Reaction of Tertiary 2-Chloroketones with Cyanide Ions: Application to 3-Chloroquinolinediones

Antonín Klásek,*[a] Stanislav Kafka,[a] Ondřej Rudolf,[a] Antonín Lyčka,[b] Michal Rouchal,[a] and Lukáš Bednář[a]

3-Chloroquinoline-2,4-diones react with cyanide ions in dimethyl formamide to give 3-cyanoquinoline-2,4-diones in small yields due to the strong hindrance of the substituent at the C-3 atom. Good yields can be achieved if the substituent at this position is the methyl group. In the methanol solution, the reaction proceeds by an addition mechanism to form 2-oxo-1a,2,3,7b-tetrahydrooxireno[2,3-*c*]quinoline-7b-carbonitriles, from which 4-hydroxy-3-methoxy-2-oxo-1,2,3,4-tetrahydroquinoline-4-carbonitriles are subsequently formed by opening of the epoxide ring with methanol. Some minor products of these reactions have also been isolated. The ^{1}H, ^{13}C and ^{15}N NMR spectra of the prepared compounds were measured, and all resonances were assigned using appropriate two-dimensional spectra.

1. Introduction

α-Haloketones belong to a group of very reactive organic compounds. In the literature, a good review was found that summarized the preparation of α-haloketones and their reactions, which are centered to the preparation of different heterocycles.[1] Several reaction mechanisms were discussed for the substitution of halogen atom in α-haloketones.[2] The review described that simple nucleophilic substitution of the bromine atom in α-bromoketone provides α-cyanoketone in good yields in a water/ethanol solvent.[3] Similar results were obtained by executing the reaction in DMSO.[4] However, scarce information is found in the literature for the reaction of cyanide ions with tertiary α-haloketones.[5,6] It is known that such compounds react inconveniently with nucleophiles, but the nucleophility can be increased, e.g., by creation of a "naked" cyanide anion using crown ethers.[1] Other problems are linked to some side reactions, e.g., the attack of the cyanide ion to the carbonyl group.[1,6a–c]

The cyanohydrin reaction is a well-known reaction of cyanide ions with the carbonyl group. If a halogen is present in the adjacent position, easy intramolecular dehalogenation proceeds and α-cyanooxiranes are formed,[7] which is a reaction that was described more frequently. Thus, α-bromoketones were converted to α-cyanooxiranes with sodium cyanide in water/dioxane.[8] Using trimethylsilyl cyanide, α-chloroketones were converted to 3-chloro-2-(trimethylsilyloxy)nitriles[9] in the presence of zinc(II) iodide. The analogous reaction also proceeds with α-bromoketones[10] and, especially, α-fluoroketones in the presence of Lewis bases.[11]

3-Chloroquinolinediones **1** constitute convenient model compounds for the study of the reactions of tertiary haloketones with nucleophiles. Due to the presence of two reactive sites in 3-chloroquinolinediones **1**, there are plenty of possible reactions capable of creating new types of heterocyclic compounds. Compounds **1** can be smoothly prepared by the reaction of 4-hydroxyquinolin-2-ones with sulfuryl chloride.[12] It is known that a considerable amount of quinolinediones are substituted in position 3 with a functional group containing heteroatom. 3-Hydroxyquinoline-2,4-diones result from the oxidation of 4-hydroxyquinolin-2-ones with peroxyacetic acid.[13] In nature, these compounds were found as metabolites of some *Pseudomonas* species.[14] The reaction of 4-hydroxyquinolin-2-ones with in situ prepared thiocyanogen leads to 3-thiocyanatoquinolinediones.[15] 3-Fluoroderivatives were prepared from 3-chloro-quinolinediones.[16] 3-Nitroquinolinediones resulted from the action of nitric acid.[12] 3-Azidoderivatives were prepared from 3-chloroquinolinediones and sodium azide.[17] Initial efforts for the conversion of 3-halogenoderivatives to corresponding amines were not very successful. The substitution of the bromine atom in position 3 of quinoline-2,4-dione moiety was accomplished by reaction with a tenfold excess of appropriate secondary amine in diethyl ether,[18] which was part of larger polycyclic patterns, such as 4*H*-pyrido[3,2,1-*jk*]carbazole-4,6(5*H*)-dione, 1*H*-pyrido[3,2,1-*kl*]phenoxazine-1,3(2*H*)-dione and 1*H*-pyrido[3,2,1-*kl*]phenothiazine-1,3(2*H*)-dione with the dimethylamino or 4-methylpiperazino group. However, the attempts at ammonolysis of 3-chloroquinolinediones with aqueous ammonia resulted in the preparation of only one desired product, namely that product bearing the 3-benzyl substituent at the C-3 atom.[13] The first 3-aminoquinolinedione

[a] *Prof. Dr. A. Klásek, Assoc. Prof. Dr. S. Kafka, Dr. O. Rudolf, Dr. M. Rouchal, L. Bednář*
Department of Chemistry
Faculty of Technology, Tomas Bata University
Vavrečkova 275, 760 01 Zlín (Czech Republic)
E-mail: klasek@utb.cz
[b] *Prof. Dr. A. Lyčka*
Department of Chemistry
Faculty of Science, University of Hradec Králové
Rokitanského 62, 500 03 Hradec Králové 3 (Czech Republic)

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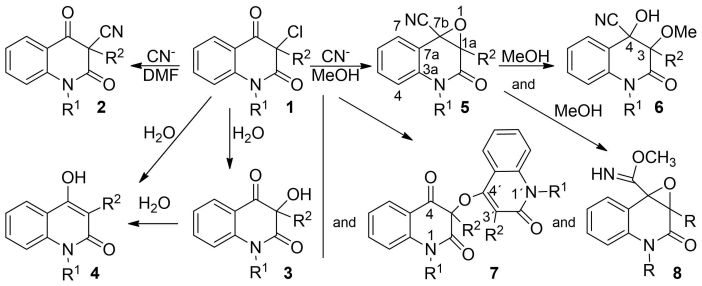
was prepared by acid hydrolysis of the corresponding 3-acetamido derivative, which was obtained by rearrangement of 6-chloro-4-hydroxy-3-imino-1-methyl-4-phenyl-3,4-dihydro-1*H*-quinolin-2-one.[17] Only when dimethyl formamide was used as the reaction medium were the appropriate 3-amino derivatives prepared in good yields from the corresponding 3-chloro derivatives and in situ generated ammonia or primary amines.[20]

To the best of our knowledge, 3-cyanoquinoline-2,4-diones were not prepared until now. Therefore, we decided to study their preparation from the reaction of 3-chloroquinolinediones **1** with cyanide ions. Compounds **1** can react with CN^- ions in two different ways: first, by simple substitution of the chlorine atom to form corresponding nitriles and, second, by a nucleophilic attack on the carbonyl group. Both possibilities are studied in this paper.

