Dyes and Pigments 86 (2010) 197–205

Contents lists available at ScienceDirect

Dyes and Pigments

journal homepage: www.elsevier.com/locate/dyepig

Review

The structure and tautomerism of azo coupled β-Enaminones

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ARTICLE INFO

Article history:
Received 15 September 2009
Received in revised form
12 January 2010
Accepted 13 January 2010
Available online 28 January 2010

Keywords:
Enaminone
Diazonium salt
Azo coupling
Azo-hydrazone tautomerism
NMR
X-ray

ABSTRACT

This paper concerns a systematic structural study of the products of the reaction between diazonium salts and β-enaminones both in solution and in solid state. Azo coupling proceeds solely at the α-carbon atom of the β-enaminone. The structure of the azo coupling products is affected mainly by that of the starting enaminone; in the case of acyclic substrates, the directing influence is the nature of the amino group. Compounds having primary and secondary amino groups exhibit azo-hydrazone tautomerism, the position of which, depends on the nature of the *N*-substitution (i.e. H, alkyl, aryl). A novel type of azo coupling that results in a new class of azo coupling products is described and discussed. For cyclic enaminones the structure of the azo coupling products is affected mainly by ring size and either the presence or absence of an annelated benzene ring. Owing to the push-pull effect of the carbonyl and amino groups, some products exhibit, besides azo-hydrazone tautomerism, *E*/*Z* isomerism connected with various kinds of hydrogen bond.

Results of the structural studies on azo coupled enaminones are summarized with regard equilibria, structure of the starting β-enaminone (acyclic, cyclic) and type of amino group (primary, secondary, tertiary). Studies were made in $CDCl_3$ solution using ^{1}H, ^{13}C and ^{15}N NMR spectroscopy and in the crystalline state using X-ray crystallography. Structural features leading to multiple azo coupling are analysed.

1. Introduction

β-Enaminones contain the conjugated system O═C–C═C–N [1] (Scheme 1) and are capable of reacting with a wide variety of both electrophilic and nucleophilic reagents. The reactivity of these compounds, which has been the focus of a number of reviews [2a–e], ensures that β-enaminones are frequently used intermediates, especially in heterocyclic syntheses [2,3a,b].

The enaminone unit has three nucleophilic centres namely the hard oxygen as well as softer nitrogen and α-carbon. In the case of reaction with a proton (hard electrophile), protonation in the kinetically driven stage occurs at oxygen (in a smaller extent also at nitrogen) and subsequently, in the thermodynamically driven stage, protonation takes place at carbon [3c] (Scheme 2).

Isocyanates are softer electrophiles compared with a proton and they react with β-enaminones both at nitrogen and carbon giving a mixture of products [3d] (Scheme 3).

Isothiocyanates, which are even softer electrophiles, attack enaminones only at the carbon atom [3d] (Scheme 3); benzoylisothiocyanate, which is a more reactive, but simultaneously softer electrophile than isocyanates, also reacts with β-enaminones solely at the carbon atom [3e]. Only in the cases when the α-carbon of the enaminone is substituted, does the attack of the benzoylisothiocyanate take place at nitrogen to form substituted thioureas [3f]. (Scheme 3).

Besides having an important synthetic potential, β-enaminones also represent convenient objects for structural studies due to the possibility of keto-enol and enamino-imino tautomerisms and due to the *E*/*Z* isomerism (given by a lowered barrier of rotation around C═C bond because of the push-pull effect) and *sE*/*sZ* (given by increased barriers of rotation around C–N and C–C═O bonds [2b]). All the processes are dynamic and equilibria between individual molecules can be established (Scheme 4).

Upon introduction of an aryldiazenyl group into the molecule of the β-enaminone this structural potential even more increases. In contrast to anilines (that can be considered as enamines) which react with diazonium ion, in dependence on conditions, either at nitrogen (reversibly) to form triazenes or at carbon (irreversibly), β-enaminones react with diazonium ions only at the α-carbon. The carbon atom is attacked solely, even in the case of the most reactive diazonium ion used so far (2,6-dichloro-4-trifluoromethylbenzenediazonium) [4a]. The products of the azo coupling to β-enaminones can theoretically exist in several tautomeric forms (Scheme 5). The individual tautomers can exist in various isomeric forms differing in a type of an intramolecular hydrogen bond (Scheme 5).

The existence of the azo-hydrazone tautomerism is an important property of azo dyes and azo pigments. The position of the

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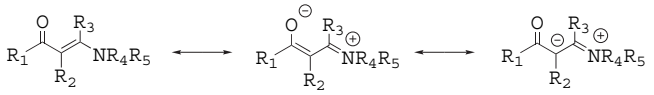
doi:10.1016/j.dyepig.2010.01.004



Scheme 1. Resonance structures of β-enaminones.

tautomeric equilibrium affects the basic characteristics of azo dyes (color tone, photostability …). The products of the reaction of β-enaminones with diazonium salts are, due to a number of the structural phenomena possible, convenient model compounds for studies of the relationships between the structure of the starting active and passive components and the position of the azo-hydrazone tautomeric equilibrium. The results obtained by their study can be used for the design of compounds having required color properties.

Reactions of enaminones with diazonium salts have found a number of applications as seen from the literature, e.g. from the review [2c] or from the works of Elnagdi's group [4b]. However, the products of azo coupling to enaminones are here only probable intermediates, because the reactions in these cases are usually carried out under the conditions leading to the hydrolysis of the enamino group to form monohydrazones of tricarbonyl compounds [4b]. During the last few years we have explored the synthesis and structure of the products formed by azo coupling to β-enaminones and having the enamino group preserved. These compounds can be isolated provided that the azo coupling is accomplished under controlled conditions so as the hydrolysis of the enamino group (both in the stage of the starting enaminone and/or the azo coupling product) is suppressed or at least limited.

2. Results and discussion

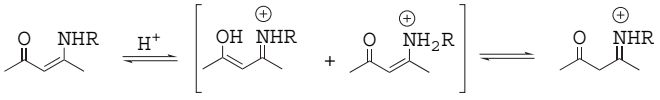
2.1. Acyclic β-enaminones having primary or secondary amino group

The first work dealing with the structure of the azo coupled enaminones was published in 1995 [5a].

