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Reaction of 1-alkyl/aryl-3-amino-1*H*,3*H*-quinoline-2,4-diones with urea. Synthetic route to novel 3-(3-acylureido)-2,3-dihydro-1*H*-indol-2-ones, 4-alkylidene-1′*H*-spiro[imidazolidine-5,3′-indole]-2,2′-diones, and 3,3a-dihydro-5*H*-imidazo[4,5-*c*]quinoline-2,4-diones

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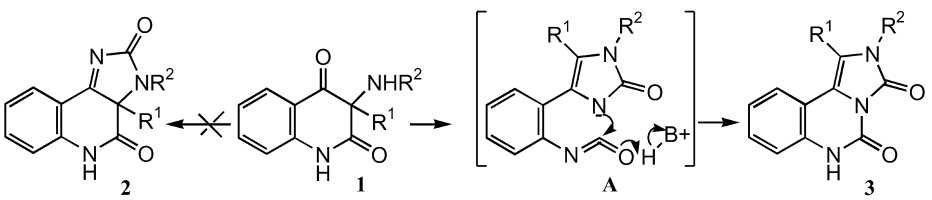
Abstract—1-Substituted 3-alkyl/aryl-3-amino-1*H*,3*H*-quinoline-2,4-diones react with urea in boiling acetic acid to give products depending on the type of substitution in position 3 and at the nitrogen atom of the 3-amino group. Starting compounds bearing a primary amino group in position 3 give 3-(3-acylureido)-2,3-dihydro-1*H*-indol-2-ones. Starting compounds bearing a secondary amino group in position 3 react according to the character of the other substituent in position 3. If there is a hydrogen atom α to the carbon atom C(3), 4-alkylidene-1′*H*-spiro[imidazolidine-5,3′-indole]-2,2′-diones arise. If a hydrogen atom is not present in this position, the reaction leads to 3,3a-dihydro-5*H*-imidazo[4,5-*c*]quinoline-2,4-diones. Reaction mechanisms for these transformations are proposed. All compounds were characterized by their ^{1}H, ^{13}C, IR and atmospheric pressure chemical ionization mass spectra and some of them also by ^{15}N NMR data.

1. Introduction

Recently, an unprecedented reaction of 3-amino-1*H*,3*H*-quinoline-2,4-diones **1** with urea in boiling acetic acid has been described.[1] The expected 3,3a-dihydro-5*H*-imidazo[4,5-*c*]-quinoline-2,4-diones **2** do not arise but a molecular rearrangement takes place, producing novel 2,6-dihydro-imidazo[1,5-*c*]quinazoline-3,5-diones **3** (Scheme 1). Their formation was proposed to take place via intermediate **A** containing an isocyanate group.

An isocyanate mechanism may, of course, be applicable only where the starting compound **1** contains a secondary lactam group in the quinoline nucleus. Therefore, we decided to study the reaction of urea with compounds analogous to **1**, but containing a tertiary lactam group in the quinoline ring. In our present study, we demonstrate that 1-alkyl/aryl-3-amino-1*H*,3*H*-quinoline-2,4-diones **5** react with urea in boiling acetic acid in a different manner to unsubstituted compounds **1**. Depending on the character of substitution in starting compounds **5**, either a molecular rearrangement of the quinolone system to indolinone system comes about with formation of hitherto undescribed 3-(3-acylureido)-2,3-dihydro-1*H*-indol-2-ones **6** or 4-alkylidene-1′*H*-spiro[imidazolidine-5,3′-indole]-2,2′-diones **7**, or



Scheme 1.

Keywords: molecular rearrangement; urea derivatives; α-aminoketones; reaction mechanism; NMR; MS.
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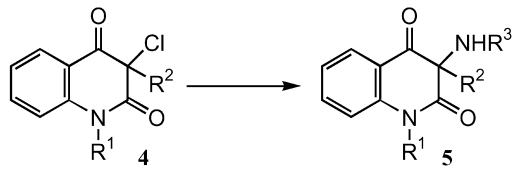


Method A: R^3NH_2 in DMF (R^3 = Alkyl)
Method B: $NH_4Cl + K_2CO_3$ in DMF (R^3 = H)

a: $R^1 = CH_3$, $R^2 = C_4H_9$, $R^3 = H$ 58%
b: $R^1 = CH_3$, $R^2 = Ph$, $R^3 = H$ Ref. 2
c: $R^1 = CH_3$, $R^2 = C_4H_9$, $R^3 = C_4H_9$ 70%
d: $R^1 = Ph$, $R^2 = C_4H_9$, $R^3 = C_4H_9$ 68%
e: $R^1 = CH_3$, $R^2 = Ph$, $R^3 = C_4H_9$ Ref. 2
f: $R^1 = CH_3$, $R^2 = Ph$, $R^3 = c\text{-}C_6H_{11}$ Ref. 2
g: $R^1 = R^2 = Ph$, $R^3 = C_4H_9$ 70%

Scheme 2.

expected 3,3a-dihydro-5*H*-imidazo[4,5-*c*]quinoline-2,4-diones **8** arise.

2. Results and discussion

Reactions were performed in the same manner as in our previous paper,[1] i.e. by boiling amines **5** with urea in a solution of acetic acid. The starting amines **5** were obtained from the corresponding chloro derivatives **4** in accordance with procedures described in Ref. 2 (Scheme 2). NMR spectral characteristics of starting compounds are presented in Table 1.

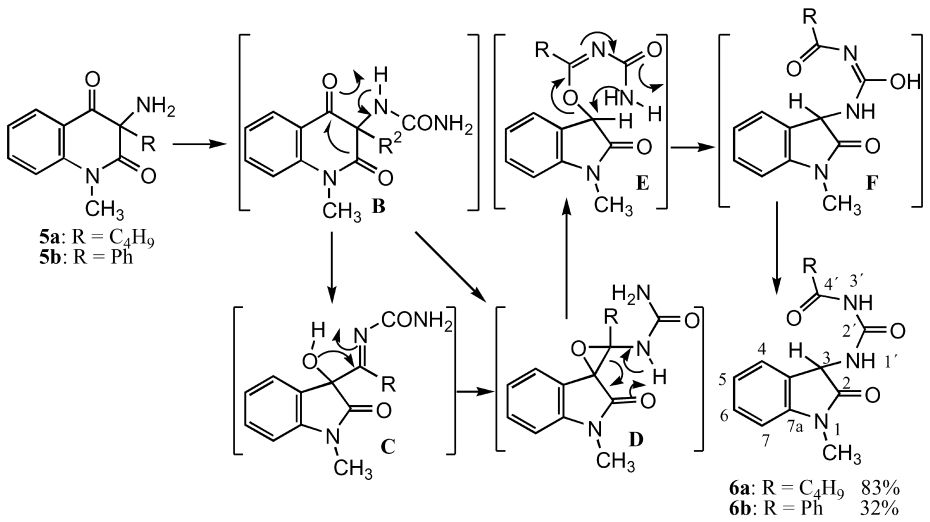
Products, which markedly differ from each other in spectral characteristics (IR, MS, NMR), were obtained in good to very good yields from the reaction of amines **5** with urea. Even the results of elemental analyses of some reaction products were not in accord with the assumed structures. We soon recognized that product structure depended both on the character of substituent in position 3 as well as on the substitution at the nitrogen atom in the same position in starting compounds **5**. Therefore, the following survey of results and discussion is divided into three parts according to this criterion.