2. Results and Discussion

In all compounds, H, Me and Ph were chosen as R^1, and Bu, Bn and Ph were chosen as R^2 (Scheme 1). The reaction of compounds **1 a–i** with cyanide ions was carried out in two different solvents – DMF and methanol. In DMF, as a polar and aprotic solvent, the main reaction products were 3-carbonitriles **2** (Table 1, NMR data in Table 2). Compounds **2** gave only one aliphatic quaternary carbon in the ^{13}C NMR spectra (Table 2). In the IR spectra of compounds **2**, a very weak band corresponding to stretching vibration of CN group appears, as could be expected, in the region of 2222–2262 cm^{-1}, since a very similar wavenumber range of CN absorption bands (2220–2273 cm^{-1}) has been reported earlier for a series of nitriles with two carbonyl groups in close proximity to the CN group, namely 2-cyanocyclopent-4-ene-l,3-diones.[21] The reaction is not absolutely regioselective. In two cases (**1 c** and **1 f**), products **5** were also isolated (Table 1). Table 1 shows that the yields of **2** were very poor or even none, whereas unreacted starting materials, 1,3-hydroxyquinolinediones **3** and 4-hydroxy-2-quinolones **4** were isolated or, at least, indicated by TLC in most cases. We believe that the poor yields of **2** are caused by the steric hindrance of the substituent R^2. This effect is very strong particularly where R^2 is the benzyl or phenyl group. In these instances, the expected compounds (**2 b, c, i**) were not isolated. Therefore, we performed experiments with three other com-



Scheme 1. Reaction of 3-chloroquinoline-2,4-diones with cyanide ions in DMF and methanol.

Table 1. The key of substituents and results of the reaction of α-chloroketones **1** with cyanide ions in DMF and in methanol (isolated yields).

	a	b	c	d	e	f	g	h	i	j	k	l
R^1	H	H	H	Me	Me	Me	Ph	Ph	Ph	H	Me	Ph
R^2	Bu	Bn	Ph	Bu	Bn	Ph	Bu	Bn	Ph	Me	Me	Me
In DMF (**Method A**)												
1 [%][a]	27	40		50	10	7	8		10		20	
2 [%]	9	0	0	8	5	0	14	24	0	58	48	55
3 [%][b]	b		12	a		7			9	a		
4 [%][b]	b		5	a		4				a		
5 [%]			12			7						
7 [%]				6		4						
In methanol (**Method B**)												
1 [%][a]		3			20		24	25				
3 [%][b]					15				47		30	19
4 [%][b]		b		5		2				a		a
5 [%]	4	0	24	0	0	53	0	0	47	0	30	19
6 [%]	5									16		
7 [%]				0							3	
8 [%]				44			32				40	7

[a] Regenerated starting compounds. [b] Compounds **3** and **4** with declared yields were isolated and their structure was confirmed by comparison of their IR spectra with those of authentic compounds. Non-isolated compounds were indicated by TLC.

Table 2. ^{1}H, ^{13}C and ^{15}N chemical shifts of compounds **2** in DMSO-d_6.

Position	**2a**		**2d**		**2e**		**2g**		**2h**		**2j**		**2k**		**2l**	
	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	–	248.9[a],[b]	–	–	–	–		235.0[a]	–	234.2[a]		–	–	–	–	–
2	–	165.8	–	165.2	–	164.6	–	165.2	–	164.5		166.5	–	166.0	–	166.0
3	–	61.0	–	61.3	–	62.3	–	61.9	–	62.8		55.0	–	55.4	–	56.1
4	–	187.6	–	187.1	–	186.7	–	187.1	–	186.8		188.1	–	187.6	–	187.7
4a	–	117.3	–	116.0	–	119.4	–	118.4	–	119.1		116.8	–	118.3	–	118.0
5	7.78	127.2	7.86	127.4	7.83	127.2	7.91	127.5	7.87	127.3	7.81	127.4	7.89	127.6	7.94	127.7
6	7.16	123.1	7.27	123.4	7.26	123.4	7.23	123.5	7.21	123.5	7.17	123.1	7.29	123.4	7.25	123.5
7	7.64	136.6	7.77	136.7	7.72	136.6	7.55	136.2	7.52	136.2	7.65	136.7	7.78	136.8	7.56	136.4
8	7.10	116.7	7.42	116.2	7.31	116.0	6.36	116.9	6.29	117.0	7.11	116.7	7.43	116.3	6.37	117.0
8a	–	141.4	–	142.5	–	142.4	–	143.5	–	143.6	–	141.6	–	142.6	–	143.6
3-CN	–	116.0	–	116.0	–	115.9	–	115.9	–	115.9	–	117.0	–	117.0	–	116.9
1'(R^1)	11.22[b]	–	3.39	30.2	3.35	30.0	–	137.0	–	137.1	11.24	–	3.40	30.2	–	137.0
2'(R^1)	–	–	–	–	–	–	7.42	129.3	7.45	129.5					7.45	129.2
	–	–	–	–	–	–	7.31	128.9	7.31	128.4	–	–	–	–	7.31	128.8
3'(R^1)	–	–	–	–	–	–	7.42	130.1	7.62	130.4					7.61	130.3
4'(R^1)	–	–	–	–	–	–	7.59	130.4	7.57	130.1	–	–	–	–	7.57	129.1
1'(R^2)	1.99	37.5	1.99	37.6	3.34	44.3	2.10	37.3	3.51	43.9	1.73	24.7	1.72	24.9	1.90	24.9
	1.91		1.90		3.31		2.19		3.54		–	–	–	–	–	–
2'(R^2)	1.36	26.6	1.35	26.7	–	132.1	1.41	26.8	–	132.2	–	–	–	–	–	–
	–	–	1.31	–	–	–	–	–	–		–	–	–	–	–	–
3'(R^2)	1.26	21.3	1.22	21.3	6.98	128.0	1.29	21.3	7.12	130.4	–	–	–	–	–	–
4'(R^2)	0.80	13.6	0.79	13.6	7.21	130.1	0.84	13.6	7.28	128.1	–	–	–	–	–	–
5'(R^2)	–	–	–	–	7.11	128.0	–	–	7.30	129.5	–	–	–	–	–	–

[a] δ(^{15}N). [b] ^{1}J(^{15}N, H) = 91.0 Hz.

pounds (**1j**–**1l**) bearing the methyl group in position 3. Our presumption was confirmed and the corresponding compounds **2j,k,l** were prepared in good yields of 48–58%.

In methanol, as a polar and protic solvent, compounds **1** reacted differently. As expected, the cyanide ion was added to the carbonyl group, whereat oxiranes **5** arose due to the intramolecular nucleophilic substitution of the chlorine atom (Scheme 1, Table 1). By analogy with compounds **2**, in the IR spectra of compounds **5**, a very weak band corresponding to stretching vibration of CN group appears in the region of 2241–2260 cm^{-1}. Oxiranes **5** contain the cyano group signal and two signals of quaternary carbons in the ^{13}C NMR spectra (Table 3), resonating at 113.7–114.6 ppm (CN), 63.1–66.1 ppm (C-1a) and 56.7–59.1 ppm (C-7b). Compounds **6** gave two aliphatic quaternary carbons in ^{13}C NMR spectra (Table 4), and the chemical shifts were considerably shifted to higher frequencies compared with those in compounds **5**. Compounds **6** resulted from

Table 3. ^{1}H, ^{13}C and ^{15}N chemical shifts of oxiranes **5** in DMSO-d_6.

