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Reaction of 1-substituted 3-aminoquinoline-2,4-diones with isothiocyanates. An easy pathway to generate novel 2-thioxo-1′*H*-spiro[imidazoline-5,3′-indole]-2,2′-diones

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ABSTRACT

3-Butyl-3-amino-1*H*,3*H*-quinoline-2,4-diones react with isothiocyanates to give novel 3a-butyl-9b-hydroxy-2-thioxo-1,2,3,3a,5,9b-hexahydro-imidazo[4,5-*c*]quinolin-2-ones in high yields. These compounds rearrange in boiling acetic acid or concd hydrochloric acid to give (*E*)- and/or (*Z*)-4-butylidene-2-thioxo-1′*H*-spiro[imidazoline-5,3′-indole]-2,2′-diones. All compounds were characterized by their ^{1}H, ^{13}C, IR and MS spectra, and some of them also by ^{15}N NMR. The structure of one compound was investigated by single-crystal X-ray diffraction.

1. Introduction

In our laboratory, attention has been given to study the reactivity of 3-alkyl/aryl-3-amino-1*H*,3*H*-quinoline-2,4-diones. We have recently investigated the reaction of these compounds with isocyanates to yield 3′-substituted 3-ureidoquinoline-2,4-diones and/or their cyclic isomers.[1,2] These compounds rearrange in boiling acetic acid to form new heterocyclic systems. In cases where the starting compounds are not substituted at position 1, their rearrangement in acetic acid produced mixtures of 3-ureidoindoles and 1,3-disubstituted ureas, whereas rearrangement in concd hydrochloric acid yielded derivatives of imidazolinone.[1,3,4] However, if position 1 in the starting compound bears an alkyl or aryl group, three different derivatives of spiro-imidazolidinyl-oxindoles arise.[2] An illustrative survey of these reactions was given in our latest paper.[2]

Molecular rearrangement of the addition products of 3-aminoquinoline-2,4-diones with isocyanates yields products displaying quite exceptional structural diversity. This gave us incentive to perform an analogous reaction of 3-aminoquinoline-2,4-diones with isothiocyanates, and to examine how the products of this reaction behave in an acidic environment. We anticipated the rise of new compounds containing a sulfur atom, which may be interesting, since many biologically active compounds belong to this group.[5,6] Molecular rearrangements of the adducts of 3-aminoquinolinediones with isocyanates[1–4] gave results that were largely dependent on the character of the substituents at positions 1 and 3 of the starting compound. Thus, according to this criterion, we now divided the starting 3-aminoquinolinediones into three different groups. The first group contained compounds substituted at position 1 with an alkyl or aryl group and at position 3 with an alkyl group. The second group contained compounds having the same type of substitution at position 1, but bearing a phenyl group at position 3. The third group comprised compounds without any substituent at position 1.

We would like to demonstrate in this work that the reaction of 1-substituted 3-butyl-3-aminoquinolinediones **1** with isothiocyanates provides—contrary to their reactions with isocyanates—a single product **3**, which rearranges in an acid environment to give 4-butylidene-2-thioxo derivatives of spiro-imidazolidinyl-oxindoles **4**.

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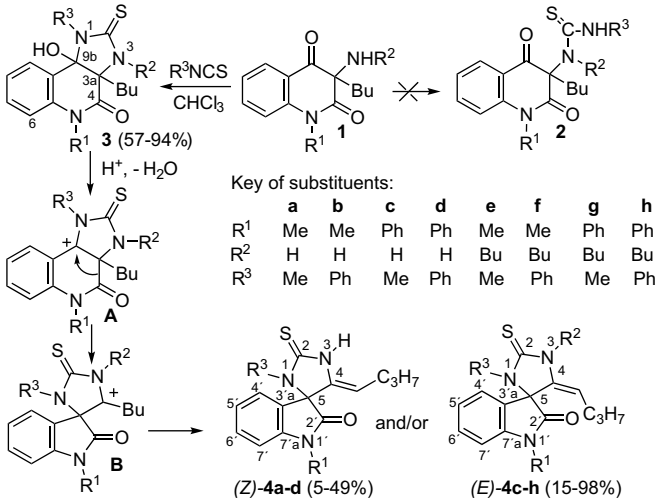
2. Results and discussion

Reactions of 3-aminoquinoline-2,4-diones **1** with isothiocyanates were performed by boiling the reaction components in chloroform (Scheme 1, Table 1). Methylisothiocyanate and phenylisothiocyanate were chosen as model isothiocyanates. All starting compounds had a butyl group at position 3, which fulfils the conditions for compounds **1** of the first group (see above). The substituent selected for position 1 was methyl or phenyl, and a primary amino or butylamino group was chosen as the second substituent at position 3. Starting aminoketones **1** were obtained from the corresponding 3-chloro derivatives in accordance with procedures described in Ref. 7. One novel amine, **1c**, was prepared and its NMR spectra are given in Table 2.



Scheme 1.

Table 1
Preparation of compounds **3** by the reaction of 3-aminoquinoline-2,4(1*H*,3*H*)-diones (**1**) with isothiocyanates

Entry	Educt	Substituents[a]			Time (h)	Product (yield, %)
		R^1	R^2	R^3		
1	**1a**	Me	H	Me	3	**3a** (94)
2	**1a**	Me	H	Ph	1	**3b** (89)
3	**1c**	Ph	H	Me	2	**3c** (57)
4	**1c**	Ph	H	Ph	1	**3d** (81)[b]
5	**1e**	Me	Bu	Me	3.5	**3e** (58)
6	**1e**	Me	Bu	Ph	4.5	**3f** (68)
7	**1g**	Ph	Bu	Me	6.5	**3g** (92)
8	**1g**	Ph	Bu	Ph	13	**3h** (86)

[a] R^3 from isothiocyanate.
[b] A mixture of **2d** and **3d**, subsequently converted in 65% yield to almost pure **3d** by heating in DMSO.

The reaction of aminoketones **1** with isothiocyanates should produce 3-thioureido-1*H*,3*H*-quinoline-2,4-diones **2** and/or 9b-hydroxy-2-thioxo-1,2,3,3a,5,9b-hexahydro-imidazo[4,5-*c*]quinolin-4-ones **3** (Scheme 1). However, compounds **3** arose (Table 1) in a total majority in good to very good yields in this case, contrary to the reaction of **1** with isocyanates.[2] The NMR spectra of **3** are presented in Table 2.

Only in one case—from starting compound **1c** and phenylisothiocyanate (Table 1, entry 4)—was a mixture of compounds obtained that could not be separated chromatographically. Nevertheless, when the NMR spectra of those reaction products were acquired in DMSO-d_6, it was found that the second component in the mixture, probably compound **2d**, diminished with time, and within 2 days, almost fully transformed into cyclic isomer **3d**. For that reason, we subjected the raw product of the reaction of **1c** with phenylisothiocyanate to heating in DMSO, and obtained nearly pure **3d**, despite the weak signals of compound **2d** (approx. 5%) always present in the NMR spectrum. Signals of trace quantities of compounds **2** were noticed in the NMR spectra of almost all of the compounds **3**, even though these were pure according to TLC. Such results indicate the possibility of a chemical equilibrium between compounds **2** and their cyclic isomers **3** in DMSO, albeit one that is strongly shifted in favour of compounds **3**. The reaction of **1** with isothiocyanates did not produce, in any case, a tautomeric compound bearing SH group that could theoretically arise from compounds having R^2=H, i.e., **3a–d**. Signals of the thioxo group of compounds **3** lie in a narrow region of 181.3–182.4 ppm, which is typical of the C=S group, and excludes the presence of the C–SH group.

The molecular rearrangement of compound **3** was carried out in accordance with our latest work[2] by boiling in acetic acid or concd hydrochloric acid. The results are presented in Table 3. A comparison of the yields of the rearrangement of **3** into **4** shows only a slight influence of the reaction medium on the reaction course, which is a different result from that observed for the rearrangement of the 2-oxaanalogues of **3**.[2,4] A suggested reaction mechanism for the rearrangement (Scheme 1) supposes that compounds **3**, by protonation and loss of water, produce intermediate **A** that is transformed into intermediate **B** through migration of the N(R^1)(C=O) group from the 3a to the 9b position. Further transformations of intermediate **B** depend on the character of the substituents at positions 3 and 4.[2,4]

A butyl group is present at position 4 in all of the compounds studied. If a butyl group is bonded to the nitrogen atom in position 3, intermediate **B** stabilizes by splitting-off of a proton, thus giving spiro-compounds **4**. Interestingly, the formation of stable enamides **4** takes place even in cases where R^2=H. The formation of tautomeric imines was not observed. We observed that coupling constants ^1J(^{15}N, ^{1}H) for the nitrogen atom at position 3 of 99.4±0.4 Hz, which unambiguously indicated the presence of an NH group.

