Asymmetric induction in the reactions of azinones with C-nucleophiles

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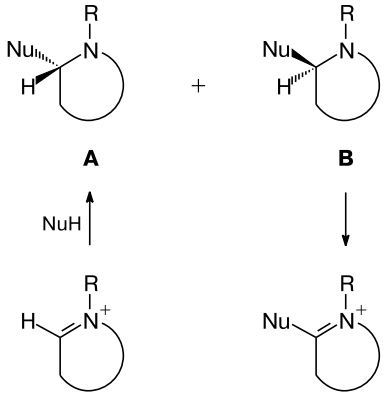
Effect of acylating agents on the course of addition of C-nucleophiles to 1,2,4- and 1,3,5-triazinones, as well as to quinoxalin-2(1*H*)-one, was studied. A series of new azinone derivatives was obtained. A method for the preparation of diastereomerically pure addition products of indoles to 1,2,4-triazinones and quinoxalin-2(1*H*)-one in the presence of *N*-Ts-L-amino acid acyl chlorides was suggested.

Key words: triazinones, 1,2,4-triazin-5(4*H*)-one, 1,2,4-triazin-3(2*H*)-one, 1,3,5-triazin-2,4(1*H*,3*H*)-one, quinoxalin-2(1*H*)-one, diastereoselective synthesis, aromatic nucleophilic addition, C-nucleophiles, amino acid acyl chlorides, indoles.

Nucleophilic substitution reactions of hydrogen (S_N^H) in the series of π-deficient (hetero)aromatic compounds are common for a wide class of two-step processes[1] (Scheme 1), which are characterized by formation in the first step of nucleophilic addition products, σ^H-adducts **A** and **B**, due to *the direct* attack by nucleophiles on the *unsubstituted* carbon atom of the azine ring.

Scheme 1



Appearance of stereoisomers during formation of σ^H-adducts in the reactions of this type can be due to the introduction of chiral catalysts into the reaction[2—4] or the use of an enantiomerically pure substrate[2,5—7] and/or nucleophile.[2,8] An asymmetric carbon atom, directly or indirectly incorporated into the substrate molecule (for example, by *in situ* acylation), should determine stereochemistry of the addition product formed, *i.e.*, induce stereoselective formation of new asymmetric center upon attack by an achiral nucleophile. In the ideal case, an individual stereoisomer can be the addition product. For instance, known addition of the Grignard reagents and allylsilanes to homochiral pyridin-4-one *N*-acylium salts, obtained *in situ* upon the action of optically active chloroformates, allows one to reach a high degree of asymmetric induction (*de* = 88—98) and leads to substituted pyridones in high yields.[2,5] Stereoselective addition of nucleophiles to quinolines or isoquinolines occurs when amino acid acyl fluorides are used as auxilliary chiral agents in the presence of Lewis acids.[6] We have briefly described a stereoselective reaction of indole with 3-phenyl-1,2,4-triazin-5-one in the presence of amino acids activated with DCC[7] and with 6-phenyl-1,2,4-triazin-5-one in the presence of mixed amino acid anhydrides.[9]

In the present work, we in details consider how the nature of acylating agents and structure of the substrate affect stereochemistry of the addition products of C-nucleophiles to 1,2,4- and 1,3,5-triazinones **1—4**, as well as to quinoxalin-2(1*H*)-one **5**.

Initially, we studied nucleophilic addition reaction to the azine ring in the presence of acetic anhydride. The whole series of azinones **1—5** studied react with C-nucleophiles under these conditions. Earlier, for 3-phenyl-1,2,4-triazin-5-one **1** we have already described addition reactions of indoles and pyrroles in acetic anhydride with the formation of the corresponding 6-indolyl- or 3-phe-

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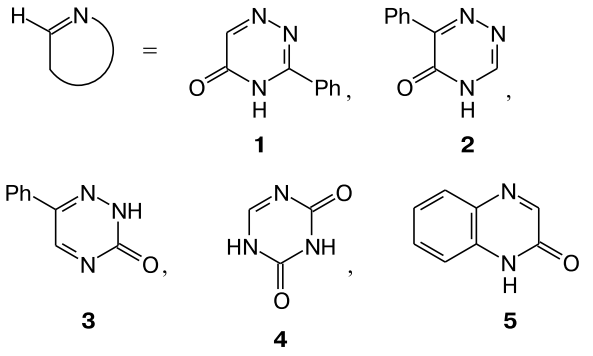
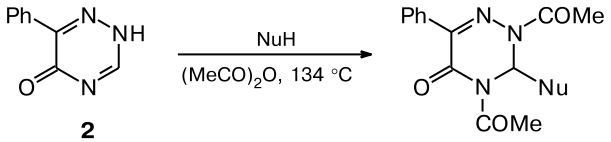


1 **2** **3** **4** **5**

nyl-6-pyrrolyl-1,6-dihydro-1,2,4-triazin-5(4*H*)-ones.[10] In the present work, it was found that reflux of 6-phenyl-1,2,4-triazin-5(2*H*)-one (**2**) with indoles in acetic anhydride smoothly leads to 2,4-diacetyl-3-indolyl-6-phenyl-1,2,4-triazin-5(2*H*)-ones **6—8** (Scheme 2, Table 1). It is noticeable that both nitrogen atoms placed in α-positions to the reaction center undergo acylation.

Scheme 2



2 **6—8**

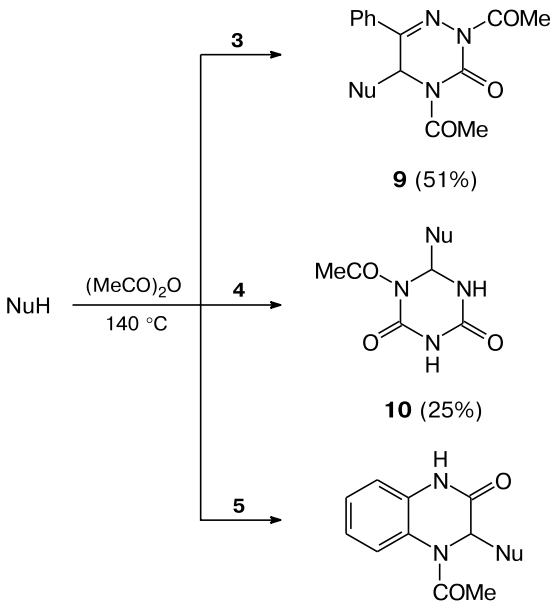
Table 1. Synthesis of compounds **6—8**

NuH	Product	Yield (%)
Indole	**6**	79
1-Me-Indole	**7**	62
2-Me-Indole	**8**	43

6-Phenyl-1,2,4-triazin-3(2*H*)-one (**3**) behaves similarly in this reaction, which leads to 2,4-diacetyl-5-(1*H*-indol-3-yl)-6-phenyl-4,5-dihydro-2*H*-1,2,4-triazin-3-one (**9**). The reaction of 1,3,5-triazine-2,4(1*H*,3*H*)-dione (**4**) with indole in acetic anhydride affords 1-acetyl-6-(1*H*-indol-3-yl)-1,3,5-triazinane-2,4-dione (**10**), whereas 4-acetyl-3-(1*H*-indol-3-yl)-3,4-dihydroquinoxalin-2(1*H*)-one (**11**) was obtained from quinoxalin-2(1*H*)-one **5** (Scheme 3).

Study of the possibility to carry out this reaction in the presence of *p*-toluenesulfonyl chloride as a compound close in structure to amino acid acyl chlorides, which were further used as the chiral acylating agents, showed that in the case of 3-phenyl-1,2,4-triazin-5(4*H*)-one (**1**) and 1,3,5-triazine-2,4(1*H*,3*H*)-dione (**4**) formation of the nucleophilic addition products of indoles, **12** and **16**, respectively, takes place in the temperature interval

Scheme 3

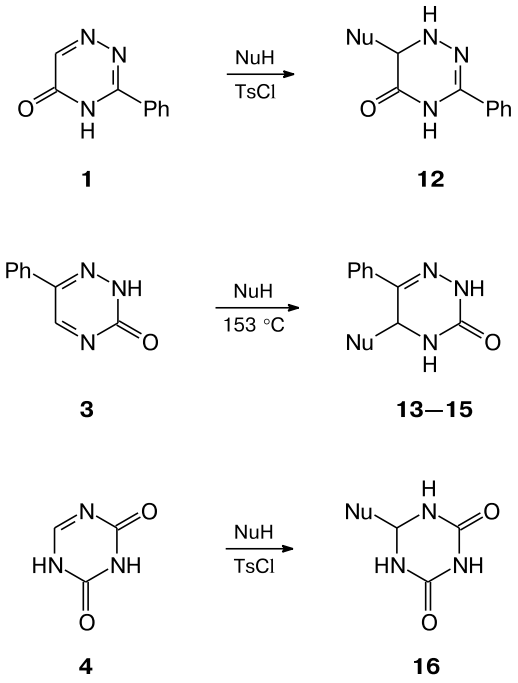


9 (51%) **10** (25%) **11** (62%)

Nu is the 3-indole

−15÷−10 °C. Compounds **12** and **16** contain no tosyl fragment, though the presence of tosyl chloride is necessary for the process to be successful, since no reaction takes place if it is absent (see Scheme 4, Table 2). 6-Phenyl-1,2,4-triazin-5(2*H*)-one (**2**) and 6-phenyl-