The first group is formed by starting compounds bearing a primary amino group in position 3 (**5a**, **5b**). From the results of elemental analyses, it followed that products of their reaction with urea have one molecule of water more than expected. In the ^{1}H NMR spectra of the products, two doublets for protons corresponding to the CH–NH grouping appear at 5.21 and 9.06 ppm or 5.31 and 9.35 ppm, respectively. The signal of CH carbon atom in this grouping, according to results of 2D experiments, appears in ^{13}C NMR spectrum at approx. 52 ppm. This implies the atom in question is C(3) of 3-acylamino-2,3-dihydro-1*H*-indol-2-one because the signal of atom C(3) in quinolone derivatives **5** ranges from 67–77 ppm[2] and the signal of C(3) in 3-acyloxy-2,3-dihydro-1*H*-indol-2-ones lies in the region 69–71 ppm.[3] Besides the signal of the mentioned NH group at 9.06 or 9.35 ppm, signals of another NH group appear in

Table 1. ^{1}H and ^{13}C NMR shifts (δ, ppm) of compounds **4a** and **5a**,**c**,**d**,**g** (in DMSO-d_6)

Position	4a		5a		5c		5d		5g	
	δ_H	δ_C	δ_H	δ_C	δ_H	δ_C	δ_H	δ_C	δ_H	δ_C
2	–	166.39	–	172.94	–	172.50	–	172.65	–	171.48
3	–	67.98	–	68.93	–	73.58	–	74.07	–	77.54
4	–	188.00	–	195.62	–	195.23	–	195.25	–	192.90
4a	–	118.91	–	120.06	–	120.62	–	120.29	–	120.59
5	7.97	128.02	7.86	126.98	7.89	126.97	7.95	127.21	7.86	127.64
6	7.33	123.71	7.27	123.00	7.25	123.00	7.24	123.28	7.18	123.48
7	7.84	137.17	7.76	136.04	7.76	136.37	7.57	136.09	7.52	136.03
8	7.49	116.32	7.41	115.66	7.40	115.75	6.38	116.59	6.39	116.74
8a	–	142.17	–	142.69	–	142.66	–	143.60	–	143.17
CH_3 (1)	3.41	30.46	3.43	29.84	3.45	29.67	–	–	–	–
NH (NH_2)	–	–	2.20	–	Not found	44.08	1.91	–	Not found	–
1′(3)	2.30	36.19	1.52, 1.57[a]	42.01	1.71, 1.77[a]	39.73	1.91[b]	39.89	–	–
2′(3)	1.31	26.64	1.02, 1.17[a]	25.16	1.06, 1.16	25.11	1.23[b]	25.33	–	–
3′(3)	1.27	22.25	1.06	22.02	1.13	22.18	1.23	22.30	–	–
4′(3)	0.85	13.64	0.72	13.77	0.74	13.70	0.82	13.90	–	–
1′(3–N)	–	–	–	–	2.28, 2.31[a]	44.08	2.44[b]	44.13	2.46, 2.60[a]	44.48
2′(3-N)	–	–	–	–	1.35	32.26	1.41[b]	32.36	1.47	32.36
3′(3-N)	–	–	–	–	1.28	19.83	1.34	19.93	1.35	20.00
4′(3-N)	–	–	–	–	0.84	13.70	0.87	13.90	0.89	13.99
ipso-Ph (1)	–	–	–	–	–	–	–	137.54	–	137.60
o-Ph (1)	–	–	–	–	–	–	7.37	129.24	7.44[b]	130.39
m-Ph (1)	–	–	–	–	–	–	7.66[b]	130.35	7.69[b]	130.60[b]
p-Ph (1)	–	–	–	–	–	–	7.58	128.98	7.60	128.79
ipso-Ph (3)	–	–	–	–	–	–	–	–	–	137.60
o-Ph (3)	–	–	–	–	–	–	–	–	7.51	126.89
m-Ph (3)	–	–	–	–	–	–	–	–	7.43	129.09
p-Ph (3)	–	–	–	–	–	–	–	–	7.37	129.19

[a] Prochiral methylene group.
[b] Broad signal.



Scheme 3.

the ^{1}H NMR spectra of products from reaction of **5a** and **5b** with urea at 10.44 or 10.88 ppm, and three signals of carbonyl groups are present in their ^{13}C NMR spectra at 152.95, 173.84 and 175.08 ppm, or at 153.25, 168.37 and 173.96 ppm, respectively. The signal at highest field must belong to the NH–CO–NH fragment, the other two are then signals for carbon atoms of amide and lactam groups. The identification of the fragments mentioned above and results of 1D and 2D NMR experiments led us to formulate structures **6a** and **6b** (Scheme 3) for products of the reaction of **5a** and **5b** with urea. Even though more than one hundred derivatives of 3-aminoindolin-2-one have been described in the literature, only six of these have an acylated amino group and none have an acylated carbamoyl group.

All signals in ^{1}H and ^{13}C NMR spectra of compounds **6a** and **6b** were assigned to the corresponding atoms (Table 2) on the basis of COSY, HMBC and HMQC experiments, and their positions are in accord with the proposed structure. Assigning the signals to the corresponding atoms is supported in particular by proved interactions C(2)O with N–CH_3, C(3)H and N(1′)H; C(2′)O with C(3)H and N(1′)H; C(4′)O with N(3′)H and pertinent protons of the R group in HMBC spectra. In addition to the peaks of protonated molecules, the MS and MS/MS spectra of **6a** and **6b** show characteristic ammonium ions $[C_6H_4N(CH_3)COCHNH_3]^+$ (*m*/*z* 163) formed by the cleavage of the bond between N-1′ and C-2′ followed by the loss of ammonia (*m*/*z* 146). Both spectra also yield other structurally important ions,

Table 2. ^{1}H and ^{13}C NMR shifts (δ, ppm) of compounds **6a**,**b**, **10e**,**g**, and **11e** (in DMSO-d_6)

Position	**6a**		**6b**		**10e**[a]		**10g**[a]		**11e**	
	δ_H	δ_C	δ_H	δ_C	δ_H	δ_C	δ_H	δ_C	δ_H	δ_C
2	–	173.84	–	173.96	–	173.92	–	173.36	–	175.18
3	5.21	52.41	5.31	52.67	5.25	53.43	5.39	53.70	5.00	52.80
3a	–	127.13	–	128.26	–	126.32	–	126.02	–	128.67
4	7.26	122.13	7.33	123.48	7.38	124.20	7.46	124.45	7.22	123.31
5	7.06	122.13	7.08	122.24	7.06	122.82	7.12	123.29	7.06	122.03
6	7.36	128.64	7.36	128.20	7.31	129.20	7.26	129.08	7.32	128.30
7	7.00	108.44	7.05	108.54	6.84	108.30	6.82	109.55	7.00	108.25
7a	–	143.99	–	144.13	–	143.90	–	144.09	–	143.85
N–CH_3	3.16	26.27	3.18	26.37	3.27	26.54	–	–	3.14	26.15
1′	9.06	–	9.35	–	9.79	–	9.90	–	6.68	–
2′	–	152.95	–	153.25	–	154.78	–	154.78	–	157.53
3′	10.44	–	10.88	–	–	–	–	–	6.18	–
4′	–	175.08	–	168.37	–	175.08	–	175.11	–	–
1-Bu	2.36	35.42	–	–	3.67	47.07	3.69	47.07	3.00	40.18
2-Bu	1.56	26.57	–	–	1.48	31.55	1.50	31.56	1.39	32.13
3-Bu	1.32	21.71	–	–	1.09	19.66	1.10	19.66	1.30	19.68
4-Bu	0.91	13.77	–	–	0.71	13.39	0.72	13.39	0.91	13.85
ipso-Ph (4′)	–	–	–	132.62	–	136.09	–	136.10	–	–
o-Ph (4′)	–	–	8.01	128.76	7.40	126.02	7.41	126.02	–	–
m-Ph (4′)	–	–	7.57	128.33	7.43	128.61	7.46	128.62	–	–
p-Ph (4′)	–	–	7.68	133.02	7.46	130.36	7.49	130.40	–	–
ipso-Ph (1)	–	–	–	–	–	–	–	134.43	–	–
o-Ph (1)	–	–	–	–	–	–	7.48	126.69	–	–
m-Ph (1)	–	–	–	–	–	–	7.53	129.62	–	–
p-Ph (1)	–	–	–	–	–	–	7.39	128.16	–	–

[a] In deuteriochloroform.

