Synthesis, Oxidation and Dehydrogenation of Cyclic *N,O*- and *N,S*-Acetals. Part III. [1,2] Transformation of *N,O*-Acetals: 3-Acyl-1,3,4-Oxadiazolines

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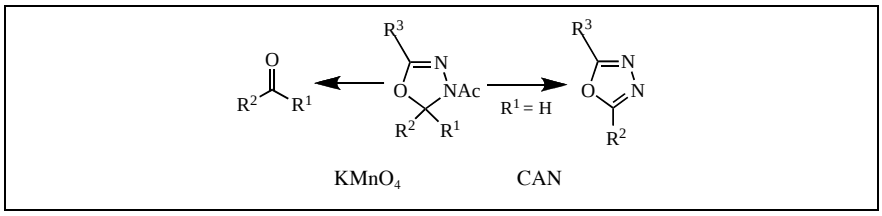

Various aldehyde and ketone acylhydrazones are synthesized and, under acylating conditions, cyclized into 3-acyl-1,3,4-oxadiazolines. The scope and limitations of these cyclizations and the possible side reactions (*e.g.* formation of the open-chain *N,O*-acylhydrazinocarbinols) are dissected. For the first time, simple, convenient and efficient dehydrogenations of 3-acyl-1,3,4-oxadiazolines to oxadiazoles by treatment with potassium permanganate, or more conveniently, with ammonium cerium(IV) nitrate (CAN) are presented. CAN oxidation of 2,2-disubstituted 3-acyl-1,3,4-oxadiazolines, as well as that of aldehyde diacylhydrazones (open-chain isomers of 2,5-disubstituted 3-acyl-1,3,4-oxadiazolines) regenerates the parent carbonyl compounds.

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INTRODUCTION

Numerous representatives of the 1,3,4-oxadiazol(in)e ring system exhibit remarkable physical [3], chemical or biological [4] properties (recently some 1,3,4-oxadiazoles, carbocyclic acid hydrazides and semicarbazides have been prepared [5] as peptidomimetics).

Cyclocondensation of *N,N'*-diacyl- or *N*-acyl-*N'*-thioacylhydrazines *via* elimination of the elements of water or hydrogen sulfide, as well as transformation of 5-substituted tetrazoles with acid chlorides or anhydrides, moreover, syntheses starting from trichloromethylarenes are convenient methods for the synthesis of 2,5-disubstituted 1,3,4-oxadiazoles. As a valuable and versatile alternative, dehydrocyclization of aldehyde acylhydrazones has been effected by treatment with a variety of oxidants such as chlorine–carbon tetrachloride [6], potassium hexacyanoferrate(III)–aq. sodium hydroxide [7], 3-methylbutylnitrite–diethyl ether [7], iodine–mercury(II) oxide [8a,b,9], lead(IV) acetate [10,12d], lead(IV) oxide–acetic acid [11], nickel(II) peroxide [10e], bromine–sodium acetate [12a-i], iodine–aq. sodium carbonate [12j], iron(III) chloride–acetic acid [13], potassium permanganate–acetone [10d], Chloramine T [14], (diacetoxyiodo)benzene [15] which transforms also *N,N'*-diacylhydrazines into oxadiazoles[16], and zinc chloride–acetic acid [17]. – Also, dehydrogenation of 2,5-disubstituted 3-acetyl-2,3-dihydro-1,3,4-oxadiazoles by treatment with lead(IV) acetate has been performed [18].

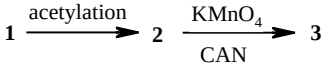
Of the various 1,3,4-oxadiazole syntheses, for this once, dehydrogenation reactions of the chemically or biologically valuable 3-acyl-1,3,4-oxadiazolines will be considered. It should also be noted that due to the diminished nucleophilicity of oxygen, in comparison to that of sulfur, acylhydrazones do not cyclize spontaneously into the isomeric 2,3-dihydro-1,3,4-oxadiazoles.

Moreover, upon chemical or enzymatic [19] deacylation 3-acyl-1,3,4-oxadiazolines cleave into acylhydrazones, and even the "heteroaromatic" 1,3,4-oxadiazole ring system can be opened [8] by intra- or intermolecular nucleophilic functionalities.

RESULTS AND DISCUSSION

In order to explore the scope and limitations of the aimed synthesis steps, a variety of substituted benzaldehyde acylhydrazones (**1**, see Table 3) was prepared and, under acetylating conditions, cyclized into 3-acetyl-1,3,4-oxadiazolines (**2**, Table 4). The products (**2**) were subjected to treatment with various oxidants and dehydrogenating agents of diverse mechanism of action (CAN, (diacetoxyiodo)benzene, potassium permanganate; see Table 5).

Scheme 1



The structure of the products, (di)acylhydrazones (**1,6**), oxadiazolines (**2**) and oxadiazoles (**3**), was supported by ^{1}H and ^{13}C nmr spectral data (see Tables 1 and 2).

Table 1
Characteristic ^{1}H nmr spectral data [a] of (di)acylhydrazones (**1,6**), oxadiazolines (**2**) and oxadiazoles (**3**).

	δ(ppm)				δ (ppm)	
Compound	N*H*/O*H*	C*H*=N	CH_3	Compound	O-C*H*(Ar)-N	CH_3
1b	11.43[b]	8.13[b]	2.20[d]	**2a**	[e]6.94	2.17
	11.31[c]	7.97[c]	1.95[f]	**2c**	[e]7.05	2.35
	[e]10.12	7.80	2.39	**2d**	[e]6.97	2.26
1c	11.94	8.46				2.15
1d	11.68[b]	8.23[b]	2.23[d]	**2e**	[e]7.16	2.37
	11.55[c]	8.06[c]	1.98[f]	**2f**	[e]7.35	2.42
1e	12.18	8.55		**2g**	[e]7.28[u]	2.37
1f	12.35	8.83				2.32
1g	12.13	8.82		**2h**	7.52	2.20
	11.74					2.11
1h	11.66[g]	8.32[g]	2.16[i]	**2i**	7.70	2.32
	11.52[h]	8.21[h]	1.97[j]	**2k**	7.01	2.95[q,r]
1i	12.17[k]	8.68[k]				2.35
1j	11.07[l]	7.98[l]	2.96[n,r]	**2o**	[e]7.01	2.34
	10.97[m]	7.84[m]	2.95[n,r]			2.29
			2.16[o]	**3d**		[e]2.68[v]
			1.90[p]	**3g**		[e]2.46
1k	11.57	8.31	2.98[q,r]	**3h**		[e]2.66
1l	10.79	7.87	2.95[q,r]	**3o**		[e]2.47
			1.22[s]			
1m	[e]8.56	7.99	1.36[s]			
1o	11.86[t]	8.47				
6a		[e]8.52	2.52[q]			
6b		[e]8.50	2.56[w]			
			2.25			
6c	[e]9.67[b]	8.20	2.35[d]			
	9.34[c]		2.17[x]			
			2.14[x]			
6d		[e]8.94	2.58[w]			
			2.25			

[a] 200 MHz, for solutions in [dimethylsulfoxide-d_6] if not otherwise stated *before* the first column. [b] 1/3 H. [c] 2/3 H. [d] 2 H, 2/3 Ac. [e] For solutions in deuteriochloroform. [f] 1 H, 1/3 Ac. [g] 1/4H. [h] 3/4H. [i] 3/4Ac. [j] 1/4Ac; ref. 66: δ 10.8 (NH) and 10.4 (CH=N, improbably downfield shifted value!). [k] Ref. 66: δ 10.6 (NH) and 10.4 (CH=N, improbably downfield shifted value!). [l] 0.4 H. [m] 0.6 H. [n] Together 6 H. [o] 1.8 H (0.6 Ac). [p] 1.2 H (0.4 Ac). [q] 6 H. [r] NMe_2. [s] t, *J* 7 Hz (CH_2CH_3). [t] 2 H (!), deuterium oxide - exchangeable (in the 500 MHz spectrum this 2 H singlet signal is somewhat broadened. The single crystal X-ray analysis supported the hydrazone structure with intramolecularly proximal OH and NH groups.); ^{13}C nmr (dimethylsulfoxide-d_6): δ 164.78 (C=O), 159.03 (=C–OH), 148.72 (CH=N), no upfield signals from 117.27 (aromatic C). [u] Dubious; beside the signal of solvent (δ 7.26) it is superimposed on the signals of aromatic hydrogens. [v] 360 MHz. [w] Presumably the *N*–Ac. [x] In total 1 H, 1/3 Ac.