A comparison of the NMR spectral characteristics of compounds **4** (Table 4) showed that these compounds differ by configuration at the double bond of the butylidene group. Key compounds for determination of the configuration turned out to be two isomeric products isolated from the rearrangement of compound **3c**. These two isomers displayed very similar MS spectra. In their NMR spectra, the same number of signals was present; however, they differed in chemical shifts. Conclusive results were obtained from 2D-NOESY measurements. A through-space interaction of the N(3)–H proton and the =CH proton of the butylidene group was observed (Fig. 1) in the 2D-NOESY spectrum of the major product of the rearrangement of **3c** (Table 3). Hence, this compound is the *E*-isomer, and the minor product of the rearrangement of **3c** (Table 3) is the *Z*-isomer (Fig. 2). The greatest differences between the NMR spectra of the (*E*)-**3c** and (*Z*)-**4c** isomers were found in the chemical shifts of the protons of the butylidene group and the carbon atoms of the C=S group, which was used in to assign the corresponding configuration of the other compounds **4** (Table 4).

The formation of an *E*- or *Z*-isomer is influenced by the steric conditions in intermediate **B** (Scheme 1). Intermediates **Be–h** display strong steric interactions between the *N*(3)-butyl and *C*(4)-butyl groups, which unambiguously preferences the formation of the (*E*)-**4e–h** isomers. In the case of compounds **4a**,**b** (R^2=H), such an interaction is absent, and elimination of a proton from intermediate **B** occurs preferentially to give formation of the *Z*-isomer. However, with compounds **4c**,**d**, which, in contrast to **4a**,**b** bear a phenyl group at position 1′, both isomers arise. This may be due to steric interaction between the 4-butyl group and the bulky phenyl substituent at C-1′.

In the case of *E*-**4f**, the structure was confirmed by single-crystal X-ray diffraction (Fig. 3). Single crystals of *E*-**4f** suitable for

Table 2
^{1}H and ^{13}C chemical shifts (δ, ppm) of compounds **1e** and **3a–h** in DMSO-d_6

Position	**1c**		**3a**		**3b**		**3c**		**3d**		**3e**		**3f**		**3g**		**3h**	
	δ_H	δ_C	δ_H	δ_C	δ_H	δ_C	δ_H	δ_C	δ_H	δ_C	δ_H	δ_C	δ_H	δ_C	δ_H	δ_C	δ_H	δ_C
2	—	173.1	—	182.1	—	181.8	—	182.4	—	182.1	—	181.9	—	181.3	—	182.2	—	181.6
3	—	69.4	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—
3a	—	—	—	68.3	—	69.3	—	68.7	—	69.8	—	71.2	—	71.1	—	71.6	—	72.7
4	—	195.5	—	169.0	—	169.0	—	169.3	—	169.2	—	168.5	—	168.4	—	168.8	—	168.7
4a	—	119.8	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—
5	7.91	127.1	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—
5a	—	—	—	137.0	—	136.9	—	138.1	—	138.0	——	136.7	—	136.9	—	137.8	—	[a]
6	7.23	123.1	7.25	115.1	7.23	114.7	6.26	116.1	6.21	115.8	7.23	115.0	7.18	114.5	6.20	116.1	6.12	115.6
7	7.54	135.5	7.52	130.7	7.38	130.5	7.33	130.4	7.32	130.8	7.51	130.7	7.35	130.4	7.26	130.4	7.08	130.5
8	6.39	116.4	7.28	123.2	6.88	122.8	7.27	123.4	6.85	122.8	7.29	123.3	6.88	122.7	7.21	123.4	6.81	122.9
8a	—	143.6	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—
9	—	—	7.84	127.5	7.07	127.6	7.90	128.0	7.16	127.7	7.86	127.4	7.16	127.4	7.86	128.8	7.22	[b]
9a	—	—	—	121.8	—	121.8	—	121.5	—	121.4	—	122.0	—	122.1	—	122.0	—	121.7
9b	—	—	—	88.7	—	90.4	—	89.1	—	90.8	—	87.9	—	89.0	—	88.2	—	89.4
OH	—	—	7.04	—	7.55	—	7.15	—	7.71	—	7.02	—	7.39	—	7.07	—	7.51	—
1′Bu)	1.84	41.7	1.90	31.0	1.93	31.1	1.98	30.9	2.07	30.9	2.07	31.0	2.18	30.7	2.12	30.5	2.21	30.7
	1.81		1.85		1.90		1.95		2.04		2.01		2.11		2.08		2.17	
2′(Bu)	1.35	25.3	0.95	24.7	0.98	24.6	1.28	24.8	1.32	24.8	0.99	24.5	1.01	24.5	1.14	24.7	1.16	24.6
	1.21						1.16		1.23		0.97		0.81					
3′ (Bu)	1.23	22.1	1.14	22.4	1.18	22.5	1.14	22.5	1.32	22.6	1.16	22.5	1.25	22.5	1.23	22.6	1.26	22.6
4′ (Bu)	0.84	13.9	0.73	13.6	0.75	13.6	0.82	13.7	0.84	13.7	0.71	13.6	0.72	13.6	0.75	13.8	0.77	13.8
1′ (R^1)	—	137.7	3.36	29.9	3.40	29.7	—	137.6	—	137.7	3.32	29.5	3.40	29.6	—	137.3	—	[a]
2′ (R^1)	7.40	129.4	—	—	—	—	7.21	129.0	7.21	129.1	—	—	—	—	7.14	130.2	7.20	130.4
	7.33	129.1																
3′(R^1)	7.65	130.3	—	—	—	—	7.63	130.3	7.67	130.2	—	—	—	—	7.57	128.9	7.62	[b]
		130.2																
4′(R^1)	7.56	128.9	—	—	—	—	7.57	128.8	7.57	128.8	—	—	—	—	7.50	127.8	7.53	[b]
1′ (R^2)	2.22	—	9.41	—	9.73	—	9.50	—	9.83	—	3.94	44.8	4.03	44.8	3.90	44.9	3.94	45.1
											3.88		3.99		3.77		3.84	
2′ (R^2)	—	—	—	—	—	—	—	—	—	—	1.87	31.6	1.97	31.6	1.82	31.6	1.91	31.6
											1.51		1.61		1.48		1.57	
3′ (R^2)	—	—	—	—	—	—	—	—	—	—	1.37	20.0	1.38	20.0	1.29	19.9	1.34	20.0
4′ (R^2)	—	—	—	—	—	—	—	—	—	—	0.97	14.0	1.01	14.0	0.91	13.8	0.93	13.8
1′ (R^3)	—	—	2.70	27.5	—	136.3	2.83	27.7	—	136.5	2.73	28.5	—	136.6	2.80	28.6	—	[a]
2′ (R^3)	—	—	—	—	7.24	130.8	—	—	7.18	130.4	—	—	[c]	130.6	—	—	[c]	[b]
3′ (R^3)	—	—	—	—	7.24	127.9	—	—	7.24	128.1	—	—	[c]	128.0	—	—	[c]	128.2
4′(R^3)	—	—	—	—	7.24	127.6	—	—	7.24	127.9	—	—	[c]	127.4	—	—	[c]	[b]

[a] 137.6, or 137.4, or 137.0.
[b] 130.2, or 129.0, or 127.8, or 127.7.
[c] 7.15–7.30 (broadened signals).

