientation of the 19-CH_3. The formation of regioisomer in which the *O* terminus of the dipole is attached to the α-carbon of the dipolarophile, and the aromatic ring is therefore bent towards the sterane portion, is considered to be hampered by steric repulsions.



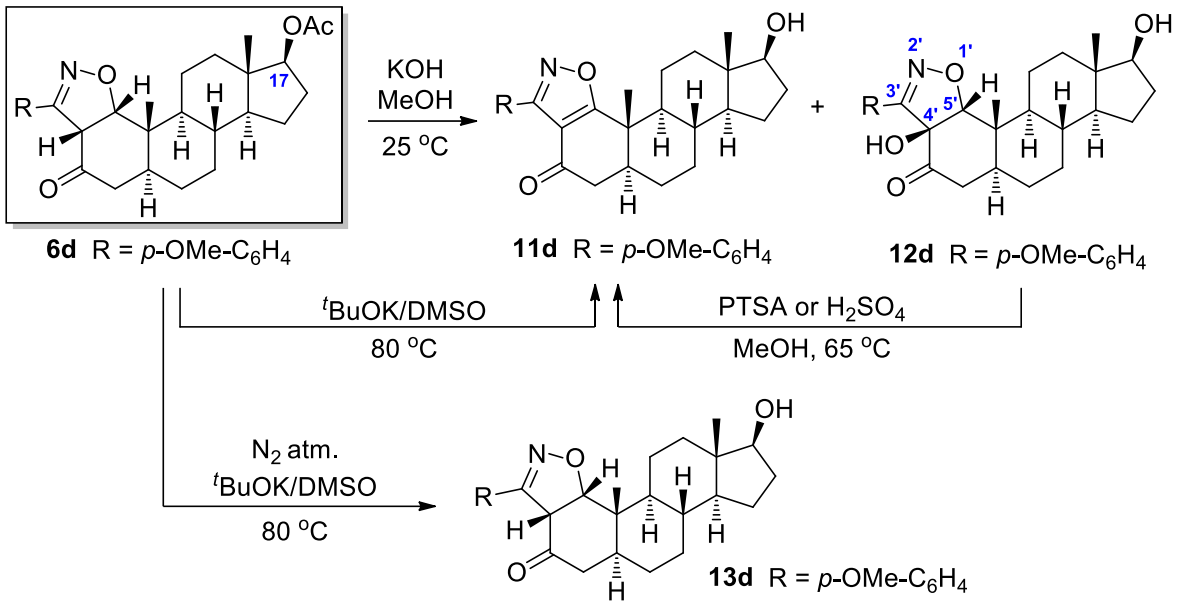
Scheme 1

3.6. During the ring-closures of **7**, a single regioisomer was formed in a stereoselective manner to furnish exclusively 15β,16β-condensed heterocycles (**8a–e**). The most facilitated isomers are undoubtedly **8a–e**, in which the anionic pole of the nitrile oxide is connected to the β carbon of **7**. The introduction of the nitrile oxide in **7** is unlikely to occur from beneath (the α side) in consequence of the steric interaction between the dipole and 14-H_α. The regio- and the stereoselectivity of the ring-closures are therefore influenced by steric factors. The exact configurations of the newly formed stereocenter was established with the aid of homonuclear 2D NMR (COSY and NOESY) and heteronuclear 2D NMR (HSQC and HMBC) measurements.

3.7. The intermolecular ring-closures of **9** with **4a–e** also occurred in a highly regio- and stereoselective manner, permitting the formation of a single 16α,17α-condensed diastereomer (**10a–e**) in which the *O* terminus of the nitrile oxide dipole is attached to C-17 of the sterane core. The regioselectivity was determined on the basis of the ^{13}C NMR spectra of **10a–e** indicating the presence of the C-17 signal at around 106 ppm, which was consistent with its linkage to an oxygen. The attack of the nitrile oxide dipole (**4a–e**) from above the general plane of the sterane framework (the β side) is unfavorable in consequence of the same spatial orientation of the 18-CH_3.

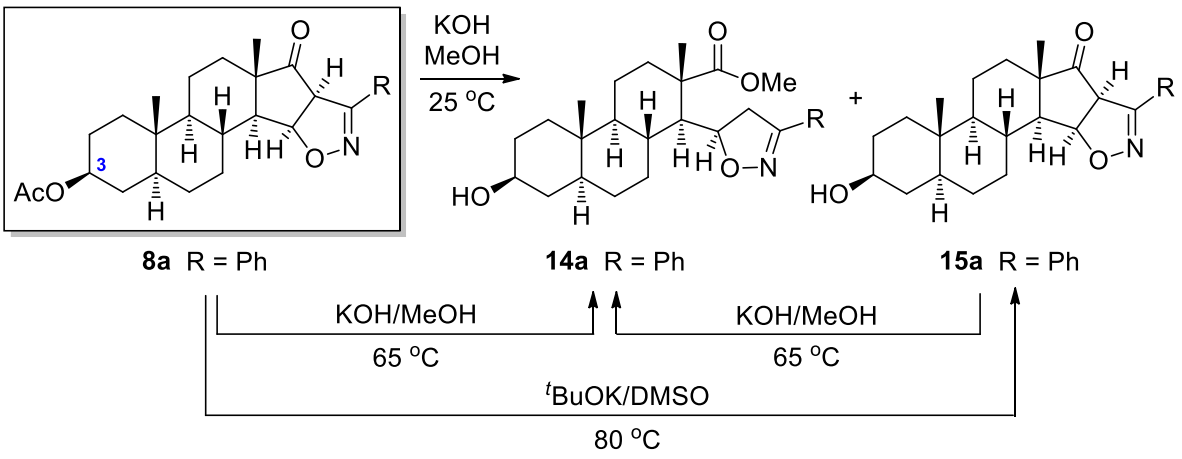
3.8. 17-Deacetylation of **6d** in alkaline MeOH at room temperature resulted in the simultaneous formation of a heteroaromatic isoxazole (**11d**) and a 4′-hydroxylated isoxazoline (**12d**) in an approximate ratio of 4:1, the structures of which were confirmed by NMR spectroscopy after separation (*Scheme 2*). The formation of the 4′-OH derivative **12d** was explained by the oxidation of the corresponding enolate produced in alkaline medium. Such hydroxylation has already been observed, especially for ketones containing a tertiary carbon at the α position. The spontaneous aromatization of the isoxazoline ring of **6d** to isoxazole **11d** was quite unusual, since the oxidation of such rings is more difficult than that of pyrazolines to pyrazoles, and the application of different oxidizing reagents is usually needed even for the dehydrogenation of six-membered ringcondensed analogues. Interestingly, repeated deacetylation of **6d** with ^{t}BuOK in DMSO at 80 °C led to the formation of **11d** alone. Although **12d** proved to be quite stable in alkaline medium, it could be converted to **11d** by elimination in the presence of