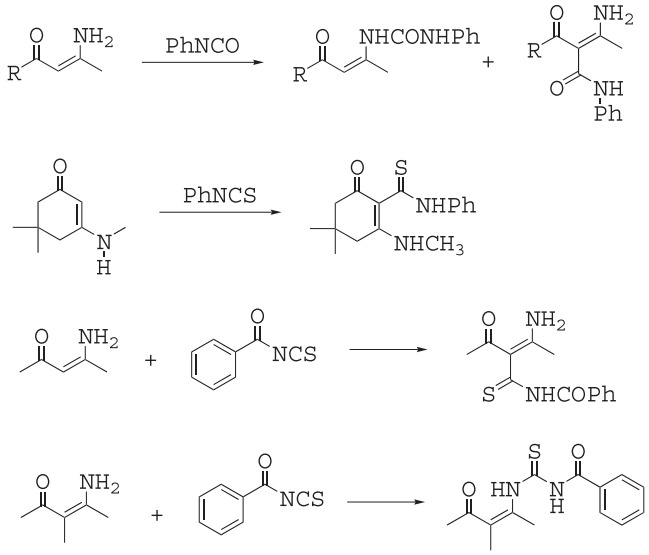
The structure of the product of azo coupling was found to be dependent on the type of amino group of the enaminone. As long as the substrate contained the primary amino group or *N*-methyl group, the product was the azo compound in the form of a mixture of *E* and *Z* isomers (**2A,B**) (Scheme 6). The isomers differ in the kind of hydrogen bond (C═O···H–N vs. N═N···H–N). In the case of the enaminone with *N*-aryl group the product was the hydrazo compound **4** in the form of the one isomer only (Scheme 6). Rožňavská [5a] also studied the kinetics of the azo coupling and proposed the mechanism of the reaction (Scheme 6, bottom). The kinetics of the azo coupling was studied only for the reactions of 4-aminopent-3-en-2-one (**1**, R═H) with substituted benzenediazonium salts. It can be supposed that the proposed mechanism is valid also for the case of enaminones bearing secondary amino group. The hydrazone **3** was a by-product in both the cases.

2.1.1. An estimation of the position of the azo-hydrazone tautomerism

The conclusions regarding the structure of the azo coupling products in the work [5a] were made on the basis of ^{1}H and ^{13}C



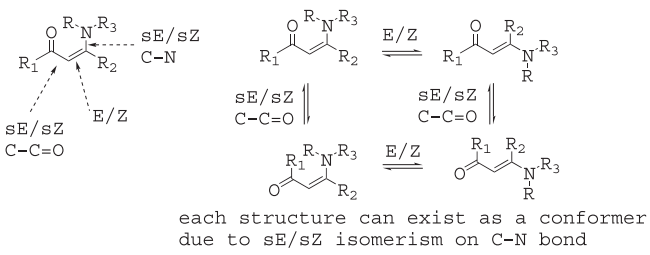
Scheme 2. Protonation of β-enaminones.



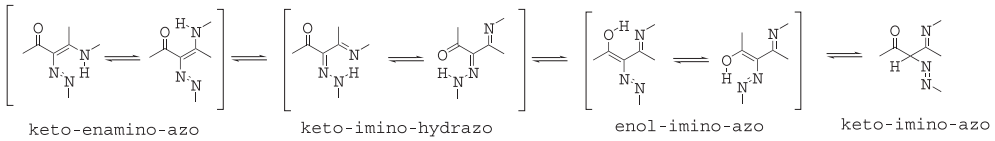
Scheme 3. The reaction of β-enaminones with isocyanates and isothiocyanates.

NMR spectra only. However, ^{15}N NMR parameters of the system studied have appeared to be much more convenient for the estimation of the azo-hydrazone equilibrium. The azo-hydrazone equilibrium mixture could be considered, from the spectral point of view, as being a single compound, because the exchange between both the tautomers proceeds only through the very fast intramolecular transfer of proton between two nitrogen atoms.

The topic of quantitative characterization of the equilibrium, being fast on the NMR time scale, has been a subject of some review articles [6a–d,f]. As the parameters, suitable for the quantification of the azo-hydrazone equilibrium, both the ^{15}N NMR chemical shifts of the nitrogens participating in the equilibrium and the values of the coupling constant $^{1}J(^{15}N,^{1}H)$ could be used. The estimation of the position of the equilibrium by means of ^{15}N NMR chemical shifts is based on the comparison of the chemical shifts of the system studied with the shifts of the standard compounds, existing as pure tautomers under the measuring conditions. ^{15}N NMR spectroscopy is especially attractive for this purpose because of the extraordinary differences between ^{15}N chemical shifts of the azo and hydrazo form [6e]. A choice of the standard compound is the key for the accuracy of the estimation. The choice of the standard compound is given by a structural similarity with the system studied (mainly by the presence or absence of hydrogen bonds, especially intramolecular ones with the participation of the tautomeric N–H group). The position of the equilibrium can be estimated by means of the equation mentioned e.g. in [6d]. Nitrogen-15 chemical shifts of representative compounds usually used as the standards for the estimation of the azo-hydrazone tautomeric equilibrium are shown in Scheme 7 [6e]. For the estimation based on the values of the



Scheme 4. *E*/*Z* ans *sE*/*sZ* isomerism possible for β-enaminones.



Scheme 5. The tautomerism possible for azo coupled β-enaminones.