Scheme 4



1 **12** **3** **13—15** **4** **16**

Table 2. Synthesis of compounds **12—16**

Triazinone	NuH	Product	*T*/°C	Yield (%)
1	Indole	**12**[10]	−15	65
2	Indole	—	−15	—
	Indole	—	153	—
3	Indole	**13**	153	92
	1-Me-Indole	**14**	153	80
	2-Me-Indole	**15**	153	95
4	Indole	**16**[11]	−15	85

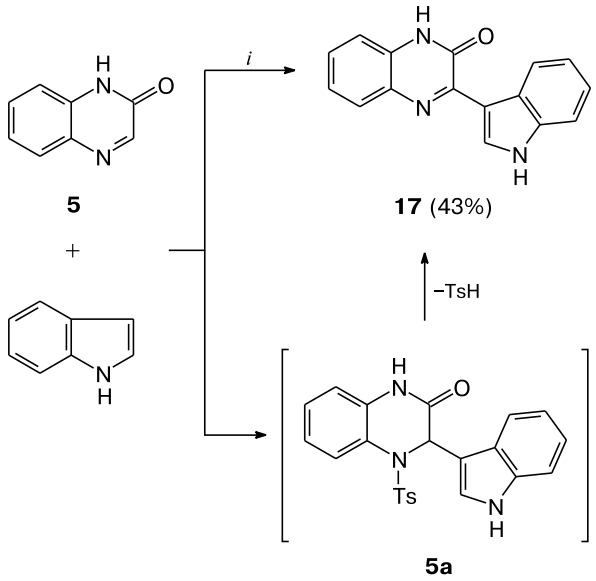
1,2,4-triazin-3(2*H*)-one (**3**) give no reaction at low temperatures, however, when the reaction was performed in boiling DMF, a number of nucleophilic addition products were obtained for triazinone **3** both in the presence and in the absence of *para*-toluenesulfonyl chloride.

In the reaction of quinoxalin-2(1*H*)-one (**5**) with indole, nucleophilic substitution product **17** was isolated. This reaction proceeds similarly to the Reissert reaction, that allows one to suggest that compound **5a** is formed as an intermediate product, possessing structure similar to that of the Reissert compounds (Scheme 5).

To sum up, the experiments described showed a principal possibility of the formation of nucleophilic addition products, as well as hydrogen substitution in the reaction of a number of triazinones **1—4** and quinoxalinone **5** with nucleophiles in the presence of acylating agents. These data allowed us to suggest a possibility to use optically active acylating agents in this reaction and obtain diastereomerically pure products. In the present work, *N*-Ts-L-valine **18** and *N*-Ts-L-leucine **19** were used as such reagents.

3-Phenyl-1,2,4-triazin-5(4*H*)-one (1). The reactions of triazinone **1** with C-nucleophiles in the presence of acyl chlorides of *N*-Ts-L-valine **18** or *N*-Ts-L-leucine **19** at temperatures of −15÷−10 °C leads to a number of 6-substituted 1-(2-tosylamino)acyl-6-aryl-3,4-dihydro-1,2,4-triazin-5(4*H*)-ones **20—25** in the yield from 15 to 77% and in some cases with high diastereoselectivity (Scheme 6). The use of *N*-Ts-L-valine as the acylating agent produces higher diastereoselectivity. The content

Scheme 5

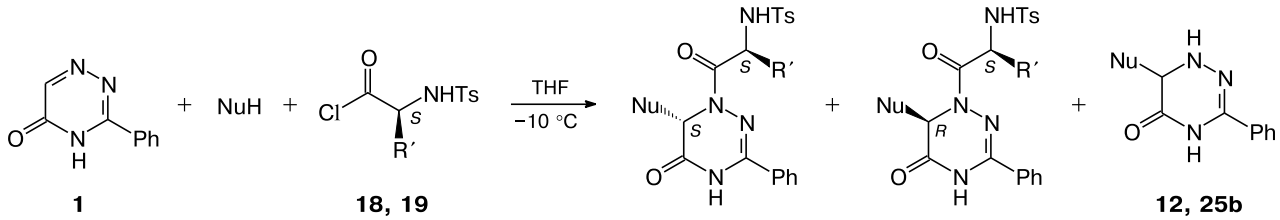


i. TsCl, −15÷−10 °C.

of *S*,*S*-isomers **21** and **24** in the reaction mixture reaches 90—95% (^{1}H NMR data). After purification on a column, the ^{1}H NMR spectrum of the product exhibits only one set of signals. Assignment of the signals was made based on the ^{1}H NMR spectrum of compound **24**, the absolute stereoconfiguration of which was determined by X-ray diffraction (Fig. 1), as well as with allowance for the known configuration of the chiral center in *N*-Ts-L-valine. In the general case, the ^{1}H NMR spectra of the reaction mixtures exhibit two close sets of signals, whereas only one set of signals is found in the spectra of isolated compounds. Adducts **12** and **25b** containing no acyl fragment are the minor products at low temperatures in some cases, which become predominant when the reaction temperature is elevated to ambient. No reaction was observed at temperatures below −15 °C (see Scheme 6, Table 3).

As an explanation of the asymmetric induction observed, it can be suggested that formation of

Scheme 6



R′ = $CHMe_2$ (**18**), CH_2CHMe_2 (**19**)

Scheme 7

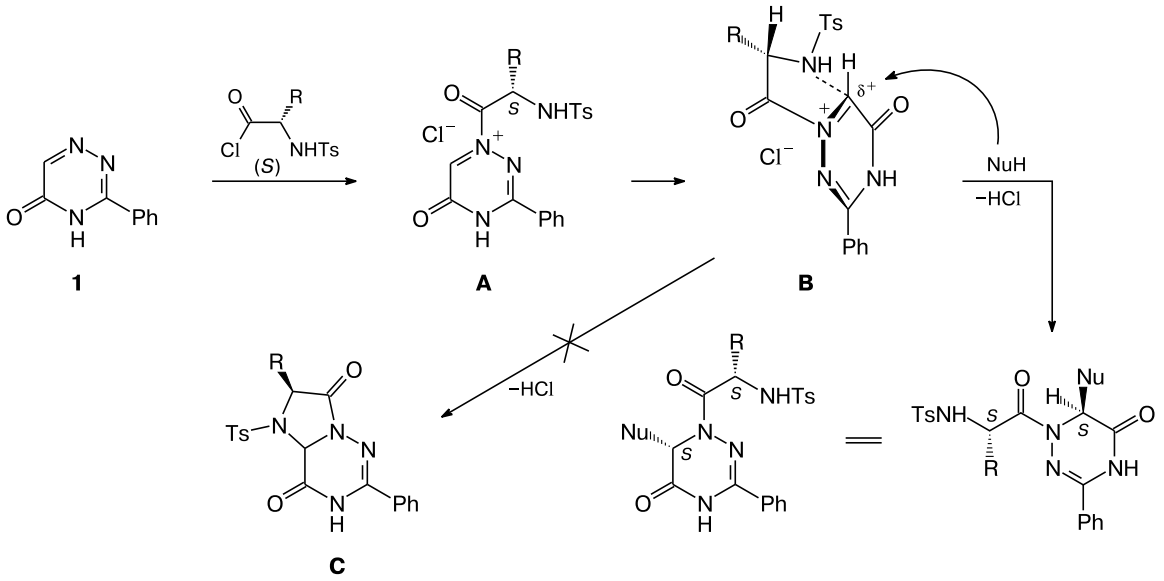


Table 3. Reactions of triazinone **1** with C-nucleophiles in the presence of acyl chlorides **18** and **19**

NuH	R´	*T*/°C	*S,S* : *S,R*[a]	*S,S* : *S,R*[b]	Product (yield (%))
Indole	CH_2CHMe_2	−15	60 : 40	>95 : 5	(*S,S*)-**20** (15)[b], **12**[10] (<5)
	CH_2CHMe_2	20	45 : 55	>95 : 5	(*S,S*)-**20** (10)[b], **12**[10] (36), (*S,R*)-**20** (5)[b]
	$CHMe_2$	−15	90:10	>95 : 5	(*S,S*)-**21** (77)[b]
1-Me-Indole	CH_2CHMe_2	−15	55 : 45	>95 : 5	(*S,S*)-**22** (65)[b]
2-Me-Indole	CH_2CHMe_2	−15	65 : 35	>95 : 5	(*S,S*)-**23** (42)[b]
	$CHMe_2$	−15	>95 : 5	>95 : 5	(*S,S*)-**24** (32)[b]
1-Me-Pyrrole	CH_2CHMe_2	−15	60 : 40	>95 : 5	(*S,S*)-**25a** (15)[b], **25b**[10] (7)

[a] *dr* in the reaction mixture.
[b] *dr* after separation on a chromatographic column.

N-acylazinium salt takes place in the course of the reaction (Scheme 7, structure **A**), in which there is present a dipole-dipole interaction between the nitrogen atom of the amino acid fragment and electrophilic carbon atom of the heterocycle (structure **B**). As a result, one of the sides of the heterocycle becomes sterically hindered for the attack by a nucleophile (see Scheme 7). According to the literature data,[6] the amino group in *N*-Ts-amino acids is a strong enough nucleophile to form a covalent bond with the carbon atom of the C=N bond of azaheterocycle (isoquinoline), however, no formation of the corresponding bicyclic product was observed in the reactions studied.