Position	**5a**		**5c**		**5f**		**5i**		**5k**		**5l**	
	δ[H]	δ[C]	δ[H]	δ[C]	δ[H]	δ[C]	δ[H]	δ[C]	δ[H]	δ[C]	δ[H]	δ[C]
1a	–	65.2	–	66.0	–	65.8	–	66.1	–	63.1	–	63.4
2	–	163.5	–	163.5	–	163.2	–	163.2	–	163.9	–	163.8
3 (N)	–	–	–	–	–	−253.5[a]	–	−233.1[a]	–	−256.0[a]	–	–
3a	–	136.5	–	136.8	–	138.0	–	139.1	–	137.8	–	137.0
4	7.08	116.1	7.15	116.2	7.42	116.2	6.32	116.8	7.23	115.9	6.24	116.5
5	7.51	132.0	7.55	132.1	7.69	132.4	7.50	132.0	7.62	132.0	7.42	131.7
6	7.21	122.9	7.23	122.9	7.33	123.3	7.33	123.4	7.32	123.1	7.28	123.2
7	7.76	128.4	7.77	128.4	7.86	128.8	7.92	128.9	7.82	128.7	7.90	128.8
7a	–	114.5	–	114.5	–	115.4	–	115.2	–	116.6	–	115.4
7b	–	56.7	–	59.1	–	59.0	–	59.1	–	57.1	–	57.1
CN	–	114.2	–	113.8	–	113.7	–	113.7	–	114.6	–	114.6
1'(R^1)	11.15	–	11.32	–	3.41	30.3	–	137.0	3.35	29.9	–	139.1
2'(R^1)	–	–	–	–	–	–	7.42	129.2	–	–	7.44	129.1
							7.28	128.6			7.24	128.7
3'(R^1)	–	–	–	–	–	–	7.63	130.4	–	–	7.60	130.3
4'(R^1)	–	–	–	–	–	–	7.55	129.1	–	–	7.54	129.1
1'(R^2)	2.38	29.0	–	130.5	–	131.1	–	130.7	1.84	16.1	1.87	15.8
	1.83											
2'(R^2)	1.61	26.3	7.63	127.9	7.63	127.8	7.73	127.8	–	–	–	–
	1.52								–	–	–	–
3'(R^2)	1.37	22.2	7.45	128.1	7.48	128.1	7.47	128.1	–	–	–	–
4'(R^2)	0.89	13.7	7.45	129.6	7.48	128.7	7.47	129.6	–	–	–	–
5'(R^2)	–	–	–	–	–	–	–	–	–	–	–	–

[a] δ(^{15}N).

Table 4. ^{1}H, ^{13}C and ^{15}N chemical shifts of compounds **6** and **7** in DMSO-d_6.

Position	**6a**		**6j**		**7d**		**7f**		**7k**	
	δ[H]	δ[C]	δ[H]	δ[C]	δ[H]	δ[C]	δ[H]	δ[C]	δ[H]	δ[C]
1	10.53		10.53	−252.6[a],[b]	-	−242.7[a]	–	−242.3[a]		−242.8[a]
2	–	169.4		170.5	–	167.0	–	168.4	–	166.4
3	–	76.8		74,0	–	88.5	–	83.9	–	89.0
4	–	83.6		83.5	–	189.7	–	190.1	–	187.6
4a	–	118.1		117.8	–	119.2	–	119.4	–	119.0
5	7.47	128.5	7.49	128.5	7.88	127.5	7.88	127.7	7.62	127.4
6	7.13	122.3	7.13	122.2	7.29	123.9	7.28	123.5	7.15	123.4
7	7.44	131.7	7.45	131.7	7.82	137.6	7.78	137.0	7.66	136.4
8	6.97	116.3	6.99	116.3	7.50	114.5	7.44	116.2	7.58	114.5
8a	–	136.5	–	136.5	–	142.3	–	142.6	–	141.6
CN	–	115.3	–	115.2	–	–	–	–	–	–
OH	5.94	–	6.11	–	–	–	–	–	–	–
OH	–	–	–	–	–	–		–	–	–
OCH_3	3.07	53.3	3.07	53.5	–	–	–	–	–	–
1'(R^1)	10.53	–	10.52	–	3.43	29.9	3.43	29.9	3.25	29.8
1'(R^2)	1.60	33.7	1.22	22.2	2.20,	40.5	1.70	21.7	–	136.2
	1.38	–	–	–	–	–	–	–	–	–
2'(R^2)	1.49	22.1	–	–	1.36	24.8	–	–	b	c–
	1.02		–	–	–			–	–	–
3'(R^2)	1.13	22.3	–	–	1.28	22.0	–	–	b	c
4'(R^2)	0.76	13.9	–	–	0.82	13.7	–	–	b	c
1'	–	–	–	–	–	−252.6[a]	–	−254.5[a]	–	−250.5[a]
2'	–	–	–	–	–	162.4	–	162.6	–	162.2
3'	–	–	–	–	–	118.8	–	117.3	–	117.6
4'	–	–	–	–	–	155.4	–	155.2	–	155.5
4a'	–	–	–	–	–	118.5	–	118.6	–	118.0
5'	–	–	–	–	7.80	123.3	7.74	123.5	7.75	124.4
6'	–	–	–	–	7.24	121.7	7.26	121.6	7.22	121.9
7'	–	–	–	–	7.58	130.2	7.59	130.3	7.41	130.2
8'	–	–	–	–	7.48	116.4	7.50	114.4	7.58	115.8
8a'	–	–	–	–	–	137.7	–	137.6	–	136.2
1'(R^1)'	–	–	–	–	3.60	29.6	3.60	29.7	3.61	29.7
1'(R^2)'	–	–	–	–	2.09	25.6	1.77	11.9	–	130.8
	–	–	–	–	2.02	–	–	–	–	–
2'(R^2)'	–	–	–	–	1.16	29.5	–	–	b	c
3'(R^2)'		–	–	–	0.97	22.4	–	–	b	c
4'(R^2)'		–	–	–	0.64	13.6	–	–	b	b

[a] δ(^{15}N). [b] ^{1}J(^{15}N, H) = 91.3 Hz. [c] δ(^{1}H) = 7.30–7.45, 6,70–6,90, broadened overlapped signals. [c] δ(^{13}C) = 133.5, 131.1, 129.3, 127.4, 126.7, 126.6.

subsequent nucleophilic attack of methanol on oxiranes **5**. The stretching vibrations of CN groups were not observed in the IR spectra of some compounds **6** (**6a** and **6j**), which is common with some cyanohydrines.[20] Table 1 shows that the sum of the yields of **5** and **6** depends on the nature of the substituent on C-3. When the starting compounds were **1e** and **1h**, wherein R^2 is a benzyl group, the corresponding compounds **5** and **6** were not isolated.

The reactions of **1d**, **1f** and **1k** took place in anomalous way yielding unsymmetrical dimers **7d**, **7f** and **7k** (NMR data in Table 4). Their origin can be explained by the providing corresponding 4-hydroxy-2-quinolone **4**, which is alkylated by the molecule of the starting compound **1**. The presence of compounds **4** in the reaction mixture was proved by TLC in almost all cases. Their formation is caused by the transfer of the "positive charged" chlorine atom in **1** to a nucleophile *(e.g.*, water, CN^-).[26]

To support our explanation of the presence of compounds **6** in the reaction mixtures, we investigated the conversion of compounds **5a** and **5l** to the corresponding compounds **6a** and **6l**. It has been shown that this conversion does not take place by the action of methanol alone, even with prolonged boiling. However, the conversions proceeded smoothly in a short time and compounds **6a,l** were obtained in good yields after addition of NaCN to the reaction mixtures, apparently due to its basicity by the effect of which methoxide anions were generated.