p-toluenesulfonic acid or sulfuric acid at elevated temperature. However, similar reaction by applying an inert atmosphere led to the desired product **13d** exclusively.



Scheme 2

3.9. When the 3-deacetylation of the ring D-fused analogue **8a** was carried out at room temperature, the major formation of a D-*seco* ester (**14a**) was observed, together with the desired product (**15a**) (*Scheme 3*), while **14a** was the sole product when either **8a** or **15a** was refluxed in alkaline MeOH. The 3β-hydroxy compound **15a** was obtained as sole product by applying ^{t}BuOK in DMSO for repeated deacetylation. The observed fragmentation was similar to the retro-*Dieckmann* reactions of 1,3-diketones and ketoesters, where the attack of the MeO^{-} nucleophile, derived from the solvent, on the carbonyl-C induces the cleavage of ring D between C-16 and C-17. Simultaneous deacetylation on C-3 also occurs to furnish **14a**. The formation of the D-*seco* derivative serves as indirect evidence of the regioselectivity of the 1,3-cycloaddition of **7** with **4a**, because the fragmentation would not be possible in the opposite regioisomer.

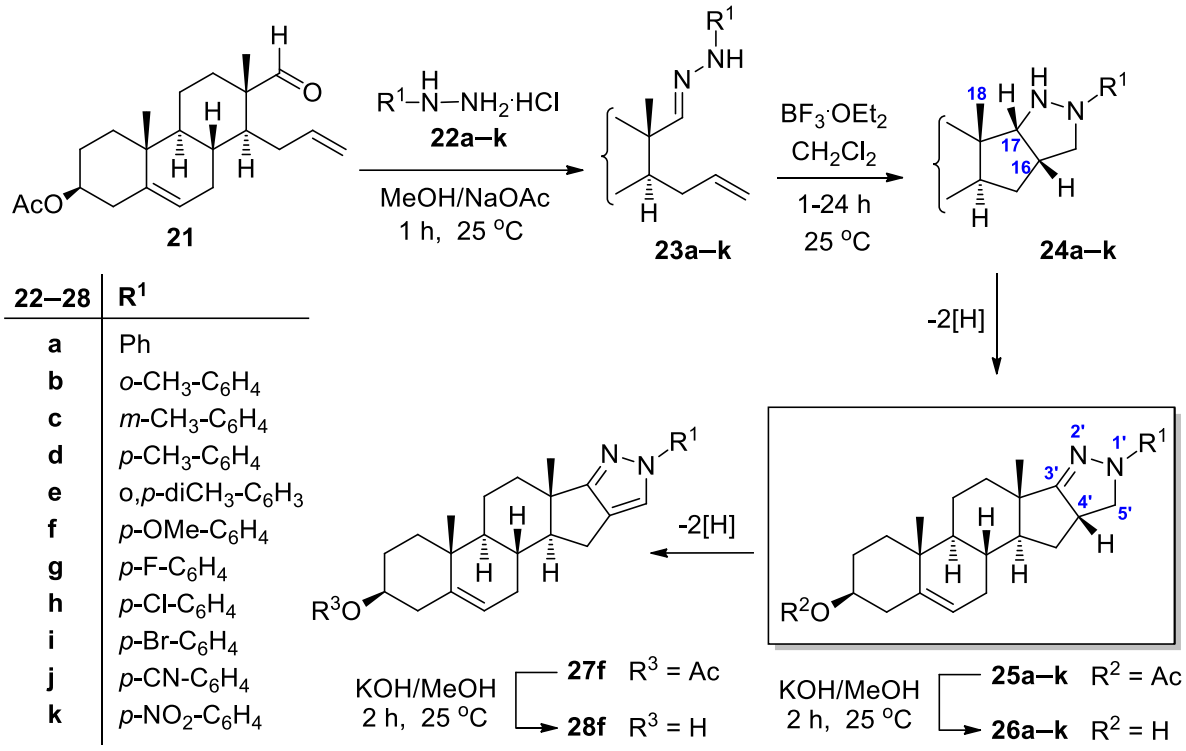


Scheme 3

3.10. The different behaviour observed for **6d** and **8a** under deacetylation conditions may be attributed to the higher rigidity and sterically more hindered character of ring D in **8a** compared to the flexible six-membered ring A in **6d**. Aromatization of the heteroring should further enhance the ring strain of ring D in **8a**, therefore, fragmentation induced by a nucleophile attack on C-17 instead of oxidation is more favourable in this case.