For the cyclization of acylhydrazones under acylating conditions among others hot acetic anhydride or, at lower temperatures, the acetic anhydride–sulfuric acid, 4-toluenesulfonic acid, trifluoroacetic acid, zinc chloride or acetic anhydride–sodium acetate, triethylamine, pyridine couples or acetic chloride and acetic chloride–dimethylanilin, respectively, were successfully applied. It should be noted, however, that similar agents are reported also to transform acylhydrazones and, as a result of degradation, semicarbazones [20,21] into acylhydrazones and diacylhydrazones. In turn, upon treatment with acetic anhydride–zinc chloride at room temperature [20], upon thermolysis in neat form [22], or in hot propionic anhydride [20] aldehyde and ketone diacylhydrazones were transformed, *via* *N,N'* acetyl migration, into the corresponding 3-acetyl-5-methyl-1,3,4-oxadiazolines.

On the other hand, thermolysis of oxadiazolines (**8a**) has been reported [22] to give, likewise with *N,N'* acetyl migration in an intermediary azomethine imine species, the isomeric benzophenone diacetylhydrazone.

Thus, while in the case of the *N,S*-acetals, unacylated benzothiazolines and 1,3,4-thiadiazolines, a ring–chain tautomerism can occur, a somewhat similar isomer transformation is potential for the acylated oxygen analogs 3-acyl-1,3,4-oxadiazolines and diacylhydrazones.

Certain aldehyde acylhydrazones (*e.g.* **1b,g,o**), some of them exhibiting also a peculiar reaction mechanism of formation [23], resisted cyclization under the given acetylating conditions (or underwent only under special

requirements) but transformed into diacylhydrazones (**6a-d**, see EXPERIMENTAL). On this subject, particularly the acetic anhydride–zinc chloride couple is capable of producing transformations of various types. This agent is known not only to effect cyclizations accompanied by acetylation [24] (**2**→**3**) but also to transform, with partial deacetylation (!), 3-acetyl-5-methyl-1,3,4-oxadiazolines [25] or diacetylhydrazones [21d] into acetylhydrazones.

Moreover, acylhydrazones of type A (Scheme 2) have been reported [20,24b] to cleave, with acetolysis of the C—N acetal bond, into acetylated aldopyranoses and 5-substituted 2-methyl-1,3,4-oxadiazoles. Treatment of some (di)acylhydrazones with the acetic anhydride–zinc chloride and acetic anhydride–sulfuric acid couples or hot acetic anhydride leads to the formation of transacylated products [21e,26] or to the regeneration of the parent carbonyl compound [21e,27]. Under acylating conditions, some acylhydrazones carrying electron-withdrawing groups do not cyclize into oxadiazolines but transform due to the competition of the acetylating agent with the carbonyl or acetoximino azomethine moiety of the substrate *via* addition of acetic anhydride onto the C=N bond [28] into acetylated hydrazinocarbinols (*e.g.* **7c** [29]) or geminal diacetates (for the preparation of **7a,b,d,e** and 4-nitrobenzylidene diacetate see EXPERIMENTAL).

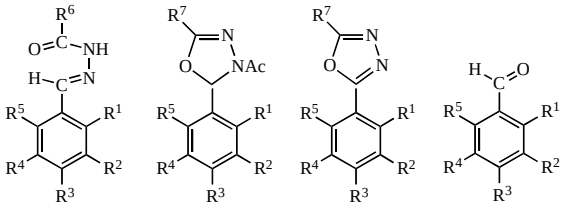
Potassium permanganate oxidation, which has been successfully used previously [30,31] and also most recently [1] for transforming 3-acetyl-1,3,4-thiadiazolines into 1,3,4-thiadiazoles, was applied efficiently for the dehydrogenation of the oxygen analogs 3-acetyl-1,3,4-oxadiazolines (**2**) to oxadiazoles (**3**) now for the first time (see Table 5). However, for the (**2**→**3**) transformation CAN oxidation now turned out to be a novel and more advantageous way, as this method is more ready and, with more simple processing, often affords almost pure crude products and in better yields in comparison to the potassium permanganate oxidation (see Table 5). Upon treatment with CAN, similarly to 3-acetyl-2,5-diphenyl-

Table 2

Characteristic ^{13}C nmr spectral data [a] of oxadiazolines (**2**) and oxadiazoles (**3**).

	δ[ppm]			
Compound	*C*=O	O–*C*(R^7)=N	O–*C*(Ar)H–N	*C*H_3[b]
2c	[c]174.89	155.67	91.48	21.38
2d	[c,d]168.07	156.18	90.26	21.26
				11.30[e]
2e	[c,d]168.21	155.77	90.69	21.35
2f	[c]167.84	153.56	90.61	21.18
2h	[c]166.83	155.57	88.63	20.93
				10.95[e]
2i	[c,d]167.41	155.33	89.29	21.18
2k	[c]167.43	155.57	92.86	40.23[f]
				21.43
2o	[c]169.17	152.81	91.46	21.53
	167.46			20.95
3d		[g]		[c,d]11.15[e]
3h		[g]		[c]11.00[e]

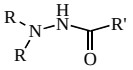
[a] 50.3 MHz, for solutions in dimethyl sulfoxide-d_6 if not stated otherwise *before* the first column. [b] *C*H_3–C=O if not stated otherwise. [c] For solutions in deuterio-chloroform. [d] 90 MHz. [e] 5-Me. [f] 2C, NMe_2. [g] C-2 and C-5 of the heterocycle cannot be unequivocally distinguished.



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

	R^1	R^2	R^3	R^4	R^5	R^6	R^7
a	H	H	H	H	H	Ph	Ph
b	H	H	Cl	H	H	Me	Me
c	H	H	Cl	H	H	Ph	Ph
d	H	H	NO_2	H	H	Me	Me
e	H	H	NO_2	H	H	Ph	Ph
f	Cl	H	Cl	H	H	4-pyridyl	4-pyridyl
g	Cl	H	Cl	H	H	2-(HO)C_6H_4	2-(AcO)C_6H_4
h	Cl	H	H	H	Cl	Me	Me
i	Cl	H	H	H	Cl	Ph	Ph
j	H	H	NMe_2	H	H	Me	Me
k	H	H	NMe_2	H	H	Ph	Ph
l	H	H	NMe_2	H	H	OEt	
m	H	H	NO_2	H	H	OEt	
n	H	OMe	OH	Br	H	OEt	
o	H	H	H	H	H	2-(HO)C_6H_4	2-(AcO)C_6H_4

1,3,4-oxadiazoline (**2a**), benzaldehyde benzoylhydrazone (**1a**) also transformed into 2,5-diphenyl-1,3,4-oxadiazole (**3a**), however, in poor yield. On the other hand, under the same conditions CAN failed to dehydrogenate 3-acetyl-2-(2,4-dichlorophenyl)-5-(4-pyridyl)-1,3,4-oxadiazoline (**2f**) to oxadiazole (**3f**), probably due to a significant tendency of pyridyl moiety to form strong cerium complexes.