Four compounds that do not have the CN group in the molecule were also isolated. These compounds exhibit signals of two quaternary carbon atoms and a signal of proton on the nitrogen atom in the range of 8.66–8.88 ppm in their NMR spectra (Table 5), which pertains to the imino group. It stands to reason that the base catalyzed (NaCN) addition of the molecule of methanol to the nitrile group[24] in compounds **5** proceeded under formation of methyl imidates **8d,g,k,l**. (NMR spectra in Table 5). ^{15}N NMR spectroscopy provided the key piece of information about the constitution of compounds **8d,g,k,l**. Gradient selected 1D ^{1}H-^{15}N-HMQC gave us relatively small ^{1}J(^{15}N, ^{1}H) coupling constants about 61 Hz while from 2D ^{1}H-^{15}N-HMQC we read ^{15}N chemical shifts of =N–H about −155 ppm, both typical of methyl imidates. These compounds were prepared also by the base catalyzed reaction of compounds **5** with methanol.

Table 5. ^{1}H, ^{13}C and ^{15}N chemical shifts of imines **8** in DMSO-d_6.

Position	**8d**		**8f**		**8g**		**8k**		**8l**	
	δ[H]	δ[C]	δ[H]	δ[C]	δ[H]	δ[C]	δ[H]	δ[C]	δ[H]	δ[C]
1a	–	64.2	–	65.5	–	64.6	–	61.8	–	62.2
2	–	164.1	–	164.5	–	164.3	–	164.8	–	164.9
3 (N)	–	−254.0[a]	–	−253.5[a]	–	−242.7[a]	–	−255.2[a]	–	−240.0[a]
3a	–	138.1	–	138.5	–	139.4	–	138.3	–	139.6
4	7.29	115.6	7.36	115.8	6.22	116.3	7.31	115.6	6.22	116.3
5	7.52	130.8	7.58	131.1	7.30	130.4	7.51	130.8	7.29	130.4
6	7.18	122.7	7.21	122.7	7.14	122.8	7.19	122.7	7.13	122.8
7	7.31	129.1	7.36	129.3	7.36	129.3	7.34	129.1	7.36	129.2
7a	–	118.2	–	118.00	–	118.0	–	118.2	–	118.0
7b	–	65.9	–	67.8	–	66.3	–	66.1	–	66.3
C=NH	–	164.0	–	162.5	–	163.9	–	164.1	–	164.1
C=***NH***	8.66	−155.0[a] J=60.1 Hz	8.52	−154.1[a] J=61.1 Hz	8.76	−154.2[a] J=61.2 Hz	8.88	−155.4[a] J=60.1 Hz	8.75	−154.8[a] J=61.0 Hz
OCH3	3.79	53.3	3.40	52.9	3.84	53.4	3.79	53.5	3.84	53.5
1'(R^1)	3.38	29.7	3.42	30.0	–	137.2	3.35	29.8	–	137.3
2'(R^1)	–	–	–	–	7.37 7.19	129.4 128.7	–	–	7.36 7.19	129.4 128.7
3'(R^1)	–	–	–	–	7.56	130.3	–	–	7.58	130.2
4'(R^1)	–	–	–	–	7.52	128.9	–	–	7.53	128.9
1'(R^2)	2.28 1.29	28.2	–	131.8	2.25 1.39	27.9	1.50	14.2	1.54	13.9
2'(R^2)	1.33 1.26	26.5	7.36	127.6	1.39	26.5	–	–	–	–
3'(R^2)	1.23	22.2	7.36	127.5	1.25	22.3	–	–	–	–
4'(R^2)	0.83	13.6	7.36	128.5	0.84	13.7	–	–	–	–

[a] δ(^{15}N).

3. Conclusion

We conclude that the presented reaction of tertiary 2-chloroketones with cyanide ions is interesting from a theoretical viewpoint, which is exemplified using 3-chloroquinoline-2,4-diones **1** as model compounds, and it also leads the way for preparing new compounds for the study of their biological activity due to the simple reaction protocol.

Although the yields of products of nucleophilic substitution of the chlorine atom in aprotic DMF are low owing to a strong steric hindrance, we demonstrated that they can be substantially enhanced by the suitable selection of the substituent in the position 3 of the starting compound. We also show that carrying out the reaction in polar protic solvent (methanol) leads to the nucleophilic addition of the cyanide ion to the carbonyl group, which allows preparation of compounds with oxirane ring **5** as the second row of products that can be smoothly converted to 4-hydroxy-3-alkoxyquinolinones **6**. Oxiranes **5** can also act as important synthetic intermediates for the synthesis of different heterocycles, *e.g.*, indoles by the reaction with anilines.[25] The reaction of compounds **1 d, g, k, l** having an alkyl group in position 3 with cyanide ions in methanol is interesting, because it does not afford or affords not only epoxides **5**, but also carbamidates **8**.

Experimental Section

General Methods

Melting points were determined on a Kofler block. IR (KBr) spectra were recorded on a FT-IR ALPHA-T spectrophotometer (Bruker). The intensities of the bands are referred to as very strong (vs), strong (s), medium (m), weak (w), and very weak (vw). NMR spectra were recorded on a Bruker AVANCE III HD spectrometer (500.13 MHz for ^{1}H, 125.76 MHz for ^{13}C), and on a Bruker AVANCE III HD 400 spectrometer (400.13 MHz for ^{1}H, 100.56 MHz for ^{13}C and 40.55 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 (δ = 0.0). The ^{15}N chemical shifts were referred to an external ^{15}N enriched nitromethane in a coaxial capillary (δ = 0.0). All 2D experiments (gradient-selected (gs)-COSY, NOESY, gs-HMQC, gs-HMBC) and 1D ^{1}H-^{15}N gs-HMQC were performed using manufacturer's software. The positive-ion EI mass spectra (EI-MS) were measured on a Shimadzu QP-2010 instrument within the mass range *m/z* = 50–600 using direct inlet probe (DI). Samples were dissolved in dichloromethane (30 μg/mL) and 10 μL of the solution was evaporated in DI cuvette at 50 °C. The ion source temperature was 200 °C; the energy of electrons was 70 eV. Only signals exceeding relative abundance of 5% are listed. The positive as well as negative electrospray ion mass spectra (ESI-MS) were recorded on an amaZon X ion-trap mass spectrometer (Bruker Daltonics, Bremen, Germany) equipped with an ESI source. Individual samples were infused into the ion source as methanol/water (1/1, v/v) solutions via a syringe pump at a constant flow rate of 4 μL min^{-1}. The other instrumental conditions were as follows: *m/z* range 50–1500, electrospray voltage ±4.2 kV, drying gas temperature 220 C, drying gas flow 6.0 dm^3 min^{-1}, nebulizer pressure 55.16 kPa, capillary exit ±140 V. Nitrogen was used as nebulizing as well as drying gas. Column chromatography was carried out on silica gel (VWR CHEMICALS) using chloroform/ethanol (in ratios from 99:1 to 8:2) (S1), benzene and then successive mixtures of benzene/ethyl

acetate (in ratios from 99:1 to 8:2) (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 and 1:1) (S4 and 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 Flash EA 1112 Elemental Analyzer (Thermo Fisher Scientific).Regenerated compounds **1** and isolated compounds **3** and **4** were identified by IR spectra.

General procedure for the reaction of 3-hloro-quinolinediones 1 with cyanide ions

Method A: NaCN (0.147 g, 3 mmol) was added to the solution of compound **1** (3 mmol) in DMF (12 mL) portionwise at 0 °C during 1 h. The orange suspension was stirred for 5 h at room temperature and then poured onto crushed ice (100 mL). The mixture was extracted with chloroform (6×25 ml). Collected extracts were dried with anhydrous sodium sulfate, evaporated to dryness and column chromatographed.