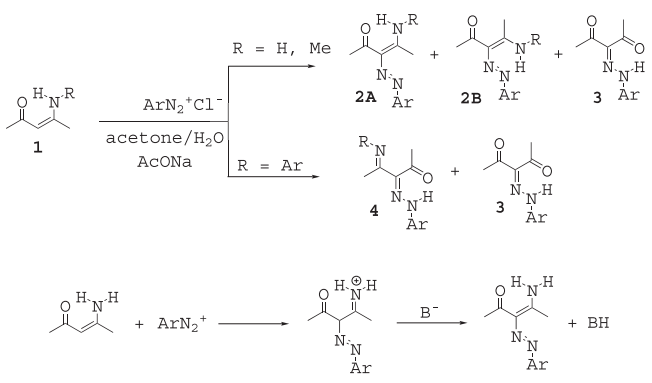
coupling constants, the method of determination of so-called *virtual coupling constant* was proposed [7]. The principle of the method consists in the fact, that the value of the coupling constant $^1J(^{15}N,^1H)$ is relatively independent on the structural surroundings. For the pure azo form the value is 0 Hz and for the pure hydrazo form it is usually 88–96 Hz depending on the presence or absence of any type of the hydrogen bond. A system in the tautomeric equilibrium has the value of the constant in an interval 0–96 Hz. The position of the equilibrium can be estimated by means of the equation mentioned e.g. in [6d] Nitrogen atoms participating in the tautomeric equilibrium have very different chemical shifts and it is then possible to read the values of both the coupling constants [$^1J(^{15}N_a,^1H)$ and $^1J(^{15}N_c,^1H)$]. A verification of the accuracy of the results lies in the calculation of the equilibrium position using the various parameters and the comparison of the results which should be close together. For schematic description see Scheme 7.

In a solid state the position of the tautomeric equilibrium is possible to estimate on the basis of bond lengths and the corresponding bond orders. Another possibility is to localize the hydrogens, participating in the tautomeric exchange, having partial occupancy on individual X-atoms (for system X–H···X where X=O, N) and to refine them. By means of this approach it is possible to determine their occupancy factors on individual X-atoms giving the populations of the tautomers [9]. The abundance of the individual tautomers in the solid state can be determined directly, in contrast to NMR, without the possible error, being introduced into the estimation by using standards.

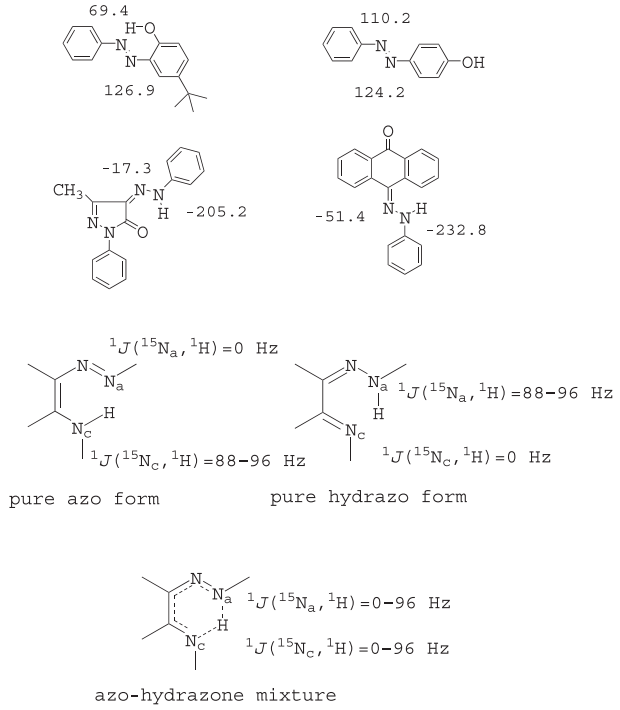
In the original study the azo coupling of β-enaminones was carried out by treatment of the solution of the enaminone in acetone with the aqueous solution of the corresponding diazonium chloride in the presence of sodium acetate [5a]. The products of the azo coupling formed had to be isolated from the reaction mixture quickly (even with only partial conversion to the product) so as the subsequent hydrolysis to the hydrazone **3** was suppressed. An alternative method of forming the hydrazone **3** is hydrolysis of the starting β-enaminone to the corresponding β-diketone with following azo coupling to form the hydrazone [5a]. Figueiredo proposed the hydrolysis in the stage of primary adduct of the diazonium salt to the enaminone [5b]. For more distinct suppresion of the hydrolysis and thereby the improvement of the yields of the azo coupling products, the method was improved by using of diazonium tetrafluoroborates (which could be isolated and, importantly, dried) and diisopropylether as a solvent [8].

The results obtained in the original work [5a] had been, with the use of ^{15}N NMR parameters measured in $CDCl_3$ solution, improved and the following conclusions were formulated [8] (Scheme 8):

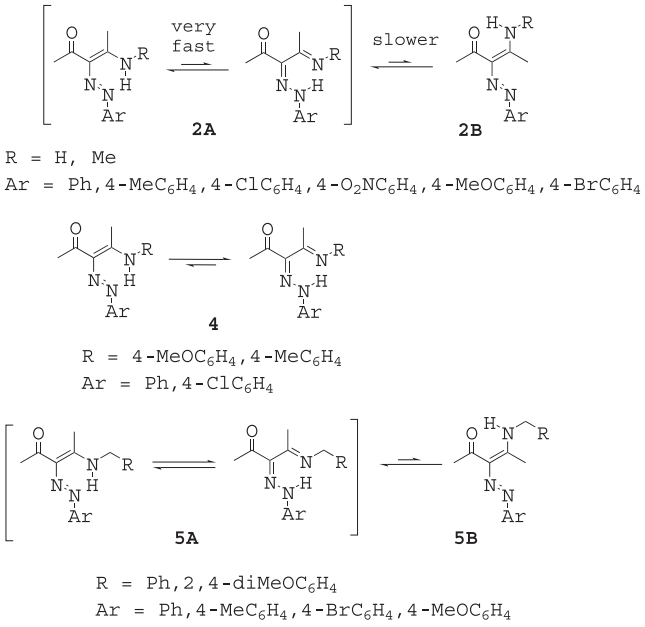
- The position of the azo-hydrazone tautomeric equilibrium for the products **2** and **4** of the azo coupling to 4-aminopent-3-en-2-ones **1** (R=H, Me, Ar) depends mainly on the substitution of the amino group of the starting enaminone. Keto-enol tautomerism does not manifest.
- The products **4** of the azo coupling to *N*-aryl-4-aminopent-3-en-2-one **1** (R=Ar) exist mainly as hydrazo compounds with a little content of the azo form (less than 15%).
- The products **2** (R=H) of the azo coupling to 4-aminopent-3-en-2-one **1** (R=H) exist as an equilibrium mixture of *E* and *Z* isomers. The *Z* isomer having the intramolecular hydrogen bond N–H···N strongly predominates (80–90%). The existence of the intramolecular hydrogen bond makes the rapid shift of a proton between the azo and hydrazo tautomers possible. The rate of the exchange between both the isomers was studied by means of TPPI-NOESY spectroscopy [8] and is depicted in Scheme 9. The major isomer is predominantly azo compound



Scheme 6. The first results obtained on azo coupling with β-enaminones. Mechanism of the reaction [5a].