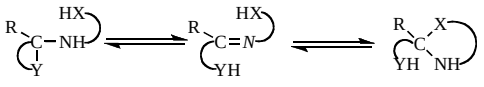


5

	R	R'
5a	H	Me
5b	H	Ph
5c	H	2-(HO)C_6H_4
5d	H	4-pyridyl
5e	H	OEt
5f	Ac	Ph

Besides potassium permanganate and CAN, in a single case, also 2,3-dichloro-5,6-dicyano-1,4-benzoquinone dehydrogenation was tested and found to be entirely inadequate for the transformation of oxadiazoline (**2i**) after boiling in benzene even for 25 hours. Moreover, treatment with (diacetoxyiodo)benzene in methanol at room temperature for 19 hours failed to transform oxadiazolines (**2f**) or 5-(2-acetoxyphenyl)-3-acetyl-2-(2,4-dichlorophenyl)-1,3,4-oxadiazoline (**2g**) into the corresponding oxadiazoles (**3f** and **3g**, respectively), the reaction **2g→3g**, however, was complete in 2.5 hours by CAN dehydrogenation at room temperature (see Table 5). On the other hand, treatment with CAN under similar conditions degraded 2,4-dichlorobenzaldehyde *N*-(2-acetoxybenzoyl)-*N*-acetylhydrazone (**6d**), the open-chain isomer of oxadiazoline (**2g**), to the parent aldehyde (**4g**), as well as 2,3,4,5,6-penta-*O*-acetyl-D-galactose diacetylhydrazone (**10**) to 2,3,4,5,6-penta-*O*-acetyl-D-galactose isolated as its ethyl hemiacetal (**11**, see EXPERIMENTAL).

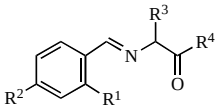
Scheme 2



A **B** **C**

Y = O X = O, S

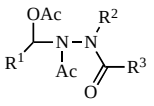
As mentioned, (diacetoxyiodo)benzene is known to dehydrocyclize [15] aldehyde acylhydrazones into 2,5-disubstituted 1,3,4-oxadiazoles in 24-68% yield. Some related compounds transform, however, differently. Hypervalent iodine oxidation [32] has been reported to transform alkoxycarbonyl (ald)imines into oxazoles with C—O bond formation [33], but to rearrange Δ^2-oxazolines with C—O bond cleavage [34]. Transformation of arylhydrazines [35] and hydrazones [36] into ethers, as well as carboxylic acid hydrazides into *N,N*-diacylhydrazines [37], heterocyclization of hydrazones with C—N [38] or N—N [39] bond formation, degradation of carboxylic acid hydrazides [40] to parent acids, Hofmann-type rearrangement [41] or conversion of carboxamides to hydrazines with N—N bond formation [42], regeneration of the carbonyl from (acyl)hydrazones [43], from oximes [44], and from dithianes [45] have also been described.



6

	R^1	R^2	R^3	R^4
6a	H	Cl	Ac	Me
6b	H	H	Ac	2-(AcO)C_6H_4
6c	H	H	H	2-(AcO)C_6H_4
6d	Cl	Cl	Ac	2-(AcO)C_6H_4

For comparsion also some related oxadiazolines (**8**) disubstituted at position 2 were synthesized and subjected to react with CAN (see Table 6, EXPERIMENTAL). In these reactions the parent ketones were formed and isolated, except the well-soluble and volatile acetone from **8e**, in good yields.



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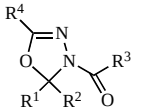
	R^1	R^2	R^3
7a	4-chlorophenyl	Ac	Me
7b	4-nitrophenyl	Ac	Me
7c	5-nitro-2-furyl	Ac	Me
7d	4-nitrophenyl	Ac	OEt
7e	4-nitrophenyl	H	OEt

CAN oxidation of bioxadiazoline (**9**), standing for both an aldehyde and ketone derivative, led to the formation of *N,N*-diacetyl-*N'*-benzoylhydrazine (**5f**, see EXPERIMENTAL) and not methyl 5-phenyl-1,3,4-oxadiazol-2-yl ketone, as expected.



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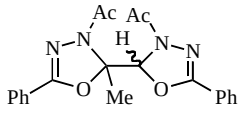
	R^1	R^2	R^3	R^4
8a	Ph	Ph	Me	Me
8b	Ph	Ph	Me	Ph
8c	Ph	Ph	Ph	Ph
8d	4-BrC_6H_4	Me	Me	Ph
8e	Me	Me	Me	Ph

CAN-mediated transformations of nitrogen and/or oxygen containing related compounds of various types are known. Treatment with ceric salts transforms carboxylic acid hydrazides into the parent acids [46] or their esters [47], substituted hydrazones, semicarbazones, oximes or oxime ethers [48], as well as azines [49] or acetals [50]



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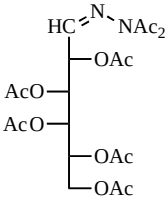

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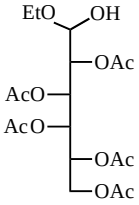

11

into the parent carbonyl compounds (regeneration of carbonyl compounds by treating dioxolanes with cerium(III) chloride has also been reported) [51], aryl-substituted carbazides into bisarylcarbodiazones [52], while some ketone phenylhydrazones into the 4- and 2-nitrophenyl derivatives [53].

EXPERIMENTAL

Melting points (uncorrected): Kofler block. Solutions were concentrated under reduced pressure in a rotary evaporator (< 50 °C, bath). tlc: Kieselgel 60 F254 (Merck, Alurolle). Ir (potassium bromide disks): Perkin-Elmer 16 PC-FT spectrophotometer. 200 MHz ^{1}H- and 50 MHz ^{13}C nmr: Bruker WP 200 SY, 360 MHz ^{1}H- and 90 MHz ^{13}C nmr: Bruker AM 360, and 500 MHz ^{1}H nmr: Bruker DRX 500 spectrometers; for recording the ^{13}C spectra, *J*-echo techniques were used. X-ray diffraction analysis for compound **1o**: Enraf Nonius MACH3 diffractometer.

General Procedure for the Preparation of Acylhydrazones (1) and Oxadiazolines (2) (see Tables 3 and 4). A mixture of the reaction components (and the solvent if used) was made to react if possible with stirring as stated in Table 3 and Table 4.

General Procedure for Potassium permanganate Oxidation (see Table 3). With slight modification of the literature method [30] to a stirred and cooled suspension of the finely powdered substrate in 99% acetic acid were added finely powdered potassium permanganate in small portions, and water in 3-4 portions. For processing the reaction mixtures see the indications in Table 5 and General Operations (see EXPERIMENTAL).

General Procedure for Ammonium cerium(IV) nitrate Oxidation (see Table 5). To a stirred suspension/solution of the powdered substrate in acetonitrile was added CAN in small portions (the proper time intervals being indicated by the change of color) and water in 3-4 portions. For processing the reaction mixtures see the indications in Table 5 and the General Operations (EXPERIMENTAL).

General Operations of Processing the Reaction Mixtures (see Tables 3-6). (A) The product was filtered off in the cold.

Table 3

Preparation and properties of acylhydrazones (**1**)