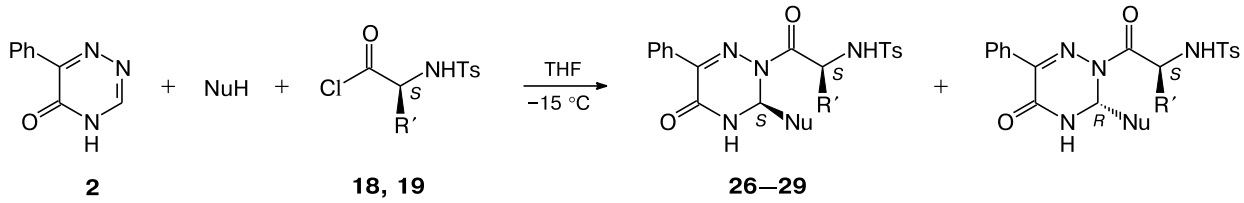
6-Phenyl-1,2,4-triazin-5(4*H*)-one (2). The reaction with C-nucleophiles and amino acid acyl chlorides (**18**, **19**) leads to the formation of a number of 3-substituted 2-(2-tosylamino)acyl-6-aryl-3,4-dihydro-1,2,4-triazin-5(4*H*)-ones (**26—29**) in moderate yields and low diastereoselectivity. After separation on a chromatographic column, diastereoisomers were isolated having only one set of signals in their ^{1}H NMR spectra (Scheme 8, Table 4).

The absolute configuration of compounds obtained was determined based on the X-ray diffraction analysis data for compound **27**,[13] as well as on the known configuration of the amino acid fragment, which showed that the compound is a *S,S*-diastereomer.

It is obvious that *N*-acyl derivative **2*** is formed in the course of the reaction, however, relatively low electrophilicity of the carbon atom C(3) of the triazine ring leads to the fact that no sterical hindrance arises for the attack by nucleophile in contrast to position C(6) in triazinone **1** and the reaction results in the formation of diastereomers in approximately equal proportion (Scheme 9).

6-Phenyl-1,2,4-triazin-3(2*H*)-one (3) gives no reaction with C-nucleophiles in the presence of amino acid acyl chlorides in the temperature range from −15 to +25 °C. The use of ester and carbodiimide methods for the activation of amino acids did not result in obtaining amino acid derivatives of triazinone **3**.

Scheme 8



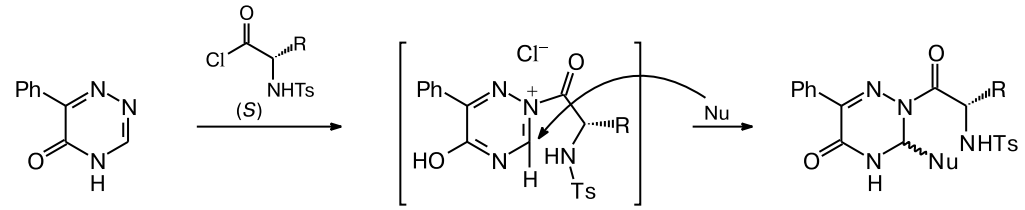
2 **18, 19** **26—29**

Table 4. Reactions of triazinone **2** with C-nucleophiles in the presence of amino acid acyl chlorides **18** and **19**

Compound	R′	NuH	*S,S* : *S,R*[a]	*S,S* : *S,R*[b]	Product	Yield[b] (%)
19	CH_2CHMe_2	Indole	55 : 45	>95 : 5	**26**	52
18	$CHMe_2$	Indole	65 : 35	>95 : 5	**27**	23
19	CH_2CHMe_2	1-Me-Pyrrol	—	>95 : 5	**28**	15
18	$CHMe_2$	1-Me-Indole	50 : 50	>95 : 5	**29**	32

[a] *dr* in the reaction mixture.
[b] *dr* after separation on a chromatographic column.

Scheme 9



2 **2***

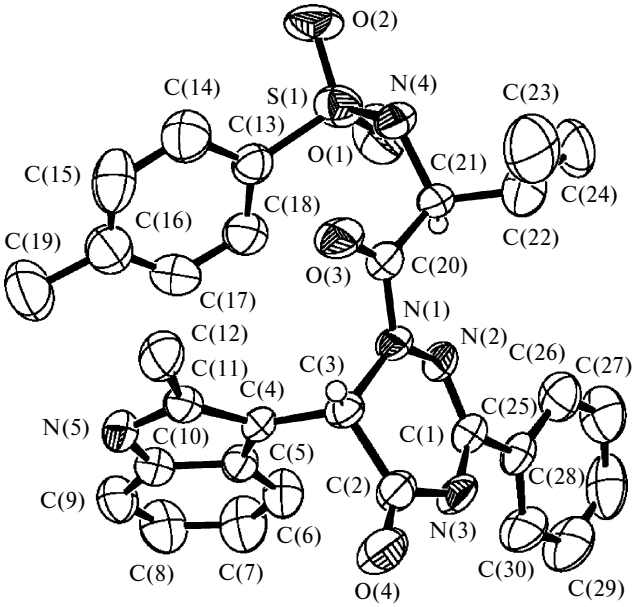
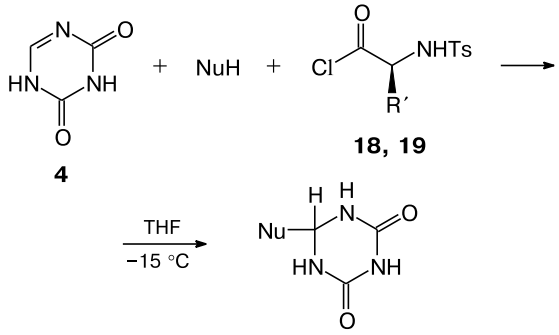


Fig. 1. General view of molecule **24** (see Ref. 12).* Nonhydrogen atoms are given as ellipsoids of thermal vibrations (p = 50 %). Hydrogen atoms are not shown.

* These data are available at: www.ccdc.cam.ac.uk/data_request/cif.

1,3,5-Triazin-2,4(1*H*,3*H*)-dione (4) forms no expected acylated σ^H-adducts with C-nucleophiles in the presence of amino acid acyl chlorides **18** and **19** in the temperature range from −15 to +25 °C either, nucleophilic addition products **16** and **30** containing no amino acid fragment were isolated instead, which are analogous to those described in the literature,[11] rather obtained in higher yields (Scheme 10, Table 5).

Scheme 10



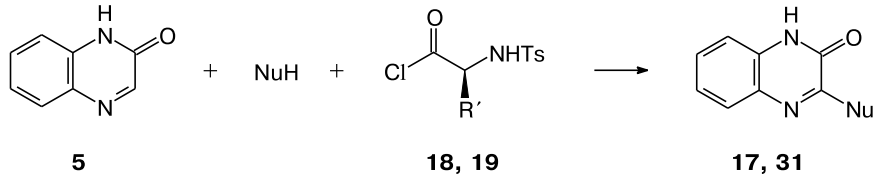
4 **18, 19** **16, 30**

Table 5. Reactions of compound **4** with C-nucleophiles in the presence of amino acid acyl chlorides **18** and **19**

Product	NuH	R´	Yield (%)
16[11]	Indole	$CHMe_2$	43
30	2-Me-Indole	CH_2CHMe_2	35

Quinoxalin-2(1*H*)-one (5). The reaction of quinoxalin-2(1*H*)-one with indoles and amino acid acyl chlorides **18** and **19** in the temperature range from −40 to +25 °C gives rise only to 3-indolylquinoxalin-2(1*H*)-ones **17** and **31** (Scheme 11, Table 6). Formation of the S_N^H products in this reaction allows us to suggest that amino acid acyl chlorides play here the same role as the acylating agent in the Reissert reaction.

Scheme 11

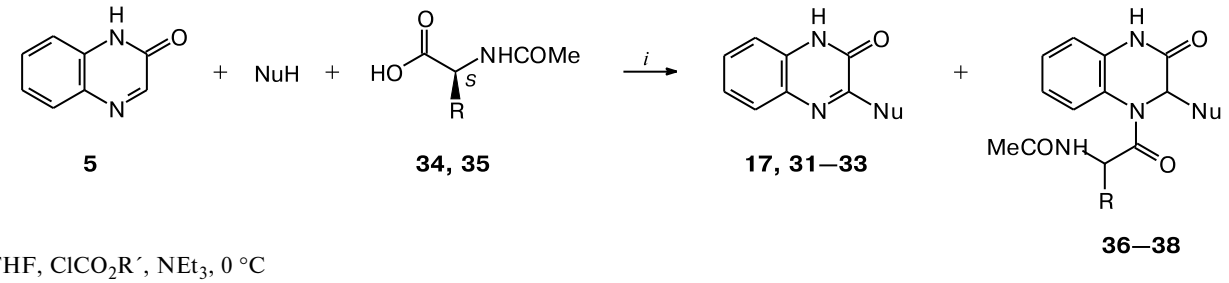


5 **18, 19** **17, 31**

Table 6. Reactions of quinoxalinone **5** with C-nucleophiles in the presence of amino acid acyl chlorides **18** and **19**

NuH	R´	Conditions		Product	Yield (%)
		Solvent	*T*/°C		
Indole	$CHMe_2$	THF	−15—−10	**17**[14,15]	37
2-Me-Indole	CH_2CHMe_2	THF	−15—−10	**31**	21
	$CHMe_2$	THF	−15—−10	**31**	35
	$CHMe_2$	THF	−40—−10	**31**	13
	$CHMe_2$	DCM	−15—−10	**31**	25

Scheme 12



i. THF, $ClCO_2R´$, NEt_3, 0 °C

R = $CHMe_2$ (**34**), CH_2CHMe_2 (**35**)

Table 7. Reactions of quinoxalinone **5** with amino acid derivatives **34** and **35**

NuH	R	R´	Solvent	Product (yield (%))
Indole	$CHMe_2$	Et	THF	**17**[12,13] (8), **36** (6)
Indole	$CHMe_2$	Et	DCM	**17** (<5%), **36** (4)
2-Me-Indole	$CH_2CH(CH_3)_2$	Et	THF	**31** (12)
	CH_2CHMe_2	Bu^i	THF	**31** (6), **37** (4)
1-Me-Indole	CH_2CHMe_2	Et	THF	**32** (12)
	$CHMe_2$	Et	THF	**32** (15), **38** (3)
Pyrrole	$CHMe_2$	Et	THF	**33**[16] (<5%)

Replacement of amino acid acyl chlorides by *N*-Ac-amino acid **34** and **35**, activated due to the formation of mixed anhydrides,[9] leads to a decrease in the yields of compounds **17**, **31—33**; expected acylated products **36—38** were isolated in low yields in some cases (Scheme 12, Table 7).