Method B: The reaction was carried out by the similar procedure as Method A, with the difference that methanol (12 mL) instead of DMF was used as solvent. The mixture was stirred for 1 h at room temperature, subsequently refluxed for 1–3 h and then poured onto crushed ice. The precipitate solid was filtered off with suction. The filtrate was extracted with chloroform (6×25 ml). Collected extracts were dried with anhydrous sodium sulfate, filtered, and evaporated to dryness. Collected portions were chromatographed on silica gel column.

2a: Compound was prepared from **1a** by Method A in 9% yield. Colorless solid, mp 226–229 °C (ethyl acetate/hexane). IR (KBr): ν= 3218 (w) ν(NH), 3081 (w) ν(CH), 2980 (w) ν(CH), 2259 (w) ν(CN), 1704 (s) ν(CO), 1683 (vs) ν(CO), 1613 (m), 1594 (w), 1484 (m), 1437 (w), 1386 (m), 1249 (w), 787 (w) cm^{-1}. ESI-MS (pos.) *m/z* (%): 507.1 $[2{\cdot}M+Na^+]^+$ (27), 281.0 $[M+Na^+]^+$ (16), 265.0 $[M+H^+]^+$ (100). ESI-MS (neg.) *m/z* (%): 240.8 $[M\text{-}H^+]^-$ (100). EI-MS: 41 (8), 58 (5), 63 (7), 64 (12), 65 (10), 90 (10), 92 (22), 102 (6), 119 (14), 120 (10), 130 (6), 144 (14), 146 (12), 171 (40), 174 (26), 175 (15), 186 (51), 187 (11), 188 (11), 199 (100), 200 (13), 242 (10). For NMR spectra see Table 1. For $C_{14}H_{14}N_2O_2$ (242.27) calcd. C 69.41, H 5.82, N 11.56; found C 69.29, H 5.87, N 11.29.

2d: Compound was prepared from **1d** by Method A in 8% yield. Colorless solid, mp 105–108 °C (benzene/cyclohexane). IR (KBr): ν= 2959 (w) ν(CH), 2932 (w) ν(CH), 2261 (w) ν(CN), 1700 (vs) ν(CO), 1675 (vs)), 1661 (vs) ν(CO), 1603 (s), 1475 (vs), 1364 (s), 1297 (m), 1112 (w), 777 (w), 757 (w) cm^{-1}. ESI-MS (pos.) *m/z* (%): 404.3 $[3{\cdot}M+H^++K^+]^{2+}$ (20), 279.2 $[M+Na^+]^+$ (100), 257.3 $[M+H^+]^+$ (89), 201.2 $[M+H^+\text{-}C_4H_8]^+$ (49). EI-MS: 41 (61), 42 (7), 43 (6), 51 (10), 55 (22), 57 (74), 63 (9), 75 (9), 76 (10), 77 (14), 85 (6), 88 (7), 89 (20), 90 (13), 101 (11), 102 (15), 103 (7), 114 (11), 115 (19), 116 (21), 117 (23), 127 (9), 128 (11), 129 (6), 130 (12), 140 (10), 142 (11), 143 (29), 144 (21), 155 (7), 156 (15), 159 (11), 160 (24), 169 (16), 170 (13), 171 (12), 172 (54), 173 (13), 183 (11), 188 (19), 189 (10), 197 (20), 198 (73), 199 (14), 200 (100), 201 (19), 211 (23), 212 (9), 213 (8), 240 (14), 241 (5), 256 (24). For $C_{15}H_{16}N_2O_2$ (256.30) calcd C 70.29, H 6.29, N 10.93; found: C 70.16, H 6.19, N 10.86.

2e: Compound was prepared from **1e** by Method A in 5% yield.. Colorless solid, mp 151–154 °C (benzene/hexane). IR: (KBr): ν= 3030 (w) ν(CH), 2936 (w) ν(CH), 2257 (w) ν(CN), 1699 (vs) ν(CO), 1664 (vs) ν(CO), 1601 (vs), 1474 (vs), 1373 (s), 1301 (m), 1247 (w), 761 (s), 700 (m) cm^{-1}. ESI-MS (pos.) *m/z* (%): 603.2 $[2{\cdot}M+Na^+]^+$ (7), 329.1 $[M+K^+]^+$ (12), 313.1 $[M+Na^+]^+$ (100). ESI-MS (neg.) *m/z* (%): 306.9 $[M\text{-}H^++H_2O]^-$ (100). For $C_{18}H_{14}N_2O_2$ (290.32) calcd C 74.47, H 4.86, N 9.65; found: C 74.24, H 4.82, N 9.43.

2g: Compound was prepared from **1g** by Method A in 14% yield. Colorless solid, mp 135–139 °C (benzene/hexane). IR (KBr): ν= 2958 (w) ν(CH), 2932 (w) ν(CH), 2258 (w) ν(CN), 1709 (vs) ν(CO), 1682 (vs) ν(CO), 1601 (s), 1492 (m), 1462 (vs), 1349 (s), 1293 (m), 761 (s), 707 (m) cm^{-1}. ESI-MS (pos.) *m/z* (%): 659.2 $[2{\cdot}M+Na^+]^+$ (11), 656.2 $[4{\cdot}M+H^++K^+]^{2+}$ (10), 497.2 $[3{\cdot}M+H^++K^+]^{2+}$ (100), 357.0 $[M+K^+]^+$ (6), 341.1 $[M+Na^+]^+$ (37), 319.1 $[M+H^+]^+$ (7). ESI-MS (neg.) *m/z* (%): 352.9 $[M+Cl^-]^-$ (100). EI-MS: 41 (76), 42 (7), 43 (36), 55 (29), 56 (10), 57 (100), 70 (11), 71 (33), 76 (12),77 (60), 78 (12), 83 (18), 84 (8), 85 (29), 97 (13), 99 (10), 102 (10), 103 (8), 111 (10), 113 (9), 115 (7), 127 (9), 128 (10), 140 (7), 143 (9), 149 (22), 151 (13), 152 (9), 156 (33), 166 (8), 167 (11), 177 (10), 178 (12), 179 (9), 193 (6), 204 (14), 205 (46), 206 (15), 221 (11), 222 (20), 229 (10), 231 (12), 232 (11), 233 (49), 234 (68), 235 (22), 244 (13), 245 (24), 248 (14), 250 (85), 251 (49), 252 (8), 258 (13), 259 (32), 260 (37), 261 (89), 262 (99), 2163 (26), 273 (12), 290 (14), 302 (9), 303 (14), 318 (63), 319 (15). For $C_{20}H_{18}N_2O_2$ (318.37) calcd C 75.45, H 5.70, N 8.80. found C 75.20, H 5.63, N 8.79.

2h: Compound was prepared from **1h** by Method A in 24% yield, Colorless solid, mp 197–200 °C (benzene/hexane). IR (KBr): ν= 3027 (w) ν(CH), 2979 (w) ν(CH), 2258 (w) ν(CN), 1712 (vs) ν(CO), 1681 (vs) ν(CO), 1599 (s), 1493 (m), 1464 (s), 1352 (s), 765 (s), 708 (m), 683 (m) cm^{-1}. ESI-MS (pos.) *m/z* (%): 727.2 $[2{\cdot}M+Na^+]^+$ (39), 705.3 $[2{\cdot}M+H^+]^+$ (8), 548.1 $[3{\cdot}M+H^++K^+]^{2+}$ (9), 391.0 $[M+K^+]^+$ (34), 375.1 $[M+Na^+]^+$ (100), 353.1 $[M+H^+]^+$ (18). ESI-MS (neg.) *m/z* (%): 368.9 $[M\text{-}H^++H_2O]^-$ (100). For $C_{23}H_{16}N_2O_2$ (352.39) calcd C 78.39, H 4.58, N 7.95; found C 78.28, H 4.65, N 7.88.