Table 3
Molecular rearrangement of compounds **3** in boiling acetic acid (method A) and concd hydrochloric acid (method B)[a]

Entry	Educt	Method	Time (h)	Products (yield, %)
1	**3a**	A	3	(*Z*)-**4a** (49)
2	**3a**	B	1	(*Z*)-**4a** (36)
3	**3b**	A	2	(*Z*)-**4b** (28), **3b** (13)[b]
4	**3b**	B	1.5	(*Z*)-**4b** (35)
5	**3c**	A	2.5	(*E*)-**4c** (61), (*Z*)-**4c** (6)
6	**3c**	B	2.5	(*E*)-**4c** (61)
7	**3d**	A	4	(*E*)-**4d** (15), (*Z*)-**4d** (5), **3d** (19)[b]
8	**3d**	B	2	(*E*)-**4d** (45), (*Z*)-**4d** (11), **3d** (17)[b]
9	**3e**	A	3	(*E*)-**4e** (62)
10	**3e**	B	3	(*E*)-**4e** (72)
11	**3f**	A	3	(*E*)-**4f** (98)
12	**3f**	B	1	(*E*)-**4f** (98)
13	**3g**	A	3	(*E*)-**4g** (76)
14	**3g**	B	2	(*E*)-**4g** (64)
15	**3h**	A	3	(*E*)-**4h** (83)
16	**3h**	B	2	(*E*)-**4h** (86)

[a] For key of substituents see Table 1.
[b] Regenerated starting compound.

analysis were prepared from a benzene–hexane mixture. Compound *E*-**4f** crystallizes in the triclinic space group *P*-1. The view of the molecular structure of *E*-**4f** (Figs. 3 and 4) shows an almost planar arrangement of the five-membered core (spiro) ring with interplanar angles of 88.2(2)°, which is comparable to the values of 88.3(2)° observed for 1-butyl-1′-methyl-4-phenyl-1′*H*-spiro-[imidazoline-5,3′-indole]-2,2′-dione and 89.3(2)° and 85.9(1)° for (4*R**,5*S**)-3-butyl-4-hydroxy-1,4,1′-triphenyl-1′*H*-spiro[imidazolidine-5,3′-indole]-2,2′-dione.[2] The C3–C18 distance (1.321(4) Å) in compound *E*-**4f** revealed a shortening that was typical of the presence of a double bond compared to the standard single bond C(sp2)–C(sp2) distance of 1.31 Å.[8] Also, the C10–O1 (1.207(3) Å) distance and the geometry of the respective groups were suggestive of the presence of a double bond. The identity of the S═C(–N)$_2$ moiety in *E*-**4f** was compared with 2648 analogous compounds in the Cambridge Structural Database, and was in very good agreement with respect to both the interatomic distances and the bond angles, thus proving such an arrangement.[9] Non-classical H-bonding interactions are taking place in the *E*-**4f** structure through O1–H22a–C22 (2.533(4) Å) and O1–H21c–C21 (2.717(3) Å) connecting the C═O group of one molecule to the first CH_2 group of the butyl moiety and the CH_3 end group of the –C═CH–C_3H_7 moiety (Fig. 4).

The APCI mass spectra of all of the compounds yielded peaks of the $[M+H]^+$ ions in the positive-ion mode and the $[M-H]^-$ ions in the negative-ion mode. In general, these ions were base peaks, or at least very intense peaks in the spectra. These mass spectra provide complementary ions in both polarity modes, which are useful for the determination and identification of the alkyl/aryl substitution, such as the neutral loss of butene for butyl substitution and similar fragmentation for other substituents (methyl, phenyl). Another typical neutral loss is NCS (or appropriate alkyl/aryl–NCS). A typical neutral loss for compounds containing a tertiary hydroxyl group is the loss of water. However, the above fragmentations were as useful for identification as water loss was is our previously published results.[1–4]

3. Conclusions

In conclusion, we would like to emphasize that the described method allows the preparation, in good to very good yields, of new spiro-oxindoles **4**, starting from aminoquinolinediones **1**. The molecular rearrangement of adduct **3** not only has theoretical significance, but enables through a simple procedure, the targeted preparation of new spiro-oxindoles suitable for biological testing and further synthetic utilization. 2-Thioxo-1′*H*-spiro[imidazoline-5,3′-indole]-2,2′-diones **4** have not been previously described in the literature. The only compounds hitherto known are their 2-oxoanalogues, whose preparation was described in our previous work.[2] The presented results expand the array of compounds containing the spiro-oxindole structural motif, which appears in several indole alkaloids,[10] and in other compounds exhibiting various biological activities.[11,12] They also increase the variety of methods for preparing spiro-oxindoles.[11] At the same time, our results expand the number of compounds containing the 4,4-spiro-2-thioxoimidazolidine structural fragment. Only a few of such compounds have been previously described in literature, and they contain a cyclohexylidene,[13,14] cyklopentylidene,[14] or dihydroacridinyl group[15] as the second component of the spiro-structure. Since a number of simple *N*-substituted 2-thioxoimidazolines exhibit, for example, inflammatory activity,[16] gentamycin nephrotoxicity,[17] dopamine β-hydroxylase inhibitory activity and anti-aggregating activity against collagen,[18] it may be assumed that 4,4-spiro-2-thioxoimidazolidines can also display significant biological activity.

4. Experimental

4.1. General considerations

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 500 spectrometer (500.13 MHz for ^{1}H, 125.76 MHz for ^{13}C, 50.68 MHz for ^{15}N) in DMSO-d_6. ^{1}H 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, gs-HMQC, gs-HMBC) were performed using manufacturer's software. Proton spectra were assigned using gs-COSY. Protonated carbons were assigned by gs-HMQC. Quaternary carbons were assigned by gs-HMBC. The positive- and negative-ion APCI mass spectra were measured on an ion trap analyser Agilent LC-MSD Trap XCT-Ultra (Agilent, Palo Alto, CA, USA) within the mass range m/z=50–500. Samples were dissolved in acetonitrile and analyzed after direct injection (2 μL) at the flow rate of 400 μL/min acetonitrile. The ion source temperature was 350 °C, the APCI probe temperature was 350 °C, 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 m/z 4 and the collision amplitude was 0.8 V. 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 (S3), chloroform–ethanol, 9:1 (S4) and/or 19:1 (S5), and chloroform–ethyl acetate, 7:3 (S6)) on Alugram® SIL G/UV_{254} foils (Macherey-Nagel). Elemental analyses (C, H, N) were performed with an EA 1108 Elemental Analyzer (Fisons Instrument).

X-ray analysis. The X-ray data for colourless crystals of (*E*)-**4f** (crystallized from a mixture of benzene and hexane) were obtained at 150(1) K using Oxford Cryostream low-temperature device on a Nonius KappaCCD diffractometer with Mo Kα radiation (λ=0.71073 Å), a graphite monochromator, and the φ and χ scan mode. Data reductions were performed with DENZO-SMN.[19] The absorption was corrected by integration methods.[20] Structures were solved by direct methods (Sir92)[21] and refined by full matrix least-square based on F^2 (SHELXL97).[22] Hydrogen atoms were mostly localized on a difference Fourier map, however, to ensure uniformity of treatment of crystal, all hydrogens were recalculated into idealized positions (riding model) and assigned temperature

Table 4
^{1}H and ^{13}C chemical shifts (δ, ppm) of 4-butylidene-3-butyl-2-thioxo-1′*H*-spiro[imidazoline-5,3′-indole]-2,2′-diones (**4**) in DMSO-d_6