3.11. Novel androsteno-arylpyrazolines (**25a–k**) were synthesized stereoselectively by *Lewis* acid-induced intramolecular 1,3-dipolar cycloaddition of alkenyl hydrazones (**23a–k**), obtained from a steroidal D-*seco*-aldehyde (**21**) with differently substituted arylhydrazines (**22a–k**) (*Scheme 4*). For the intramolecular ring-closures, **21** was synthesized from dehydroepiandrosterone acetate in a multistep sequence, using MW-assisted technique. The opening of the ring D – with *Grob* fragmentation to furnish D-*seco*-androsten aldehyde – was also performed by both conventional and MW heating techniques, and during the MW synthesis the yield increased from 77% to 92%, while the required reaction time decreased from 3 h to only 1 min.

3.12. Olefinic D-*seco*-aldehyde phenylhydrazones (**23a–k**) were prepared *via* simple condensation reactions. The *E*/*Z* isomerization of hydrazones (**23a–k**) in solution during NMR measurements and on acidic-based TLC plates was not observed in these cases, and the formation of the sterically more favorable *E* isomers is assumed.



22–28	R^1
a	Ph
b	*o*-CH_3-C_6H_4
c	*m*-CH_3-C_6H_4
d	*p*-CH_3-C_6H_4
e	o,*p*-diCH_3-C_6H_3
f	*p*-OMe-C_6H_4
g	*p*-F-C_6H_4
h	*p*-Cl-C_6H_4
i	*p*-Br-C_6H_4
j	*p*-CN-C_6H_4
k	*p*-NO_2-C_6H_4

Scheme 4

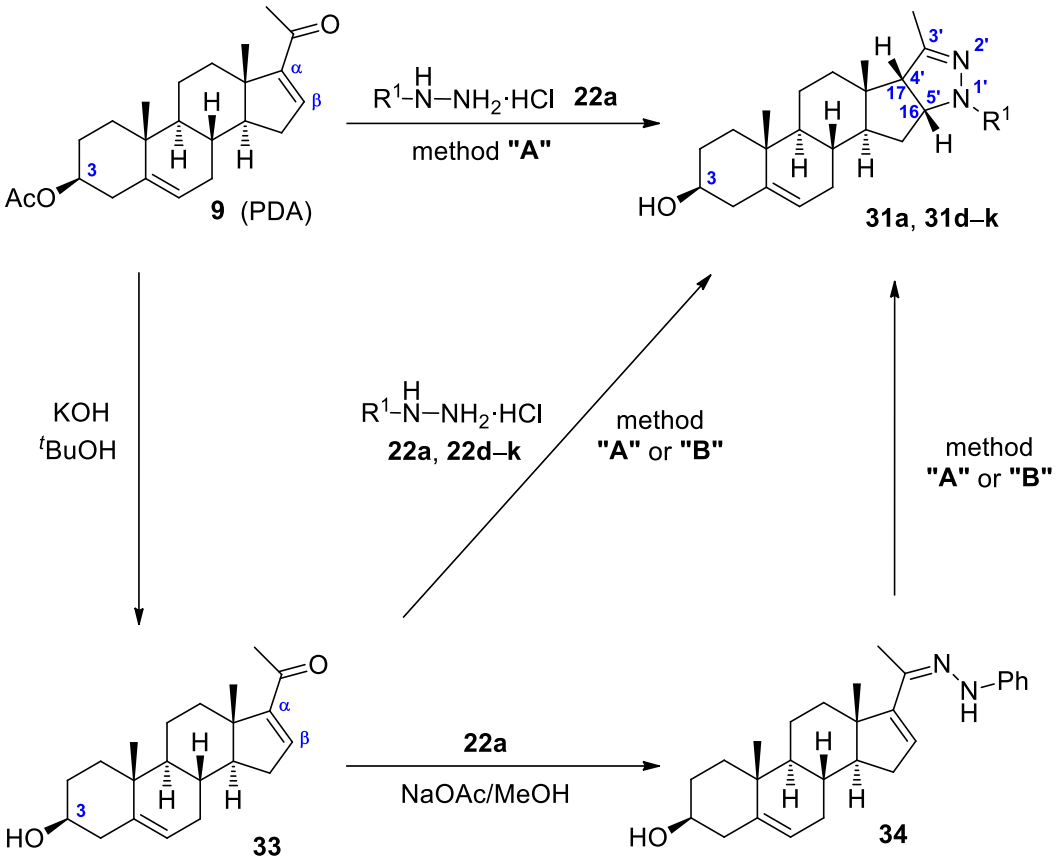
3.13. Arylhydrazones (**23a–k**) were subjected to cyclization directly after preparation in view of their instability. The 1,3-dipolar cycloadditions of **23a–k** were carried out in the presence of $BF_3{\cdot}OEt_2$ in CH_2Cl_2. The cyclizations are assumed to follow a stepwise rather than a pure concerted mechanism, to afford arylpyrazolidines (**24a–k**) as primary products. Spontaneous oxidation of the saturated *N*,*N*-heterocycles (**24a–k**) under the reaction conditions led to 2′-pyrazoline derivatives (**25a–k**) in good to excellent yields. The stabilities of the hydrazones (**23a–k**), the intramolecular ring-closures and the readiness of the newly formed heteroring to undergo oxidation were all observed to be affected significantly by the electronic character of the substituent on the aromatic moiety. Steric effect of the *ortho*-CH_3 substituent on the ring-closures of **23b** and **23e** was not observed.