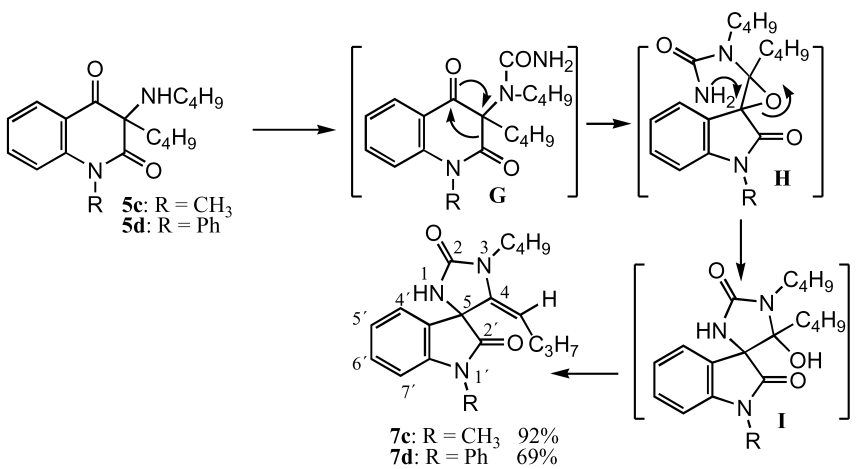
Table 3. ^{1}H and ^{13}C NMR shifts (δ, ppm) of compounds **7c** and **7d** (in DMSO-d_6)

Position	**7c**		**7d**	
	δ_H	δ_C	δ_H	δ_C
2	–	157.76	–	157.72
4	–	137.49	–	137.55
5	–	63.31	–	63.54
2′	–	173.57	–	173.16
3a′	–	129.23	–	128.58
4′	7.24	124.13	7.36	124.83
5′	7.16	124.40	7.24	124.11
6′	7.45	130.12	7.41	130.22
7′	7.14	109.08	6.86	109.54
7a′	–	143.65	–	143.35
NH	7.79	–	7.97	–
1 (3)	3.39, 3.47	38.93	3.46, 3.5?	39.06
2 (3)	1.54	28.43	1.57	28.10
3 (3)	1.35	19.36	1.38	19.41
4 (3)	0.97	13.84	0.97	13.88
1 (4)	4.51	98.54	4.61	99.04
2 (4)	1.23, 1.35	28.06	1.48, 1.62	27.12
3 (4)	0.95, 1.05	22.66	1.02, 1.29	22.83
4 (4)	0.54	13.45	0.59	13.57
CH_3 (1′)	3.22	26.43	–	–
ipso-Ph (1′)	–	–	–	133.98
o-Ph (1′)	–	–	7.44	126.28
m-Ph (1′)	–	–	7.68	130.07
p-Ph (1′)	–	–	7.56	128.42

$[C_6H_4N(CH_3)COCH(NCO)]^+$, $[C_6H_5CONH_3]^+$, and $[C_6H_5CO]^+$ for **6b** and $[C_6H_4N(CH_3)COCH(NHCONH_3)]^+$ for **6a**.

Recently, base catalysed or thermally induced rearrangement of 3-alkyl/aryl-3-hydroxy-1*H*,3*H*-quinoline-2,4-diones to 3-acyloxy-1,3-dihydro-2*H*-indol-2-ones have been described.[3,4] In the case of 3-amino derivatives **5**, their rearrangement to compounds **6** could be its nitrogeneous analogy and the reaction mechanism should be similar. Using TLC monitoring, we proved that amines **5a** and **5b** themselves do not change even at temperatures high above their melting points, and that only at temperatures above 260°C does their undefined breakdown to a complex mixture of compounds occur. It is hence obvious, for facilitating rearrangement, that the presence of an acidic hydrogen atom on a heteroatom in position 3 is important. The acidic hydrogen atom of the hydroxyl group, being able to shift to the oxygen atom in position 4, is present in the molecule of 3-hydroxy-1*H*,3*H*-quinoline-2,4-diones and, therefore, these smoothly rearrange.[3,4] However, the hydrogen atom of the amino group in compounds **5** becomes acidic only after substitution of the ureido group for an amino group. The suggested reaction mechanism (Scheme 3) presumes in the first stage a reaction of **5** with isocyanic acid (arising by thermal breakdown of urea) producing intermediate **B** containing a sufficiently acidic hydrogen atom. This intermediate rearranges similarly to 3-hydroxy-1*H*,3*H*-quinoline-2,4-diones[3,4] and intermediate **C** is produced through a 1,2-shift of the carboxamide group. An analogous intermediate, bearing an acyl group in position 3, arises as a by-product of the rearrangement of 3-hydroxy-1*H*,3*H*-quinoline-2,4-diones.[3] Further transformation of intermediate **C** produces epoxide **D**, which opens giving rise to intermediate **E**. It is only at this stage that a further course of rearrangement appears, differentiated from rearrangements of 3-hydroxy-1*H*,3*H*-quinoline-2,4-diones. Intramolecular substitution of the amino group for the iminoester group in position 3 gives rise to intermediate **F**, which is tautomeric with product **6**. However, even direct formation of epoxide **D** from intermediate **B** cannot be ruled out.

The second group of starting compounds **5** consists of compounds bearing a mono-substituted amino group in position 3 (**5c**–**g**). These compounds react with urea in a different manner depending on whether the substituent bound in position 3 is aliphatic or aromatic. Compounds **5c** and **5d** bear a butyl group in position 3 as well as on the nitrogen atom of the amino group. Products of their reaction with urea again possess a basic 2,3-dihydro-1*H*-indol-2-one structure as with **6a** and **6b**, which was deduced from a signal present at approx. 63 ppm in their ^{13}C NMR spectra (Table 3). This signal corresponds to carbon atom C(3) and is shifted to a lower field compared to signals of carbon atoms C(3) in compounds **6a** and **6b**. Both products of the reaction **5c** and **5d** with urea show the presence of an N-butyl group in ^{1}H and ^{13}C NMR spectra. However, the second butyl group, initially bound to carbon C(3) in compounds **5c** and **5d**, transformed after the reaction in both cases into a butylidene group. Protons of the two methylenes of this group and the N–CH_2 group are diastereotopic. From the proton-detected ^{1}H–^{15}N HMBC experiment it follows



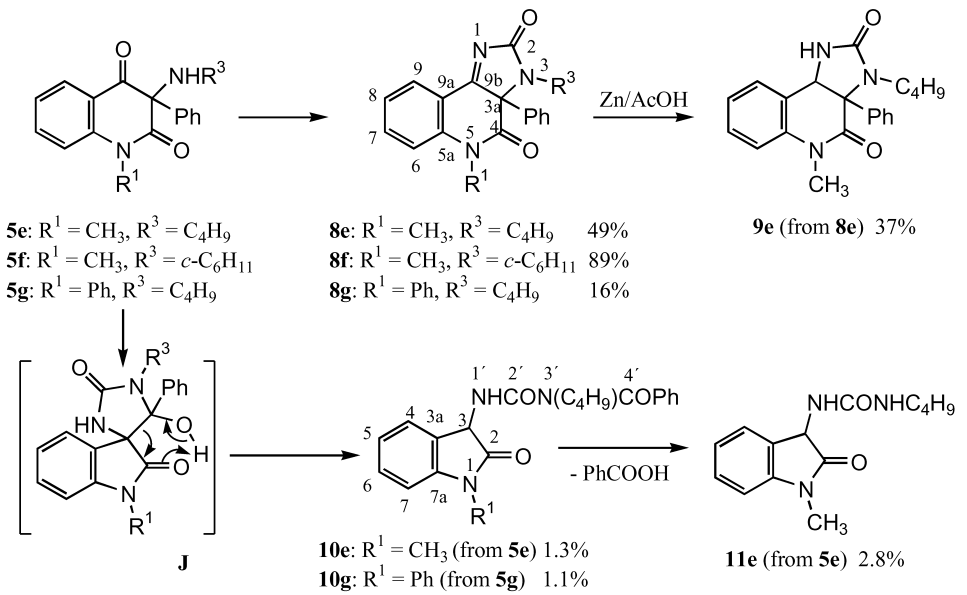
Scheme 4.