Position	(*Z*)-**4a**		(*Z*)-**4b**		(*Z*)-**4c**		(*E*)-**4c**		(*Z*)-**4d**		(*E*)-**4d**		(*E*)-**4e**		(*E*)-**4f**		(*E*)-**4g**		(*E*)-**4h**	
	δ_H	δ_C	δ_H	δ_C	δ_H	δ_C	δ_H	δ_C	δ_H	δ_C	δ_H	δ_C	δ_H	δ_C	δ_H	δ_C	δ_H	δ_C	δ_H	δ_C
1	—	—	—	—	—	−265.8[a]	—	−264.9[a]	—	—	—	—	—	—	—	—	—	—	—	—
2 (C=S)	—	181.2	—	181.5	—	181.4	—	179.4	—	181.4	—	179.5	—	179.8	—	179.9	—	179.8	—	179.8
3	—	—	—	—	—	−243.9[a,b]	—	−253.4[a,c]	—	—	—	—	—	—	—	—	—	—	—	—
4	—	137.1	—	137.3	—	137.2	—	136.9	—	137.2	—	137.0		137.2		137.4	—	137.3	—	137.1
5	—	73.9	—	75.5	—	73.7	—	72.4	—	75.6	—	74.3	—	71.0	—	72.6	—	71.1	—	72.6
1′	—	—	—	—	—	−233.5[a]	—	−230.0[a]	—	—	—	—	—	—	—		—	—	—	—
2′	—	171.9	—	172.4	—	171.6	—	171.7	—	171.9	—	170.9	—	171.0	—	171.6	—	170.6	—	170.9
3a′	—	127.6	—	127.1	—	126.4	—	124.9	—	126.9	—	125.6	—	125.2	—	125.8	—	125.0	—	125.7
4′	7.28	124.5	7.53	125.3	7.37	125.1	7.42	125.4	7.59	126.0	7.65	126.1	7.21	124.5	7.47	125.2	7.32	125.2	7.58	125.8
5′	7.18	123.8	7.15	123.6	7.26	124.5	7.28	124.7	7.16	124.4	7.18	124.5	7.21	124.0	7.18	123.8	7.29	124.8	7.26	124.5
6′	7.50	130.9	7.37	130.7	7.45	131.1	7.45	131.3	7.25	131.0	7.31	131.2	7.53	131.2	7.40	131.0	7.48	131.4	7.37	131.2
7′	7.20	109.8	7.00	109.4	6.88	110.1	6.91	110.2	6.65	109.7	6.58	109.7	7.26	109.8	7.01	109.5	6.93	110.2	6.64	109.8
7a′	—	144.2	—	143.7	—	143.9	—	143.4	—	143.6	—	143.1	—	143.9	—	143.5	—	143.5	—	143.2
1′(C-4)	3.89	99.9	3.93	100.1	4.15	100.3	4.91	102.3	4.21	100.9	4.99	102.6	4.92	102.8	5.04	103.3	5.02	103.2	5.16	103.8
2′(C-4)	2.05	26.7	2.11	27.3	2.10	27.4	1.59	27.9	2.17	27.4	1.56	27.8	1.44	27.4	1.47	27.4	1.70	27.8	1.69	27.9
	2.02		2.08		2.07		1.43		2.13		1.38		1.27		1.30		1.50		1.53	
3′(C-4)	1.24	22.3	1.26	22.3	1.28	22.3	1.12	22.4	1.34	22.3	1.09	22.4	1.08	22.2	1.12	22.2	1.18	22.3	1.22	22.3
	1.20		1.23		1.24		0.99		1.30		0.98		0.98		1.02		1.05		1.10	
4′(C-4)	0.79	13.3	0.82	13.5	0.82	13.3	0.58	13.6	0.87	13.3	0.55	13.6	0.55	13.4	0.57	13.4	0.61	13.5	0.63	13.6
1′(R^1)	3.22	27.1	3.09	27.2	—	133.6	—	133.4	—	133.4	—	133.2	3.29	26.7	3.09	26.5	—	133.4	—	133.2
2′(R^1)	—	—	—	—	7.54	126.8	7.50	126.4	7.17	126.5	7.03	126.0	—	—	—	—	7.52	126.4	7.06	126.0
3′(R^1)	—	—	—	—	7.65	129.9	7.69	130.2	7.55	130.0	7.57	130.2	—	—	—	—	7.69	130.1	7.61	130.2
4′(R^1)	—	—	—	—	7.57	128.8	7.58	129.0	7.47	128.8	7.48	128.9	—	—	—	—	7.59	129.0	7.53	128.9
1′(R^2)	10.95	—	11.31	—	11.03	—	11.02	—	11.42	—	11.35	—	3.96	43.3	4.06	43.4	3.99	43.4	4.10	43.5
													3.85		3.95		3.90		4.00	
2′(R^2)	—	—	—	—	—	—	—	—	—	—	—	—	1.60	27.8	1.69	27.8	1.64	27.8	1.72	27.9
3′(R^2)	—	—	—	—	—	—	—	—	—	—	—	—	1.39	19.4	1.48	19.5	1.48	19.4	1.43	19.5
4′(R^2)	—	—	—	—	—	—	—	—	—	—	—	—	0.97	14.0	1.01	14.0	0.98	14.0	1.02	14.0
1′(R^3)	2.70	29.5	—	136.8	2.86	29.6	2.77	28.8	—	136.7	—	136.2	2.70	29.5	—	136.2	2.85	29.6	—	136.4
2′(R^3)	—	—	7.08	129.3	—	—	—	—	7.09	129.3	6.98	129.6	—	—	6.94	129.6	—	—	6.99	129.7
3′(R^3)	—	—	7.28	128.7	—	—	—	—	7.28	128.9	7.28	128.9	—	—	7.28	128.8	—	—	7.33	128.9
4′(R^3)	—	—	7.25	128.1	—	—	—	—	7.26	128.4	7.26	128.5	—	—	7.28	128.4	—	—	7.33	128.6

[a] δ (^{15}N).
[b] ^{1}J (^{15}N, ^{1}H)=99.8 Hz.
[c] ^{1}J (^{15}N, ^{1}H)=99.0 Hz.

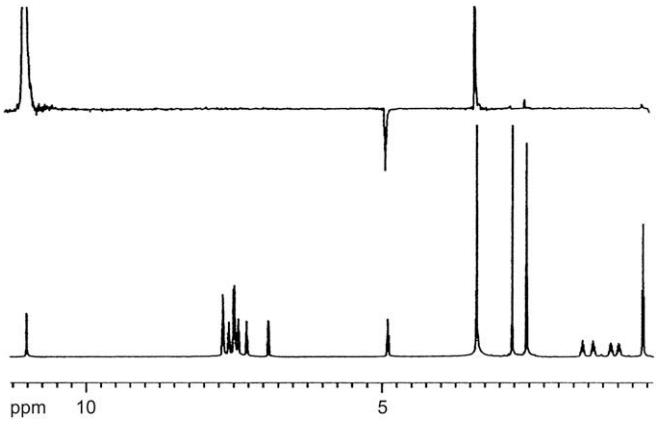


Figure 1. The ^{1}H NMR spectrum (bottom trace) and a trace from gradient-selected 2D NOESY spectrum (upper trace) showing through-space interaction of N(3)–H proton (δ (^{1}H)=11.02) and =CH proton of butylidene group (δ (^{1}H)=4.91) in compound (*E*)-**4c**. Positive signal at 3.49 ppm is due to an exchange of N(3)–H protons and protons of water present in the solvent.

factors $H_{iso}(H)=1.2\ U_{eq}$(pivot atom) or of $1.5\ U_{eq}$ for the methyl moiety with C–H=0.96, 0.97 and 0.93 Å for methyl, methylene and hydrogen atoms in aromatic ring or a double bond, respectively. Crystallographic data for (*E*)-**4f**: $C_{25}H_{29}N_3OS$, M=419.57, triclinic, *P*-1, a=9.1510(4) Å, b=10.6580(4) Å, c=13.3390(8) Å, α=112.814(4)°, β=100.639(5)°, γ=98.897(4)°, Z=2, V=1141.23(9) Å^3, D_c=1.221 g cm^{-3}, μ=0.163 mm^{-1}, T_{min}=0.949, T_{max}=0.981; 21,250 reflections measured (θ_{max}=27.5°), 5175 independent (R_{int}=0.0450), 3716 with $I>2\sigma(I)$, 271 parameters, S=1.127, $R1$ (obsd data)=0.0600, $wR2$ (all data)=0.1391; max, min residual electron density=0.315, −0.275 e Å^{-3}.

Crystallographic data for structural analysis have been deposited with the Cambridge Crystallographic Data Centre, CCDC No. 702717. Copies of this information may be obtained free of charge from The Director, CCDC, 12 Union Road, Cambridge CB2 1EY, UK (fax: +44 1223 336033; e-mail: deposit@ccdc.cam.ac.uk orwebsite: http://www.ccdc.cam.ac.uk).

4.2. Preparation of 3-amino-1*H*,3*H*-quinoline-2,4-diones (1)

Starting 3-substituted 3-amino-1*H*,3*H*-quinoline-2,4-diones (**1**) were prepared from corresponding 3-chloro derivatives according to the protocol described in literature.[10] One new amine was prepared.

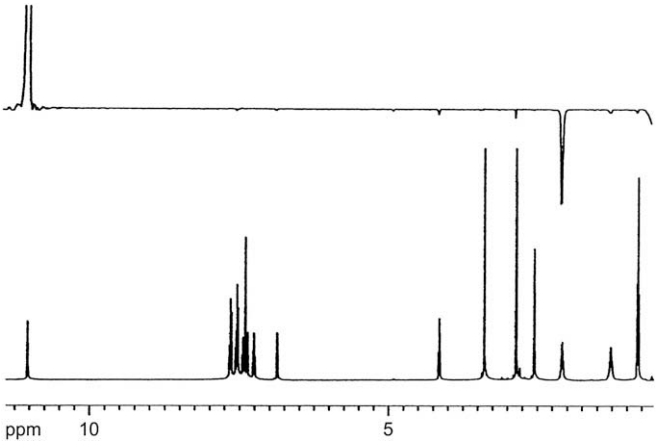


Figure 2. The ^{1}H NMR spectrum (bottom trace) and a trace from gradient-selected 2D NOESY spectrum (upper trace) showing through-space interaction of N(3)–H proton (δ (^{1}H)=11.03) and =CHCH_2 protons of butylidene group (δ (^{1}H)=2.07–2.10) in compound (*Z*)-**4c**.