3.14. Electron-donating groups in **23b–f** favored ring-closure in comparison to unsubstituted phenylhydrazone **23a**, to afford the desired products (**25b–f**) in high yields within shorter time (1–6 h), while for the arylhydrazones containing electron-withdrawing groups (**23g–k**) a longer time (24 h) was necessary at room temperature for sufficient conversion.

3.15. The intramolecular 1,3-dipolar cycloadditions of **23a–k** occurred in a stereoselective manner to afford androstene-fused arylpyrazolines (**25a–k**) as single diastereomers, with 16-H in the β position. The diastereofacial selectivity is not surprising, since the 16α,17α-*cis* formation of the fused pyrazolidine ring in the primary products (**24a**–**k**) is more favorable due to the β orientation of the bulky angular methyl group on C-13.

3.16. In the next stage of the work, novel ring D-condensed 2′-pyrazolines in the androstene (**31a** and **31d–k**) and in the estrone series (**48a**, **48b** and **48d–k**) were efficiently synthesized from steroidal α,β-unsaturated ketones under microwave irradiation leading to the fused heterorings stereoselectively with a 16α,17α-*cis* heteroring junction (*Scheme 5*). During preliminary experiments, PDA (**9**) was reacted with phenylhydrazine hydrochloride (**22a**) in the presence of 1 equiv. of PTSA under conventional heating. After refluxing of the reaction mixture in EtOH for 6 h, full conversion was achieved and **31a** was obtained in a yield of 82% after chromatographic purification. Since the transformation led directly to the 3β-OH analog of the desired product by simultaneous cyclization and deacetylation in acidic medium, 16-dehydropregnenolone (**33**) was used for further reactions. The ring-closure of **33** with **22a** in refluxing EtOH occurred within 5 h, while MW irradiation at 100 °C shortened the reaction time to 20 min, leading to **31a** in yields exceeding 90% almost independently of the method applied. Other strong acids, such as H_2SO_4 or trifluoroacetic acid (TFA), were also suitable for the promotion of the reaction.

3.17. The reactions are assumed to occur via hydrazone intermediates, followed by intramolecular 1,4-addition. In order to determine whether the reaction proceeds via 1,2- or 1,4-addition of **22a**, the phenylhydrazone derivative **34** of **33** was prepared as reference compound. During the repeated reaction of **33** with **22a** under conventional heating, the phenylhydrazone (**34**) was detected by TLC as the sole intermediate of the transformation.



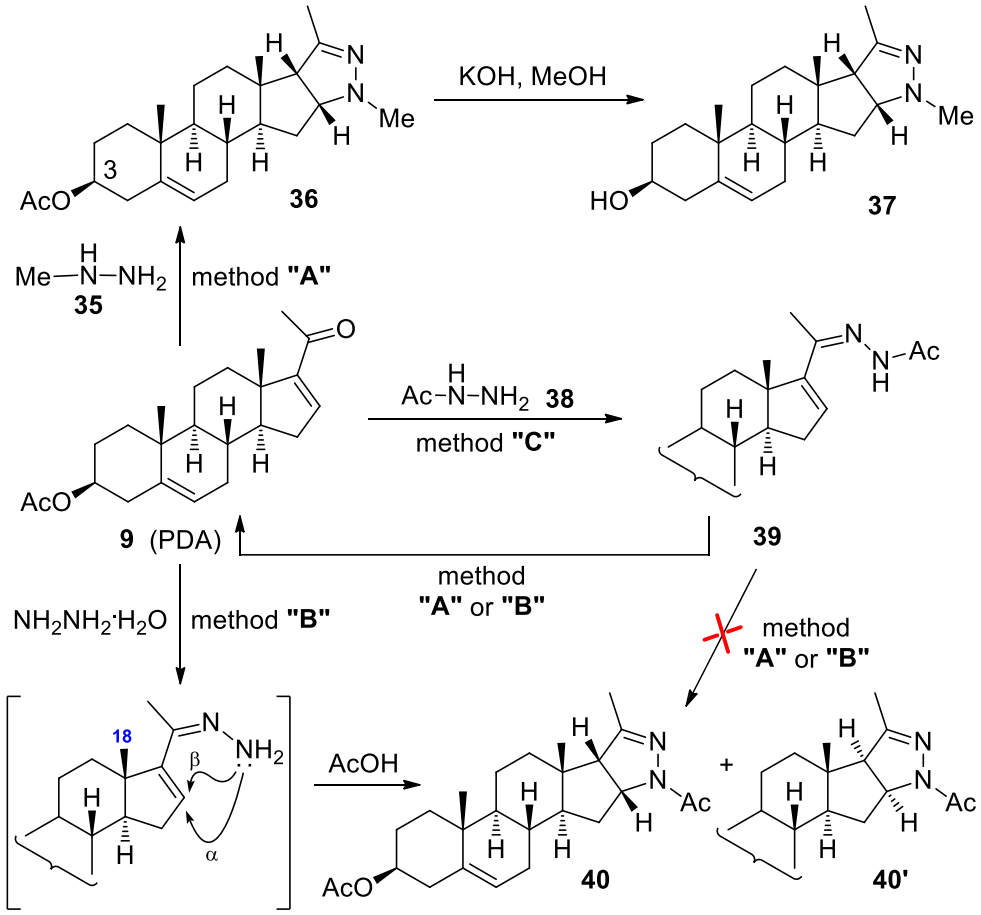
method **"A"** : PTSA (1 eq.), EtOH, reflux, 78 °C
method **"B"** : PTSA (1 eq.), EtOH, MW, 100 °C