Product	Reaction components (mmol)		Solvent (mL)	Reaction temp. (°C)[a] (time, h)	Workup[b]	Yield[c] %	Mp (°C) (solvent)	Lit. mp (°C) (solvent)	Formula[d] (mol. mass)
1a	**4a** (50)	**5b** (50)	EtOAc (50)	bp (3.5)	A	99	212[e]	206 (EtOH)[f] 209 (EtOH)[g]	$C_{14}H_{12}N_2O$ (224.3)
1b	**4b** (30)	**5a** (35)	EtOAc[h] (30)	bp (4)[i]	A[j]	70	154 (50% 2-PrOH)	151-153 (EtOH)[k]	$C_9H_9N_2OCl$ (196.6)
1c	**4c** (60)	**5b** (60)	EtOAc[h] (50)	bp (4)	A	80	176[e] 178 ($CHCl_3$)	175[l] (MeOH)	$C_{14}H_{11}N_2OCl$ (258.7)
1d	**4d** (60)	**5a** (70)	EtOAc[h] (80)	bp (4.5)	A	78	188[e] 201 (2-PrOH)	202[m] (EtOH)	$C_9H_9N_3O_3$ (207.2)
1e	**4e** (60)	**5b** (60)	EtOAc[h] (80)	bp (4)	A	85	246[e] 242 (ME–H_2O)[n]	240[o] (EtOH)	$C_{14}H_{11}N_3O_3$ (269.3)
1f	**4f** (30)	**5d** (30)	EtOAc (60)	bp (2.5)	A	93	228[e] 228 (EtOH)	228–229 (aq. EtOH)[p]	$C_{13}H_9N_3OCl_2$ (294.1)
1g	**4g** (40)	**5c** (40)	EtOAc (80)	bp (2.5)	A	94	240[e] 241 (EtOAc)	—	$C_{14}H_{10}N_2O_2Cl_2$ (309.1)
1h[q]	**4h** (30)	**5a** (35)	EtOAc[h] (30)	bp (3.5)	A	91	199–200[e] 199 (2-PrOH)[r]	200–201 (EtOH)[s]	$C_9H_8N_2OCl_2$ (231.1)
1i	**4i** (30)	**5b** (30)	EtOAc (30)	bp (2.5)	A	94	232[e]	231[t] (EtOH)	$C_{14}H_{10}N_2OCl_2$ (293.2)
1j	**4j** (50)	**5a** (60)	EtOAc (30)	bp (2)	A[u]	97	175–176[e] 177 (EtOAc)	173–174[v]	$C_{11}H_{15}N_3O$ (205.3)
1k	**4k** (50)	**5b** (50)	EtOAc (15)	bp (2)	A	97	190[e] 188 (EtOAc)	191–192 (EtOH)[w]	$C_{16}H_{17}N_3O$ (267.3)
1l	**4l** (40)	**5e** (40.7)	EtOAc (10)	bp (2)	A[x]	95	155[e] 156 (EtOAc)	154–155[y] (aq. EtOH)	$C_{12}H_{17}N_3O_2$ (235.3)
1m	**4m** (40)	**5e** (40.7)	EtOAc (40)	bp (4)	A	75	146[e] 147 (EtOAc)	147–148 (EtOAc)[z]	$C_{10}H_{11}N_3O_4$ (237.2)
1n	**4n** (5)	**5e** (5.1)	EtOAc (5)	bp (1)	A	96	210[e] 211 (ME–H_2O)[n]	—	$C_{11}H_{13}N_2O_4Br$ (317.1)
1o	**4o** (20)	**5c** (20)	EtOAc (50)	bp (3)	A[bb]	94	254[e] 250 (EtOH)	250–252[cc] (EtOH)	$C_{14}H_{12}N_2O_2$ (240.3)

[a] Bath if not bp. [b] For general operations of processing the reaction mixtures see EXPERIMENTAL. [c] Without workup of the mother liquors. [d] The C, H, N, as well as Br or Cl analyses data for the products are agreeing with the theoretical values within ±0.3–0.4% limit. [e] Crude product. [f] Ref. 59. [g] Ref. 60. [h] In the presence of a catalytic amount of 4-toluenesulfonic acid. [i] The formed water was removed azeotropically. [j] The mother liquor was concentrated. [k] Ref. 23. [l] Ref. 61. [m] Ref. 62. [n] 2-Methoxyethanol with addition of water. [o] Ref. 63. [p] Ref. 64. [q] For the preparation by acetylating 2,6-dichlorobenzaldehyde hydrazone see EXPERIMENTAL. [r] With addition of water to the hot solution. [s] Ref. 65; ref. 66: 105 °C (sic!; ethanol). [t] Ref. 66. [u] Previously hexane (30 mL) was added. [v] Ref. 67. [w] Ref. 68. [x] Previously hexane (20 mL) was added. [y] Ref. 69. [z] Ref. 70. [bb] Previously hexane (40 mL) was added to the warm mixture. [cc] Ref. 71a; ref. 71b: 249-250 °C (from ethanol); ref. 71c: 230 °C (from ethanol); ref. 71d: 208 °C (sic!; from ethanol).

(B) The cold reaction mixture was poured into ice and water. (C) The reaction mixture was concentrated. (D) The cold residue was triturated with a small amount of anhydrous ethanol and kept at room temperature for 0.5–1 hour then hexane was added. (E) The cold residue was triturated with ice–water. (F) The cold residue was triturated with ethyl acetate–hexane. (G) The solution of the product in chloroform was washed with aq. sodium hydrogen carbonate and water, dried (magnesium sulfate), and then concentrated. (H) The residue was crystallized from methanol and then from hexane. (I) sodium hydrogen carbonate was added in excess to the mixture, which was then extracted with chloroform. The chloroform solution was washed with water, dried (magnesium sulfate) and concentrated. The residue was triturated with ether. (J) Under ice–water cooling, to the stirred reaction mixture was added 30% hydrogen peroxide in small portions until discoloration was complete. (K) The mixture was diluted with 2–3-fold volume of water. (L) The mixture was extracted with ether, the organic phase was washed with aq. sodium hydrogencarbonate and water, dried (magnesium sulfate), and then concentrated.

2,6-Dichlorobenzaldehyde hydrazone. To a solution of hydrazine hydrate (2 mL, 98%, 40 mmol) in isopropyl alcohol (50 mL) was added 2,6-dichlorobenzaldehyde (5.00 g, 28.6 mmol) with stirring. The mixture was boiled for 2.5 hours then concentrated to give crude (5.03 g, 93%, mp 136-137 °C) or recrystallized hydrazone, mp 138 °C (from ethanol). *Anal.* Calcd. for $C_7H_6N_2Cl_2$: C, 44.47; H, 3.20; N, 14.82; Cl, 37.51. Found: C, 44.56; H, 3.19; N, 14.55; Cl, 38.03.

2,6-Dichlorobenzaldehyde acetylhydrazone (1h). To a suspension of 2,6-dichlorobenzaldehyde hydrazone (14.18 g, 75 mmol) in anhyd. pyridine (50 mL) was added acetic anhydride (25 mL, 265 mmol). The mixture was kept at room temperature for 4 hours and then poured into ice–water to give crude **1h** (17.17 g, 99%), mp 197-198 °C. For the preparation of **1h** from 2,6-dichlorobenzaldehyde with acethydrazide (**5a**) see Table 3.

Ammonium cerium(IV) nitrate Oxidation of Bioxadiazoline (9), Preparation of *N*,*N*-Diacetyl-*N*'-benzoylhydrazine (5f).

Procedure A. To a stirred solution of **9** (the higher-melting isomer [24d,f], mp 155 °C; 1.962 g, 5 mmol) in acetonitrile (25 mL) were added water (0.5 ml) and in small portions CAN (5.613 g, 10.2 mmol) during 4 hours at room temperature. The mixture was stirred more for 1 hour, then filtered and the filtrate concentrated. The residue was partitioned in chloroform–water, the chloroform solution was washed with water, aq. sodium hydrogencarbonate and water, dried (magnesium sulfate), treated with charcoal, and then concentrated. The residue was triturated with diethyl ether (3 mL) and hexane (15 mL) was added to give crude (1.008 g, 91.5%) or recrystallized **5f** (0.572 g, 52%), mp 150 °C (from water). Ir: 3216, 3014, 1734, 1716, 1664, 1602, 1578 cm^{-1}. ^1H nmr (200 MHz, deuteriochloroform): δ 8.40 (br s, 1H, deuterium oxide - exchangeable, NH), 7.87-7.83 (m, 2H) and 7.59-7.42 (m, 3H, Ph), 2.49, 2.47, 2.44, and 2.43 (superimposed, 6H, 2Ac); ^{13}C nmr (50.3 MHz, deuteriochloroform): δ 171.82 (2C=O), 167.71 (C=O), 132.90 (aromatic CH), 131.08 (quat. aromatic C), 128.83 (2 aromatic

Table 4

Preparation and properties of 1,3,4-oxadiazolines (**2**)