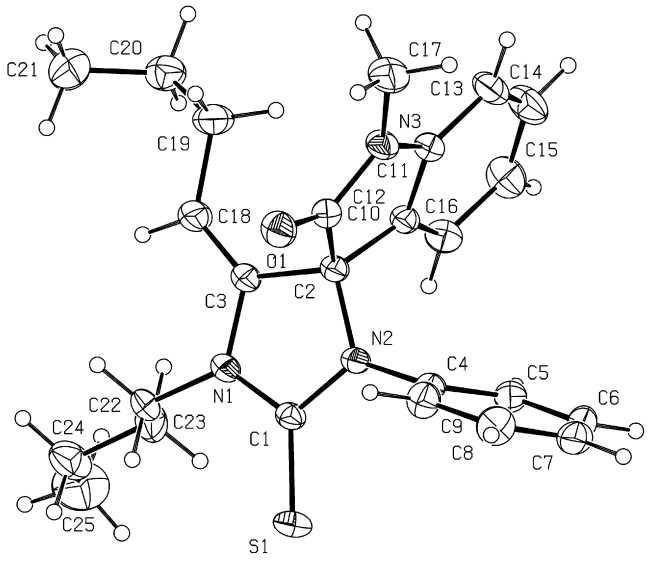


Figure 3. Molecular structure of compound (*E*)-**4f** with atom numbering scheme. ORTEP 50% probability level, arbitrary spheres for hydrogen atoms.

4.2.1. 3-Amino-3-butyl-1-phenyl-1H,3H-quinoline-2,4-dione (**1c**)

Compound was prepared from 3-butyl-3-chloro-1-phenyl-1*H*,3*H*-quinoline-2,4-dione, ammonium chloride and potassium carbonate in 47% yield. Colourless crystals, mp 119–120 °C (benzene–hexane); IR: 3385, 3320, 2951, 2922, 2870, 1714, 1677, 1599, 1491, 1465, 1345, 1299, 1229, 1218, 1155, 1102, 1072, 1025, 957, 852, 768, 758, 707, 645, 526, 509 cm^{-1}. Anal. Calcd (found) for $C_{19}H_{20}N_2O_2$: C 74.00 (74.22); H 6.54 (6.39); N 9.08 (9.15). For ^{1}H and ^{13}C NMR see Table 2. Positive-ion APCI-MS: *m*/*z* 309 $[M+H]^+$ (100%). Positive-ion APCI-MS/MS of *m*/*z* 309: 292 $[M+H-NH_3]^+$ (100%). Negative-ion APCI-MS: *m*/*z* 307 $[M-H]^-$ (31%), 292 $[M-CH_3]^-$ (100%). Negative-ion APCI-MS/MS of *m*/*z* 307: 249 $[M-H-CH_3-C_3H_7]^-$ (100%), 188 $[M-H-C_6H_5NCO]^-$.

4.3. General method for the preparation of 9b-hydroxy-2-thioxo-1,2,3,3a,5,9b-hexahydro-imidazo[4,5-*c*]quinolin-2-ones (3) from 3-aminoquinolinediones 1

Phenylisothiocyanate (0.144 mL, 1.2 mmol) or methylisothiocyanate (88 mg, 1.2 mmol) was added to the cooled (0 °C) and stirred solution of **1** (1 mmol) in chloroform (5 mL). After stirring at rt for 3 h, the solution was heated to reflux for the time given in Table 1. The course of the reaction was monitored by TLC. After cooling and evaporating in vacuo to dryness, the residue was crystallized from appropriate solvent. In the case of the reaction of **1a** with phenyl isothiocyanate, the residue was column chromatographed.

4.3.1. 3a-Butyl-1,5-dimethyl-9b-hydroxy-2-thioxo-1,2,3,3a,5,9b-hexahydro-imidazo[4,5-c]quinolin-4-one (**3a**)

Colourless crystals, yield 94%, mp 176–180 °C (benzene–hexane); IR: 3368, 3247, 2959, 2931, 2859, 1646, 1603, 1473, 1443, 1398, 1372, 1315, 1280, 1212, 1160, 1138, 1115, 1077, 1048, 997, 969, 942, 911, 850, 759, 698, 679, 616, 576, 526 cm^{-1}. For ^{1}H and ^{13}C NMR see Table 2. Positive-ion APCI-MS: *m*/*z* 320 $[M+H]^+$ (100%), 302 $[M+H-H_2O]^+$, 247 $[M+H-CH_3NCS]^+$. Positive-ion APCI-MS/MS of *m*/*z* 320: 247 $[M+H-CH_3NCS]^+$ (100%), 230 $[M+H-CH_3NHCSNH_2]^+$. Negative-ion APCI-MS: *m*/*z* 318 $[M-H]^-$ (100%). Negative-ion APCI-MS/MS of *m*/*z* 318: 261 $[M-H-C_4H_9]^-$, 245 $[M-H-CH_3NCS]^-$,185 $[M-H-C_4H_8-NHCS-H_2O]^-$ (100%). Anal. Calcd (found) for $C_{16}H_{21}N_3O_2S$: C 60.16 (60.23); H 6.63 (6.72); N 13.16 (13.31).

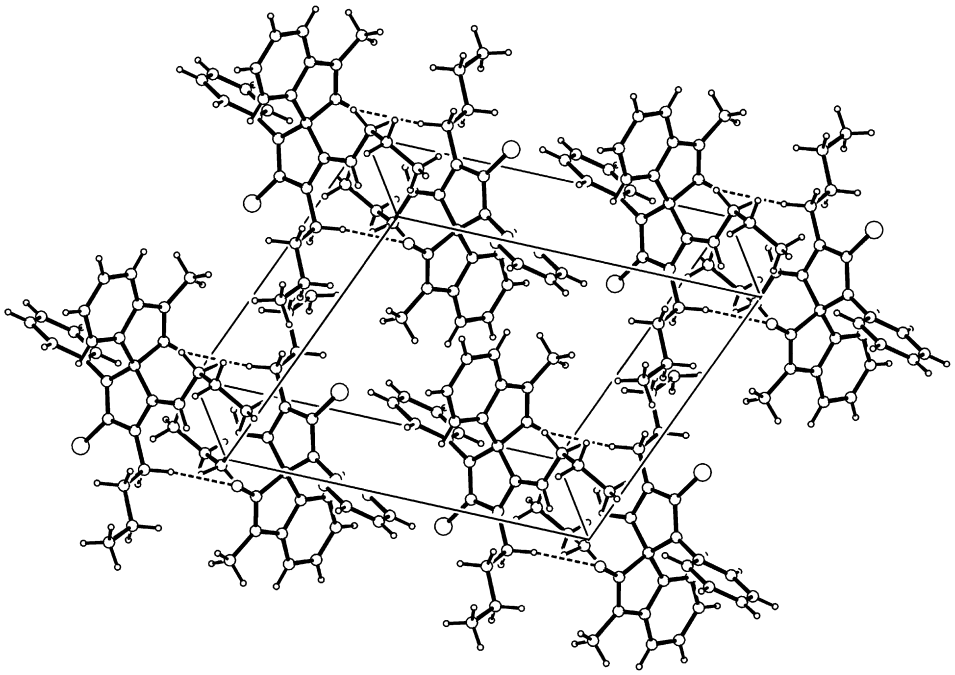


Figure 4. View of non-classical H-bonding in (*E*)-**4f**.

*4.3.2. 3a-Butyl-9b-hydroxy-5-methyl-1-phenyl-2-thioxo-1,2,3,3a,5,9b-hexahydro-imidazo[4,5-c]quinolin-4-one (**3b**)*

Colourless crystals, yield 81%, mp 170–176 °C (benzene–hexane); IR: 3618, 3246, 2961, 2931, 2860, 1648, 1606, 1474, 1405, 1373, 1341, 1304, 1268, 1226, 1179, 1120, 1099, 1072, 1053, 995, 940, 863, 757, 703, 652, 578, 546 cm^{-1}. For ^{1}H and ^{13}C NMR see Table 2. Positive-ion APCI-MS: *m*/*z* 382 $[M+H]^+$ (100%), 348, 247 $[M+H-C_6H_5NCS]^+$. Positive-ion APCI-MS/MS of *m*/*z* 382: 247 $[M+H-C_6H_5NCS]^+$ (100%), 230 $[M+H-C_6H_5NHCSNH_2]^+$. Negative-ion APCI-MS: *m*/*z* 380 $[M-H]^-$ (100%). Negative-ion APCI-MS/MS of *m*/*z* 318: 261 $[M-H-C_6H_5NCO]^-$ (100%). Anal. Calcd (found) for $C_{21}H_{23}N_3O_2S$: C 66.12 (66.32); H 6.08 (6.21); N 11.01 (11.21).