22, **31**	**R**^{1}
a	Ph
d	*p*-CH_3-C_6H_4
e	o,*p*-diCH_3-C_6H_3
f	*p*-OMe-C_6H_4
g	*p*-F-C_6H_4
h	*p*-Cl-C_6H_4
i	*p*-Br-C_6H_4
j	*p*-CN-C_6H_4
k	*p*-NO_2-C_6H_4

Scheme 5

3.18. After determination of the optimal conditions under MW conditions, similar reactions of **33** were carried out with different substituted phenylhydrazine hydrochlorides (**22d–k**), which furnished the corresponding ring D-fused arylpyrazolines (**31d–k**) in good to excellent yields, independently of the substituents on the aromatic ring in **22d–k**. Based on the NOESY spectra, the newly formed pyrazoline ring was assigned to be 16α,17α-*cis*, supporting the conception that the intramolecular attack of the aryl-substituted nitrogen in hydrazones could occur from the opposite direction relative to the angular Me group on C-13.

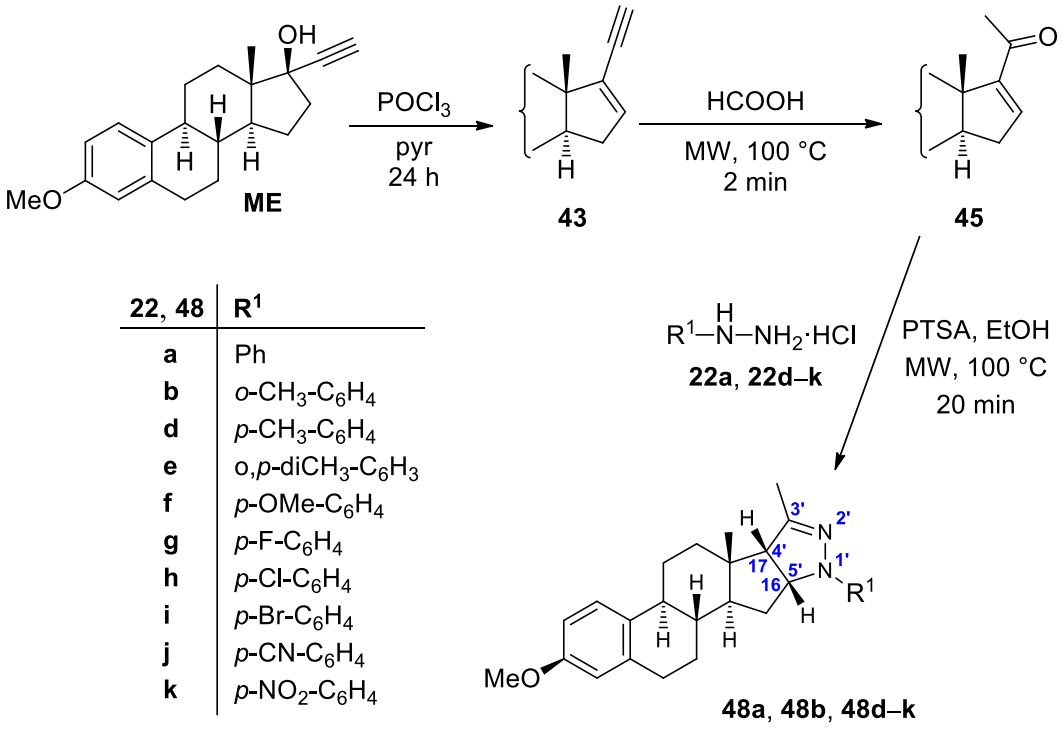
3.19. The reaction between **33** and methylhydrazine (**35**), which was not applied as its hydrochloride, proved to be very sluggish when PTSA was used in EtOH under either reflux or MW irradiation (at 100 °C), presumably because of the low nucleophilicity of the terminal nitrogen in **35**. In view of the moderate productivity, an alternative route was developed for the synthesis of **37**, involving the MW-assisted reaction of PDA (**9**) with methylhydrazine in AcOH for 2 min at 150 °C in the presence of PTSA and subsequent deacetylation (*Scheme 6*). Interestingly, when the unsubstituted hydrazine-hydrate was used instead of methylhydrazine, the stereoselectivity of the process proved to be low, and the ^{1}H NMR spectrum of the crude product indicated that an inseparable mixture of the two possible *cis*-fused pyrazolines (**40** + **40′**) were obtained in an isomeric ratio of 1:2. The exact ratio of the product and the structures were determined from the NMR data of the isomeric mixture (**50a**).



Scheme 6

3.20. In an effort to find evidence for the preliminary cyclization and subsequent acetylation process, the MW-assisted reaction of PDA (**9**) with **38** in AcOH was also attempted, but the intermediate **39**, which was also synthesized by an independent route, was transformed back to the starting PDA in acidic medium instead of undergoing cyclization to **40**. This was not surprising in view of the low nucleophilicity of the amide nitrogen in **39**.

3.21. Novel ring A-condensed pyrazoles in the 5α-androstene series (**48a**, **48b** and **48d–k**) were also efficiently synthesized from steroidal α,β-unsaturated ketone under microwave irradiation. The preparations were carried out from mestranol (**ME**) in a two-step sequence (*Scheme 7*). The previously applied MW-assisted tandem condensation/1,4-addition process and subsequent oxidation of the pyrazoline rings to aromatic pyrazoles resulted the corresponding products (**48a**, **48b** and **48d–k**).