Product	Substrate (mmol)	Agents (mmol)	Reaction temp. (°C)[a] (time, h)	Workup[b]	Yield[c] %	Mp (°C) (solvent)	Formula[d] (mol. mass)
2a	**1a** (9)	AcCl (252)	bp (6)	C, F	35	91[e] (EtOH)	$C_{16}H_{14}N_2O_2$ (266.3)
2c	**1c** (20)	Ac_2O (265)	bp (2)	C, E, A, G, H	70	80 (hexane)	$C_{16}H_{13}N_2O_2Cl$ (300.7)
2d	**1d** (15)	Ac_2O (159)	150±5 (2.5)	C, D	68 [g]	92-94[f] 96 (Et_2O–hexane)	$C_{11}H_{11}N_3O_4$ (249.2)
2e	**1e** (26)	Ac_2O (371)	150 (2)	C, D	76	104-106[f] 107 (2-PrOH–hexane)	$C_{16}H_{13}N_3O_4$ (311.3)
2f	**1f** (10)	Ac_2O (265) py[h] (31)	105±2 (5)	C, D	86	129-130 (EtOAc–hexane)	$C_{15}H_{11}N_3O_2Cl_2$ (336.2)
2g	**1g** (3)	Ac_2O (42.5) py[h] (12.4)	105 (4.25)	C, E	73	140-141 (2-PrOH–H_2O)	$C_{18}H_{14}N_2O_4Cl_2$ (393.2)
2h	**1h** (74)	Ac_2O (901)	bp (3.5)	C, D	70	140-141 141 (2-PrOH–H_2O)	$C_{11}H_{10}N_2O_2Cl_2$ (273.1)
2i	**1i** (24)	Ac_2O (742)	bp (2)	C, D	93	164-165[f] 169-170 (EtOAc)	$C_{16}H_{12}N_2O_2Cl_2$ (335.2)
2k	**1k** (20)	Ac_2O (212)	150 (1)	C, E, I	52	153-156[f] 158 (EtOAc)	$C_{18}H_{19}N_3O_2$ (309.4)
2o	**1o** (3)	Ac_2O (106) py[h] (12.4)	118 (6)	B	78 [i]	130 (EtOAc–hexane)	$C_{18}H_{16}N_2O_4$ (324.3)

[a] Bath if not bp. [b] For general operation of processing the reaction mixtures see EXPERIMENTAL. [c] Without workup of the mother liquors. [d] The C, H, N, as well as Br or Cl analyses data for the products are agreeing with the theoretical values within ±0.3–0.4% limit. [e] Lit. m.p. 84–86 °C (ethanol), ref. 72; 98 °C (ethanol), ref. 73; 98–93 °C (ethanol), ref. 18. [f] Crude product. [g] After purification by column chromatography (Silica Woelm, 100-200 μm, chloroform) and subsequent crystallization. [h] Anhydrous. [i] Tlc chloroform:ethyl acetate (95:5, v/v) homogeneous.

CH), 127.48 (2 aromatic CH), 24.82 (CH_3). *Anal.* Calcd. for $C_{11}H_{12}N_2O_3$: C, 59.99; H, 5.49; N, 12.72. Found: C, 60.10; H, 5.44; N, 12.63.

Procedure B. A similar treatment of the lower-melting isomer [24d,f] of **9** (mp 140 °C) afforded crude (yield 89%) or recrystallized **5f**, mp 148-149 °C, in 43% yield.

Procedure C. A solution of benzohydrazide (**5b**, 0.408 g, 3 mmol) in a mixture of acetic anhydride (5 mL, 53 mmol) and trifluoroacetic acid (0.5 mL, ~6.5 mmol, > 98%) was kept at 48-50 °C for 7 hours and then concentrated. A solution of the residue in chloroform was washed with water, aq. sodium hydrogen-carbonate, and water, dried (magnesium sulfate) and concentrated. The residue was treated with a small amount of diethyl ether to give **5f** (0.103 g, 16%), mp 149-150 °C [ref. 54a: 152 °C (from water); ref. 54b: 149 °C (from benzene)], identical (tlc, ^{1}H nmr) with the product obtained in (A) and (B).

4-Chlorobenzaldehyde diacetylhydrazone (6a). A mixture of acetylhydrazone (**1b**, 3.343 g, 17 mmol) and acetic anhydride (30 mL, 318 mmol) was boiled for 2 hours and then concentrated. The cold residue was triturated with anhydrous ethanol (1 mL), kept at room temperature for 1 h and, after addition of hexane (4 mL) in small portions, at 5 °C for 2 hours to give **6a** (1.091 g, 27%), mp 109 °C. ^{13}C nmr (50 MHz, deuteriochloroform): δ 171.29 (2C=O), 161.90 (CH=N), 137.80, 131.70, 129.36 (2C), and 129.08 (2C) (6 aromatic C), 26.22 (2 CH_3). For ^{1}H nmr data see Table 1. *Anal.* Calcd. for $C_{11}H_{11}N_2O_2Cl$: C, 55.35; H, 4.65; N, 11.74; Cl, 14.86. Found: C, 55.39; H, 4.41; N, 11.64; Cl, 15.24.

Benzaldehyde *N*-(2-acetoxybenzoyl)-*N*-acetylhydrazone (6b) and Benzaldehyde 2-acetoxybenzoylhydrazone (6c). A mixture of acetic anhydride (5 mL, 53 mmol), anhydrous pyridine (1.5 mL, 18.5 mmol) and salicyloylhydrazone (**10**) (0.3604 g, 1.5 mmol) was stirred until dissolution was complete (~5 minutes) and kept at room temperature for 1 day, then poured into ice–water to give a mixture (0.418 g) of oxadiazoline (**2o**) (for preparation and spectral characteristics see Tables 2,4 and 5), and hydrazones (**6b,c**). Separation by column chromatography (Kieselgel 60 (0.040-0.063 mm, Merck), chloroform:ethyl acetate (98:2, v/v)) afforded pure *N*-diacylhydrazone (**6b**, 0.010 g, 2.1%; during separation it was, in part, transformed into **6c**), mp 108-110 °C (from hexane). Ir: 1772, 1694, 1658, 1604, 1540 cm^{-1}. For ^{1}H nmr data see Table 1. *Anal.* Calcd. for $C_{18}H_{16}N_2O_4$: C, 66.66; H, 4.97; N, 8.64. Found: C, 66.74; H, 4.94; N, 8.66.

Second eluate was **6c** (0.105 g, 25%), mp 159-160 °C (from ethyl acetate). Ir: 3228, 3062, 2982, 2832, 1766, 1652, 1606, 1562 cm^{-1}. For ^{1}H nmr data see Table 4. *Anal.* Calcd. for $C_{16}H_{14}N_2O_3$: C, 68.07; H, 5.00; N, 9.92. Found: C, 68.20; H, 5.04; N, 9.98.

Table 5

Preparation and properties of oxadiazoles (**3**) [a]