that one of the three nitrogen atoms present in the molecule is of NH type and its proton interacts with the other nitrogen atom by means of ^{3}J (^{15}N, ^{1}H), which supports the presence of an NH(CO)N arrangement in the molecule. The third nitrogen atom shows—with the product of the reaction of **5d** with urea—correlation with *ortho* protons of the phenyl group and also with a proton whose chemical shift has a value of 6.86 ppm. All these results led to formulating structures **7c** and **7d** (Scheme 4) for products of the reaction of **5c** and **5d** with urea. All signals in ^{1}H and ^{13}C NMR spectra of compounds **7c** and **7d** were assigned to the corresponding atoms on the basis of COSY, HMBC and HMQC experiments (Table 3) and their positions are in accord with the proposed structure. Assignment of the signals to the corresponding atoms is especially supported by proving an interaction of C(2)O with N(1)H and protons of α-methylene group at N(3); C(2′)O with =CH proton of butylidene group (**7c**,**d**) and N–CH_3 (**7c**). *E*-Stereochemistry at the double bond of compounds **7c** and **7d** follows from a NOE experiment proving a spatial interaction of the proton of the C(4)=CH group with protons of the first two methylenes of the *N*-butyl group.

The APCI mass spectra of compounds **7c** and **7d** exhibit predominant $[M+H]^{+}$ ions with very low fragmentation. The appearance of both spectra is identical but shifted in *m*/*z* values according to the difference between methyl and phenyl substituent. The characteristic cleavage for these compounds containing an imidazole moiety is the neutral loss of the whole aliphatic chain from the position N(3) yielding the corresponding ammonium fragment ions followed by the loss of HNCO or NH_3.

To the best of our knowledge, spiro-compounds of type **7** have not been described in the literature so far and only their analogues having an oxygen atom in position 4 instead of an alkylidene group are known. A proposed reaction mechanism for compounds **5c**,**d** transforming into **7c**,**d** is given in Scheme 4. In this case, it must be also assumed that the primary reaction is the addition of the amino groups of compounds **5c**,**d** to isocyanic acid, forming through breakdown of urea, with production of intermediate **G**. In the case of intermediate **G**, however, a hydrogen atom at the 3-amino group is not available as it was with intermediate **B** in the case of rearranging compounds **5a**,**b** (Scheme 3). For this reason a 1,4-hydrogen shift cannot occur and intermediate **H** must directly arise, analogous to intermediate **D** in Scheme 3. When starting compounds for this intermediate were **5a**,**b**, the C–C bond of the epoxide ring would open, conditioned by the 1,5-hydrogen shift in intermediate **D**. However, in the case of rearranging compounds **5c**,**d** (Scheme 4) this position in intermediate **H** is occupied by a butyl group. For this reason, an opening of the epoxide ring comes about in the C–O bond by a nucleophilic attack of the carbamoyl group with the formation of aminal intermediate **I**. If a hydrogen atom is present α to the hydroxyl group of **I**, a molecule of water eliminates and compounds **7c**,**d** arise (Scheme 4). When proposing the transformation of compounds **5a**,**b** (Scheme 3), we took into account two paths for producing intermediate **D**. In the light of the results provided by compounds **5c**,**d** transforming into **7c**,**d** (Scheme 4) we regard the path leading directly through intermediate **D** as being the more probable.

Compounds **5e**–**g** bear a phenyl group in position 3. If their rearrangement took place during the reaction with urea, we should expect a similar reaction course up to the intermediate stage, which would be similar to intermediate **I** in Scheme 4. In such an intermediate, however, a hydrogen atom in α to the hydroxyl group would not be available and elimination of water would have to occur only during a subsequent molecular rearrangement. Surprisingly, we isolated products **8e**–**g** (Scheme 5) from the reaction of compounds **5e**–**g** with urea. More than one hundred imidazo[4,5-*c*]quinolin-2-ones are known and a number of these display biological activity, but none are substituted in position 3a. Three signals of carbonyl groups appear in the ^{13}C NMR spectra of products of the reactions of **5e**,**f**,**g** with urea; two of these are at approx. 166 ppm and the third at approx. 183 ppm (Table 4). This last signal should not



Scheme 5.

Table 4. ^{1}H and ^{13}C NMR shifts (δ, ppm) of compounds **8e**,**f**,**g** and **9e** (in DMSO-d_6)

Position	**8e**				**8f**		**8g**		**9e**	
	δ_H	δ_H[a]	δ_C	δ_C[a]	δ_H	δ_C	δ_H[a]	δ_C[a]	δ_H[a]	δ_C[a]
2	–	–	166.23	166.55	–	164.59	–	166.48	–	161.51
3a	–	–	77.43	78.05	–	77.54	–	78.49	–	70.28
4	–	–	166.62	166.90	–	166.72	–	167.22	–	169.19
5a	–	–	141.07	140.90	–	141.03	–	142.02	–	138.72
6	7.39	7.03	116.71	115.47	7.35	116.70	6.37	117.42	7.06	114.91
7	7.66	7.46	135.38	134.74	7.64	135.25	7.29	134.43	7.36	130.17
8	7.28	7.12	124.09	123.97	7.28	124.10	7.15	124.22	7.01	123.39
9	7.90	7.89	126.48	126.85	7.90	126.40	8.01	126.85	7.12	130.23
9a	–	–	117.31	117.76	–	117.46	–	117.38	–	119.04
9b	–	–	183.83	183.38	–	183.12	–	183.26	4.77	61.95
N–H	–	–	–	–	–	–	–	–	5.22	–
N–CH_3	3.47	3.44	30.20	29.95	3.44	30.22	–	–	3.52	29.81
N–Ph	–	–	–	–	–	–	[b]	[b]	–	–
1 (3)	3.12, 3.40	3.40, 3.15	42.19	42.76	3.29	54.24	3.42, 3.18	42.78	3.48, 3.20	43.95
2 (3)	1.27, 1.53	1.62, 1.36	30.04	30.19	[c]	[c]	1.68, 1.41	30.19	1.79, 1.37	31.45
3 (3)	1.18	1.17	19.74	20.12	[c]	[c]	1.20	20.21	1.15	20.26
4 (3)	0.79	0.77	13.72	13.56	[c]	[c]	0.79	13.61	0.79	13.30
ipso-Ph (3a)	–	–	133.15	134.75	–	132.97	–	136.76	–	135.53
o-Ph (3a)	7.07	7.01	126.14	126.13	7.12	126.46	7.01	126.47	7.32	127.33
m-Ph (3a)	7.43	7.27	129.96	129.74	7.43	129.79	7.27	129.72	7.34	128.77
p-Ph (3a)	7.43	7.24	130.07	129.74	7.43	130.16	7.24	130.04	7.32	128.99

[a] In deuteriochloroform.
[b] *N*-Phenyl group is not symmetrical at the NMR timescale, all hydrogen and carbon atoms are non-equivalent and considerably broadened (*ipso*-C: –/132.98; other detectable signals: 7.59, 7.52, 7.31, 7.18/130.76, 130.22).
[c] All hydrogen and carbon atoms of cyclohexyl group are non-equivalent. ^{1}H NMR: 3.29, 2.15, 2.03, 1.98, 1.82, 1.51 (2H), 1.24, 1.06, 0.82, and 0.52 ppm. ^{13}C NMR: 54.24 (CH), 29.64, 28.12, 25.92, 25.53, and 25.06 (all CH_2). From HMQC spectra the following correlations for methylene groups were found: 2.15 and 2.03/29.64, 1.98 and 0.52/28.12, 1.82 and 1.24/25.92, 1.51 and 0.82/25.53, 1.51 and 1.06/25.06.