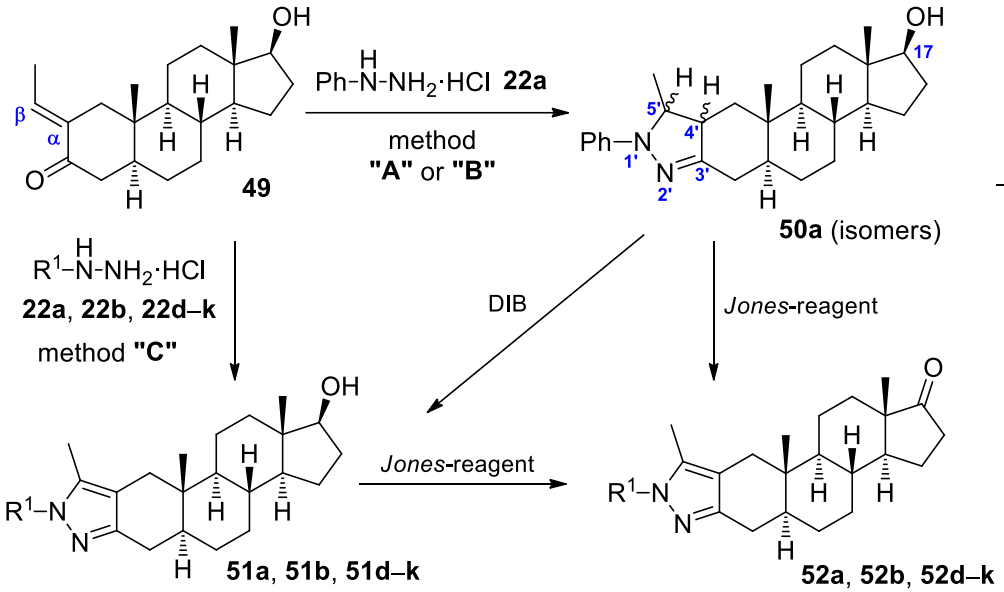
22, 48	R^1
a	Ph
b	*o*-CH_3-C_6H_4
d	*p*-CH_3-C_6H_4
e	o,*p*-diCH_3-C_6H_3
f	*p*-OMe-C_6H_4
g	*p*-F-C_6H_4
h	*p*-Cl-C_6H_4
i	*p*-Br-C_6H_4
j	*p*-CN-C_6H_4
k	*p*-NO_2-C_6H_4

Scheme 7

3.22. In the final period of the work, novel androstane-fused arylpyrazoles (**51a**, **51b**, **51d–k**) efficiently synthesized from a steroidal α,β-unsaturated ketone (**49**), which was obtained in good yield from 5α-dihydrotestosterone (DHT) and acetaldehyde by aldol condensation (*Scheme 8*). Preliminary ring-closure experiments on **49** with phenylhydrazine **22a** were first

carried out both under conventional heating and MW conditions, and a mixture of pyrazoline diastereomers (**50a**) was obtained. The MW-assisted method greatly shortened the reaction time, but the yields of the desired products were only slightly better than in the thermally-induced version. The stereoisomers of **50a** could not be separated by column chromatography and spontaneous oxidation of the pyrazoline to the corresponding pyrazole during purification was also observed. In view of the instability of pyrazolines (**50a**), further experiments were not performed toward their stereoselective synthesis.

3.23. A one-pot procedure for the regioselective formation of fused pyrazoles has been developed instead, involving the I_2-mediated oxidative cyclization of **49** with different arylhydrazines (**22a**, **22b**, **22d–k**) under MW condition. The improved practical protocol led to ring A-fused arylpyrazoles (**51a**, **51b**, **51d–k**) in excellent yields without the necessity of isolation of the less stable intermediates. Subsequent oxidation of the 17β-hydroxy derivatives with the *Jones* reagent resulted in the 17-keto analogs (**52a**, **52b**, **52d–k**), which may also deserve attention from a pharmacological point of view.



22, 48	R^1
a	Ph
b	*o*-CH_3-C_6H_4
d	*p*-CH_3-C_6H_4
e	o,*p*-diCH_3-C_6H_3
f	*p*-OMe-C_6H_4
g	*p*-F-C_6H_4
h	*p*-Cl-C_6H_4
i	*p*-Br-C_6H_4
j	*p*-CN-C_6H_4
k	*p*-NO_2-C_6H_4

method **"A"** : PTSA (0,5 eq.), EtOH, reflux, 78 °C, 1 h
method **"B"** : PTSA (0,5 eq.), EtOH, MW, 100 °C, 2 min
method **"C"** : I_2 (0,5 eq.), EtOH, MW, 100 °C, 2 min

Scheme 8

3.24. All the novel synthesized steroids were subjected to *in vitro* pharmacological studies. Antiproliferative effects were determined by our cooperation partner at the Department of Pharmacodynamics and Biopharmacy, University of Szeged. The measurements on different human gynecological cancer cell lines indicated that several derivatives exerted significant antiproliferative activities.