*4.3.3. 3a-Butyl-9b-hydroxy-1-methyl-5-phenyl-2-thioxo-1,2,3,3a,5,9b-hexahydro-imidazo[4,5-c]quinolin-4-one (**3c**)*

Colourless crystals, yield 67%, mp 190–191 °C (benzene); IR: 3310, 3208, 2961, 2939, 2873, 1678, 1604, 1490, 1464, 1455, 1399, 1353, 1336, 1299, 1176, 1127, 1119, 1106, 1057, 984, 938, 766, 705, 628, 579, 552, 508 cm^{-1}. For ^{1}H and ^{13}C NMR see Table 2. Positive-ion APCI-MS: 382 $[M+H]^+$ (100%), 364 $[M+H-H_2O]^+$, 350 $[M+H-S]^+$ (100%). Positive-ion APCI-MS/MS of *m*/*z* 382: 309 $[M+H-CH_3NCS]^+$ (100%). Negative-ion APCI-MS: *m*/*z* 380 $[M-H]^-$ (100%), 362 $[M-H_2O]^-$. Negative-ion APCI-MS/MS of *m*/*z* 380: 323 $[M-H-C_4H_9]^-$, 185 $[M-H-C_6H_5NCO-C_4H_9-H_2O]^-$ (100%). Anal. Calcd (found) for $C_{21}H_{23}N_3O_2S$: C 66.12 (66.27); H 6.08 (6.27); N 11.01 (11.24).

*4.3.4. 3a-Butyl-1,5-diphenyl-9b-hydroxy-2-thioxo-1,2,3,3a,5,9b-hexahydro-imidazo[4,5-c]quinolin-4-one (**3d**)*

Colourless crystals, yield 81%, mp 191–197 °C (benzene–hexane); IR: 3352, 2958, 2928, 2870, 2858, 1695, 1654, 1599, 1529, 1493, 1463, 1353, 1324, 1298, 1258, 1238, 1162, 1113, 1068, 1026, 971, 903, 759, 724, 704, 661, 648, 597, 520, 509 cm^{-1}. According to ^{1}H and ^{13}C NMR, this product is a mixture of **2d** and **3d**. The mixture was heated to 60 °C in a 5% solution of DMSO for 5 h, the solution was evaporated in vacuo to dryness and the residue was crystallized from benzene–hexane mixture. Compound **3d**, containing ca. 5% of **2d** in an equilibrium (see text), was obtained in 65% yield. Colourless crystals, mp 191–199 °C (benzene–hexane); IR: 3424, 3352, 2957, 2928, 280, 1665, 1601, 1530, 1495, 1463, 1406, 1350, 1312, 1300, 1251, 1162, 1128, 1094, 1067, 1023, 1004, 981, 938, 909, 834, 755, 705, 661, 624, 597, 584, 571, 539, 520 cm^{-1}. For ^{1}H and ^{13}C NMR see Table 2. Positive-ion APCI-MS: *m*/*z* 444 $[M+H]^+$ (41%), 309 $[M+H-C_6H_5NCS]^+$ (100%). Positive-ion APCI-MS/MS of *m*/*z* 444: 309 $[M+H-C_6H_5NCS]^+$ (100%), 292 $[M+H-C_6H_5NHCSNH_2]^+$, 208. Negative-ion APCI-MS: *m*/*z* 442 $[M-H]^-$ (100%). Negative-ion APCI-MS/MS of *m*/*z* 442: 382, 323 $[M-H-C_6H_5NCO]^-$ (100%). Anal. Calcd (found) for $C_{26}H_{25}N_3O_2S$: C 70.40 (70.21); H 5.68 (5.73); N 9.47 (9.54).

*4.3.5. 3,3a-Dibutyl-1,5-dimethyl-9b-hydroxy-2-thioxo-1,2,3,3a,5,9b-hexahydro-imidazo[4,5-c]quinolin-4-one (**3e**)*

Colourless crystals, yield 58%, mp 178–182 °C (benzene); IR: 3355, 2957, 2931, 2862, 1651, 1606, 1503, 1476, 1423, 1412, 1371, 1286, 1223, 1189, 1172, 1123, 1088, 1052, 1039, 1023, 977, 944, 866, 844, 772, 733, 692, 648, 582, 535 cm^{-1}. For ^{1}H and ^{13}C NMR see Table 2. Positive-ion APCI-MS: *m*/*z* 376 $[M+H]^+$ (77%), 358 $[M+H-H_2O]^+$ (100%). Positive-ion APCI-MS/MS of *m*/*z* 376: 303 $[M+H-CH_3NCS]^+$ (100%). Positive-ion APCI-MS/MS of *m*/*z* 358: 302 $[M+H-C_4H_8-H_2O]^+$ (100%), 268 $[M+H-C_4H_9-H_2OCH_3]^+$, 246 $[M+H-2\times C_4H_8-H_2O]^+$. Negative-ion APCI-MS: *m*/*z* 374 $[M-H]^-$ (47%), 356 $[M-H-H_2O]^-$ (100%). Negative-ion APCI-MS/MS of *m*/*z* 374: 330 $[M-H-C_3H_8]^-$, 241 $[M-H-C_4H_9NCS]^-$ (100%). Negative-ion APCI-MS/MS of *m*/*z* 356: 341 $[M-H-CH_3]^-$ (100%), 270 $[M-H-2\times C_3H_7]^-$. Anal. Calcd (found) for $C_{20}H_{29}N_3O_2S$: C 63.97 (63.81); H 7.78 (7.58); N 11.19 (11.26).

*4.3.6. 3,3a-Dibutyl-9b-hydroxy-5-methyl-1-phenyl-2-thioxo-1,2,3,3a,5,9b-hexahydro-imidazo[4,5-c]quinolin-4-one (**3f**)*

Colourless crystals, yield 68%, mp 188–190 °C (benzene); IR: 3436, 2957, 2931, 2870, 1661, 1605, 1499, 1474, 1403, 1378, 1286, 1229, 1125, 1052, 1023, 915, 834, 760, 729, 709, 693, 650, 617, 585, 550 cm^{-1}. For ^{1}H- and ^{13}C NMR see Table 2. Positive-ion APCI-MS: *m*/*z* 438 $[M+H]^+$ (65%), 420 $[M+H-H_2O]^+$ (100%), 404, 303 $[M+H-C_6H_5NCS]^+$ (100%). Positive-ion APCI-MS/MS of *m*/*z* 438: 303 $[M+H-C_6H_5NCS]^+$ (100%). Negative-ion APCI-MS: *m*/*z* 436 $[M-H]^-$ (100%), 356 $[M-H-OH]^-$. Negative-ion APCI-MS/MS of *m*/*z* 436: 392 $[M-H-C_3H_8]^-$, 317 $[M-H-C_6H_5NCO]^-$, 303

$[M-H-C_4H_9NCS-H_2O]^-$, 244 $[M-H-C_4H_9NCS-C_6H_5]^-$ (100%). Anal. Calcd (found) for $C_{25}H_{31}N_3O_2S$: C 68.62 (68.57); H 7.14 (7.29); N 9.60 (9.72).

4.3.7. 3,3a-Dibutyl-9b-hydroxy-1-methyl-5-phenyl-2-thioxo-1,2,3,3a,5,9b-hexahydro-imidazo[4,5-c]quinolin-4-one (**3g**)

Colourless crystals, yield 92%, mp 172–175 °C (benzene–hexane); IR: 3415, 3290, 2957, 2931, 2868, 1684, 1659, 1604, 1594, 1555, 1497, 1464, 1412, 1367, 1331, 1287, 1232, 1182, 1125, 1084, 1070, 1050, 1022, 973, 943, 834, 757, 730, 702, 650, 581, 529, 510 cm^{-1}. For ^1H and ^{13}C NMR see Table 2. Positive-ion APCI-MS: *m/z* 438 $[M+H]^+$ (28%), 420 $[M+H-H_2O]^+$ (100%), 406, 365 $[M+H-CH_3NCS]^+$. Positive-ion APCI-MS/MS of *m/z* 438: 365 $[M+H-CH_3NCS]^+$ (100%). Positive-ion APCI-MS/MS of *m/z* 420: 364 $[M+H-H_2O-C_4H_8]^+$, 330 $[M+H-H_2O-C_4H_9-CH_3]^+$, 308 $[M+H-H_2O-2\times C_4H_8]^+$. Negative-ion APCI-MS: *m/z* 436 $[M-H]^-$ (100%). Negative-ion APCI-MS/MS of *m/z* 436: 241 $[M-H-C_6H_5NHCO-C_4H_9-H_2O]^-$ (100%). Anal. Calcd (found) for $C_{25}H_{31}N_3O_2S$: C 68.62 (68.51); H 7.14 (7.29); N 9.60 (9.48).