The low yields of compounds **36—38** did not allow us to carry out X-ray diffraction analysis to determine their absolute stereochemical structures. The use of activation method for the amino acids including formation of mixed anhydrides leads to racemization of the asymmetric center in the amino acid.[9] However, only one set of signals is observed in the ^{1}H NMR spectra of compounds **36—38**, this indicates that they are a single pare of diastereomers (*SS*,*RR* or *SR*,*RS*).

Experimental

Azinones **1**,[17] **3**,[18] amino acid acyl chlorides **18**, **19** used in the work were synthesized according to the known procedures, the rest of starting materials are commercially available. The solvents were dried using standard procedures; TLC analysis was performed on Merck silica gel $60F_{254}$ plates using the UV light for visualization. Column chromatography was performed using Merck 60 silica gel. ^{1}H and ^{13}C NMR spectra were recorded on a Bruker DRX-400 and Bruker WH-250 spectrometers using $SiMe_4$ as an internal standard. Optical rotation was measured on a Perkin Elmer model 341 polarimeter. X-ray diffraction analysis for compound **24** (Table 8) was performed using Oxford Diffraction Xcalibur S CCD diffractometer with the CrysAlisPro soft ware. The structure was solved by the direct method using the SHELXS-97 program package and refined by the least-squares full-matrix method on F^2 using the SHELXL-97 program.

6-Phenyl-1,2,4-triazin-5(2*H*)-one (2). A solution of 5-cyano-6-phenyl-1,2,4-triazine[19] (10 g, 0.055 mol) in dichloromethane (100 mL) was added to aqueous NaOH (2 *M*, 200 mL). The mixture was stirred for 3 h at room temperature, then the aqueous layer was separated and washed with dichloromethane. Concentrated hydrochloric acid was added with stirring to the aq. solution obtained to pH 5. A precipitate formed was filtered off and recrystallized from ethanol. The yield was 5.3 g (55%), cream crystalline powder, m.p. 203—204 °C. ^{1}H NMR (400 MHz, DMSO-d_6), δ: 13.73 (br.s, 1 H, NH); 8.56 (s, 1 H, CH); 8.10—8.13 (m, 2 H, Ph); 7.40—7.45 (m, 3 H, Ph). Found (%): C, 62.23; H, 4.33; N, 24.52. $C_9H_7N_3O$. Calculated (%): C, 62.42; H, 4.07; N, 24.26.

Quinoxalin-2(1*H*)-one (5). A solution of glyoxalic acid monohydrate (11.9 g, 0.13 mol) in water (10 mL) was slowly added to a solution of *ortho*-phenylenediamine (14 g, 0.13 mol) in methanol (50 mL) at 0 °C. The dense mass obtained was stirred for 30 min, a precipitate formed was filtered off and recrystallized from ethanol. The yield was 15.1 g (80%), colorless crystalline powder, m.p. 268—269 °C. ^{1}H NMR (400 MHz, DMSO-d_6), δ: 12.33 (br.s, 1 H, NH); 8.07 (s, 1 H, C(3)H); 7.72 (dd, 1 H, J = 8.0 Hz, J = 1.2 Hz); 7.44—7.48 (m, 1 H); 7.29 (dd, 1 H, J = 8.2 Hz, J = 1.0 Hz); 7.21—7.26 (m, 1 H, CH). Found (%): C, 65.71; H, 4.09; N, 19.22. $C_9H_7N_3O$. Calculated (%): C, 65.75; H, 4.14; N, 19.17. Physico-chemical characteristics and spectral data of compound obtained agree with those reported in the literature.[20]

Synthesis of compounds 6—8 (general procedure). A mixture of 6-phenyl-1,2,4-triazin-5(2*H*)-one (**2**) (1 mmol) and the corresponding nucleophile (1.1 mmol) was refluxed in acetic anhydride (3 mL) for 3 h. A precipitate was formed upon cooling to room temperature. If no precipitate was formed immediately, the reaction mixture was diluted with hot water. A precipitate formed was filtered off and recrystallized from 50% aq. propan-2-ol.

2,4-Diacetyl-3-(1*H*-indol-3-yl)-6-phenyl-3,4-dihydro-2*H*-[1,2,4]triazin-5-one (6). The yield was 79%, yellow crystalline powder, m.p. 232—233 °C. ^{1}H NMR (400 MHz, DMSO-d_6), δ: 11.14 (br.s, 1 H, NH); 8.41 (d, 1 H, C(3)H, J = 0.6 Hz); 7.78—7.80 (m, 2 H, Ph); 7.54 (d, 1 H, $C(4)H_{indole}$, J = 8.1 Hz); 7.32 (d, 1 H, $C(7)H_{indole}$, J = 8.1 Hz); 7.31—7.42 (m, 3 H, Ph); 7.17—7.18 (m, 1 H, indole); 7.06—7.10 (m, 1 H, indole); 6.97—7.01 (m, 1 H, indole); 2.63 (s, 3 H, CH_3CO); 2.45 (s, 3 H, CH_3CO). Found (%): C, 67.30; H, 4.95; N, 14.82. $C_{21}H_{18}N_4O_3$. Calculated (%): C, 67.37; H, 4.85; N, 14.96.

2,4-Diacetyl-3-(1-methyl-1*H*-indol-3-yl)-6-phenyl-3,4-dihydro-2*H*-[1,2,4]triazin-5-one (7). The yield was 60%, yellow crystalline powder, m.p. 203—205 °C. ^{1}H NMR (250 MHz, DMSO-d_6), δ: 8.51 (d, 1 H, C(3)H, J = 0.8 Hz); 7.79—7.83 (m, 2 H, Ph); 7.58—7.63 (m, 1 H, indole, $C(4)H_{indole}$); 7.39—7.46 (m, 3 H, Ph); 7.32—7.46 (m, 1 H, $C(7)H_{indole}$); 7.19—7.26 (m, 1 H, indole); 7.07—7.13 (m, 2 H, indole); 3.69 (s, 3 H, NCH_3); 2.62 (s, 3 H, CH_3CO); 2.45 (s, 3 H, CH_3CO). Found (%): C, 68.24; H, 5.26; N, 14.53. $C_{22}H_{20}N_4O_3$. Calculated (%): C, 68.03; H, 5.19; N, 14.42.

2,4-Diacetyl-3-(2-methyl-1*H*-indol-3-yl)-6-phenyl-3,4-dihydro-2*H*-[1,2,4]triazin-5-one (8). The yield was 40%, yellow crystalline powder, m.p. 195—197 °C. ^{1}H NMR (250 MHz, DMSO-d_6), δ: 8.32 (s, 1 H, C(3)H); 7.84—7.89 (m, 2 H, Ph); 7.43—7.49 (m, 3 H, Ph); 7.23—7.30 (m, 2 H, indole); 7.00—7.07 (m, 1 H, indole); 6.89—6.96 (m, 1 H, indole); 2.54 (s, 3 H, CH_3); 2.46 (s, 3 H, CH_3); 2.41 (s, 3 H, CH_3). Found (%): C, 68.18; H, 5.14; N, 14.51. $C_{22}H_{20}N_4O_3$. Calculated (%): C, 68.03; H, 5.19; N, 14.42.

Synthesis of compounds 9 and 11 (general procedure). A mixture of the corresponding azinone **3**, **5** (1 mmol) and indole (1.1 mmol) in acetic anhydride (3 mL) was refluxed for 60 min. Upon standing at room temperature, clusters of colorless crystals grew from the solution. After 6 h a precipitate formed was filtered off, washed with diethyl ether, and recrystallized from ethanol.

2,4-Diacetyl-5-(1*H*-indol-3-yl)-6-phenyl-4,5-dihydro-2*H*-[1,2,4]triazin-3-one (9). The yield was 51%, colorless crystalline powder, m.p. 183—185 °C. ^{1}H NMR (250 MHz, DMSO-d_6), δ: 11.10 (br.s, 1 H, NH); 7.81—7.85 (m, 2 H); 7.67—7.70 (m, 1 H); 7.33—7.43 (m, 4 H); 7.03—7.14 (m, 4 H); 2.57 (s, 3 H, CH_3CO); 2.51 (s, 3 H, CH_3CO). Found (%): C, 67.43; H, 4.88; N, 14.87. $C_{21}H_{18}N_4O_3$. Calculated (%): C, 67.37; H, 4.85; N, 14.96.