belong to the keto group because the signal of the C=O group in **5** has a value of approx. 196 ppm.[2] Nevertheless, it could relate to the C=N–C(O)–N fragment even though, in our opinion, it lies at a field value too low and does not correspond to the respective value in simulated ^{13}C NMR spectra of compounds **8**. Several imidazolin-2-ones containing the C=N–C(O)–N grouping are known, for instance Δ^3-adamantano[2,1-*d*]imidazolin-2-one,[5] 4,5,5-triphenyl-1,5-dihydroimidazol-2-one,[6] 4,5-diphenyl-5-methyl-1,5-dihydroimidazol-2-one,[7] and 3-acetyl-4,5-dimethyl-2-oxo-3,4-dihydro-2*H*-imidazole-4-carboxylic acid dimethyl ester.[8] We did not, however, succeed in finding any ^{13}C NMR data for these or similar compounds in the literature. In the NMR spectra of compound **8e** (Table 4), the *N*-methyl group was correlated with the C=O group at 166.62 ppm and the *N*-methylene group was correlated with the C=O group at 166.23 ppm. Protons of the first two methylenes of the butyl group are prochiral and, in HMBC, correlations of this sp^3 carbon atom (77.43 ppm) with the *ortho* protons of the phenyl group and protons of the N–CH_2 group are clear. Also in HMBC, correlation of the signal at 183.83 ppm with the *peri*-proton H(9) (7.90 ppm, ^3J) is quite clear as well as a weak interaction with proton H(6) (^4J). From these it follows that the carbon resonating at 183.83 ppm is bound directly to an aromatic nucleus. When measuring the proton-detected correlation $^{1}H-^{15}N$ in DMSO-d_6, merely two chemical shifts obtained by correlation through ^3J were found. When measuring a more concentrated solution in deuteriochloroform, a correlation additionally found was that of the nitrogen atom of the C=N group with the proton H(9) (7.89 ppm, ^4J), a weak interaction with the proton H(6) (7.03 ppm, ^5J), and no correlation was found (by means of ^4J) with protons of the *N*-methyl group which should be detectable in the case of condensation with lactam carbonyl. The ^{15}N chemical shifts (measured in deuteriochloroform and referred to external nitromethane) are −72.7 (=N–), −253.7 (N–CH_3), and −259.5 (N–C_4H_9) ppm. All these data support the structure **8e**.

In order to obtain further evidence for the correctness of the structure as presented, compound **8e** was reduced with zinc in acetic acid (Scheme 5). The structure of the reduction product **9e** followed unambiguously from interpretation of its NMR spectra (Table 4). The mutual NOE enhancement between protons H-9b and H-9 due to their space proximity in compound **9e** independently proves the site of condensation of compound **5a** with urea. The site in which reduction of **8e** occurred is also confirmed by the ^{15}N NMR spectrum of **9e**. Existence of the NH group (created in the reduction) was proved by means of ^1J (^{15}N,H) (88.3 Hz) and the ^{15}N chemical shift of the C=N group (−72.7 ppm in **8e**) changed to a value −290.7 ppm for the CH–NH group in **9e**. Chemical shifts of the remaining nitrogen atoms are −275.0 ppm (N–C_4H_9) and −251.1 ppm (N–CH_3) (in deuteriochloroform). The molecular mass of **9e** was confirmed on the basis of $[M+H]^+$ ion as the only peak in the MS spectrum. The fragmentation paths observed in MS/MS measurements follow the same rules as described for other compounds and hence they enable confirmation of the structure.

More complex NMR spectra than those of compound **8e** are exhibited by cyclohexyl derivative **8f** (Table 4), in which all hydrogen and carbon atoms of the cyclohexyl group are non-equivalent due to its restricted rotation. In the case of diphenyl derivative **8g** all hydrogen and carbon atoms of the *N*-phenyl group are non-equivalent, which is caused by the

fact that the group is not symmetrical on the NMR timescale (Table 4). The protonated molecules are the only peaks observed in APCI mass spectra of compounds **8e** and **8g**. In the case of compound **8f**, the base peak of $[M+H]^+$ ion is accompanied by a less intensive peak corresponding to the neutral loss of cyclohexene from the protonated molecule which is also the only peak in MS/MS spectrum of *m/z* 374. The neutral losses of H_2O, HNCO, CO, and butene are observed in MS/MS spectra of **8e** and **8g** and additionally the loss of C_6H_4 for **8g**. The fragmentation behaviour is in accordance with the suggested structures.

Employing column chromatography of mother liquors after crystallization of the main product (**8e**) of the reaction of **5e** with urea, we succeeded in isolating three further minor compounds (Scheme 5). The first of them is urea derivative **11e**, as determined from the NMR (Table 2) and mass spectra. Compound **11e** dissociates so easily that the $[M+H]^+$ ion has only 2% relative abundance in the APCI mass spectrum measured under standard conditions. The special soft setting of tuning parameters (i.e. 'compound stability' parameter reduced to 20%) increases the relative abundance of $[M+H]^+$ ion to 100%, which confirms the expected molecular weight. The structures of fragment ions with *m/z* 146 and 163 are the same as for compounds **6a** and **6b**. The characteristic cleavage of the whole aliphatic chain (*m/z* 146) leading to the base peak in the MS/MS spectrum of compound **11e** distinguishes between two potential structures with a five-membered indole ring and a six-membered quinoline ring. The latter possibility is reasonably excluded, because the main loss of $CH_3CH_2CH_2CH_2$-$NHCONH_2$ from $[M+H]^+$ ion is a logical fragmentation path for the indole-containing structure but highly improbable for the quinoline-containing alternative.

The second isolated minor product of the reaction of **5e** with urea is the benzoyl derivative of **11e**. Its structure (**10e**), analogous to that of compounds **6a** and **6b**, results from interpreting NMR spectra (Table 2). Compound **11e** almost certainly originates through hydrolysis of **10e** during processing of the reaction mixture. Benzoic acid, arising simultaneously during hydrolysis of **10e**, was isolated as the third minor product.

From the reaction of the 1,3-diphenyl derivative **5g** with urea, which proceeds with relatively low yield as compared to similar reactions of other compounds **5**, we managed to isolate (using column chromatography), besides the main product **8g**, minor product **10g**. Its structure was resolved by interpreting NMR spectra (Table 2) and it is in good agreement with those of compounds **6a**,**b**, **10e** and **11e**. The MS and MS/MS spectra of compounds **10e** and **10g** are nearly identical differing only in the relative abundances of particular ions but with the mass shift of 62 mass units similarly to the pair of compounds **7c** and **7d**. The base peaks in MS spectra are $[M+H]^+$ ions used for the molecular weight determination and $[M+H-CH_3CH_2CH_2CH_2NCO]^+$ ions are the base peaks in MS/MS spectra. All identified fragment ions can be correlated with the structures.

From the structure of the side-products **10e**, **10g**, and **11e** it follows that even starting compounds **5** that do not have available a hydrogen atom capable of elimination in substituent R^3 may rearrange, though to a limited extent. The mechanism of this rearrangement is not quite clear yet but we presume that aminal intermediate **J** (Scheme 5) might originate to a limited degree through a succession of reactions similar to rearrangement of compounds **5c**,**d**. A molecule of water cannot split off from intermediate **J** owing to the phenyl group present in position 4. Therefore, an opening of the imidazole ring thus occurs, maybe with a 1,5-hydrogen shift, to give compounds **10**.

From the text above it is apparent that a reaction—very simple at first glance—of α-aminoketones with urea can proceed in a very complex manner and offer great surprises. However, it should be realized that the system in question is really quite complex, and apart from urea in excess contains isocyanic acid, ammonia, perhaps also biuret and cyanuric acid. The described reaction of 3-amino-1*H*,3*H*-quinoline-2,4-diones (**5**) with urea is not merely interesting from a theoretical point of view but, owing to the simple reaction protocol, presents an easy pathway to preparing novel heterocyclic systems that might be interesting structures for studying biological activity.