4.3.8. 3,3a-Dibutyl-1,5-diphenyl-9b-hydroxy-2-thioxo-1,2,3,3a,5,9b-hexahydro-imidazo[4,5-c]quinolin-4-one (**3h**)

Colourless crystals, yield 86%, mp 206–212 °C (benzene–hexane); IR: 3255, 2955, 2932, 2869, 1685, 1603, 1591, 1498, 1463, 1416, 1378, 1332, 1307, 1288, 1273, 1257, 1229, 1185, 1144, 1129, 1114, 1078, 1021, 957, 911, 839, 798, 758, 746, 726, 707, 662, 645, 619, 594, 582, 533 cm^{-1}. For ^1H and ^{13}C NMR see Table 2. Positive-ion APCI-MS: *m/z* 500 $[M+H]^+$ (51%), 482 $[M+H-H_2O]^+$, 468 $[M+H-S]^+$, 450, 365 $[M+H-C_6H_5NCS]^+$ (100%). Positive-ion APCI-MS/MS of *m/z* 500: 365 $[M+H-C_6H_5NCS]^+$ (100%). Negative-ion APCI-MS: *m/z* 498 $[M-H]^-$ (100%). Negative-ion APCI-MS/MS of *m/z* 498: 454 $[M-H-C_3H_8]^-$ (100%). Anal. Calcd (found) for $C_{30}H_{33}N_3O_2S$: C 72.11 (72.30); H 6.66 (6.81); N 8.41 (8.58).

4.4. General methods for the molecular rearrangement of compounds 3

Method A. The solution of starting compound **3** (1 mmol) in acetic acid (8 mL) was heated to reflux for the time given in Table 3. The course of the reaction was monitored using TLC. After cooling, the reaction mixture was evaporated to dryness in vacuo and the residue was crystallized from appropriate solvent or separated by column chromatography on silica gel.

Method B. The solution of starting compound **3** (1 mmol) in concd hydrochloric acid (5 mL) was heated to reflux for the time given in Table 4. In same cases, a small quantity of acetic acid was added to dissolute the starting compound. The course of the reaction was monitored using TLC. After cooling, the precipitated product was filtrated off with suction and recrystallized from appropriate solvent. In cases when the reaction mixture was homogenous, the reaction mixture was evaporated to dryness in vacuo and the residue was crystallized from appropriate solvent or separated by column chromatography on silica gel.

4.4.1. (Z)-4-Butylidene-1,1′-dimethyl-2-thioxo-1′H-spiro[imidazoline-5,3′-indole]-2,2′-dione ((Z)-**4a**)

Yellow crystals, yield 49% (method A) or 36% (method B), mp 152–160 °C (benzene–hexane); IR: 3326, 2957, 2932, 2871, 1714, 1698, 1611, 1490, 1469, 1451, 1426, 1391, 1369, 1347, 1269, 1180, 1154, 1131, 1093, 1008, 973, 761, 696, 641, 611 cm^{-1}. For ^1H and ^{13}C NMR see Table 4. Positive-ion APCI-MS: *m/z* 302 $[M+H]^+$ (100%). Positive-ion APCI-MS/MS of *m/z* 302: 246 $[M+H-C_4H_8]^+$ (100%), 229 $[M+H-CH_3NCS]^+$. Negative-ion APCI-MS: *m/z* 300 $[M-H]^-$ (100%). Negative-ion APCI-MS/MS of *m/z* 338: 285 $[M-H-CH_3]^-$, 272 $[M-H-CO]^-$, 257 $[M-H-C_3H_7]^-$, 227 $[M-H-CH_3NCS]^-$ (100%). Anal. Calcd (found) for $C_{16}H_{19}N_3OS$: C 63.76 (63.59); H 6.35 (6.48); N 13.94 (13.81).

4.4.2. (Z)-4-Butylidenene-1′-methyl-1-phenyl-2-thioxo-1′H-spiro[imidazoline-5,3′-indole]-2,2′-dione ((Z)-**4b**)

Yellowish crystals, yield 28% (method A), or 35% (method B), mp 268–273 °C (acetic acid); IR: 3449, 3187, 3139, 2954, 2928, 2869, 1733, 1702, 1613, 1493, 1471, 1399, 1368, 1343, 1256, 1181, 1155, 1131, 1105, 1081, 1042, 1025, 851, 749, 696, 661, 646, 625, 564 cm^{-1}. For ^1H and ^{13}C NMR see Table 4. Positive-ion APCI-MS: *m/z* 364 $[M+H]^+$ (100%). Positive-ion APCI-MS/MS of *m/z* 364: 321 $[M+H-C_3H_7]^+$, 308 $[M+H-C_4H_8]^+$, 306 $[M+H-NCS]^+$, 271, 249 $[M+H-C_4H_9NCS]^+$, 229 $[M+H-C_6H_5NCS]^+$ (100%). Negative-ion APCI-MS: *m/z* 362 $[M-H]^-$ (100%). Negative-ion APCI-MS/MS of *m/z* 362: 319 $[M-H-C_3H_7]^-$ (100%), 227 $[M-H-C_6H_5NCS]^-$. Anal. Calcd (found) for $C_{21}H_{21}N_3OS$: C 69.39 (69.27); H 5.82 (5.99); N 11.56 (11.71).

4.4.3. (E)-4-Butylidene-1-methyl-1′-phenyl-2-thioxo-1′H-spiro[imidazoline-5,3′-indole]-2,2′-dione ((E)-**4c**)

Yellow crystals, yield 61% by both methods, mp 202–207 °C (benzene–hexane); IR: 3275, 2954, 2924, 2865, 1719, 1684, 1610, 1592, 1497, 1467, 1454, 1436, 1395, 1370, 1325, 1295, 1284, 1265, 1208, 1173, 1103, 1046, 968, 887, 784, 756, 703, 682, 669, 644, 608, 519 cm^{-1}. For ^1H and ^{13}C NMR see Table 4. Positive-ion APCI-MS: *m/z* 364 $[M+H]^+$ (100%), 332 $[M+H-S]^+$. Positive-ion APCI-MS/MS of *m/z* 364: 308 $[M+H-C_4H_8]^+$ (100%), 291 $[M+H-CH_3NCS]^+$. Negative-ion APCI-MS: *m/z* 362 $[M-H]^-$ (100%). Negative-ion APCI-MS/MS of *m/z* 362: 334 $[M-H-CO]^-$ (100%). Anal. Calcd (found) for $C_{21}H_{21}N_3OS$: C 69.39 (69.59); H 5.82 (5.63); N 11.56 (11.42).

4.4.4. (Z)-4-Butylidene-1-methyl-1′-phenyl-2-thioxo-1′H-spiro[imidazoline-5,3′-indole]-2,2′-dione ((Z)-**4c**)

Yellowish crystals, yield 6% (method A), mp 150–160 °C (benzene–hexane); IR: 3325, 2958, 2928, 2893, 2964, 1714, 1687, 1609, 1593, 1484, 1467, 1425, 1371, 1353, 1330, 1294, 1252, 1176, 1103, 1070, 1038, 985, 935, 869, 756, 702, 588, 480, 469 cm^{-1}. For ^1H and ^{13}C NMR see Table 4. Positive-ion APCI-MS: *m/z* 364 $[M+H]^+$ (100%), 332 $[M+H-S]^+$. Positive-ion APCI-MS/MS of *m/z* 364: 321 $[M+H-C_3H_7]^+$, 308 $[M+H-C_4H_8]^+$ (100%), 291 $[M+H-CH_3NCS]^+$. Negative-ion APCI-MS: *m/z* 362 $[M-H]^-$ (100%). Negative-ion APCI-MS/MS of *m/z* 362: 334 $[M-H-OH-C_2H_4]^-$ (100%). Anal. Calcd (found) for $C_{21}H_{21}N_3OS$: C 69.39 (69.31); H 5.82 (5.97); N 11.56 (11.43).

4.4.5. (E)-4-Butylidene-1,1′-diphenyl-2-thioxo-1′H-spiro[imidazoline-5,3′-indole]-2,2′-dione ((E)-**4d**)

Yellowish crystals, yield 15% (method A) or 45% (method B), mp 228–231 °C (benzene–hexane); IR: 3453, 3189, 3144, 2956, 2926, 2867, 1733, 1699, 1612, 1596, 1498, 1474, 1357, 1368, 1324, 1248, 1210, 1175, 1109, 1071, 1026, 987, 936, 822, 798, 753, 693, 663, 620, 547 cm^{-1}. For ^1H and ^{13}C NMR see Table 4. Positive-ion APCI-MS: *m/z* 426 $[M+H]^+$ (100%). Positive-ion APCI-MS/MS of *m/z* 426: 383 $[M+H-C_3H_7]^+$, 370 $[M+H-C_4H_8]^+$, 333, 311 $[M+H-C_4H_8NHCS]^+$, 291 $[M+H-C_6H_5NCS]^+$ (100%), 274 $[M+H-C_6H_5NHCSNH_2]^+$, 210. Negative-ion APCI-MS: *m/z* 424 $[M-H]^-$ (100%). Negative-ion APCI-MS/MS of *m/z* 424: 396 $[M-H-CO]^-$ (100%), 381 $[M-H-C_3H_7]^-$. Anal. Calcd (found) for $C_{26}H_{23}N_3OS$: C 73.38 (73.51); H 5.45 (5.57); N 9.87 (9.75).