4-Acetyl-3-(1*H*-indol-3-yl)-3,4-dihydro-1*H*-quinoxalin-2-one (11). The yield was 62%, colorless crystalline powder, m.p. > 260 °C. ^{1}H NMR (400 MHz, DMSO-d_6), δ: 10.78—10.80 (m, 2 H, 2 NH); 7.68 (d, 1 H, J = 7.9 Hz); 7.27 (d, 1 H, J = 8.0 Hz); 7.20—7.21 (m, 1 H); 7.11 (t, 1 H, J = 7.4 Hz); 7.03—7.06 (m, 2 H); 6.96—7.00 (m, 1 H); 6.92 (t, 1 H, J = 7.2 Hz); 6.73 (d, 1 H, J = 1.5 Hz); 6.55 (s, 1 H); 2.26 (s, 3 H, CH_3CO). Found (%): C, 70.53; H, 4.97; N, 13.80. $C_{18}H_{15}N_3O_2$. Calculated (%): C, 70.81; H, 4.95; N, 13.76.

1-Acetyl-6-(1*H*-indol-3-yl)-[1,3,5]triazinane-2,4-dione (10). A mixture of 1,3,5-triazine-2(1*H*),4(3*H*)-dione (**4**) (1 mmol)

and indole (1.1 mmol) in acetic anhydride (3 mL) was refluxed for 60 min. Then the reaction mixture was cooled and diluted with water (50 mL). A precipitate formed was subjected to chromatography on silica gel. The yield was 25%, colorless crystalline powder, m.p. 215—216 °C, R_f = 0.6 (ethyl acetate). ^{1}H NMR (400 MHz, DMSO-d_6), δ: 11.02 (s, 1 H, NH); 10.17 (s, 1 H, NH); 8.80 (d, 1 H, N(5)H, J = 4.7 Hz); 7.61 (d, 1 H, C(4)H_{indole}, J = 8.0 Hz); 7.35 (d, 1 H, C(7)H_{indole}, J = 8.1 Hz); 7.12—7.03 (m, 2 H, C(2)H+C(5)H_{indole}); 6.96—6.70 (m, 1 H, C(6)H_{indole}); 6.84 (d, 1 H, C(6)H, J = 4.4 Hz); 2.49 (s, 3 H, CH_3CO). ^{13}C NMR (75 MHz, DMSO-d_6), δ: 170.35, 152.52, 151.20, 137.12, 124.90, 123.16, 122.13, 119.65, 119.33, 113.63, 112.37, 57.48, 26.01. Found (%): C, 57.03; H, 4.23; N, 20.24. $C_{13}H_{12}N_4O_3$. Calculated (%): C, 57.35; H, 4.44; N, 20.58.

Synthesis of compounds 12,[10] 16,[11] and 17[12,13] (general procedure). Indole (1.2 mmol) was added to a suspension of the corresponding azinone (**1**, **4**, **5**) (1.2 mmol) and *p*-toluenesulfonyl chloride (1.2 mmol) in THF (5 mL) at −15 °C. The mixture was stirred for 1 h at −15 °C, then the temperature was raised to ambient over 1 h. A precipitate formed was filtered off, washed with THF and diethyl ether, and recrystallized from ethanol.

Synthesis of compounds 13—15 (general procedure). A solution of 6-aryl-1,2,4-triazin-3(2*H*)-one (1.2 mmol) and the corresponding nucleophile (1.2 mmol) in DMF (3 mL) was refluxed for 60 min and concentrated *in vacuo*, A resin-like residue obtained was stirred with water, a precipitate formed was filtered off, dried, and recrystallized from ethanol.

5-(1*H*-Indol-3-yl)-6-phenyl-4,5-dihydro-1,2,4-triazin-3(2*H*)-one (13). The yield was 92%, colorless crystalline powder, m.p. 272—273 °C. ^{1}H NMR (250 MHz, DMSO-d_6), δ: 11.04 (br.s, 1 H, NH, indole); 10.26 (br.s, 1 H, N(2)H); 7.81 (d, 1 H, N(4)H, J = 3.0 Hz); 7.68—7.33 (m, 3 H); 7.28—7.35 (m, 4 H, Ph); 7.21—7.22 (m, 1 H); 7.08—7.09 (m, 1 H); 7.01—7.03 (m, 1 H); 5.97 (d, 1 H, C(5)H, J = 3.0 Hz). Found (%): C, 70.21; H, 4.80. $C_{17}H_{14}N_4O$. Calculated (%): C, 70.33; H, 4.86.

5-(1-Methylindol-3-yl)-6-phenyl-4,5-dihydro-1,2,4-triazin-3(2*H*)-one (14). The yield was 95%, colorless crystalline powder, m.p. 265—267 °C. ^{1}H NMR (250 MHz, DMSO-d_6), δ: 10.22 (br.s, 1 H, N(2)H); 7.69—7.79 (m, 2 H); 7.50 (br.s, 1 H, N(4)H); 7.28—7.38 (m, 5 H); 7.06—7.18 (m, 2 H); 5.95 (d, 1 H, C(5)H, J = 1.9 Hz); 3.69 (s, 3 H, CH_3). Found (%): C, 71.02; H, 5.35. $C_{18}H_{16}N_4O$. Calculated (%): C, 71.04; H, 5.30.

5-(2-Methyl-1*H*-indol-3-yl)-6-phenyl-4,5-dihydro-1,2,4-triazin-3(2*H*)-one (15). The yield was 80%, colorless crystalline powder, m.p. 275—276 °C. ^{1}H NMR (250 MHz, DMSO-d_6), δ: 10.25 (br.s, 1 H, N(2)H); 7.58—7.61 (m, 2 H); 7.45—7.51 (m, 2 H); 7.20—7.27 (m, 4 H); 6.92—6.98 (m, 2 H); 5.97 (d, 1 H, C(5)H, J = 2.2 Hz); 2.46 (s, 3 H, CH_3). Found (%): C, 71.30; H, 5.06. $C_{18}H_{16}N_4O$. Calculated (%): C, 71.04; H, 5.30.

Synthesis of compounds 20—25 (general procedure). Triazinone **1** (1.2 mmol) was added to a solution of (*S*)-*N*-Ts-amino acid acyl chloride (**18** or **19**) (1.2 mmol) in THF (3 mL) at −15 °C, after 5 min the corresponding nucleophile (1.2 mmol) was added to the solution. The mixture was stirred for 1 h at −15 °C, then the temperature was raised to ambient over 2 h. Then the reaction mixture was poured into cold water and extracted with ethyl acetate (2×20 mL). The organic layer was washed with water and brine, dried with calcined Na_2SO_4. The solution was concentrated, the residue was dissolved in chloroform and subjected to chromatographic separation on a column with silica gel using the ethyl acetate—chloroform (1 : 1) mixture as an eluent.

(*S*)-1-[(*S*)-4-Methyl-2-tosylaminopentanoyl]-6-(1*H*-indol-3-yl)-3-phenyl-1,6-dihydro-1,2,4-triazin-5(4*H*)-one (*S*,*S*-20). The yield was 15%, colorless crystalline powder, m.p. 244—245 °C, R_f = 0.9 (ethyl acetate), $[\alpha]_D^{20}$ = +309.2 (c = 1.0, DMF). ^{1}H NMR (400 MHz, DMSO-d_6), δ: 11.51 (s, 1 H, NH); 10.98 (d, 1 H, NH, J = 2.1 Hz); 7.90—7.92 (m, 2 H, Ph); 7.81 (d, 1 H, NH, J = 9.1 Hz); 7.73 (d, 1 H, C(4)H_{indole}, J = 8.0 Hz); 7.54 (d, 2 H, Ts, J = 8.2 Hz); 7.44—7.50 (m, 3 H, Ph); 7.35 (d, 1 H, C(7)H_{indole}, J = 8.1 Hz); 7.07—7.11 (m, 1 H, C(6)H_{indole}); 6.99—7.02 (m, 1 H, C(5)H_{indole}); 6.93—6.96 (m, 3 H, Ts+C(2)H_{indole}); 6.07 (s, 1 H, C(6)H); 5.11 (dt, 1 H, CH, J = 10.3 Hz, J = 3.8 Hz); 2.21 (s, 3 H, Ts); 1.81—1.62 (m, 1 H, CH); 1.55—1.42 (m, 1 H, CH_2); 1.31—1.38 (m, 1 H, CH_2); 0.83 (d, 3 H, CH_3, J = 6.6 Hz); 0.75 (d, 3 H, CH_3, J = 6.6 Hz). Found (%): C, 64.55; H, 5.56; N, 12.53. $C_{30}H_{31}N_5O_4S$. Calculated (%): C, 64.61; H, 5.60; N, 12.56.

(*R*)-1-[(*S*)-4-Methyl-2-tosylaminopentanoyl]-6-(1*H*-indol-3-yl)-3-phenyl-1,6-dihydro-1,2,4-triazin-5(4*H*)-one (*S*,*R*-20). The yield was 5%, colorless crystalline powder, m.p. 270—272 °C, R_f = 0.8 (ethyl acetate), $[\alpha]_D^{25}$ = −127.6 (c = 0.5, DMF). ^{1}H NMR (400 MHz, DMSO-d_6), δ: 11.48 (s, 1 H, NH); 10.90 (d, 1 H, NH, J = 1.5 Hz); 7.91—7.93 (m, 2 H, Ph); 7.79 (d, 1 H, NH, J = 10.3 Hz); 7.59 (d, 1 H, C(4)H_{indole}, J = 7.9 Hz); 7.47—7.50 (m, 5 H, Ts+Ph); 7.28 (d, 1 H C(7)H_{indole}, J = 8.1 Hz); 7.17 (d, 2 H, Ts, J = 8.2 Hz); 7.04 (t, 1 H, C(6)H_{indole}, J = 7.3 Hz); 6.95 (t, 1 H, C(5)H_{indole}, J = 7.5 Hz); 6.89 (d, 1 H, C(2)H_{indole}, J = 2.5 Hz); 5.69 (s, 1 H, C(6)H); 4.95 (dt, 1 H, CH, J = 5.3 Hz, J = 9.7 Hz); 2.41 (s, 3 H, Ts); 1.62—1.72 (m, 1 H, CH); 1.27—1.42 (m, 1 H, CH_2); 1.31—1.38 (m, 1 H, CH_2); 0.85 (d, 6 H, 2 CH_3, J = 6.5 Hz). Found (%): C, 64.49; H, 5.58; N, 12.52. $C_{30}H_{31}N_5O_4S$. Calculated (%): C, 64.61; H, 5.60; N, 12.56.