3. Experimental

Melting points were determined on a Kofler block or Gallencamp apparatus. IR (KBr) spectra were recorded on a Mattson 3000 spectrophotometer. NMR spectra were recorded on a Bruker Avance spectrometer (500.13 MHz for ^1H, 125.76 MHz for ^{13}C, 50.68 MHz for ^{15}N) in DMSO-d_6 or $CDCl_3$. ^1H and ^{13}C chemical shifts are given on the δ scale (ppm) and are referenced to internal TMS. ^{15}N chemical shifts were referred to external neat nitromethane in co-axial capillary (δ=0.0). All 2D experiments (gradient-selected (gs)-COSY, NOESY, proton-detected gs-HMQC, gs-HMBC) were performed using manufacturer's software. Proton spectra were assigned using gs-COSY. Benzene ring protons were assigned according to their characteristic multiplet pattern. Protonated carbons were assigned by gs-HMQC. Quaternary carbons were assigned by gs-HMBC. The positive-ion APCI mass spectra were measured on an ion trap analyser Esquire 3000 (Bruker Daltonics, Bremen, Germany) within the mass range *m/z*=50–500. Samples were dissolved in acetonitrile and analysed by direct infusion at the flow rate of 50 μl/min. The ion source temperature was 350EC, the APCI probe temperature was 350EC, the flow rate and the pressure of nitrogen were 4 l/min and 45 psi, respectively. For MS/MS measurements, the isolation width of precursor ions was 4 *m/z* and the collision amplitude was in the range 0.7–0.8 V. The tuning parameter 'compound stability' was reduced to 20% for the measurement of compound **9e**. Column chromatography was carried out on Silica gel (Merck, grade 60, 70–230 mesh) using chloroform and then successive mixtures of chloroform–ethanol (in ratios from 99:1 to 8:2, solvent system S1) or benzene and then successive mixtures of benzene–ethyl acetate (in ratios from 99:1 to 8:2, solvent system S2). Reactions as well as the course of separation and also the purity of substances were monitored by TLC (elution systems benzene–ethyl acetate, 4:1, and chloroform–ethanol, 9:1 and/or 19:1) on Alugram® SIL G/UV_{254} foils (Macherey-Nagel). Elemental analyses (C, H, N) were

performed with a EA 1108 Elemental Analyzer (Fisons Instrument).

3.1. General procedure for the preparation of 3-chloro-1*H*,3*H*-quinoline-2,4-diones (4a–g)

Compounds **4a**–**g** were prepared by reaction of appropriate 4-hydroxy-1*H*-quinolone-2-one with sulfuryl chloride according to procedure described in Ref. 2.

3.1.1. 3-Butyl-3-chloro-1-methyl-1*H*,3*H*-quinoline-2,4-dione (4a). Yield 58% (after column chromatography, solvent system S2). Yellow oil, IR: 2958, 2933, 2871, 1707, 1675, 1602, 1472, 1359, 1302, 1108, 1089, 764, 751, 672, 643, 529 cm^{-1}. Anal. calcd (found) for $C_{14}H_{16}ClNO_2$: C 63.28 (63.07); H 6.07 (6.15); N 5.27 (5.01).

3.2. General procedure for the preparation of 3-amino-1*H*,3*H*-quinoline-2,4-diones (5a–g)

Compounds **5a**–**g** were prepared by the reaction of appropriate 3-chloro-1*H*,3*H*-quinoline-2,4-dione with an amine (Method A) or a mixture of ammonium chloride and potassium carbonate (Method B), respectively, in dimethylformamide according to the general procedures described in Ref. 2.

3.2.1. 3-Amino-3-butyl-1-methyl-1*H*,3*H*-quinoline-2,4-dione (5a). Yield 58% (method B, 160 h). Colorless plates, mp 85–86°C (benzene–hexane), IR: 3389, 3316, 3112, 2953, 2936, 2904, 1706, 1665, 1605, 1475, 1358, 1301, 1221, 1193, 1108, 972, 844, 778, 755, 666, 617, 533 cm^{-1}. Anal. calcd (found) for $C_{14}H_{18}N_2O_2$: C 68.27 (68.38); H 7.37 (7.59); N 11.37 (11.18).

3.2.2. 3-Butyl-3-butylamino-1-methyl-1*H*,3*H*-quinoline-2,4-dione (5c). Yield 70% (method A, 3 h, chromatography with solvent system S2). Yellow oil, IR: 3332, 3083, 2957, 2930, 2871, 1703, 1665, 1602, 1471, 1356, 1302, 1167, 1109, 1046, 996, 952, 863, 758, 664, 530 cm^{-1}. Anal. calcd (found) for $C_{18}H_{26}N_2O_2$: C 71.49 (71.33); H 8.67 (8.69); N 9.26 (9.08).

3.2.3. 3-Butyl-3-butylamino-1-phenyl-1*H*,3*H*-quinoline-2,4-dione (5d). Yield 68% (method A, 23 h). Colorless prisms, mp 64–67°C (hexane), IR: 3438, 3343, 2957, 2928, 2870, 2857, 1708, 1674, 1602, 1461, 1342, 1297, 1243, 1178, 1160, 1121, 1071, 929, 760, 705, 649, 585, 518 cm^{-1}. Anal. calcd (found) for $C_{23}H_{28}N_2O_2$: C 75.79 (75.49); H 7.74 (7.73); N 7.69 (7.47).

3.2.4. 3-Butylamino-1,3-diphenyl-1*H*,3*H*-quinoline-2,4-dione (5g). Yield 70% (method A, 1 h). Colorless needles, mp 110–112°C (hexane), IR: 3416, 3380, 3329, 3064, 2959, 2922, 2851, 1706, 1673, 1600, 1492, 1459, 1338, 1302, 1247, 1149, 1109, 1034, 978, 912, 876, 834, 766, 718, 695, 655, 605 cm^{-1}. Anal. calcd (found) for $C_{25}H_{24}N_2O_2$: C 78.10 (77.89); H 6.29 (6.19); N 7.29 (7.07).

3.3. General procedure for the reaction of 3-amino-1*H*,3*H*-quinoline-2,4-diones (5a–g) with urea

A mixture of appropriate 3-amino-1*H*,3*H*-quinoline-2,4 dione (**5**) (5 mmol) and urea (1.8 g, 30 mmol) in acetic acid (10 ml) was refluxed for 30–50 min and the course of the reaction was monitored by TLC. After cooling, the reaction mixture was diluted with water (150 ml). The precipitated product (**6a**,**b**, **7c**,**d**, **8f**) was filtered off with suction and recrystallized from the appropriate solvent.

The reaction (30 min) of **5e** (4.84 g, 15 mmol) with urea (5.36 g, 90 mmol) in acetic acid (12 ml) afforded a crude reaction product (3.98 g, portion A), which was, according to TLC, a mixture of several compounds. The filtrate after separation of portion A was extracted with benzene (3×15 ml). The combined extracts were dried over sodium sulfate and evaporated in vacuo (0.62 g, portion B). The main reaction product (**8e**) (2.35 g, 45%) was obtained by crystallization of crude reaction product (portion A) with benzene. The mother liquors after crystallization of **8e** were column chromatographed on silica gel using solvent system S2. After evaporation of combined fractions and crystallization, three substances were isolated in the following elution order: **10e** (70 mg, 1.3%), **8e** (180 mg, 3.5%), and **11e** (69 mg, 1.8%). Portion B was column chromatographed on silica gel using solvent system S1. After evaporation of combined fractions and crystallization, two substances were isolated in the following elution order: **8e** (12 mg, 0.2%) and **11e** (48 mg, 1.0%). The non-crystallized portions after chromatography were collected and, after evaporation to dryness, extracted with 5% solution sodium hydrogen carbonate (5×3 ml). The combined extracts were filtered and the filtrate was acidified with conc. hydrochloric acid. Separated crystals were filtered off and identified (mp, IR) as benzoic acid (16 mg, 0.8%).