Product	Substrate (mmol)	Agent (mmol)	Solvent (mL)	Reaction temp. (°C) (time, h)[b,c]	Workup[d]	Yield %	Mp (°C) (solvent)	Lit. mp (°C) (solvent)	Formula[e] (mol. mass)
3a	**2a** (0.5)	CAN (0.99)	MeCN (3) H_2O (1)	23 (0.17; 0.25)	K, A	60	139[f]	139-140 (Et_2O)[g]	$C_{14}H_{10}N_2O$ (222.2)
	1a (0.5)	CAN (1.07)	MeCN (10) H_2O (3)	23 (0.3; 0.5)	C, G	14	138 (heptane)	138[h] (petr. ether)	
3c	**2c** (3)	CAN (5.48)	MeCN (10) H_2O (3)	23 (0.4; 0.1)	K, A	59	158[f] 166 (MeOH)	163[i] (EtOH)	$C_{14}H_9N_2OCl$ (256.7)
3d	**2d** (6)	CAN (11.6)	MeCN (15) H_2O (1.5)	23 (0.6; 0.5)	K, A	33	171[f] 172 (2-PrOH)	169-170 (MeOH)[j]	$C_9H_7N_3O_3$ (205.2)
3e	**2e** (3)	CAN (5.99)	MeCN (15) H_2O (4)	23 (0.3; 0.25)	K, A	77	205-206[f] 211 ($CHCl_3$–MeOH)	210-211 (PhH)[k]	$C_{14}H_9N_3O_3$ (267.2)
3f	**2f** (3)	$KMnO_4$ (15.4)	AcOH (20) H_2O (10)	< 20 (3.5; 4)	J, C, G	16[l]	150 (EtOAc)	—	$C_{13}H_7N_2O_3Cl_2$ (292.1)
3g	**2g** (0.5)	CAN (1)	MeCN (8) H_2O (0.6)	23 (1.5; 1)	K, A	80[m]	162 (EtOAc–heptane)	—	$C_{16}H_{10}N_2O_3Cl_2$ (349.2)
3h	**2h** (2)	$KMnO_4$ (10.2)	AcOH (9) H_2O (1)	< 20 (5; 4)	J, C, G	24	125 (Et_2O–hexane)	—	$C_9H_6N_2OCl_2$ (229.1)
	2h (2)	CAN (4)	MeCN (10) H_2O (1)	23 (0.75; 1)	C, G	35	126-127 (Et_2O)	—	
3i	**2i** (0.5)	$KMnO_4$ (2.5)	AcOH (7) H_2O (3)	< 20 (3; 3)	J, K	72	96-98[f,n]	—	
	2i (1)	CAN (1.85)	MeCN (10) H_2O (2)	23 (2; 1)[o]	K, A	76	106[f] 98-99 (EtOAc–hexane)[n]	—	$C_{14}H_8N_2OCl_2$ (291.1)
3o	**2o** (0.5)	CAN (0.98)	MeCN (4) H_2O (0.3)	23 (0.45; 1.5)	K, A	66	96 (2-PrOH–hexane)	—	$C_{16}H_{12}N_2O_3$ (280.3)

[a] For a general method of preparation see EXPERIMENTAL. [b] Input. [c] Additional reaction time. [d] For general operations of processing the reaction mixtures see EXPERIMENTAL. [e] The C, H, N, as well as Br or Cl analyses data for the products are agreeing with the theoretical values within ±0.3–0.4% limit. [f] Crude product. [g] Ref. 74; 139.5 °C (ethanol), ref. 75; 140 °C (methanol), ref. 76; 140-141 °C (benzene), ref. 77; 138-139 °C (ethanol), ref. 18; 138 °C (ethanol), ref. 78. [h] Ref. 79; the product is identical (tlc) with that obtained from **2a**. [i] Ref. 78; 162 °C (ethanol), ref. 75; 156-157 °C (ethanol), ref. 80; 155-157 °C (methanol), ref. 76; 130 °C, ref. 8b. [j] Ref. 81; 172-173.5 °C (benzene), ref. 82. [k] Ref. 83; 209-210 °C (benzene), ref. 84; 209 °C (ethanol), ref. 75; 206.5-208 °C (acetone), ref. 82. [l] After purification by column chromatography: silica gel 60, chloroform:methanol (95:5, v/v). [m] tlc chloroform:ethyl acetate (95:5, v/v) homogeneous. [n] The crystals, formed from the melt upon cooling, had mp 106 °C. [o] During the reaction the substrate dissolves with difficulty.

2,4-Dichlorobenzaldehyde *N*-(2-acetoxybenzoyl)-N-acetylhydrazone (6d). A mixture of acetic anhydride (10 mL, 106 mmol), anhydrous pyridine (10 mL, 124 mmol) and salicyloylhydrazone (**1g**, 1.000 g, 3.235 mmol) was kept at room temperature for 3.5 days and then concentrated. The cold residue was triturated with ice-water to give crude (1.251 g, 98%) or recrystallized **6d** (0.836 g, 66%), mp 121-122 °C (from isopropyl alcohol with addition of water). For ^{1}H nmr spectral data see Table 1. For preparation and spectral characteristics of the structure-isomer oxadiazoline (**2g**) see Tables 4 and 1. *Anal.* Calcd. for $C_{18}H_{14}N_2O_4Cl_2$: C, 54.98; H, 3.59; N, 7.12. Found: C, 55.14; H, 3.62; N, 7.08.

Ammonium cerium(IV) nitrate Oxidation of Diacylhydrazone (6d): Regeneration to 2,4-Dichlorobenzaldehyde (4g). To a solution of diacylhydrazone (**6d**, 0.0983 g, 0.25 mmol) in acetonitrile (3 mL) were added water (0.3 mL) and in small portions during 1.5 hours CAN (0.2737 g, 98%, ~0.5 mmol) with stirring. The solution was stirred for an additional 1 hour and then diluted with water (20 mL) to give **4g** (0.0292 g, 67%), mp 68-73 °C, tlc hexane:chloroform (1:1, v/v) homogeneous and identical with an authentic (Aldrich, 99%, mp 69-73 °C) specimen.

1-(α-Acetoxy-4-chlorobenzyl)-1,2,2-triacetylhydrazine (7a).

Procedure A. A mixture of acetic anhydride (25 mL, 265 mmol), trifluoroacetic acid (2.5 mL, 32.5 mmol, >98%) and acetylhydrazone (**1b**, 5.000 g, 25.43 mmol) was stirred until dissolution was complete, kept at room temperature for an additional 28 hours, and then concentrated. The cold residue was triturated with ice-water to give crystalline material. A solution of the crude product in chloroform was washed with aq. sodium hydrogencarbonate and water, dried (magnesium sulfate), treated with charcoal, and then concentrated. Crystallization of the residue twice from diethyl ether (5 mL) with addition of hexane (5 mL) afforded pure tlc chloroform:diethyl ether (9:1, v/v) homogeneous **7a** (4.412 g, 51%), mp 83 °C. ^{1}H nmr (200 MHz, deuteriochloroform): δ 8.01 (s, ~0.6H) and 7.49 (s, ~0.4H) AcO-CHR-N, 7.37-7.30 (m, 4H, H-Ar), 2.57 (s, ~1.3H, 0.43Ac), 2.54 (s, 1.8H, 0.6Ac), 2.45 (s, 1.1H, 0.37Ac), 2.14 (s, 1.3H, 0.43Ac), 2.10 (s, 1.8H, 0.6Ac), 1.97 (s, 1.8H, 0.6Ac), 1.86 (s, 1.8H, 0.6Ac) and 1.68 (s, 1.1H, 0.37Ac), altogether 4Ac. The double singlets of carbinolamine and the acetyl groups are due presumably to hindered rotations. Ir: 1740, 1718, 1702, 1600 cm^{-1}.

Procedure B. A mixture of acetic anhyride (2 mL, 21.2 mmol), trifluoroacetic acid (0.2 mL, ~2.6 mmol, >98%) and diacetylhydrazone (**6a**, 0.2387 g, 1 mmol) was stirred until dissolution was complete (~15 minutes), kept at room temperature for 2 days, and then concentrated. The residue was crystallized from diethyl ether (0.5 mL) to give **7a** (0.168 g, 49%), mp 83 °C, identical (tlc, ir) with the product obtained in (A). *Anal.* Calcd. for $C_{15}H_{17}N_2O_5Cl$: C, 52.87; H, 5.03; N, 8.22; Cl, 10.41. Found: C, 52.60; H, 5.04; N, 8.30; Cl, 10.42.