(R/*S*)-1-[(*S*)-4-Methyl-2-tosylaminopentanoyl]-6-(1*H*-indol-3-yl)-3-phenyl-1,6-dihydro-1,2,4-triazin-5(4*H*)-one (*S*,*RS*-20). The yield was 25%, colorless crystalline powder, m.p. 244—245 °C. $[\alpha]_D^{20}$ = +179.3 (c = 1.0, DMF). Found (%): C, 64.51; H, 5.47; N, 12.42. $C_{30}H_{31}N_5O_4S$. Calculated (%): C, 64.61; H, 5.60; N, 12.56.

(*S*)-1-[(*S*)-3-Methyl-2-tosylaminobutanoyl]-6-(1*H*-indol-3-yl)-3-phenyl-1,6-dihydro-1,2,4-triazin-5(4*H*)-one (21). The yield was 77%, pink crystalline powder, m.p. 248 °C, R_f = 0.9 (ethyl acetate), $[\alpha]_D^{20}$ = +329.8 (c = 1.0, DMF). ^{1}H NMR (400 MHz, DMSO-d_6), δ: 11.65 (s, 1 H, NH); 11.11 (d, 1 H, NH, J = 1.8 Hz); 7.92 (d, 1 H, NH, J = 9.4 Hz); 7.82—7.90 (m, 2 H, Ph); 7.70 (d, 1 H, C(4)H_{indole}, J = 8.0 Hz); 7.52—7.62 (m, 3 H, Ph); 7.48 (d, 2 H, Ts, J = 8.2 Hz); 7.40 (d, 1 H, C(7)H_{indole}, J = 8.1 Hz); 7.13—7.16 (m, 1 H, C(6)H_{indole}); 7.01—7.05 (m, 1 H, C(5)H_{indole}); 6.97 (d, 1 H, C(2)H_{indole}, J = 2.3 Hz); 6.88 (d, 2 H, Ts, J = 8.0 Hz); 6.12 (s, 1 H, C(6)H); 4.88—4.92 (m, 1 H, CH); 2.14 (s, 3 H, Ts); 1.94—2.05 (m, 1 H, CH); 0.87 (d, 3 H, CH_3, J = 6.8 Hz); 0.80 (d, 3 H, CH_3, J = 6.8 Hz). Found (%): C, 63.95; H, 5.41; N, 12.77. $C_{29}H_{29}N_5O_4S$. Calculated (%): C, 64.07; H, 5.38; N, 12.88.

(*S*)-1-[(*S*)-4-Methyl-2-tosylaminopentanoyl]-6-(1-methyl-1*H*-indol-3-yl)-3-phenyl-1,6-dihydro-1,2,4-triazin-5(4*H*)-one (22). The yield was 65%, colorless crystalline powder, m.p. 252—253 °C, R_f = 0.9 (ethyl acetate), $[\alpha]_D^{25}$ = +262.7 (c = 1.0, DMF). ^{1}H NMR (400 MHz, DMSO-d_6), δ: 11.55 (s, 1 H, NH); 7.88—7.92 (m, 3 H, Ph, NH); 7.76 (d, 1 H, C(4)H_{indole},

J = 8.0 Hz); 7.57 (d, 2 H, Ts, J = 8.1 Hz); 7.44—7.52 (m, 3 H, Ph); 7.34 (d, 1 H, C(7)H_{indole}, J = 8.2 Hz); 7.18 (t, 1 H, C(6)H_{indole}, J = 7.6 Hz); 7.04—7.08 (m, 2 H, C(5)H_{indole} + C(2)H_{indole}); 6.96 (d, 2 H, Ts, J = 8.1 Hz); 6.08 (s, 1 H, C(6)H); 5.10 (dt, 1 H, CH, J = 10.4 Hz, J = 3.6 Hz); 3.74 (s, 3 H, NCH_3); 2.23 (s, 3 H, Ts); 1.74—1.59 (m, 1 H, CH); 1.58—1.43 (m, 1 H, CH_2); 1.30—1.37 (m, 1 H, CH_2); 0.82 (d, 1 H, J = 6.6 Hz); 0.70 (d, 1 H, J = 6.5 Hz). Found (%): C, 65.14; H, 5.86; N, 12.47. $C_{31}H_{33}N_5O_4S$. Calculated (%): C, 65.13; H, 5.82; N, 12.25.

(*S*)-1-[(*S*)-4-Methyl-2-tosylaminopentanoyl]-6-(2-methyl-1*H*-indol-3-yl)-3-phenyl-1,6-dihydro-1,2,4-triazin-5(4*H*)-one (23). The yield was 42%, colorless crystalline powder, m.p. 274—275 °C, R_f = 0.9 (ethyl acetate). ^{1}H NMR (400 MHz, DMSO-d_6), δ: 11.59 (s, 1 H, NH); 10.96 (s, 1 H, NH); 8.08—7.96 (m, 2 H, Ph); 7.47—7.61 (m, 4 H, Ph+NH); 7.29 (d, 1 H, C(4)H_{indole}, J = 8.0 Hz); 7.20 (d, 2 H, Ts, J = 8.2 Hz); 7.16 (d, 1 H, C(7)H_{indole}, J = 8.0 Hz); 6.99 (t, 1 H, C(6)H_{indole}, J = 7.5 Hz); 6.81 (t, 1 H, C(5)H_{indole}, J = 7.5 Hz); 6.44 (d, 2 H, Ts, J = 8.1 Hz); 5.92 (s, 1 H, C(6)H); 5.08 (dt, 1 H, CH, J = 10.0 Hz, J = 3.8 Hz); 2.36 (s, 3 H, CH_3); 2.15 (s, 3 H, CH_3); 1.90—1.73 (m, 1 H, CH); 1.53—1.32 (m, 2 H); 0.87 (t, 6 H, 2 CH_3, J = 7.2 Hz). Found (%): C, 64.85; H, 5.90; N, 12.20. $C_{31}H_{33}N_5O_4S$. Calculated (%): C, 65.13; H, 5.82; N, 12.25.

(*S*)-1-[(*S*)-3-Methyl-2-tosylaminobutanoyl]-6-(2-methyl-1*H*-indol-3-yl)-3-phenyl-1,6-dihydro-1,2,4-triazin-5(4*H*)-one (24). The yield was 32%, colorless crystalline powder, m.p. > 300 °C, R_f = 0.9 (ethyl acetate). ^{1}H NMR (400 MHz, DMSO-d_6), δ: 11.64 (s, 1 H, NH); 10.96 (s, 1 H, NH); 7.96—7.99 (m, 2 H, Ph); 7.51—7.63 (m, 3 H, Ph); 7.27—7.31 (m, 2 H, C(4)H_{indole}+NH); 7.20 (d, 2 H, Ts, J = 8.2 Hz); 7.15 (d, 1 H, C(7)H_{indole}, J = 8.1 Hz); 6.99 (t, 1 H, C(6)H_{indole}, J = 7.3 Hz); 6.81 (t, 1 H, C(5)H_{indole}, J = 7.3 Hz); 6.37 (d, 2 H, Ts, J = 8.0 Hz); 5.96 (s, 1 H, C(6)H); 4.89 (dd, 1 H, CH, J = 9.0 Hz, J = 3.5 Hz); 2.39 (s, 3 H, CH_3); 2.01—2.19 (m, 4 H, CH+CH_3); 0.99 (d, 3 H, CH_3, J = 6.70 Hz); 0.85 (d, 3 H, CH_3, J = 6.81 Hz). Found (%): C, 64.75; H, 5.43; N, 12.85. $C_{30}H_{31}N_5O_4S$. Calculated (%): C, 64.61; H, 5.60; N, 12.56.

(*S*)-1-[(*S*)-3-Methyl-2-tosylaminobutanoyl]-6-(1-methyl-1*H*-pyrrol-3-yl)-3-phenyl-1,6-dihydro-1,2,4-triazin-5(4*H*)-one (25). The yield was 15%, colorless crystalline powder, m.p. 177—178 °C, R_f = 0.9 (ethyl acetate). ^{1}H NMR (400 MHz, DMSO-d_6), δ: 11.65 (s, 1 H, NH); 7.99—7.89 (m, 2 H, Ph); 7.75 (d, 1 H, NH, J = 9.5 Hz); 7.57—7.43 (m, 5 H, Ph+Ts); 7.01 (d, 2 H, Ts, J = 8.1 Hz); 6.60—6.67 (m, 1 H, pyrrole); 5.84—5.88 (m, 1 H, pyrrole); 5.81 (s, 1 H, C(6)H); 5.72—5.75 (m, 1 H, pyrrole); 5.01 (dt, 1 H, CH, J = 10.6 Hz, J = 3.6 Hz); 3.57 (s, 3 H, NCH_3); 2.35 (s, 3 H, Ts); 1.67—1.87 (m, 1 H, CH); 1.38—1.53 (m, 1 H, CH_2); 1.24—1.31 (m, 1 H, CH_2); 0.80—0.84 (m, 6 H, 2 CH_3). Found (%): C, 61.97; H, 6.00; N, 13.41. $C_{27}H_{31}N_5O_4S$. Calculated (%): C, 62.17; H, 5.99; N, 13.43.