The reaction (25 min) of **5g** (1.43 g, 3.7 mmol) with urea (1.34 g, 22.3 mmol) in acetic acid (4 ml) afforded a crude reaction product (1.07 g), which was column chromatographed on silica gel using solvent system S2. After evaporation of combined fractions and crystallization, two substances were isolated in the following elution order: **10g** (17 mg, 1.1%) and **8g** (235 mg, 15.6%).

3.3.1. 1-Methyl-3-(3-pentanoylureido)-2-oxo-2,3-dihydro-1*H*-indole (6a). Yield 83% (45 min). Colorless plates, mp 190–196°C (ethanol), IR: 3320, 3231, 3096, 2976, 2958, 2930, 1722, 1704, 1686, 1614, 1537, 1511, 1494, 1378, 1354, 1324, 1266, 1235, 1188, 1121, 1091, 1046, 863, 763, 697, 672, 638, 588, 555 cm^{-1}. Anal. calcd (found) for $C_{15}H_{19}N_3O_3$: C 62.27 (62.06); H 6.62 (6.60); N 14.52 (14.37). APCI-MS: *m/z* 290 $[M+H]^+$ (80%), 272 $[M+H-H_2O]^+$, 206 $[C_6H_4N(CH_3)COCH(NHCONH_3)]^+$, 188 $[C_6H_4N(CH_3)COCH(NCO)]^+$, 163 $[C_6H_4N(CH_3)COCH(NH_3)]^+$, 161 $[C_6H_4N(CH_3)COCH(NH)]^+$, 146 $[C_6H_4N(CH_3)COCH)]^+$ (100%). APCI-MS/MS of precursor ion *m/z* 290: 206 $[C_6H_4N(CH_3)COCH(NHCONH_3)]^+$, (100%), 188 $[C_6H_4N(CH_3)COCH(NCO)]^+$, 163 $[C_6H_4N(CH_3)COCH(NH_3)]^+$, 146 $[C_6H_4N(CH_3)COCH]^+$.

3.3.2. 3-(3-Benzoylureido)-1-methyl-2-oxo-2,3-dihydro-1*H*-indole (6b). Yield 32% (30 min). Colorless plates, mp 213–214°C (ethanol), IR: 3295br, 3059, 2935br, 1726, 1698, 1671, 1614, 1531, 1495, 1470, 1374, 1318, 1273, 1227, 1117, 1087, 1018, 901, 852, 751, 709br, 634, 594, 558, 541 cm^{-1}. Anal. calcd (found) for $C_{17}H^{15}N_3O_3$: C

66.01 (66.10); H 4.89 (4.82); N 13.58 (13.43). APCI-MS: *m/z* 310 $[M+H]^+$ (100%), 292 $[M+H-H_2O]^+$, 267 $[M+H-NHCO]^+$, 188 $[C_6H_4N(CH_3)COCH(NCO)]^+$, 163 $[C_6H_4N(CH_3)COCH(NH_3)]^+$, 161 $[C_6H_4N(CH_3)COCH(NH)]^+$, 146 $[C_6H_4N(CH_3)COCH)]^+$, 122 $[C_6H_5CONH_3]^+$, 105 $[C_6H_5CO]^+$. APCI-MS/MS of precursor ion *m/z* 310: *m/z* 267 $[M+H-NHCO]^+$, 188 $[C_6H_4N(CH_3)COCH(NCO)]^+$, 163 $[C_6H_4N(CH_3)COCH(NH_3)]^+$, 146 $[C_6H_4N(CH_3)COCH)]^+$ (100%), 122 $[C_6H_5CONH_3]^+$, 105 $[C_6H_5CO]^+$.

3.3.3. (*E*)-3-Butyl-4-butylidene-1′-methyl-1′*H*-spiro[imidazolidine-5,3′-indole]-2,2′-dione (7c). Yield 92% (30 min). Colorless needles, mp 196–200°C (ethanol), IR: 3214, 3090, 2959, 2932, 2867, 1729, 1712, 1675, 1611, 1493, 1453, 1428, 1372, 1341, 1259, 1234, 1192, 1126, 1087, 1020, 934, 879, 764, 737, 695, 676, 612, 538 cm^{-1}. Anal. calcd (found) for $C_{19}H_{25}N_3O_2$: C 69.70 (69.51); H 7.70 (7.51); N 12.83 (12.66). APCI-MS: *m/z* 328 $[M+H]^+$ (100%), 272 $[M+H-CH_3CH_2CH{=}CH_2]^+$. APCI-MS/MS of precursor ion *m/z* 328: *m/z* 285 $[M+H-NHCO]^+$, 272 $[M+H-CH_3CH_2CH{=}CH_2]^+$, 255 $[M+H-CH_3CH_2CH{=}CH_2-NH_3]^+$, 229 $[M+H-CH_3CH_2CH{=}CH_2-NHCO]^+$ (100%), 148.

3.3.4. (*E*)-3-Butyl-4-butylidene-1′-phenyl-1′*H*-spiro[imidazolidine-5,3′-indole]-2,2′-dione (7d). Yield 69% (50 min). Yellowish needles, mp 124–128°C (benzene–hexane), IR: 3219, 2957, 2931, 2870, 1742, 1674, 1612, 1594, 1499, 1451, 1423, 1365, 1175, 1130, 940, 750, 704, 623 cm^{-1}. Anal. calcd (found) for $C_{24}H_{27}N_3O_2$: C 74.01 (73.73); H 6.99 (6.95); N 10.79 (10.47). APCI-MS: *m/z* 390 $[M+H]^+$ (100%), 334 $[M+H-CH_3CH_2CH{=}CH_2]^+$, 291 $[M+H-CH_3CH_2CH{=}CH_2\text{-}NHCO]^+$. APCI-MS/MS of precursor ion *m/z* 390: *m/z* 373 $[M+H-NH_3]^+$, 347 $[M+H-NHCO]^+$, 334 $[M+H-CH_3CH_2CH{=}CH_2]^+$, 317 $[M+H-CH_3CH_2CH{=}CH_2\text{-}NH_3]^+$, 291 $[M+H-CH_3CH_2CH{=}CH_2\text{-}NHCO]^+$ (100%), 250, 210.

3.3.5. 3-Butyl-5-methyl-3a-phenyl-3,3a-dihydro-5*H*-imidazo[4,5-*c*]quinoline-2,4-dione (8e). Yield 49% (40 min). Yellowish plates, mp 198–200°C (benzene–hexane), IR: 2957, 2938, 2893, 2873, 1736, 1690, 1611, 1468, 1359, 1286, 1154, 1070, 1042, 974, 772, 755, 699, 608 cm^{-1}. Anal. calcd (found) for $C_{21}H_{21}N_3O_2$: C 72.60 (72.46); H 6.09 (6.07); N 12.10 (11.97). APCI-MS: *m/z* 348 $[M+H]^+$ (100%). APCI-MS/MS of precursor ion *m/z* 348: *m/z* 330 $[M+H-H_2O]^+$, 305 $[M+H-NHCO]^+$, 292 $[M+H-CH_3CH_2CH{=}CH_2]^+$ (100%), 264 $[M+H-CH_3CH_2CH{=}CH_2-CO]^+$, 249 $[M+H-CH_3CH_2CH{=}CH_2-NHCO]^+$, 221, 217, 160, 146, 104.