4. Scientific publications directly related to the Ph.D. Thesis

1. **Gergő Mótyán**, Zalán Kádár, Dóra Kovács, János Wölfling, Éva Frank
   Regio- and stereoselective access to novel ring-condensed steroidal isoxazolines
   Steroids, **2014**, *87*, 76–85.
   IF=2.639

2. **Gergő Mótyán**, István Zupkó, Renáta Minorics, Gyula Schneider, János Wölfling, Éva Frank
   Lewis acid-induced intramolecular access to novel steroidal ring D-condensed arylpyrazolines exerting *in vitro* cell-growth-inhibitory effects
   Molecular Diversity, **2015**, *19*, 511–527.
   IF=2.080

3. **Gergő Mótyán**, Ferenc Kovács, János Wölfling, András Gyovai, István Zupkó, Éva Frank
   Microwave-assisted stereoselective approach to novel steroidal ring D-fused 2-pyrazolines and an evaluation of their cell-growth inhibitory effects *in vitro*
   Steroids, **2016**, 112, 36–46.
   IF=2.282

4. **Gergő Mótyán**, Ádám Baji, István Zupkó, Éva Frank
   Regio- and stereoselective synthesis of pregnane-fused isoxazolines by nitril-oxide/alkene 1,3-dipolar cycloaddition and an evaluation of their cell-growth inhibitory effect *in vitro*
   Journal of Molecular Structure, **2016**, *1110*, 143–149.
   IF=1.753

Total IF: 8.754

MTMT identifier: 10035549

5. Other scientific publications

1. Dóra Kovács, Zalán Kádár, **Gergő Mótyán**, Gyula Schneider, János Wölfling, István Zupkó, Éva Frank
Synthesis, characterization and biological evaluation of some novel 17-isoxazoles in the estrone series
Steroids, **2012**, *77*, 1075–1085.
IF=2.803

2. Ágnes Berényi, Renáta Minorics, Zoltán Iványi, Imre Ocsovszki, Eszter Ducza, Hubert Thole, Josef Messinger, János Wölfling, **Gergő Mótyán**, Erzsébet Mernyák, Éva Frank Gyula Schneider, István Zupkó
Synthesis and investigation of the anticancer effects of estrone-16-oxime ethers *in vitro*
Steroids, **2013**, *78*, 69–78.
IF=2.716

3. Dóra Kovács, **Gergő Mótyán**, János Wölfling, Ida Kovács, István Zupkó, Éva Frank
A facile access to novel steroidal 17-2′-(1′,3′,4′)-oxadiazoles, and an evaluation of their cytotoxic activities *in vitro*
Bioorganic & Medicinal Chemistry Letters, **2014**, *24*, 1265–1268.
IF=2.420

4. Ádám Baji, Ferenc Kovács, **Gergő Mótyán**, Gyula Schneider, János Wölfling, Izabella Sinka, István Zupkó, Imre Ocsovszki, Éva Frank
Investigation of pH and substituent effects on the distribution ratio of novel steroidal ring D- and A-fused arylpyrazole regioisomers and evaluation of their cell-growth inhibitory effects *in vitro*
Steroids, **2017**, *126*, 35–49.
$IF_{(2016)}$=2.282

Total IF: 10.221

6. Lectures and posters related to the Ph.D. Thesis

1. **Gergő Mótyán**, Réka Kiss-Faludy, János Wölfilng, Éva Frank; Sterane-fused pyrazoles: An efficient microwave-assisted sythesis on ring A, *10th Joint Meeting on Medicinal Chemistry*, Dubrovnik, Croatia, 2017. jun. 25–28. (Poster presentation)

2. **Gergő Mótyán**, Ferenc Kovács, János Wölfling, Éva Frank: Application of microwave irradiation for the stereoselective synthesis of androstenefused 2-pyrazolines, *16th Tetrahedron Symposium - Challenges in Bioorganic & Organic Chemistry*, Berlin, Germany, 2015. jun. 16–19. (Poster presentation)

3. **Gergő Mótyán**, Dóra Kovács, Éva Frank: Regio- And Stereoselective Synthesis Of Ring-Condensed Steroidal Isoxazolines By 1,3-Dipolar Cycloaddition, *9th Joint Meeting on Medicinal Chemistry*, Athens, Greece, 2015. jun. 7–10. (Poster presentation)

4. **Gergő Mótyán**: Androsztánvázhoz kondenzált pirazolin és izoxazolin származékok szintézise, *MTA Szteroid és Terpenoidkémiai Munkabizottság és a MTA Szegedi Akadémiai Bizottság Szerves és Gyógyszerkémiai Munkabizottság közös rendezvénye*, Szeged, Hungary, 2015. oct. 12. (Oral presentation)

5. **Gergő Mótyán**, Dóra Kovács, Éva Frank: Stereoselective synthesis of androstene-fused pyrazoline derivatives by microwave irradiation, *22th Conference on Isoprenoids*, Prague, Czech Republic, 2014. sept. 7–10. (Poster presentation)
   Chem. Listy **2014**, *108*, 138. ISSN 0009-2770, **IF=0.272**

6. **Gergő Mótyán**: Az androsztánváz D-gyűrűjéhez kondenzált pirazolinok szintézise, *MTA Szteroid és Terpenoidkémiai Munkabizottság és a MTA Szegedi Akadémiai Bizottság Szerves és Gyógyszerkémiai Munkabizottság közös rendezvénye*, Szeged, Hungary, 2014. oct. 31. (Oral presentation)

7. **Gergő Mótyán**, Dóra Kovács, Ferenc Kovács, Gyula Schneider, Éva Frank: Stereoselective synthesis of new androstene-fused arylpyrazolines as potent antiproliferative agents, *20th International Conference on Organic Chemistry*, Budapest, Hungary, 2014. jun. 29. – jul. 4. (Poster presentation)

8. **Gergő Mótyán**, Dóra Kovács, Gyula Schneider, Éva Frank: Efficient approach to novel androstene-fused arylpyrazolines as potent antiproliferant agents, *4th Meeting of the Paul Ehrlich MedChem Euro-PhD Network*, Hradec Králové, Czech Republic, 2014. jun. 20–22. (Poster presentation)

9. **Gergő Mótyán**: Synthesis of androstene-fused arylpyrazolines, *33rd Edition of European School of Medicinal Chemistry - ESMEC 2013*, Urbino, Italy, 2013. jun. 7–12. (Poster presentation)