2j: Compound was prepared from **1j** by Method A in 58% yield. Colorless solid, mp 239–240 °C (ethyl acetate). IR (KBr): ν= 3220 (w) ν(NH), 3082 (w) ν(CH), 3001 (w) ν(CH), 2262 (w) ν(CN), 1706 (s) ν(CO), 1683 (vs) ν(CO), 1614 (m), 1594 (m), 1484 (m), 1395 (m), 1359 (w), 1188 (w), 787 (w) cm^{-1}. ESI-MS (pos.) *m/z* (%): 439.1 $[2{\cdot}M+K^+]^+$ (4), 423.1 $[2{\cdot}M+Na^+]^+$ (25), 320.2 $[3{\cdot}M+H^++K^+]^{2+}$ (12), 239.1 $[M+K^+]^+$ (75), 223.2 $[M+Na^+]^+$ (100), 218.2 $[M+NH_4^+]^+$ (13), 201.2 $[M+H^+]^+$ (4). ESI-MS (neg.) *m/z* (%): 199.0 $[M\text{-}H^+]^-$ (100). EI-MS: 50 (10), 51 (8), 52 (16), 63 (24), 64 (32), 65 (12), 76 (9), 77 (6), 90 (16), 91 (14), 92 (56), 119 (100), 120 (10), 146 (14), 149 (12), 171 (14), 172 (9), 199 (6), 200 (41), 201 (5). For $C_{11}H_8N_2O_2$ (200.19) calcd C 66.00, H 4.03, N 13.99; found: C 66.15, H 3.96, N 13.82.

2k: Compound was prepared from **1k** by Method A in 48% yield. Colorless solid, mp 139–141 °C (benzene/hexane). IR (KBr): ν= 2999 (w) ν(CH), 2942 (w) ν(CH), 2253 (w) ν(CN), 1711 (s) ν(CO), 1673 (vs) ν(CO), 1602 (s), 1471 (vs), 1380 (m), 1360 (s), 1298 (m), 1105 (s), 759 (s). ESI-MS (pos.) *m/z* (%): 451.2 $[2{\cdot}M+Na^+]^+$ (32), 341.2 $[3{\cdot}M+H^++K^+]^{2+}$ (69), 253.1 $[M+K^+]^+$ (52), 237.2 $[M+Na^+]^+$ (100), 232.2 $[M+NH_4^+]^+$ (23), 215.2 $[M+H^+]^+$ (21). For $C_{12}H_{10}N_2O_2$ (214.22) calcd C 67.28, H 4.71, N 13.08); found: C 67.30, H 4.53, N 13.11).

2l: Compound was prepared from **1l** by Method A in 55% yield. Colorless solid, mp 196–199 °C (benzene/hexane). IR (KBr): ν= 3007 (w) ν(CH), 2948 (w) ν(CH), 2236 (w) ν(CN), 1722 (vs) ν(CO), 1684 (vs) ν(CO), 1597 (vs), 1492 (m), 1460 (vs), 1336 (vs), 1300 (m), 754 (s), 701 (m) cm^{-1}. ESI-MS (pos.) *m/z* (%): 591.0 $[2{\cdot}M+K^+]^+$ (32), 575.1 $[2{\cdot}M+Na^+]^+$ (100), 434.1 $[3{\cdot}M+H^++K^+]^{2+}$ (19), 315.0 $[M+K^+]^+$ (60), 299.0 $[M+Na^+]^+$ (97), 277.0 $[M+H^+]^+$ (17). EI-MS: 41 (54), 42 (15), 43 (100), 44 (54), 51 (19), 55 (47), 56 (20), 57 (41), 71 (37), 83 (17), 84 (13), 85 (34), 96 (6), 99 (16), 104 (9), 112 (6), 135 (17), 149 (23), 157 (11), 196 (10), 205 (22), 206 (6), 224 (8), 233 (31), 234 (26), 248 (7), 159 (19), 260 (16), 276 (35) For $C_{17}H_{12}N_2O_2$ (276.29) calcd C 73.90, H 4.38, N 10.14; found C 73.75, H 4.24, N 10.17.

5a: Compound was prepared from **1a** by Method B in 4% yield. Colorless solid, mp 108–112 °C (benzene/hexane).. IR (KBr): ν= 3207

(w) ν(NH), 3087 (w) ν(CH), 2934 (w) ν(CH), 2246 (vw) ν(CN), 1691 (vs) ν(CO), 1613 (m), 1599 (m), 1498 (w), 1486 (m), 833 (w), 758 (w), 601 (w) cm^{-1}. ESI-MS (pos.) *m/z* (%): 265.0 $[M+Na^+]^+$ (100), 242.9 $[M+H^+]^+$ (29). ESI-MS (neg.) *m/z* (%): 240.8 $[M\text{-}H^+]^-$ (100). EI-MS: 41 (100), 42 (12), 43 (26), 44 (21), 45 (7), 51 (20), 52 (10), 53 (9), 55 (51), 56 (18), 57 (62), 63 (10), 64 (8), 69 (9), 73 (12), 75 (33), 76 (22), 77 (17), 89 (9), 101 (15), 102 (27), 103 (26), 115 (9), 116 (8), 117 (11), 128 (11), 129 (12), 130 (32), 145 (12), 146 (20), 155 (16), 156 (11), 157 (6), 158 (45), 159 (12), 168 (11), 169 (21), 174 (13), 175 (10), 182 (14), 183 (15), 184 (51), 186 (58), 187 (11), 197 (14), 207 (27), 226 (7), 242 (14). For $C_{14}H_{14}N_2O_2$ (242.27) calcd C 69.41, H 5.82, N 11.56; found C 69.22, H 5.71, N 11.34.

5c: Compound was prepared from **1c** by *Method A* in 12% yield, as well as by *Method B* in 24% yield. Colorless solid, mp 214–218 C (benzene). IR (KBr): $\tilde{\nu}$ = 3214 (w) ν(NH), 3069 (w) ν(CH), 2925 (w) ν(CH), 2250 (vw) ν(CN), 1699 (vs) ν(CO), 1599 (m), 1495 (m), 1449 (w), 891 (w), 756 (m), 697 (m) cm^{-1}. ESI-MS (pos.) *m/z* (%): 301.0 $[M+K^+]^+$ (22), 285.0 $[M+Na^+]^+$ (100), 263.0 $[M+H^+]^+$ (19). ESI-MS (neg.) *m/z* (%): 260.8 $[M\text{-}H^+]^-$ (100). For $C_{16}H_{10}N_2O_2$ (262.26) calcd C 73.27, H 3.84, N 10.68; found: C 73.22, H 3.67, N 10.42.