1-(α-Acetoxy-4-nitrobenzyl)-1,2,2-triacetylhydrazine (7b). To a mixture of acetic anhydride (15 mL, 159 mmol) and trifluoroacetic acid (>98%, 1.5 mL, 19.5 mmol) was added acetylhydrazone (**1d**, 3.000 g, 14.48 mmol). The mixture was stirred for 15 hours, kept at room temperature for additional 48 hours, and then concentrated. A chloroform solution of the residue was washed with aq. sodium hydrogen carbonate and water, dried (magnesium sulfate), treated with charcoal, and concentrated. The residue was triturated with diethyl ether (4 mL) to give tlc chloroform:ether (8:2, v/v) homogeneous **7b** (3.409 g, 67%), mp 123 °C. ^{1}H nmr (200 MHz, deuteriochloroform): δ 8.29-8.20 (m, 2H, 3,5-H), 8.13 (s, 2/3H, O-CHR-N), 7.64-7.55 (m, 2.4H, 1/3 O-CHR-N superimposed on the signals of 2,6-H), 2.60 (s, ~1H, ~1/3Ac), 2.55 (s, ~2H, ~2/3Ac), 2.43 (s, ~1H, ~1/3Ac), 2.20 (s, ~1H, ~1/3Ac), 2.15 (s, ~2H, ~2/3Ac), 1.99 (s, ~2H, ~2/3Ac), 1.95 (s, ~2H, ~2/3Ac), 1.78 (s, ~1H, ~1/3Ac), thus altogether 4Ac. ^{13}C nmr (50.3 MHz, deuteriochloroform): δ 172.63, 171.89, 170.64, 168.81, 168.43, and 167.72 (C=O), 81.66 and 78.29 (AcO-CHR-N; signals of the solvent 77.63, 77.00 and 76.36), 24.74, 24.32, 23.78, 21.16, 20.44, and 20.24 (CO–CH_3). The product seems to be a mixture of rotamers also in a dimethylsulfoxide-d_6 solution. Ir: 1774, 1732, 1696, 1608, 1558, 1522 cm^{-1}. *Anal.* Calcd. for $C_{15}H_{17}N_3O_7$: C, 51.28; H, 4.88; N, 11.96. Found: C, 50.94; H, 4.89; N, 11.85.

1-(α-Acetoxy-4-nitrobenzyl)-1,2-diacetyl-2-ethoxycarbonylhydrazine (7d). To a solution of anhydrous zinc chloride (5.00 g, 36.7 mmol) in acetic anhydride (50 mL, 530 mmol) was added ethoxycarbonylhydrazone (**1m**, 4.744 g, 20 mmol). The solution was kept at 40-41 °C (bath temp.) for 22 hours, then cooled and poured into ice–water. A chloroform solution of the

Table 6

Ammonium cerium(IV) nitrate oxidation of 2,2-disubstituted 1,3,4-oxadiazolines (**8**)

Substrate (mmol)	CAN mmol	Solvents (mL)	Reaction[a] time, h [b]	Workup[c]	Product[d]	Yield %	Mp (ºC)[e]
8a[f,k] (1)	2.88	MeCN (5) H_2O (1)	3.5+1	K,L	Ph_2CO	99	46-48
8b[f] (1)	2.08	MeCN (10) H_2O (2)	5+2	K,L [g]	Ph_2CO	92	47-48
					$PhCO_2H$	25	118-119
8c[f] (1)	1.92	MeCN (10) H_2O (2)	5+2	K,L [g]	Ph_2CO	96	46-48
					$PhCO_2H$	30[h]	121-123
8d[i] (1)	2.11	MeCN (5) H_2O (1)	1.75+0.75	K,L [g]	4-BrC_6H_4Ac	81	48-50
					$PhCO_2H$	28	119-121
8e[j] (4)	7.20	MeCN (5) H_2O (1.5)	1.3+0.5	K,L [g]	$PhCO_2H$	25	118-119

[a] At room temperature. [b] Input + additional. [c] For general operations of processing the reaction mixtures see EXPERIMENTAL. [d] Identical (mp, tlc, ir) with an authentic sample. [e] For the crude product. [f] Ref. 85. [g] The aq. sodium hydrogen carbonate extract was acidified with 5 N hydrochloric acid to Congo Red and kept at 5 °C to give benzoic acid. [h] Note, 1 mol **8c** should give 2 mols of benzoic acid. [i] Ref. 24d. [j] Ref. 86. [k] Analogous treatment of the structure-isomer benzophenone diacetylhydrazone[85] with ammonium cerium(IV) nitrate (2.66 mmol) afforded similarly benzophenone (99.3%), mp 46-48 °C.

doughy product, containing (tlc) traces of the starting material, was washed with aq. sodium hydrogen carbonate and water, dried (magnesium sulfate), treated with charcoal, and concentrated. The syrupy residue was triturated with ether (6 mL) to give crude (4.656 g, 61%, mp 127-128 °C) or recrystallized, tlc homogeneous **7d** (4.602 g, 60%), mp 132-133 °C (from ethyl acetate with addition of hexane). ^{1}H nmr (200 MHz, deuteriochloroform): δ 8.26-8.16 (m, 2 H, 3,5-H), 7.90 (s, 0.75 H, AcO-CHR-NAc), 7.70-7.59 (m, 2H, 2,6-H), 7.47 (s, 0.25H, AcO-CHR-NAc), 4.53-4.29 (m, 2H, CH_2), 2.62-1.92 (7 s, 9H, 3Ac), 1.48-1.33 and 1.06-0.97 (mixtures of triplets, 2.7H, and 0.3H, 0.9 and 0.1 CH_2CH_3, respectively). ^{13}C nmr (90 MHz, deuteriochloroform): δ 171.42, 170.21, 169.45, 166.42, and 166.33 (C=O), 81.31, 80.46, 78.00, and 76.43 (AcO-CHR-NAc; signals of the solvent at 77.35, 77.00 and 76.65, distinguished by *J*-echo techniques), 64.82, 64.36, 64.27, and 63.72 (CH_2CH_3), 25.53, 25.02, 21.43, 20.63, 20.52, and 20.28 ($CO-CH_3$), 14.16 and 13.73 (CH_2CH_3). Ir: 1760, 1750, 1740, 1702, 1610, 1526 cm^{-1}. *Anal.* Calcd. for $C_{16}H_{19}N_3O_8$: C, 50.39; H, 5.02; N, 11.02. Found: C, 50.40; H, 5.05; N, 10.97.

1-(α-Acetoxy-4-nitrobenzyl)-1-acetyl-2-ethoxycarbonylhydrazine) (7e). To a solution of anhydrous zinc chloride (7.5 g, 55 mmol) in acetic anhydride (75 mL, 795 mmol) was added ethoxycarbonylhydrazone (**1m**, 6.908 g, 29.12 mmol). The solution was kept at room temperature for 15 hours and then poured into ice–water to give a tlc-multicomponent solid (6.821 g). A chloroform solution of the crude product was treated with fuller's earth and charcoal then concentrated. The residue was crystallized from ethyl acetate (8 mL) with addition of heptane (5 mL) to give the tlc homogeneous title compound (**7e**, 3.881 g, 39%), mp 131 °C. Due to the formation of isomers (tautomers and rotamers) in deuteriochloroform or dimethylsulfoxide-d_6 solution some signals in the ^{1}H nmr (200 MHz) spectra are doubled *e.g.* (deuteriochloroform): δ 10.17 and 7.90 (s and br s, respectively, each 0.5H, NH) or 2.21-2.04 (4 s, altogether 6H, 2Ac). Ir: 3444, 1770, 1744, 1662, 1606, 1518 cm^{-1}. From the ethyl acetate–heptane mother liquor of **7e** pure unchanged **1m** (0.213 g, 3.1%) could be recovered. *Anal.* Calcd. for $C_{14}H_{17}N_3O_7$: C, 49.55; H, 5.05; N, 12.39. Found: C, 49.54; H, 5.13; N, 12.37.