7. Other lectures and posters

1. Éva Frank, Ádám Baji, **Gergő Mótyán,** István Zupkó: Synthesis of ring A-fused pyrazole regioisomers in the androstane series and an evaluation of their cell-growth inhibitory effects *in vitro*, *10th Joint Meeting on Medicinal Chemistry*, Dubrovnik, Croatia, 2017. jun. 25–28. (Poster presentation)

2. Barnabás Molnár, **Gergő Mótyán**, Ádám Baji, Éva Frank: Pirazolin- és triazolgyûrûvel módosított ösztron származékok előállítása mikrohullámú aktiválással, *MKE Vegyészkonferencia*; Hajdúszoboszló, Hungary, 2017. jun. 19–21. (Poster presentation)

3. Ádám Baji, **Gergő Mótyán**, Éva Frank: Pirazolgyűrűvel módosított androsztánvázas vegyületek mikrohullámú szintézise, *MKE 2. Nemzeti Konferencia*, Hajdúszoboszló, Hungary, 2015. aug. 31. – sept. 2. (Poster presentation)

4. Dóra Kovács, **Gergő Mótyán,** Ádám Baji, Éva Frank, János Wölfling: Efficient approach to novel ring-condensed steroidal isoxazolines by 1,3-dipolar cycloaddition, *20th International Conference on Organic Chemistry*, Budapest, Hungary, 2014. jun. 29. – jul. 4. (Poster presentation)

5. Dóra Kovács, **Gergő Mótyán**, János Wölfling, Éva Frank: Synthesis, characterization and biological effects of 16-spiro-izoxazolines in the androstane series, *4th Meeting of the Paul Ehrlich MedChem Euro-PhD Network*, Hradec Králové, Czech Republic, 2014. jun. 20–22. (Poster presentation)

6. **Gergő Mótyán**, Dóra Kovács, János Wölfling, Éva Frank: Synthesis and structure determination of steroidal 16-spiroizoxazolines, *VIIIth Joint Meeting on Medicinal Chemistry*, Lublin, Poland, 2013. jun. 30. – jul. 4. (Poster presentation)

7. Dóra Kovács, **Gergő Mótyán**, Ádám Baji, Gyula Schneider, Éva Frank: Efficient approach to steroidal 1,2,4-oxadiazoles in androstane series, *VIIIth Joint Meeting on Medicinal Chemistry*, Lublin, Poland, 2013. jun. 30. – jul. 4. (Poster presentation)

8. **Gergő Mótyán**, Dóra Kovács, János Wölfling, Éva Frank: Androsztánvázas 16-spiro-izoxazolinek szintézise és szerkezetvizsgálata, *MKE Vegyészkonferencia*, Hajdúszoboszló, Hungary, 2013. jun. 26–28. (Poster presentation)

9. Dóra Kovács, **Gergő Mótyán**, Ádám Baji, Gyula Schneider, Éva Frank: 1,2,4-Oxadiazolgyűrűvel módosított androsztánvázas vegyületek szintézise, *MKE Vegyészkonferencia*, Hajdúszoboszló, Hungary, 2013. jun. 26–28. (Poster presentation)

10. **Gergő Mótyán:** Triazol gyűrűt tartalmazó dehidroepiandroszteron származékok szintézise 1,3-dipoláris cikloaddícióval, *XXXI. Országos Tudományos Diákköri Konferencia*, Eger, Hungary, 2013. apr. 4–6. (Oral presentation)

11. **Gergő Mótyán**, Kádár Zalán, Éva Frank, Judit Huber, Gyula Schneider, János Wölfling: Nem várt átrendeződések azidoszteroidok 1,3-dipoláris cikloaddíciós reakciói során, *XXXV. Kémiai Előadói Napok*, Szeged, Hungary, 2012. oct. 29–31. (Oral presentation)

12. **Gergő Mótyán**: Triazol gyűrűt tartalmazó dehidroepiandroszteron származékok szintézise 1,3-dipoláris cikloaddícióval, *Szegedi Ifjú Szerves Kémikusok Támogatásáért Alapítvány és a SZAB Szerves és Gyógyszerkémiai Munkabizottságának 12. tudományos előadóülése*, Szeged, Hungary, 2012. may 8. (Oral presentation)

13. **Gergő Mótyán**, Zalán Kádár, Judit Huber, Éva Frank, Gyula Schneider, János Wölfling: Új típusú, triazol gyűrűt tartalmazó dehidroepiandroszteron származékok előállítása 1,3-dipoláris cikloaddícióval, *XXXIV. Kémiai Előadói Napok*, Szeged, Hungary, 2011. nov. 2–4. (Oral presentation)

14. János Wölfling, Gyula Schneider, Éva Frank, Zalán Kádár, Zoltán Iványi, Dóra Kovács, **Gergő Mótyán**, István Zupkó: Triazolil-szteroidok – új, potenciális gyógyszerhatóanyagok, *A Magyar Tudomány Ünnepe*, Szeged, Hungary, 2010. nov. 15. (Oral presentation)

15. **Gergő Mótyán**, Zalán Kádár, Gyula Schneider, Éva Frank, János Wölfling: Új típusú, triazol gyűrűt tartalmazó dehidroepiandroszteron származékok előállítása 1,3-dipoláris cikloaddícióval, *MKE Vegyészkonferencia és 53. Magyar Spektrokémiai Vándorgyűlés*, Hajduszoboszló, Hungary, 2010. jun. 30. – jul. 2. (Poster presentation)

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