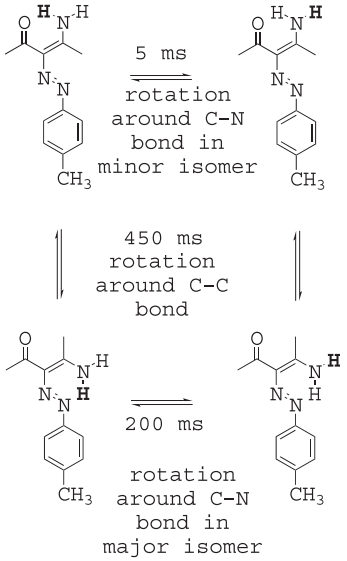
Scheme 7. Upper part: Nitrogen-15 chemical shifts (referenced to a neat nitromethane) of pure azo and hydrazo compounds with and without the intramolecular hydrogen bond. Bottom part: Values of the coupling constants $^1J(^{15}N,^1H)$ for the estimation of the azo-hydrazone tautomerism.



Scheme 8. The improved results on the structure of the azo coupling products from β-enaminones.

with the content of the hydrazo form about 30% (Ar=Ph, 4-MeC_6H_4, 4-ClC_6H_4). The highest content of the hydrazo form was noted for the 4-nitroderivative (Ar = 4-$O_2NC_6H_4$, about 45% hydrazo form) [9]. The minor *E* isomer has substantially higher content of the azo form (owing to its low content in the equilibrium mixture the values of only some ^{15}N NMR parameters could be obtained and only for some compounds).

- The structure of the products **2** (R=Me) of the azo coupling to *N*-methyl-4-aminopent-3-en-2-one **1** (R=Me) was also studied [8,10]. From the results of the ^{15}N NMR measurements it follows that the introduction of the methyl group to the amino group of the starting β-enaminone led to a moderate increase of the hydrazone content in the azo coupling products. The content of the hydrazone form depends also on the benzenediazonium salt substitution (4-OMe < 4-Me ≈ 4-Br < H < 4-NO_2). Differences between the individual substituents are more striking here and the nitro group does not stand out from the trend as in the case of the derivative bearing primary amino group [9]. The products with an *N*-methyl group also form the equilibrium mixture *E* and *Z* isomers in ratio from 1:9 to 1:16, with exception of 4-nitroderivative existing as the single *E* isomer. The minor isomer in all cases is almost pure azo compound [8,10].

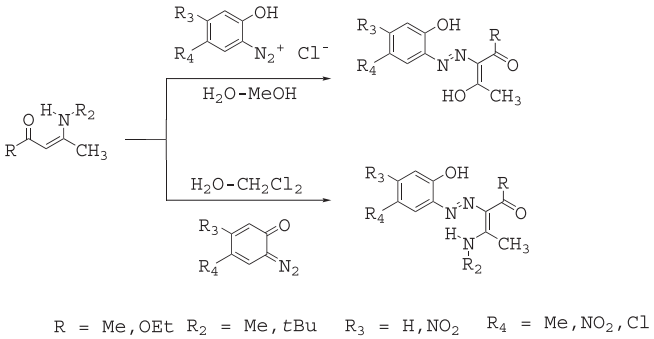


Scheme 9. Rates of the exchange between *E* and *Z* isomers of the azo coupling product based on EXSY measurements [8].

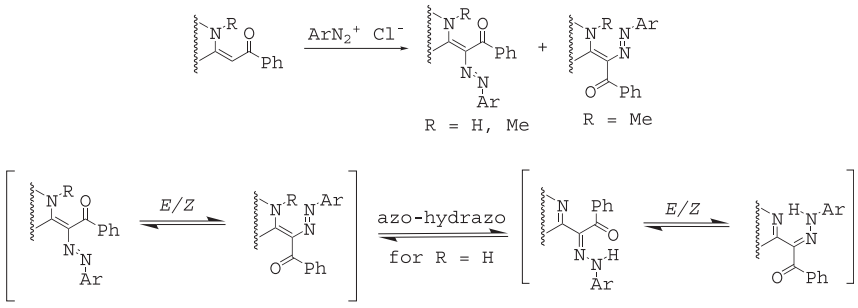
During the study of the structure of the azo coupling products **5** from *N*-benzylderivatives and confrontation of the results with the other azo coupling products it follows that the hydrazo form abundance increases in the order NH_2 < N–CH_3 < N–CH_2Ph < N–Ph [10]. The position of the tautomeric equilibrium is also affected by the substitution at the benzene ring of the benzyl group (enhancement of the azo form content in the order *N*-benzyl < *N*-(2,4-dimethoxybenzyl), in the latter compound the azo form strongly predominated [10]). The benzyl derivatives also form the mixture of *E* and *Z* isomers **5A,B**. Owing to a very low abundance of the minor isomers, no conclusions regarding their tautomeric composition could be drawn and their structure was suggested only on the basis of the analogy with the related NH_2 and NHMe derivatives [10]. The structure of the azo coupling products from the derivatives of 4-aminopent-3-en-2-one in $CDCl_3$ is expressed in Scheme 8.

The reaction of some enaminones having a secondary amino group with diazotized aminophenols and quinone diazides was studied by Figueiredo [5b]. Upon using diazonium chlorides in aqueous methanol only the corresponding azo coupled β-dicarbonyl compounds were isolated [5b] (Scheme 10). The products of hydrolysis were assigned a structure of the azo compounds but the conclusions were made on the basis of proton NMR spectra only. When quinone diazides, in a two-phase system water-dichloromethane, were used as the active components, no hydrolysis took place and the products were azo coupled β-enaminones. Their structures (Scheme 10) was assumed based on AM1 geometry optimizations [5b].