Transformation of Acetylhydrazone (1d) into 4-Nitrobenzylidene diacetate. To a solution of anhydrous zinc chloride (2.07 g, 14.68 mmol) in acetic anhydride (20 mL, 212 mmol) was added acetylhydrazone (**1d**, 2.072 g, 10 mmol). The solution was kept at 40-41 °C (bath temp.) for 2.5 days and then poured into ice– water to give crystalline crude (2.263 g, 91%) or pure title product (2.093 g, 84%), mp 126.5-127.5 °C (from ethyl acetate with addition of hexane), ref. 55, mp 126.5 °C (from ethanol); ref. 56, mp 127 °C (from ethanol); ref. 57, mp 125-126 °C (from ethanol). ^{1}H nmr (200 MHz, deuteriochloroform): δ 8.30-8.25 (d shaped m, 2H, 3,5-H), 7.73 (s, 1H, superimposed on one of the signals of 2,6-H, O-CHR-O), 7.73-7.68 (d shaped m, 2H, 2,6-H), 2.16 (s, 6H, 2Ac). ^{13}C nmr (90 MHz, deuteriochloroform): δ 168.43 (2C!, C=O), 148.80, 142.03, 127.84 (2C), and 123.83 (2C) C-Ar, 88.44 (O-CHR-O), 20.64 (2C, $2CO-CH_3$). Ir: 1764, 1610, 1530 cm^{-1}. *Anal.* Calcd. for $C_{11}H_{11}NO_6$: C, 52.17; H, 4.38; N, 5.53. Found: C, 52.13; H, 4.21; N, 5.44.

Ammonium cerium(IV) nitrate Degradation of 2,3,4,5,6-Penta-*O*-acetyl-D-galactose diacetylhydrazone (10) to Ethyl hemiacetal (11). To a stirred suspension of powdered **10**[58] (1.465 g, 3 mmol) in acetonitrile (45 mL) were added ammonium acetate (0.463 g, 6 mmol), water (6 mL), and in small portions, during 1.5 hours, ammonium cerium(IV) nitrate (2.149 g, 3.92 mmol). The mixture was stirred for an additional 7 hours and then concentrated. The residue was diluted with water (~30 mL) and extracted several times with chloroform. The chloroform solution was washed with aq. sodium hydrogencarbonate and water, dried (magnesium sulfate), treated with charcoal and concentrated. The solid residue was boiled in anhydrous ethanol (6 mL) for 30 minutes and then hexane (12 mL) was added to give a crude product (1.174 g, 90%). Purification by column chromatography (Silica Woelm 100-200 μm, chloroform:acetone (95:5, v/v)) and subsequent crystallization from anhydrous ethanol with addition of hexane afforded pure **11** (0.793 g, 60.5%), mp 127-129 °C, identical tlc chloroform:acetone (9:1, v/v), ir (potassium bromide), ^{1}H nmr (deuteriochloroform) with an authentic [58] specimen.

Names of Substrates and Products Figuring in Tables 1-6.

Benzaldehyde benzoylhydrazone (**1a**); 4-Chlorobenzaldehyde acetylhydrazone (**1b**); 4-Chlorobenzaldehyde benzoylhydrazone (**1c**); 4-Nitrobenzaldehyde acetylhydrazone (**1d**); 4-Nitrobenzaldehyde benzoylhydrazone (**1e**); 2,4-Dichlorobenzaldehyde isonicotinoylhydrazone (**1f**); 2,4-Dichlorobenzaldehyde salicyloylhydrazone (**1g**); 2,6-Dichlorobenzaldehyde acetylhydrazone (**1h**); 2,6-Dichlorobenzaldehyde benzoylhydrazone (**1i**); 4-Dimethylaminobenzaldehyde acetylhydrazone (**1j**); 4-Dimethyiaminobenzaldehyde benzoylhydrazone (**1k**); 4-Dimethylaminobenzaldehyde ethoxycarbonylhydrazone (**1l**); 4-Nitrobenzaidehyde ethoxycarbonylhydrazone (**1m**); 5-Bromo-4-hydroxy-3-methoxybenzaldehyde ethoxycarbonylhydrazone (5-Bromovanillin ethoxycarbonylhydrazone) (**1n**); Benzaldehyde salicyloylhydrazone (**1o**); 3-Acetyl-2,5-diphenyl-1,3,4-oxadiazoline (**2a**); 3-Acetyl-2-(4-chlorophenyl)-5-phenyl-1,3,4-oxadiazoline (**2c**); 3-Acetyl-5-methyl-2-(4-nitrophenyl)-1,3,4-oxadiazoline (**2d**); 3-Acetyl-2-(4-nitrophenyl)-5-phenyl-1,3,4-oxadiazoline (**2e**); 3-Acetyl-2-(2,4-dichlorophenyl)-5-(4-pyridyl)-1,3,4-oxadiazoline (**2f**); 5-(2-Acetoxyphenyl)-3-acetyl-2-(2,4-dichlorophenyl)-1,3,4-oxadiazoline (**2g**); 3-Acetyl-2-(2,6-dichlorophenyl)-5-methyl-1,3,4-oxadiazoline (**2h**); 3-Acetyl-2-(2,6-dichlorophenyl)-5-phenyl-1,3,4-oxadiazoline (**2i**); 3-Acetyl-2-(4-dimethylaminophenyl)-5-phenyl-1,3,4-oxadiazoline (**2k**); 5-(2-Acetoxyphenyl)-3-acetyl-2-phenyl-1,3,4-oxadiazoline (**2o**); 2,5-Diphenyl-1,3,4-oxadiazole (**3a**); 2-(4-Chlorophenyl)-5-phenyl-1,3,4-oxadiazole (**3c**); 5-Methyl-2-(4-nitrophenyl)-1,3,4-oxadiazole (**3d**); 2-(4-Nitrophenyl)-5-phenyl-1,3,4-oxadiazole (**3e**); 2-(2,4-Dichlorophenyl)-5-(4-pyridyl)-1,3,4-oxadiazole (**3f**); 5-(2-Acetoxyphenyl)-2-(2,4-dichlorophenyl)-1,3,4-oxadiazole (**3g**); 2-(2,6-Dichlorophenyl)-5-methyl-1,3,4-oxadiazole (**3h**); 2-(2,6-Dichlorophenyl)-5-phenyl-1,3,4-oxadiazole (**3i**); 5-(2-Acetoxyphenyl)-2-phenyl-1,3,4-oxadiazole (**3o**); Benzaldehyde (**4a,o**); 4-Chlorobenzaldehyde (**4b,c**); 4-Nitrobenzaldehyde (**4d,e,m**); 2,4-Dichlorobenzaldehyde (**4f,g**); 2,6-Dichlorobenzaldehyde (**4h,i**); 4-Dimethylaminobenzaldehyde (**4j,k,1**); 5-Bromo-4-hydroxy-3-methoxybenzaldehyde (5-Bromovanillin) (**4n**); Acetohydrazide (**5a**); Benzohydrazide (**5b**); Salicylohydrazide (**5c**); Isonicotinohydrazide (Isoniazid) (**5d**); Ethoxycarbohydrazide (ethyl carbazate) (**5e**); 4-Chlorobenzaldehyde diacetylhydrazone (**6a**); Benzaldehyde *N*-(2-acetoxybenzoyl)-*N*-acetylhydrazone (**6b**); Benzaldehyde 2-acetoxybenzoylhydrazone (**6c**); 2,4-Dichlorobenzaldehyde *N*-(2-acetoxybenzoyl)-*N*-acetylhydrazone (**6d**); 1-(α-Acetoxy-4-chlorobenzyl)-1,2,2-triacetylhydrazine (**7a**); 1-(α-Acetoxy-4-

nitrobenzyl)-1,2,2-triacetylhydrazine (**7b)**; 1-(α-Acetoxy-5-nitro-2-furylmethyl)-1,2,2-triacetylhydrazine (**7c);** 1-(α-Acetoxy-4-nitrobenzyl)-1,2-diacetyl-2-ethoxycarbonylhydrazine (**7d)**; 1-(α-Acetoxy-4-nitrobenzyl)-1-acetyl-2-ethoxycarbonylhydrazine (**7e)**; 3-Acetyl-5-methyl-2,2-diphenyl-1,3,4-oxadiazoline (**8a)**; 3-Acetyl-2,2,5-triphenyl-1,3,4-oxadiazoline (**8b)**; 3-Benzoyl-2,2,5-triphenyl-1,3,4-oxadiazoline (**8c)**; 3-Acetyl-2-(4-bromophenyl)-2-methyl-5-phenyl-1,3,4-oxadiazoline (**8d)**; 3-Acetyl-2,2-dimethyl-5-phenyl-1,3,4-oxadiazoline (**8e)**.

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