Table 8. Crystallographic data and parameters of X-ray diffraction experiment for compound **24**

Parameter	Value
Molecular formula	$C_{30}H_{31}N_5O_4S$
Molecular weight	557.66
Crystal system	Orthorhombic
Space group	$P2(1)2(1)2(1)$
a/Å	11.9669(9)
b/Å	14.1290(15)
c/Å	18.1570(14)
α/deg	90.00
β/deg	90.00
γ/deg	90.00
V/Å^3	3070.0(5)
Z	4
ρ_{calc}/g cm^{-3}	1.207
μ/mm^{-1}	0.146
F(000)	1176
Crystal size/mm	0.47×0.31×0.26
θ/deg	2.67—33.29
Total number of reflections measured/independent	11075/5228
R_{int}	0.0386
Number of observed reflections with $I > 2\sigma(I)$	2029
R_1 ($I > 2\sigma(I)$)	0.0402
wR_2 ($I > 2\sigma(I)$)	0.0490
Residual electron density/e Å^{-3}, ρ_{max}/ρ_{min}	0.196/−0.230

Synthesis of compounds 26—29 (general procedure). Triazinone **2** (1.2 mmol) was added to a solution of (*S*)-*N*-Ts-amino acid acyl chloride (**18** or **19**) (1.2 mmol) in THF (3 mL) at −15 °C, after 5 min the corresponding nucleophile (1.2 mmol) was added to the solution. The mixture was stirred for 1 h at −15 °C, then the temperature was raised to ambient over 2 h. The reaction mixture was filtered off the unreacted residue of triazine, the filtrate was poured into cold water and extracted with ethyl acetate (2×20 mL). The organic layer was washed with water and brine, dried with calcined Na_2SO_4. The solution was concentrated, the residue was dissolved in chloroform and subjected to chromatographic separation on a column with silica gel using the ethyl acetate—chloroform (1 : 1) mixture as an eluent.

(*S*)-2-[(*S*)-4-Methyl-2-tosylaminopentanoyl]-3-(1*H*-indol-3-yl)-6-phenyl-3,4-dihydro-1,2,4-triazin-5(2*H*)-one (26). The yield was 52%, colorless crystalline powder, m.p. 134—135 °C, R_f = 0.8 (ethyl acetate), $[\alpha]_D^{25}$ = +444.8 (c = 1.0, DMF). ^{1}H NMR (400 MHz, DMSO-d_6), δ: 11.04 (d, 1 H, NH, J = 1.8 Hz); 9.71 (d, 1 H, NH, J = 5.3 Hz); 8.10 (d, 1 H, NH, J = 8.7 Hz); 7.86—7.90 (m, 2 H, Ph); 7.75 (d, 1 H, C(4)H_{indole}, J = 8.0 Hz); 7.54 (d, 2 H, Ts, J = 8.2 Hz); 7.33—7.46 (m, 4 H, Ph+C(7)H_{indole}); 7.08—7.11 (m, 1 H, C(6)H_{indole}); 6.98—7.05 (m, 5 H, C(5)H_{indole}+ + C(2)H_{indole}, Ts, C(3)H); 5.02 (dt, 1 H, CH, J = 10.1 Hz, J = 4.1 Hz); 2.27 (s, 3 H, Ts); 1.72—1.48 (m, 2 H, CH+CH_2); 1.35—1.42 (m, 1 H, CH_2); 0.82 (d, 3 H, CH_3, J = 6.6 Hz); 0.65 (d, 3 H, CH_3, J = 6.5 Hz). Found (%): C, 64.72; H, 5.71; N, 12.48. $C_{30}H_{31}N_5O_4S$. Calculated (%): C, 64.61; H, 5.60; N, 12.56.

(*S*)-2-[(*S*)-3-Methyl-2-tosylaminobutanoyl]-3-(1*H*-indol-3-yl)-6-phenyl-3,4-dihydro-1,2,4-triazin-5(2*H*)-one (27). The yield was 23%, colorless crystalline powder, m.p. 210—211 °C, R_f = 0.8 (ethyl acetate), $[\alpha]_D^{20}$ = +616.4 (c = 1.0, DMF). ^{1}H NMR (400 MHz, DMSO-d_6), δ: 11.03 (d, 1 H, NH, J = 2.1 Hz); 9.70 (d, 1 H, NH, J = 5.3 Hz); 7.97 (d, 1 H, NH, J = 9.1 Hz); 7.89—7.81 (m, 2 H, Ph); 7.75 (d, 1 H, C(4)H_{indole}, J = 8.0 Hz); 7.50 (d, 2 H, Ts, J = 8.2 Hz); 7.46—7.38 (m, 3 H, Ph); 7.36 (d, 1 H, C(7)H_{indole}, J = 8.1 Hz); 7.07—7.12 (m, 2 H); 6.97—7.00

(m, 2 H); 6.87 (d, 2 H, Ts, J = 8.1 Hz); 4.80 (dd, 1 H, CH, J = 8.9 Hz, J = 6.2 Hz); 2.21 (s, 3 H, CH_3); 1.99—2.08 (m, 1 H, CH); 0.88 (d, 3 H, CH_3, J = 6.7 Hz); 0.84 (d, 3 H, CH_3, J = 6.7 Hz). Found (%): C, 64.28; H, 5.42; N, 12.85. $C_{29}H_{29}N_5O_4S$. Calculated (%): C, 64.07; H, 5.38; N, 12.88.

(*S*)-2-[(*S*)-4-Methyl-2-tosylaminopentanoyl]-3-(1-methyl-1*H*-pyrrol-3-yl)-6-phenyl-3,4-dihydro-1,2,4-triazin-5(2*H*)-one (28). The yield was 15%, colorless crystalline powder, m.p. 196—197 °C, R_f = 0.8 (ethyl acetate). ^{1}H NMR (400 MHz, DMSO-d_6), δ: 9.41 (d, 1 H, N(4)H, J = 5.2 Hz); 8.11 (d, 1 H, NH, J = 8.8 Hz); 7.82—7.85 (m, 2 H, Ph); 7.62 (d, 1 H, Ts, J = 8.2 Hz); 7.30—7.47 (m, 3 H, Ph); 7.21 (d, 2 H, Ts, J = 8.1 Hz); 6.63 (d, 1 H, C(3)H, J = 5.2 Hz); 6.54 (br.s, 1 H, pyrrole); 6.50 (t, 1 H, pyrrole, J = 2.4 Hz); 5.60—5.69 (m, 1 H, pyrrole); 4.98—4.82 (m, 1 H, CH); 3.58 (s, 3 H, NCH_3); 2.40 (s, 3 H, CH_3CO); 1.78—1.61 (m, 1 H, CH); 1.59—1.47 (m, 1 H, CH_2); 1.30—1.38 (m, 1 H, CH_2); 0.82 (d, 3 H, CH_3, J = 6.6 Hz); 0.66 (d, 3 H, CH_3, J = 6.5 Hz). Found (%): C, 62.08; H, 5.95; N, 13.36. $C_{27}H_{31}N_5O_4S$. Calculated (%): C, 62.17; H, 5.99; N, 13.43.

(*S*)-2-[(*S*)-4-Methyl-2-tosylaminobutanoyl]-3-(1-methyl-1*H*-indol-3-yl)-6-phenyl-3,4-dihydro-1,2,4-triazin-5(2*H*)-one (29). The yield was 32%, colorless crystalline powder, m.p. 236—237 °C, R_f = 0.8 (ethyl acetate). ^{1}H NMR (400 MHz, DMSO-d_6), δ: 9.28 (d, 1 H, NH, J = 5.2 Hz); 7.91—7.94 (m, 3 H, NH+Ph); 7.62 (d, 1 H, C(4)H_{indole}, J = 8.0 Hz); 7.56 (d, 2 H, Ts, J = 8.2 Hz); 7.44—7.46 (m, 3 H, Ph); 7.28 (d, 1 H, C(7)H_{indole}, J = 8.2 Hz); 7.21—7.07 (m, 4 H, Ts+C(6)H_{indole}+ C(2)H_{indole}); 6.97 (t, 1 H, C(5)H_{indole}, J = 7.2 Hz); 6.83 (d, 1 H, J = 5.1 Hz); 4.62 (dd, 1 H, J = 10.0 Hz, J = 7.1 Hz); 3.73 (s, 3 H, CH_3); 2.40 (s, 3 H, CH_3); 1.81—1.90 (m, 1 H); 0.81 (d, 3 H, CH_3, J = 6.7 Hz); 0.58 (d, 3 H, CH_3, J = 6.7 Hz). Found (%): C, 64.52; H, 5.55; N, 12.61. $C_{30}H_{31}N_5O_4S$. Calculated (%): C, 64.61; H, 5.60; N, 12.56.