3.3.6. 3-Cyclohexyl-5-methyl-3a-phenyl-3,3a-dihydro-5*H*-imidazo[4,5-*c*]quinoline-2,4-dione (8f). Yield 89% (40 min). Colorless plates, mp 291–294°C (ethanol), IR: 2957, 2932, 2918, 2853, 1734, 1692, 1621, 1605, 1469, 1449, 1359, 1312, 1285, 1206, 1156, 1126, 1073, 984, 942, 892, 773, 750, 702, 651, 609, 529 cm^{-1}. Anal. calcd (found) for $C_{23}H_{23}N_3O_2$: C 73.97 (73.89); H 6.21 (6.19); N 11.25 (11.07). APCI-MS: *m/z* 374 $[M+H]^+$ (100%), 292 $[M+H-C_6H_{10}]^+$. APCI-MS/MS of precursor ion *m/z* 374: *m/z* 292 $[M+H-C_6H_{10}]^+$ (100%).

3.3.7. 3-Butyl-3a,5-diphenyl-3,3a-dihydro-5*H*-imidazo[4,5-*c*]quinoline-2,4-dione (8g). Yield 16% (25 min). Colorless plates, mp 83–86°C (benzene–hexane), IR: 2960, 2938, 2871, 1728, 1706, 1613, 1491, 1464, 1447, 1352, 1308, 1277, 1246, 1133, 1072, 772, 755, 737, 699, 686, 611 cm^{-1}. Anal. calcd (found) for $C_{26}H_{23}N_3O_2$: C 76.26 (76.32); H 5.66 (5.80); N 10.26 (10.15). APCI-MS: *m/z* 410 $[M+H]^+$ (100%). APCI-MS/MS of precursor ion *m/z* 410: *m/z* 392 $[M+H-H_2O]^+$, 354 $[M+H-CH_3CH_2CH{=}CH_2]^+$ (100%), 311 $[M+H-CH_3CH_2CH{=}CH_2-HNCO]^+$, 279 $[M+H-CH_3CH_2CH{=}CH_2-C_6H_4]^+$, 251 $[M+H-CH_3CH_2CH{=}CH_2-C_6H_4-CO]^+$, 208 $[M+H-CH_3CH_2CH{=}CH_2-C_6H_4-HNCO-CO]^+$, 160.

3.3.8. 3-Butyl-5-methyl-3a-phenyl-3,3a,5,9b-tetrahydro-1*H*-imidazo[4,5-*c*]quinoline-2,4-dione (9e). Powdered zinc (327 mg, 5 mmol) was added in small portions to the stirred solution of **8e** (347 mg, 1 mmol) in acetic acid (10 ml) during 10 min at 100°C. The mixture was for stirred additional 30 min, cooled, evaporated in vacuo to one half of its volume and diluted with water (20 ml). The yellow precipitate was filtered with suction and column chromatographed using solvent system S2. Collected fractions were crystallized. Yield 129 mg (37%). Colorless prisms, mp 246–248°C (benzene), IR: 3216br, 2956, 2930, 2874, 1706, 1672, 1640, 1606, 1475, 1398, 1367, 1278, 1140, 1106, 752, 703, 636 cm^{-1}. Anal. calcd (found) for $C_{21}H_{23}N_3O_2$: C 72.18 (72.29); H 6.63 (6.80); N 12.03 (12.15). APCI-MS: *m/z* 350 $[M+H]^+$ (100%). APCI-MS/MS of precursor ion *m/z* 350: *m/z* 333 $[M+H-NH_3]^+$, 322 $[M+H-CO]^+$, 307 $[M+H-HNCO]^+$, 294 $[M+H-CH_3CH_2CH{=}CH_2]^+$, 277 $[M+H-CH_3CH_2CH{=}CH_2\text{-}NH_3]^+$, 251 $[M+H-CH_3CH_2CH{=}CH_2-HNCO]^+$, 160 $[C_6H_4N(CH_3)COCHCH_2]^+$ (100%), 146 $[C_6H_4NHCOCHCH_2]^+$, 104 $[C_6H_5CH_2CH]^+$.

3.3.9. 3-(3-Benzoyl-3-butylureido)-1-methyl-2-oxo-2,3-dihydro-1*H*-indole (10e). Side product of the reaction of **5e** with urea, yield 1.3%. Colorless prisms, mp 156–158°C (benzene–hexane), IR: 3295, 3053, 2959, 2927, 2871, 1718, 1684, 1657, 1612, 1503, 1468, 1376, 1355, 1294, 1222, 1084, 1018, 757, 724, 697, 671, 657 cm^{-1}. Anal. calcd (found) for $C_{21}H_{23}N_3O_3$: C 69.02 (69.23); H 6.34 (6.45); N 11.50 (11.37). APCI-MS and APCI-MS/MS of precursor ion: *m/z* 366 are the same: *m/z* 366 $[M+H]^+$ (100% for MS spectrum), 348 $[M+H-H_2O]^+$, 267 $[M+H-CH_3CH_2CH_2\text{-}CH_2NCO]^+$ (100% for MS/MS spectrum), 244 $[M+H-C_6H_5CONH_3]^+$, 178 $[C_6H_5CONH_2(CH_2CH_2CH_2CH_3)]^+$, 161 $[C_6H_4N(CH_3)COCH(NH)]^+$, 146 $[C_6H_4N(CH_3)COCH]^+$, 105 $[C_6H_5CO]^+$.

3.3.10. 3-(3-Benzoyl-3-butylureido)-1-phenyl-2-oxo-2,3-dihydro-1*H*-indole (10g). Side product of the reaction of **5 g** with urea, yield 1.1%. Colorless plates, mp 183–188°C (benzene–hexane), IR: 3251, 3050, 2959, 2930, 2873, 1732, 1676, 1642, 1613, 1530, 1500, 1467, 1451, 1375, 1321, 1301, 1225, 1176, 1107, 757, 724, 704, 648 cm^{-1}. Anal. calcd (found) for $C_{26}H_{25}N_3O_3$: C 73.05 (73.16); H 5.89 (5.97); N 9.83 (9.72). Both APCI-MS and APCI-MS/MS of precursor ion *m/z* 428: *m/z* 428 $[M+H]^+$ (100% for MS spectrum), 410 $[M+H-H_2O]^+$, 385 $[M+H-HNCO]^+$ (only in MS spectrum), 329 $[M+H-CH_3CH_2CH_2CH_2NCO]^+$ (100% for MS/MS spectrum), 306 $[M+H-C_6H_5CONH_3]^+$, 288 $[M+H-C_6H_5CO-NH_3\text{-}H_2O]^+$ (only in MS spectrum),

250 $[M+H-C_6H_5CO-CH_3CH_2CH_2CH_2NH_2]^+$, 223 $[C_6H_4N(C_6H_5)COCH(NH)]^+$, 208 $[C_6H_4N(C_6H_5)COCH]^+$, 178 $[C_6H_5CONH_2(CH_2CH_2CH_2CH_3)]^+$.

3.3.11. 3-(3-Butylureido)-1-methyl-2-oxo-2,3-dihydro-1*H*-indole (11e). Side product of the reaction of **5e** with urea, yield 2.8%. Colorless plates, mp 192–195°C (benzene), IR: 3323, 3058, 2957, 2931, 2861, 1712, 1629, 1579, 1495, 1469, 1375, 1348, 1307, 1262, 1125, 1091, 749, 652 cm^{-1}. Anal. calcd (found) for $C_{14}H_{19}N_3O_2$: C 64.35 (64.06); H 7.33 (7.30); N 16.08 (15.85). APCI-MS: *m/z* 262 $[M+H]^+$ (100%), 188 $[C_6H_4N(CH_3)COCH(NCO)]^+$, 163 $[C_6H_4N(CH_3)COCH(NH_3)]^+$, 161 $[C_6H_4N(CH_3)COCH(NH)]^+$, 146 $[C_6H_4N(CH_3)COCH]^+$. APCI-MS/MS of precursor ion *m/z* 262: *m/z* 188 $[C_6H_4N(CH_3)COCH(NCO)]^+$, 163 $[C_6H_4N(CH_3)COCH(NH_3)]^+$, (100%), 146 $[C_6H_4N(CH_3)COCH]^+$, 74 $[CH_3CH_2CH_2CH_2NH_3]^+$.

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