Polygalova [5c] described the reaction of enaminones derived from 1,2,3,4-tetrahydroisoquinoline with variously substituted benzenediazonium chlorides (Scheme 11). The authors concluded that the products of azo coupling to secondary enaminones (R=H) exist in $CDCl_3$ solution as pure azo compounds. The products of azo coupling to tertiary enaminones (R=Me) also exist as pure azo compounds in the form of a mixture of *E*/*Z* isomers. However, because this assignment was made on the basis of ^1H NMR spectra only, the conclusions mentioned in the work [5c] are not reliable. The presence of one set of signals for the compounds in the work [5c] means the presence of either of the *E*/*Z* isomers only, but the isomer can be a mixture of azo/hydrazo tautomers. The possibilities of



Scheme 10. Products of azo coupling of some diazotized aminophenols to β-enaminones in dependence on reaction conditions [5b].



Scheme 11. Azo coupling to some 1,2,3,4-tetrahydroisoquinoline-based β-enaminones [5c].

azo-hydrazo and *E*/*Z* isomerisms for the compounds mentioned in the work [5c] are shown in the Scheme 11 bottom.

The structures of some products of azo coupling to enaminones were also studied in the solid state [9–12a]. Compound **4** (R = 4-MeOC$_6$H$_4$, Ar=Ph) exists in the solid state as the equilibrium mixture of the major hydrazo tautomer and the minor azo compound with an intramolecular hydrogen bond N–H···N [11]. In contrast to the situation in $CDCl_3$ solution, compounds **2** (R=H, Ar = 4-ClC$_6$H$_4$ a 4-O$_2$NC$_6$H$_4$) exist in the solid state as azo compounds where the content of the minor hydrazo tautomer is approximately the same for both the compounds (about 80–84% of the azo compound) [9]. In a crystal, the compounds **2** (R=H, Ar = 4-ClC$_6$H$_4$ and 4-O$_2$NC$_6$H$_4$) exist exclusively as *Z* isomers (lit. [9]) each containing a strong RAHB (Resonance Assisted Hydrogen Bond) [12b] N–H···N. The molecules hold together in a crystal packing through intermolecular hydrogen bonds C=O···H–N. A similar arrangement have also been found for the compound **2** (R=H, Ar = 2-ClC$_6$H$_4$) but only azo-enamino tautomer have been observed [12a]. For the enaminoester [13] ethyl 3-amino-2-(5-chloro-2-hydroxy-4-nitrophenyl)diazenylbut-2-enoate it could be concluded that, based upon the N–N bond length, the compound exists as a mixture of azo and hydrazo tautomers, where the abundance of the azo form is lower than in the case of the analogous enaminones with primary amino group. The molecule contains two intramolecular hydrogen bonds O–H···N and N–H···N.

N-Methylderivatives 2 exist in the crystalline state also as the mixtures of both the tautomeric forms [10]. In the methyl derivatives **2** studied (Ar = 4-O$_2$NC$_6$H$_4$, 4-CH$_3$OC$_6$H$_4$, 4-CH$_3$C$_6$H$_4$) the azo form predominated (80–91%) [10]. The substitution at the diazonium salt does not significantly affects the position of the tautomeric equilibrium in the solid state. The product of the azo coupling always existed as the sole Z isomer [10]. All the derivatives studied have shown similar structural features: short intramolecular RAHB N–H···N, an extended conjugation within the enaminone arrangement C=C–N and, on the contrary, a lower delocalization within diazenyl group [10].

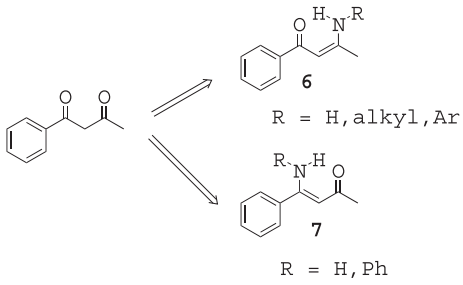
Unsymmetrical β-diketones can form two different kinds of enaminones (for the case of benzoylacetone see Scheme 12). The benzoylacetone was used as a model example for the study how different groups close to carbonyl or enamino group affect the structure of the azo coupling products.

It was established that the β-enaminone **6** (R = H), having primary amino group and benzoyl-enamino arrangement, forms the azo coupling products **8** (R=H) existing in $CDCl_3$ solution as sole *Z* isomers and the equilibrium mixture of azo and hydrazo tautomers (Scheme 13). The content of the hydrazo form depends on the substitution at the diazonium salt and increased in the order 4-NMe$_2$ ≈ 4-OMe < 4-Me < 4-NO$_2$ (the nitro derivative is practically equimolar mixture of the tautomers) [14a]. The products **8** (R = Me) of the azo coupling to 3-methylamino-1-phenylbut-2-en-1-one have the similar structure (sole *Z* isomer, the similar effect of the substituent at the diazonium salt on the tautomeric equilibrium) (Scheme 13). Branching of the alkyl chain at the amino group does not have a significant effect on the position of the tautomeric equilibrium, a *tert.*butyl group slightly favours azo compound compared to *sec.*butyl group [10]. From the data obtained by ^{15}N NMR measurements it results, that the crossing from the enaminone type **1** to the substrate type **6** does not cause a significant change of the composition of the tautomeric mixture [10,14a].