5f: Compound was prepared from **1f** in 7% yield by Method A. as well as by method B in 53%.yield. Colorless solid, mp 224–228 °C (benzene/hexane). IR (KBr): $\tilde{\nu}$ = 3088 (w) ν(CH), 2952 (w) ν(CH), 2250 (vw) ν(CN), 1673 (vs) ν(CO), 1604 (m), 1504 (w), 1471 (m), 1356 (m), 1140 (m), 756 (s), 701 (m), 648 (w) cm^{-1}. ESI-MS (pos.) *m/z* (%): 575.1 $[2{\cdot}M+Na^+]^+$ (72), 315.0 $[M+K^+]^+$ (74), 299.0 $[M+Na^+]^+$ (100), 277.0 $[M+H^+]^+$ (75). EI-MS: 51 (22), 63 (11), 75 (9), 76 (9), 77 (58), 78 (8), 88 (12), 89 (11), 102 (15), 105 (52), 115 (7), 130 (17), 190 (11), 204 (10), 219 (10), 229 (8), 231 (15), 232 (19), 234 (9), 259 (100), 260 (84), 261 (16), 276 (15). For $C_{17}H_{12}N_2O_2$ (276.29) calcd. C 73.90, H 4.38, N 10.14; found C 73.86, H 4.18, N 9.97.

5i: Compound was prepared from **1i** by Method B in 47% yield. Colorless solid, mp 179–182 °C (benzene/hexane). IR (KBr): $\tilde{\nu}$ = 3071 (w) ν(CH), 2241 (vw) ν(CN), 1678 (vs) ν(CO), 1604 (w), 1499 (w), 1458 (m), 1347 (m), 1295 (w), 755 (m), 695 (m) cm^{-1}. ESI-MS (pos.) *m/z* (%): 699.1 $[2{\cdot}M+Na^+]^+$ (50), 377.0 $[M+K^+]^+$ (47), 361.1 $[M+Na^+]^+$ (100), 339.1 $[M+H^+]^+$ (49). For $C_{22}H_{14}N_2O_2$ (338.36) calcd C 78.09, H 4.17, N 8.28; found: C 78.24, H 4.11, N 8.15.

5k: Compound was prepared from **1k** in 30% yield by Method B. Colorless solid, mp 136–140 °C (cyclohexane). IR (KBr): $\tilde{\nu}$ = 2985 (w) ν(CH), 2945 (w) ν(CH), 2247 (vw) ν(CN), 1677 (vs) ν(CO), 1604 (m), 1506 (w), 1473 (m), 1367 (m), 1110 (m), 777 (w), 761 (m), 739 (w) cm^{-1}. ESI-MS (pos.) *m/z* (%): 451.0 $[2{\cdot}M+Na^+]^+$ (41), 236.9 $[M+Na^+]^+$ (100). EA: $C_{12}H_{10}N_2O_2$ (214.22) calc: C 67.28, H 4.71, N 13.08; found: C 66.96, H 4.63, N 13.14.

5l: Compound was prepared from **1l** by Method B in 19% yield. Colorless solid, mp 135–138 °C (hexane). IR (KBr): $\tilde{\nu}$ = 3071 (w) ν(CH), 2249 (vw) ν(CN), 1681 (vs) ν(CO), 1601 (m), 1497 (m), 1460 (m), 1353 (s), 1299 (w), 1214 (w), 1143 (w), 753 (m), 705 (m) cm^{-1}. ESI-MS (pos.) *m/z* (%): 575.1 $[2{\cdot}M+Na^+]^+$ (100), 314.9 $[M+K^+]^+$ (27), 299.0 $[M+Na^+]^+$ (88), 277.0 $[M+H^+]^+$ (48), 277.0 $[M+H^+\text{-}CHNO]^+$ (28). For $C_{17}H_{12}N_2O_2$ (276.28) calcd C 73.90, H 4.38, N 10.14. found: C 73.64, H 4.60, N 9.83.

6a: Compound was prepared from **1a** by Method B in 5% yield and from **5a** in 17% yield. Colorless solid, mp 176–180 °C (benzene/hexane). IR (KBr): $\tilde{\nu}$ = 3460 (m) ν(OH), 3268 (m) ν(NH), 2955 (m) ν(CH), 2932 (w) ν(CH), 2238 (vw) ν(CN), 1706 (vs), 1665 (vs), ν(CO), 1613 (m), 1594 (m), 1481 (m), 1174 (m), 1096 (s), 771 (m) cm^{-1}. ESI-MS (pos.) *m/z* (%): 571.2 $[2{\cdot}M+Na^+]^+$ (100), 431.1 $[3{\cdot}M+H^++K^+]^{2+}$ (18), 313.0 $[M+K^+]^+$ (19), 297.0 $[M+Na^+]^+$ (40), 275.0 $[M+H^+]^+$ (2). ESI-MS (neg.) *m/z* (%): 272.9 $[M\text{-}H^+]^-$ (100). EI-MS: 41 (23), 55 (9), 57 (49), 85 (22), 102 (6), 103 (12), 130 (7), 146 (7), 147 (100), 148 (12), 157 (29), 158 (8), 161 (15), 162 (24), 187 (8), 274 (12). For $C_{15}H_{18}N_2O_3$ (274.32) calcd C 65.68, H 6.61, N 10.21; found C 65.49, H 6.49, N 9.93.

6j: Compound was prepared from **1j** by Method B in 16% yield. Colorless solid, mp 189–193 °C (benzene). IR (KBr): $\tilde{\nu}$ = 3423 (m) ν(OH), 3265 (m) ν(NH), 3068 (w) ν(CH), 2984 (w) ν(CH), 2245 (vw) ν(CN), 1699 (vs) ν(CO), 1671 (m), 1494 (m), 1389 (w), 1356 (m), 1183 (m), 1073 (m), 761 (m) cm^{-1}. ESI-MS (pos.) *m/z* (%): 503.0 $[2{\cdot}M+K^+]^+$ (11), 487.1 $[2{\cdot}M+Na^+]^+$ (100), 270.9 $[M+K^+]^+$ (21), 255.0 $[M+Na^+]^+$ (49), 232.9 $[M+H^+]^+$ (< 1). ESI-MS (neg.) *m/z* (%): 230.8 $[M\text{-}H^+]^-$ (100). For $C_{12}H_{12}N_2O_3$ (232.24) calcd C 62.06, H 5.21, N 12.06, found C 61.75, H 5.10, N 12.27.

7d: Compound was prepared from **1d** by Method A in 6% yield. Colorless solid, mp 147–150 °C (cyclohexane). IR (KBr): $\tilde{\nu}$ = 2957 (m) ν(CH), 2871 (w) ν(CH), 1704 (s) ν(CO), 1672 (s) ν(CO), 1629 (vs) ν(CO), 1598 (s) ν(CO), 1472 (s), 1363 (m), 1300 (w), 1153 (m), 1120 (w), 758 (m) cm^{-1}. ESI-MS (pos.) *m/z* (%): 499.2 $[M+K^+]^+$ (7), 483.2 $[M+Na^+]^+$ (100), 461.2 $[M+H^+]^+$ (40). For $C_{28}H_{32}N_2O_4$ (460.56) calcd C 73.02, H 7.00, N 6.08; found: C 72.98, H 7.06, N 6.12.

7f: Compound was prepared from **1f** *by* Method A *in 4%* yield.. Colorless solid, mp 192–197 C (ethyl acetate). IR (KBr): $\tilde{\nu}$ = 3058 (w) ν(CH), 2939 (w) ν(CH), 1709 (s) ν(CO), 1676 (s) ν(CO), 1625 (vs) ν(CO), 1599 (s), 1495 (m), 1473 (s), 1347 (s), 1312 (m), 1114 (m), 700 (m) cm^{-1}. ESI-MS (pos.) *m/z* (%): 1023.3 $[2{\cdot}M+Na^+]^+$ (16), 539.1 $[M+K^+]^+$ (33), 523.1 $[M+Na^+]^+$ (100), 501.2 $[M+H^+]^+$ (80). For $C_{32}H_{24}N_2O_4$ calcd. C 76.78, H 4.83, N 5.60; found C 76.70, H 4.63, N 5.65.