4.4.6. (Z)-4-Butylidene-1,1′-diphenyl-2-thioxo-1′H-spiro[imidazoline-5,3′-indole]-2,2′-dione ((Z)-**4d**)

Colourless crystals, yield 5% (method A) or 11% (method B), mp 212–216 °C (benzene–hexane); IR: 3446, 3193, 3110, 2955, 2930, 2868, 1735, 1689, 1611, 1595, 1499, 1466, 1402, 1368, 1358, 1324, 1295, 1236, 1181, 1110, 1070, 1025, 937, 809, 754, 697, 660, 591, 542 cm^{-1}. Positive-ion APCI-MS: *m/z* 426 $[M+H]^+$ (100%). Positive-ion APCI-MS/MS of *m/z* 426: 383 $[M+H-C_3H_7]^+$, 370 $[M+H-C_4H_8]^+$, 333, 311 $[M+H-C_4H_8NHCS]^+$, 291 $[M+H-C_6H_5NCS]^+$ (100%), 274 $[M+H-C_6H_5NHCSNH_2]^+$, 210. Negative-ion APCI-MS: *m/z* 424 $[M-H]^-$

(100%). Negative-ion APCI-MS/MS of *m*/*z* 424: 396 $[M-H-CO]^-$ (100%), 381 $[M-H-C_3H_7]^-$. Anal. Calcd (found) for $C_{26}H_{23}N_3OS$: C 73.38 (73.29); H 5.45 (5.53); N 9.87 (9.78).

*4.4.7. (E)-3-Butyl-4-butylidene-1,1′-dimethyl-2-thioxo-1′H-spiro[imidazoline-5,3′-indole]-2,2′-dione ((E)-**4e**)*

Colourless crystals, yield 62% (method A) or 72% (method B), mp 83–87 °C (hexane); IR: 2955, 2929, 2868, 1732, 1677, 1608, 1468, 1410, 1383, 1355, 1304, 1191, 1131, 1093, 1000, 949, 891, 758, 751, 692, 668, 630 cm^{-1}. For ^1H and ^{13}C NMR see Table 4. Positive-ion APCI-MS: *m*/*z* 358 $[M+H]^+$ (100%). Positive-ion APCI-MS/MS of *m*/*z* 358: 302 $[M+H-C_4H_8]^+$ (100%), 268 $[M+H-C_4H_9-H_2O-CH_3]^+$, 246 $[M+H-2\times C_4H_8]^+$. Negative-ion APCI-MS: *m*/*z* 356 $[M-H]^-$ (100%). Negative-ion APCI-MS/MS of *m*/*z* 356: 341 $[M-H-CH_3]^-$ (100%), 326 $[M-H-2\times CH_3]^-$, 312 $[M-H-C_3H_8]^-$, 300 $[M-H-C_4H_8]^-$, 284, 270 $[M-H-2\times C_3H_7]^-$. Anal. Calcd (found) for $C_{20}H_{27}N_3OS$: C 67.19 (67.24); H 7.61 (7.81); N 11.75 (11.58).

*4.4.8. (E)-3-Butyl-4-butylidene-1′-methyl-1-phenyl-2-thioxo-1′H-spiro[imidazoline-5,3′-indole]-2,2′-dione ((E)-**4f**)*

Colourless crystals, yield 98% by both methods, mp 163–166 °C (benzene–hexane); IR: 3436, 3061, 2957, 2931, 2869, 1724, 1672, 1609, 1496, 1470, 1451, 1416, 1383, 1361, 1296, 1258, 1191, 1127, 1108, 1085, 1023, 981, 861, 790, 763, 751, 696, 683, 661, 588, 537 cm^{-1}. For ^1H and ^{13}C NMR see Table 4. Positive-ion APCI-MS: *m*/*z* 420 $[M+H]^+$ (100%). Positive-ion APCI-MS/MS of *m*/*z* 420: 364 $[M+H-C_4H_8]^+$ (100%), 330 $[M+H-C_4H_9-H_2O-CH_3]^+$ (100%), 308 $[M+H-2^*C_4H_8]^+$, 249 $[M+H-C_4H_9NCS-C_4H_8]^+$. Negative-ion APCI-MS: *m*/*z* 418 $[M-H]^-$ (100%). Negative-ion APCI-MS/MS of *m*/*z* 418: 388, 362 $[M-H-C_4H_8]^-$, 332 $[M-H-2^*C_3H_7]^-$ (100%), 303 $[M-H-C_4H_9NCS]^-$, 260 $[M-H-C_4H_9NCS-C_3H_7]^-$. Anal. Calcd (found) for $C_{25}H_{29}N_3OS$: C 71.56 (71.49); H 6.97 (7.03); N 10.01 (9.92).

*4.4.9. (E)-3-Butyl-4-butylidene-1-methyl-1′-phenyl-2-thioxo-1′H-spiro[imidazoline-5,3′-indole]-2,2′-dione ((E)-**4g**)*

Colourless crystals, yield 76% (method A) or 64% (method B), mp 80–85 °C (hexane); IR: 3444, 2961, 2930, 2870, 1731, 1677, 1613, 1594, 1497, 1463, 1413, 1362, 1322, 1294, 1241, 1208, 1174, 1146, 1102, 1072, 1023, 982, 936, 893, 845, 803, 764, 745, 702, 675, 623, 576, 527, 484 cm^{-1}. For ^1H and ^{13}C NMR see Table 4. Positive-ion APCI-MS: *m*/*z* 420 $[M+H]^+$ (100%), 404, 388, 362. Positive-ion APCI-MS/MS of *m*/*z* 420: 364 $[M+H-C_4H_8]^+$ (100%), 330 $[M+H-C_4H_9-H_2O-CH_3]^+$, 308 $[M+H-2\times C_4H_8]^+$. Negative-ion APCI-MS: *m*/*z* 434 (5%), 418 $[M-H]^-$ (100%). Negative-ion APCI-MS/MS of *m*/*z* 418: 403 $[M-H-CH_3]^-$ (100%), 388, 383 $[M-H-H_2S]^-$, 362 $[M-H-C_4H_8]^-$, 332 $[M-H-2\times C_3H_7]^-$, 314, 272. Anal. Calcd (found) for $C_{25}H_{29}N_3OS$: C 71.56 (71.43); H 6.97 (7.03); N 10.01 (9.89).

*4.4.10. (E)-3-Butyl-4-butylidene-1,1′-diphenyl-2-thioxo-1′H-spiro[imidazoline-5,3′-indole]-2,2′-dione ((E)-**4h**)*

Colourless crystals, yield 83% (method A) or 86% (method B), mp 139–143 °C (benzene–hexane); IR: 3447, 2953, 2927, 2867, 1734, 1677, 1613, 1594, 1497, 1465, 1417, 1362, 1321, 1294, 1260, 1238, 1224, 1209, 1190, 1175, 1157, 1146, 1125, 1110, 1070, 1025, 990, 953, 937, 868, 815, 753, 732, 717, 698, 662, 619, 571, 531, 513 cm^{-1}. For ^1H and ^{13}C NMR see Table 4. Positive-ion APCI-MS: *m*/*z* 482 $[M+H]^+$ (69%), 450 $[M+H-S]^+$ (100%). Positive-ion APCI-MS/MS of *m*/*z* 482: 426 $[M+H-C_4H_8]^+$ (100%), 392 $[M+H-C_4H_9-SH]^+$, 370 $[M+H-2\times C_4H_8]^+$, 311 $[M+H-C_4H_9NCS-C_4H_8]^+$. Negative-ion APCI-MS: *m*/*z* 480 $[M-H]^-$ (100%). Negative-ion APCI-MS/MS of *m*/*z* 480: 450, 424 $[M-H-C_4H_8]^-$, 394 $[M-H-2\times C_3H_7]^-$ (100%), 365 $[M-H-C_4H_9NCS]^-$, 322 $[M-H-C_4H_9NCS-C_3H_7]^-$, 272. Anal. Calcd (found) for $C_{30}H_{31}N_3OS$: C 74.81 (74.67); H 6.49 (6.57); N 8.72 (8.91).

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