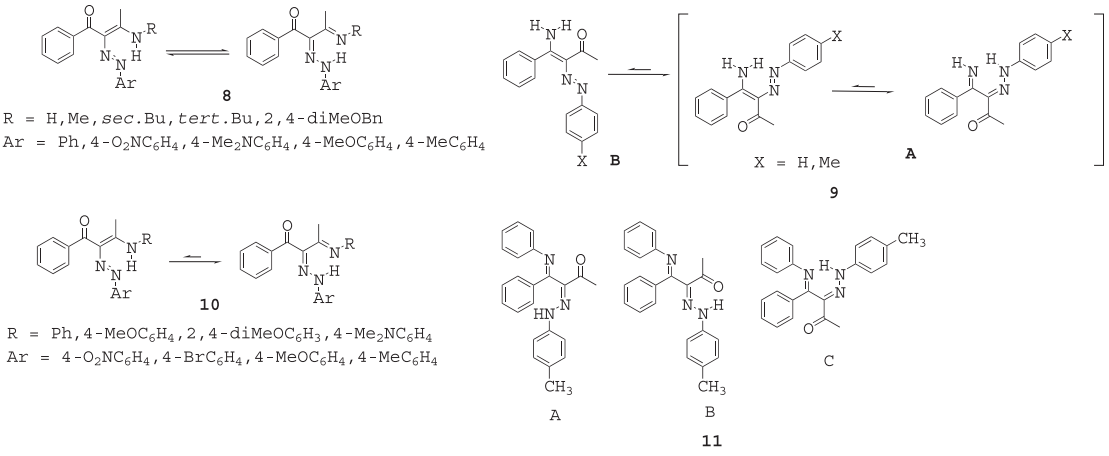
4-Amino-4-phenylbut-3-en-2-one **7** (R=H) is the representative of the β-enaminones having acetyl-enamino arrangement. The products **9** of its azo coupling with benzenediazonium and 4-methylbenzenediazonium ion exist in $CDCl_3$ solution as the equilibrium mixture of *E*/*Z* isomers **9A,B** in ratio 1:2 [14a] which is a considerable contrast to the acetylacetone derived analogues. The major isomer **9A** is predominantly the hydrazo compound (54% for X=Me, 64% for X=H) which is a remarkable difference compared to the compounds **2** and **8**. The minor isomer **9B** is practically pure azo compound, similar to the derivatives **2** (data could be acquired only for X=H with using –^{15}N=^{15}N– izotopomer). An equilibrium, having been studied by means of EXSY spectroscopy, exists between both the isomers and can be described by the scheme analogous to the Scheme 9 [14a].

In a solid state the compounds **8** (R=H, Ar = 4- Me$_2$NC$_6$H$_4$) and **9** (X=Me) are tautomeric mixtures with marked predominance of the azo form (82–85%), containing RAHB N–H···N. The molecules in the crystal hold together by means of intermolecular hydrogen bonds N–H···O=C [14a]. The simple azo coupling product **8** (R=H, X=NMe$_2$) is capable of forming 3D supramolecular channels approximately a cylindrical shape, where molecules of some aromatic compounds (benzene, toluene, chlorobenzene, *p*-xylene) are closed in a defined way [14b]. The products **8** (R = alkyl) of the azo coupling to 3-alkylamino-1-phenylbut-2-en-1-one **6** (R = alkyl) form in the solid state predominantly azo compounds (82–91%) solely in the form of the *Z* isomer [10].

The enaminones derived from benzoylacetone bearing *N*-aryl group and having the benzoyl-enamino arrangement (**6**, R = Ar)



Scheme 12. Possible β-enaminones derived from benzoylacetone.



Scheme 13. The structure of the azo coupling products from benzoylacetone enaminones.

gave by the azo coupling the products **10** existing in $CDCl_3$ solution as single isomers formed by the tautomeric mixture with strong majority of the hydrazo form (80–97% in dependence on the substitution of the starting diazonium salt, the nitroderivatives are pure hydrazo compounds) (Scheme 13). Electron donating substituents shift the equilibrium rather in favor of the azo form [14a]. This trend is similar to the one shown by acetylacetone derivatives [8]. β-Enaminone **7** (R=Ph) having acetyl-enamino arrangement allowed access, by reaction with 4-methylbenzenediazonium ion, to the compound **11**, which is the pure hydrazo form and in $CDCl_3$ solution exists as the equilibrium mixture of three isomers in the ratio 10:2:1. Their structures were determined by means of ^1H, ^{13}C and ^{15}N NMR and are shown in Scheme 13.

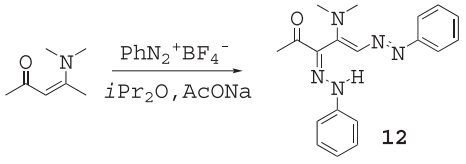
In a solid state the molecule **10** (R=Ph, Ar=4-BrC_6H_4) forms only single tautomer hydrazo-imino with RAHB N–H···N. In the crystalline state the individual molecules are bound together via intermolecular short-contact Br···O which can be interpreted as an intermolecular charge–transfer complex between the free electron pair on oxygen and LUMO of the C–Br bond [14a].

By comparing the structure of the products **2**,**4**,**5**,**8**–**10** in the solid state and in the solution it could be stated that the structure in the solution is much more sensitive both to the influence of the substituents at the diazonium salts and to the structure of the starting β-enaminone than in the solid state. In the solid state the most significant effect on the structure of the azo coupling products has the substitution of the enamino group. There is no large difference between primary amino group and *N*-alkyl group or between the type of the enaminone (acetylacetone vs. benzoylacetone derivatives). In contrast to the other compounds type **10** (Scheme 13) studied the derivative **10** (R=Ph, Ar=4-BrC_6H_4) exists in the solid state only as a sole tautomer hydrazo-imino, where the hydrazo and imino group are connected through an intramolecular hydrogen bond [14a]. In the similar derivative **4** (R = 4-$MeOC_6H_4$, Ar=Ph) a considerable shortening of the intramolecular hydrogen bond has been observed. The hydrogen of the intramolecular hydrogen bond is situated in the middle of both the nitrogens [11]. These differences compared to the other acetylacetone derivatives have been explained by electronic effects of the substituents (MeO and Br) [14a].