Synthesis of compounds 16 and 30 (general procedure). 1,3,5-Triazin-2,4-dione (**4**) (1.2 mmol) was added to a solution of (*S*)-*N*-Ts-amino acid acyl chloride (**18** and **19**) (1.2 mmol) in THF at −15 °C, after 5 min the corresponding nucleophile (1.2 mmol) was added to the solution. The mixture was stirred for 1 h at −15 °C, then the temperature was raised to ambient over 2 h. A precipitate formed was filtered off, washed with THF and diethyl ether, and recrystallized from ethanol.

6-(2-Methyl-1*H*-indol-3-yl)-[1,3,5]triazinane-2,4-dione (30). The yield was 32%, pink crystalline powder, m.p. 188—190 °C. ^{1}H NMR (400 MHz, DMSO-d_6), δ: 10.86 (s, 1 H, NH); 9.15 (s, 1 H, NH); 7.56—7.58 (m, 3 H); 7.24—7.26 (m, 1 H); 6.92—7.01 (m, 2 H); 5.89 (s, 1 H, C(6)H); 2.40 (s, 3 H, CH_3). Found (%): C, 59.12; H, 5.05; N, 22.98. $C_{12}H_{12}N_4O_2$. Calculated (%): C, 59.01; H, 4.95; N, 22.94.

Synthesis of compounds 17 and 31 (general procedure). The corresponding quinoxalin-2(1*H*)-one (**5**) (1.2 mmol) was added to a solution of (*S*)-*N*-Ts-amino acid acyl chloride (**18** and **19**) (1.2 mmol) in THF (10 mL) at −15 °C, after 5 min the corresponding nucleophile (1.2 mmol) was added to the solution. The mixture was stirred for 1 h at −15 °C, then the temperature was raised to ambient over 2 h. The reaction mixture was poured into cold water and extracted with ethyl acetate (2×20 mL). The organic layer was washed with water and brine, dried with calcined Na_2SO_4. The solution was concentrated, the residue was dissolved in ethyl acetate and subjected to chromatographic separation on a column with silica gel using ethyl acetate as an eluent.

3-(1*H*-Indol-3-yl)quinoxalin-2(1*H*)-one (17). Yellow crystalline powder, m.p. > 300 °C (Refs 14 and 15: m.p. >300 °C), R_f = 0.7 (ethyl acetate). ^{1}H NMR (400 MHz, DMSO-d_6), δ: 12.27 (br.s, 1 H, NH); 11.54 (br.s, 1 H, NH); 8.90 (d, 1 H, C(2)H_{indole}, J = 3.0 Hz); 8.83—8.85 (m, 1 H); 7.82 (d, 1 H, J = 7.8 Hz); 7.43—7.46 (m, 1 H); 7.28—7.35 (m, 2 H); 7.21—7.26 (m, 1 H); 7.14—7.19 (m, 2 H); 2.59 (s, 3 H, CH_3). Physico-chemical characteristics and spectral data for the compound obtained agree with those given in Refs 14 and 15.

3-(2-Methyl-1*H*-indol-3-yl)quinoxalin-2(1*H*)-one (31). Yellow crystalline powder, m.p. 282—283 °C, R_f = 0.7 (ethyl acetate). ^{1}H NMR (400 MHz, DMSO-d_6), δ: 12.17 (br.s, 1 H, NH); 11.23 (s, 1 H, NH); 7.75 (dd, 2 H, J = 16.6 Hz, J = 7.8 Hz); 7.38 (t, 1 H, J = 7.6 Hz); 7.31 (dd, 2 H, J = 7.7 Hz, J = 4.4 Hz); 7.22 (t, 1 H, J = 7.4 Hz); 7.03 (t, 1 H, J = 7.4 Hz); 6.98 (t, 1 H, J = 7.4 Hz); 2.59 (s, 3 H, CH_3). Found (%): C, 74.05; H, 4.67; N, 15.18. $C_{17}H_{13}N_3O$. Calculated (%): C, 74.17; H, 4.76; N, 15.26.

Synthesis of compounds 17, 31—33, 36—38 (general procedure). Triethylamine (1.2 mmol) was added to a magnetically stirred suspension of *N*-substituted amino acid **34** or **35** (1 mmol) in THF (3 mL) at room temperature. The solution was cooled to 0 °C in an ice-water bath, followed by addition of the corresponding chloroformate (1.1 mmol). After 5 min, quinoxalinone **5** (1 mmol) and the corresponding nucleophile (1.1 mmol) were added. The ice-water bath was removed in 30 min and the reaction mixture was stirred for 12—18 h at room temperature (TLC monitoring). A precipitate of unreacted starting compounds was filtered off, the filtrate was concentrated, the residue was dissolved in chloroform and subjected to chromatographic separation on a column with silica gel using the ethyl acetate—chloroform (1 : 1) mixture as an eluent.

3-(1-Methyl-1*H*-indol-3-yl)quinoxalin-2(1*H*)-one (32). Yellow crystalline powder, m.p. 289—290 °C, R_f = 0.7 (ethyl acetate). ^{1}H NMR (400 MHz, DMSO-d_6), δ: 12.34 (br.s, 1 H, NH); 8.86—8.89 (m, 2 H); 7.82 (d, 1 H, J = 7.9 Hz); 7.45 (d, 1 H, J = 7.3 Hz); 7.21—7.36 (m, 5 H); 3.94 (s, 3 H, CH_3). Found (%): C, 74.12; H, 4.71; N, 15.20. $C_{17}H_{13}N_3O$. Calculated (%): C, 74.17; H, 4.76; N, 15.26.

3-(1*H*-2-Pyrrol-2-yl)quinoxalin-2(1*H*)-one (33). Yellow crystalline powder, m.p. 242—243 °C, R_f = 0.8 (ethyl acetate). ^{1}H NMR (400 MHz, DMSO-d_6), δ: 12.39 (s, 1 H, NH); 11.44 (s, 1 H, NH); 7.69 (d, 1 H, J = 7.8 Hz); 7.26—7.40 (m, 3 H); 7.19—7.25 (m, 1 H); 6.99 (dd, 1 H, J = 3.9 Hz, J = 2.5 Hz); 6.19 (dd, 1 H, J = 5.8 Hz, J = 2.4 Hz). Physico-chemical characteristics and spectral data of the compound obtained agree with those given in Ref. 16.

4-[2-Acetylamino-4-methylpentanoyl]-3-(1*H*-indol-3-yl)-3,4-dihydroquinoxalin-2(1*H*)-one (36). The yield was 6%, colorless crystalline powder, m.p. 187—188 °C, R_f = 0.4 (ethyl acetate), $[\alpha]_D^{25}$ = +14.9 (c = 1.0, DMF). ^{1}H NMR (250 MHz, DMSO-d_6), δ: 10.80 (br.s, 1 H, NH); 10.78 (br.s, 1 H, NH); 8.19 (d, 1 H, NH, J = 8.3 Hz); 7.70 (d, 2 H, J = 7.8 Hz); 7.25—7.27 (m, 1 H); 7.13—7.17 (m, 1 H); 7.02—7.06 (m, 2 H); 6.95—6.99 (m, 2 H); 6.69 (d, 1 H, J = 2.0 Hz); 6.50 (s, 1 H); 4.92 (t, 1 H, CH, J = 8.1 Hz); 1.94 (s, 3 H, CH_3CO); 1.75—1.83 (m, 1 H, CH); 0.79 (d, 3 H, CH_3, J = 6.7 Hz); 0.66 (d, 3 H, CH_3, J = 6.7 Hz).

4-[2-Acetylamino-4-methylpentanoyl]-3-(2-methyl-1*H*-indol-3-yl)-3,4-dihydroquinoxalin-2(1*H*)-one (37). The yield was 4%, colorless crystalline powder, m.p. >260 °C, R_f = 0.5 (ethyl acetate). ^{1}H NMR (400 MHz, DMSO-d_6), δ: 10.91 (s, 1 H,

NH); 10.80 (s, 1 H, NH); 8.13 (d, 1 H, J = 7.6 Hz); 7.53 (d, 1 H, J = 7.9 Hz); 7.13—7.16 (m, 3 H); 6.94—6.97 (m, 2 H); 6.87 (t, 1 H, J = 7.5 Hz); 6.72 (t, 1 H, J = 7.5 Hz); 6.42 (s, 1 H, C(3)H); 5.05—5.10 (m, 1 H, CH); 2.30 (s, 3 H, CH_3); 1.88 (s, 3 H, CH_3); 1.35—1.44 (m, 2 H, CH_2); 0.94—1.01 (m, 1 H, CH); 0.61 (d, 3 H, CH_3, J = 6.3 Hz); 0.41 (d, 3 H, CH_3, J = 6.3 Hz).

4-[2-Acetylamino-3-methylbutanoyl]-3-(1-methyl-1*H*-indol-3-yl)-3,4-dihydroquinoxalin-2(1*H*)-one (38). The yield was 4%, colorless crystalline powder, m.p. >260 °C, R_f = 0.5 (ethyl acetate). ^{1}H NMR (250 MHz, DMSO-d_6), δ: 10.76 (s, 1 H, NH); 8.11 (d, 1 H, NH, J = 7.5 Hz); 7.68—7.72 (m, 2 H); 6.93—7.25 (m, 6 H); 6.84 (s, 1 H); 6.49 (s, 1 H); 4.90—4.97 (m, 1 H, CH); 3.61 (s, 3 H, NCH_3); 1.94 (s, 3 H, CH_3CO); 1.67—1.87 (m, 1 H, CH); 0.78 (d, 3 H, CH_3, J = 6.5 Hz); 0.65 (d, 3 H, CH_3, J = 6.5 Hz).

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