7k: Compound was prepared from **1k** by Method B in 3% yield. Colorless solid, mp 174–178 °C (hexane). IR (KBr): $\tilde{\nu}$ = 2986 (w) ν(CH), 2933 (w) ν(CH), 2887 (w) ν(CH), 1706 (vs) ν(CO), 1675 (vs) ν(CO), 1636 (vs) ν(CO), 1596 (vs), 1475 (s), 1374 (s), 1349 (s), 1094 (s), 734 (m) cm^{-1}. ESI-MS (pos.) *m/z* (%): 775.3 $[2{\cdot}M+Na^+]^+$ (30), 584.2 $[3{\cdot}M+H^++K^+]^{2+}$ (7), 415.1 $[M+K^+]^+$ (26), 399.1 $[M+Na^+]^+$ (100), 377.1 $[M+H^+]^+$ (43). For $C_{22}H_{20}N_2O_4$ (376.41) calcd C 70.20, H 5.36, N 7.14; found C 70.31, H 5.42, N 6.95.

8d: Compound was prepared from **1d** by Method B in 44% yield. Colorless solid, mp 75–78 °C (cyclohexane). IR (KBr): $\tilde{\nu}$ = 3319 (w) ν(NH), 2965 (w) ν(CH), 2942 (w) ν(CH), 2862 (w) ν(CH), 1677 (vs) ν(CO), 1474 (m), 1443 (m), 1375 (m), 1362 (m), 1349 (m), 1097 (m), 763 (m) cm^{-1}. ESI-MS (pos.) *m/z* (%): 599.2 $[2{\cdot}M+Na^+]^+$ (77), 327.0 $[M+K^+]^+$ (22), 311.0 $[M+Na^+]^+$ (98), 289.1 $[M+H^+]^+$ (100), 254.0 $[M+Na^+\text{-}C_4H_9]^+$ (21), 232.0 $[M+H^+\text{-}C_4H_9]^+$ (57). For $C_{16}H_{20}N_2O_3$ (288.34) calcd C 66.65, H 6.99, N 9.72; found: C 66.46, H 6.73, N 9.65.

8g: Compound was prepared from **1g** by Method B in 32% yield Colorless solid, mp 84–88 °C (hexane), IR (KBr): $\tilde{\nu}$ = 3317 (w) ν(NH), 2958 (w) ν(CH), 2869 (w) ν(CH), 1677 (vs) ν(CO), 1605 (m), 1461 (m), 1439 (m), 1368 (m), 1347 (m), 1094 (m), 1078 (m), 751 (m) cm^{-1}. ESI-MS (pos.) *m/z* (%): 723.2 $[2{\cdot}M+Na^+]^+$ (35), 545.2 $[3{\cdot}M+H^++K^+]^{2+}$ (20), 389.0 $[M+K^+]^+$ (56), 373.1 $[M+Na^+]^+$ (75), 351.1 $[M+H^+]^+$ (100). For $C_{21}H_{22}N_2O_3$ (350.41) calcd C 71.98, H 6.33, N 7.69; found C 71.89, H 6.37, N 7.90.

8k: Compound was prepared from **1k** by Method B in 40% yield and from **5k** in 8% yield. Colorless solid, mp 96–102 °C cyclohexane). IR (KBr): $\tilde{\nu}$ = 3303 (m) ν(NH), 2991 (w) ν(CH), 2944 (w) ν(CH), 1665 (vs) ν(CO), 1606 (m), 1475 (m), 1366 (m), 1113 (m), 1093 (m), 1069 (m), 752 (m) cm^{-1}. ESI-MS (pos.) *m/z* (%): 285.0 $[M+K^+]^+$ (19), 269.0 $[M+Na^+]^+$ (100), 247.0 $[M+H^+]^+$ (10). ESI-MS (neg.) *m/z* (%): 244.8 $[M\text{-}H^+]^-$ (100). For $C_{13}H_{14}N_2O_3$ (246.26) calcd C 63.40, H 5.73, N 11.38; found: C 63.66, H 5.66, N 11.35.

8l: Compound was prepared from **2l** in 7% yield by Method B and from **5l** in 38% yield. Colorless solid, mp 183–189 °C (benzene/hexane). IR (KBr): $\tilde{\nu}$ = 3314 (w) ν(NH), 2979 (w) ν(CH), 2941 (w) ν(CH), 1678 (vs) ν(CO), 1662 (s), 1603 (m), 1439 (m), 1368 (s), 1349 (m),

1098 (m), 759 (m), 715 (m) cm^{-1}. ESI-MS (pos.) *m/z* (%): 639.2 $[2{\cdot}M+Na^+]^+$ (100), 482.1 $[3{\cdot}M+H^++K^+]^{2+}$ (8), 347.0 $[M+K^+]^+$ (33), 331.0 $[M+Na^+]^+$ (86), 309.0 $[M+H^+]^+$ (40). For $C_{18}H_{16}N_2O_3$ (308.33) calcd C 70.12, H 5.23, N 9.09. Found: C 70.12, H 5.34, N 8.81.

General procedure for the conversion of compounds 5 to 6 and 8

The solution of **5** (0.3 mmol) in methanol (4 mL) was heated to reflux for 6 h. According to TLC, the reaction did not proceed. Then NaCN (0.66 mmol) was added and the mixture was refluxed for another hour. Methanol was evaporated in vacuo to dryness, water (6 mL) was added to the residue and the mixture was extracted with chloroform (4×6 mL). Collected extract was dried, the solvent was evaporated in vacuo and the residue was column chromatographed.

From **5a**, 36% of **6a**, from **5k**, 8% of **8k**, and from **5l**, 38% of **8l** was prepared. All these compounds were identical with those prepared from corresponding compounds **1** (Table 1). From **5f**, compound **8f** was prepared:

8f: Compound was prepared from **5f** in 56% yield by Method B. Colorless solid, mp 202–205 °C (benzene/hexane). IR (KBr): $\tilde{\nu}$ = 3313 (w) ν(NH), 3076 (w) ν(CH), 2974 (w) ν(CH), 2939 (w) ν(CH), 1667 (vs) ν(CO), 1603 (m), 1470 (m), 1444 (m), 1374 (m), 1347 (m), 1105 (m), 768 (m), 758 (m) cm^{-1}. ESI-MS (pos.) *m/z* (%): 639.2 $[2{\cdot}M+Na^+]^+$ (71), 617.1 $[2{\cdot}M+H^+]^+$ (18), 347.0 $[M+K^+]^+$ (35), 331.0 $[M+Na^+]^+$ (58), 309.0 $[M+H^+]^+$ (100), 252.0 $[M+H^+\text{-}C_2H_3NO]^+$ (47). For $C_{18}H_{16}N_2O_3$ (308.33) calcd C 70.12, H 5.23, N 9.09. Found: C 70.13, H 5.10, N 9.09.

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Conflict of Interest

The authors declare no conflict of interest.

Keywords: Cyanides · Cyanohydrin reaction · α-Cyanooxiranes · α-Haloketones · Solvent effects

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