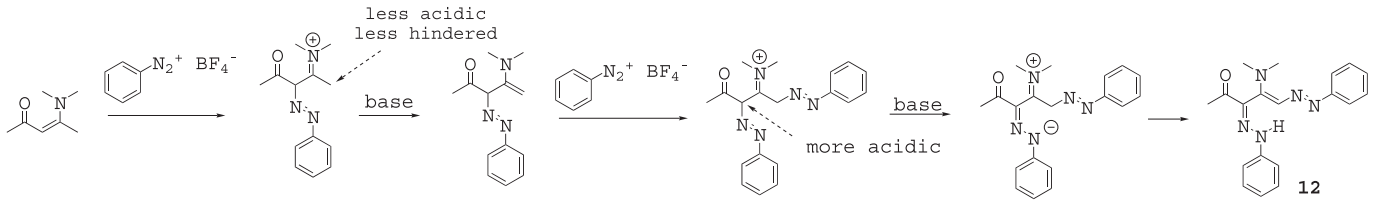
2.2. Acyclic β-enaminones bearing a tertiary amino group

In the case of the enaminone with tertiary amino group it was possible to expect a different behaviour towards diazonium ion due to the absence of N–H proton whose elimination stabilizes the positively charged intermediate, formed during the course of the azo coupling reaction, and forms the azo coupling product (see the mechanism in Scheme 6). Reaction of 4-dimethylaminopent-3-en-2-one with benzenediazonium tetrafluoroborate in the molar ratio 1:1 gave a red substance with the elemental composition expressed with formula $C_{19}H_{21}N_5O$ [15]. Based on the NMR analysis (especially on ^{15}N NMR), the structure of the substance was proved to be 4-dimethylamino-5-phenyldiazenylpent-4-en-2,3-dione 3-phenylhydrazone (**12**) (Scheme 14) i.e. the reaction of two molecules of diazonium ion with one molecule of the enaminone took place. In the case of the acyclic enaminones bearing primary and secondary amino group the formation of the double azo coupling product has not been observed so far [8–10,14a]. Another azo coupling to enaminones with tertiary amino group has been mentioned above and quite different behaviour towards diazonium salts have been observed (Scheme 11) [5c].

The structure of **12** was subsequently confirmed by X-ray analysis. In addition to that, the X-ray analysis also proved the molecule formed dimers having a centre of symmetry. The molecules in the dimer are held together through weak intermolecular hydrogen bonds N–H···N. Temperature and concentration NMR studies of the product revealed that the equilibrium between monomer and dimer also existed in $CDCl_3$ solution [15]. Beside compound **12** the 3-phenylhydrazone of pentane-2,3,4-trione **3** (Ar=Ph) has always been formed as a by-product. The optimal molar ratio diazo: enaminone has appeared to be 2:1 (yield of **12** being about 30%). Further increasing of the ratio led to increased contamination of the reaction mixture with the decomposition products from the diazonium salt and, hence, to decreasing of the yield of the compound **12**. The product **12** is very sensitive to acidic impurities. The course of the azo coupling described by Šimůnek represented a new kind of double azo coupling at aliphatic substrates [15]. The only products of double azo coupling at aliphatic substrates described by that time had been formazans. Similar behaviour has not been so far observed in the reaction of acyclic enaminone bearing primary or secondary amino group. An attempt was made to explain the difference in behaviour of the enaminone with tertiary amino



Scheme 14. Formation of the unusual azo coupling product [15].



Scheme 15. Suggested reaction path to the unusual azo coupling product 12 [15].

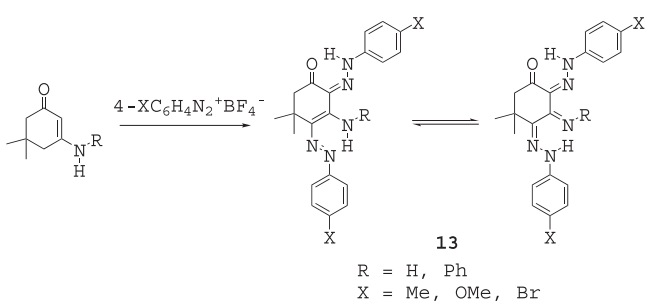
group compared to the enaminones bearing primary or secondary amino group and a hypothesis was created on the mechanism of formation of the product **12** (Scheme 15). The tautomeric form of the potential intermediate is unknown. The product of the single azo coupling have never been isolated, hence, the second attack of the diazonium salt must be faster than the first one.

2.3. Cyclic β-enaminones

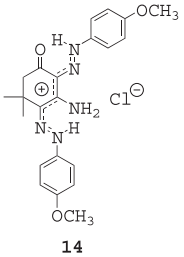
The goal of further research was to study the structure of the products of azo coupling of benzenediazonium ions with cyclic β-enaminones [16a,17]. The structure of the products **13** from the reaction of 3-amino-5,5-dimethylcyclohex-2-en-1-one derivatives with substituted benzenediazonium ions is presented in Scheme 16. The products of the double azo coupling have been formed in every case, regardless of the type of amino group substituent, even at the equimolar ratio of the reacting component. Only in one case of **13** (R═H, X═OMe) were there observed traces of the single azo coupled product [16a]. These observations suggest that the second azo coupling is faster than the first one. The reason why the enaminones derived from dimedone behave differently to the acyclic examples in not clear. On the other hand Al-Mousawi by reaction of 3-amino-5,5-dimethylcyclohex-2-en-1-one with benzenediazonium chloride in aqueous ethanol obtained a product of single azo coupling [16b] (Scheme 17). The tautomeric form hydrazo-imino was, however, determined on the basis of proton NMR spectroscopy only [16b].

Tautomeric equilibrium of the group at the 2- position is always shifted quite to the hydrazo form (Scheme 16). The tautomeric form of the group at the 4- position is affected by both the kind of the amino group and the substituents at the diazonium salt [16a]. In the case of the *N*-phenylderivatives **13** (R═Ph) the substituent at the 4-position is in the tautomeric hydrazo form, whereas at the products **13** bearing primary amino group (R═H) the tautomeric mixture was formed, where the azo-hydrazone equilibrium at the 4-position was affected by the kind of the substituent X at the diazonium salt (4-Me and 4-Br derivatives were predominantly hydrazones and 4-OMe derivative predominantly the azo compound) [16a].

The product of the reaction of 3-amino-5,5-dimethylcyclohex-2-en-1-one (Scheme 16, R═H) with 4-methoxybenzenediazonium tetrafluoroborate forms on standing in chloroform the stable hydrochloride **14** whose structure was studied in the solid state [17].

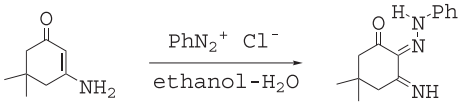


Scheme 16. Azo coupling to the dimedone-derived β-enaminones [16a].

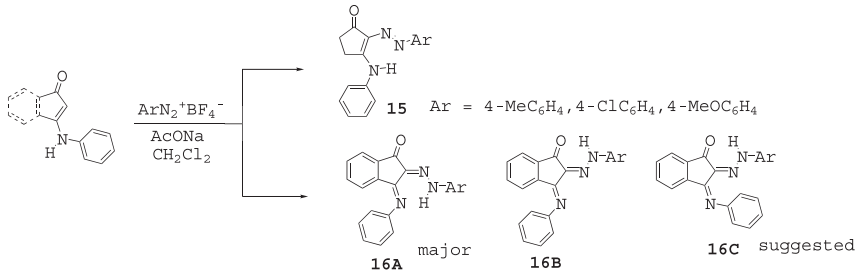


Reduction of the ring size of the starting enaminone led to a significant change of the behaviour towards diazonium ions. 3-Phenylaminocyclopent-2-en-1-one reacts with only one molecule of the diazonium salt even in the case of the double molar excess of the diazonium salt [17]. The products **15** exist in $CDCl_3$ solution (Scheme 18) as the practically pure azo compounds. By that time the presence of the *N*-phenyl group in the molecule of the starting enaminone had always meant the shift the equilibrium distinctively towards the hydrazo form. Practically pure azo form was in the case of **15** (Ar = 4-MeC_6H_4) evidenced also in a solid state [17].

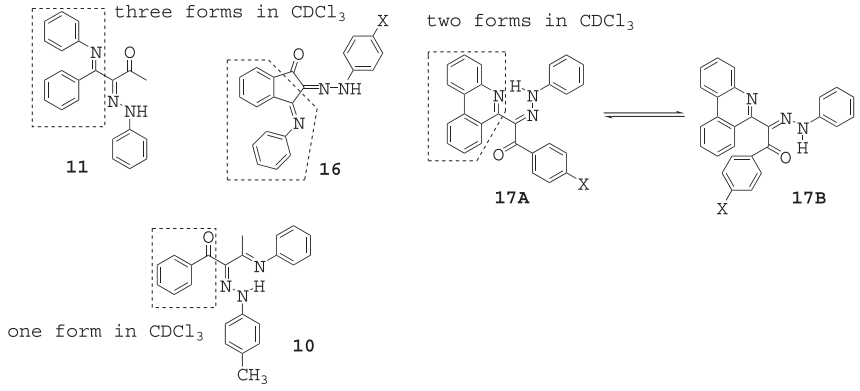
An annelation of the benzene ring to the molecule of the five-membered cyclic enaminone caused inversion of the position of the tautomeric equilibrium [17]. 3-Phenylamino-1*H*-inden-1-one gave by the reaction with benzenediazonium and 4-methylbenzenediazonium tetrafluoroborate, a mixture of practically pure hydrazo compounds **16A**–**C** in spite of the fact that the molecules of the product **16A**–**C** having azo-enamino arrangement would experienced more extended conjugated system (Scheme 18). The ratio of hydrazones **16A**–**C** in $CDCl_3$ solution is approximately 30:6:1. The ratio practically did not change after either the change of the solvent to DMSO (26:9:1) or a repeated recrystallization from various solvents. The structures of the first two forms (**16A,B**) were determined by the help of selectively ^{15}N enriched sample and the structure of the third one (**16C**) was, with regard to the low abundance, estimated on the basis of the uncomplete set of NMR parameters [17] (Scheme 18). In a crystalline state the compound **16** (Ar═Ph) exists as the form **16A** being a mixture of the imino-hydrazono and enamino-diazenyl tautomers in the ratio 89:11, i.e. even in the solid state the annelation of the benzene ring to the five-membered cyclic enaminone caused the shift towards the hydrazo form [17]. The similar trend have also been observed in aromatic row where the shift from phenols towards naphthalenols and anthracene-9-ol induced the shift of the azo-hydrazone tautomerism towards the hydrazo form [6e].



Scheme 17. Observation of single azo coupled β-enaminone upon azo coupling to dimedone-based β-enaminone [16b].



Scheme 18. Azo coupling products from five-membered cyclic β-enaminones [17].



Scheme 19. Relationships between the structure of the azo coupling product and the number of its forms.

The azo coupling products **16A–C** were the second case where the existence of the several forms in the product of azo coupling to the enaminone with *N*-phenyl group was observed. The first one was described in the [14a]. The common feature of each case is the presence of a phenylimino group in the neighbourhood of a phenyl group. In accordance with this are results obtained for some azo coupled derivatives of phenanthridine **17**, where the presence of two isomeric hydrazones (**17A,B**) differing in the kind of an intramolecular hydrogen bond was observed [18]. In the case when there was a carbonyl group next to the phenyl group (e.g. product **10**) only a single form of the azo coupling product has been observed [14a] (Scheme 19).

3. Conclusions

The products of the reaction of substituted benzenediazonium salts with various kinds of β-enaminones have shown a number of interesting structural phenomena.

From the amount of experimental data, obtained during a long-term study of the tautomerism of the azo coupling products it has been found out that the shift from oxygen substrates (phenols, naphthalenols, anthracene-9-ol) towards their nitrogen analogues (anilines, naphthylamines, aminoanthracenes) have meant the shift of the position of the tautomeric equilibrium towards the azo form. A survey of the results on this field was made by Lyčka [6b,c].

The above-mentioned trend is also manifested in the aliphatic series, where change from β-diketones (pure hydrazo compounds [19]) to their nitrogen derivatives β-enaminones (a mixture of tautomers) means the enhancement of the tendency of making up the azo form in this order.

In the product **8** (Ar = 4-$Me_2NC_6H_4$) the ability of formation of supramolecular structures with some aromatic guest-molecules (toluene, benzene, chlorobenzene, *m*- and *p*-xylene) has recently been proved [14b]. For some products of azo coupling to β-enaminones a potential for nonlinear optics was proposed [5b]. These results, together with the above-mentioned structural properties, indicate that the products of azo coupling to β-enaminones, although simple and easily preparable, exhibit a number of interesting and ofter surprising properties.

Acknowledgement

Authors are indebted to the Ministry of Education, Youth and Sports of the Czech Republic for finantial support (Project MSM 002 162 7501).

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