ISSN 1070-3632, Russian Journal of General Chemistry, 2011, Vol. 81, No. 4, pp. 756–761. © Pleiades Publishing, Ltd., 2011. Original Russian Text © I.V. Svistunova, N.P. Shapkin, O.V. Nikolaeva, O.A. Apanasenko, 2011, published in Zhurnal Obshchei Khimii, 2011, Vol. 81, No. 4, pp. 666–671.

# Nitrogen-Containing Heterocycles from Metal β-Diketonates

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## Received February 9, 2010

**Abstract**—Factors determining the reaction of metal  $\beta$ -diketonates with hydrazine, in particular the nature of central metal ion and structure of  $\beta$ -diketonate ligand, are discussed. The possibility for the preparation of other heterocyclic compounds via reaction of metal acetylacetonates with phenylhydrazine, *o*-phenylenediamine, urea, and thiourea was studied.

# DOI: 10.1134/S1070363211040244

We previously studied reactions of hydrazine with chromium and boron difluoride acetylacetonates having various substituents at the central carbon atom in the chelate ring ( $\alpha$ -substituent) [1, 2]. It was found that substituted acetylacetonate complexes reacted with hydrazine in a way similar to free diketone ligands with formation of 4-substitued 3,5-dimethylpyrazoles. In some cases, the reactions were accompanied by side processes with participation of the  $\alpha$ substituent. The resulting pyrazoles were identified by gas chromatography–mass spectrometry, and the reaction with hydrazine was proposed to use as a method for confirming the structure of substituted acetylacetonate complexes.

In the present work we examined how the nature of central metal ion,  $\alpha$ -substituent, and substituents at the carbonyl carbon atoms ( $\beta$ -substituents) affects the process of decomposition of acetylacetonate metal complexes. In addition, analogous reactions were performed with diketonate complexes containing other  $\alpha$ -substituents with a view to obtain pyrazoles possessing organometallic groups. We also tried to use other reagents to decompose metal chelates with formation of heterocyclic compounds. A few examples of the synthesis of heterocyclic compounds from  $\beta$ -diketonate metal complexes were reported previously [3].

By treatment of metal  $\beta$ -diketonates containing the simplest  $\alpha$ - and  $\beta$ -substituents with hydrazine we obtained the expected pyrazoles (Pz) as shown in Scheme 1.



The reactions were carried out by heating complexes **I–XXIII** with hydrazine hydrate in alcohol, the ratio chelate (g)–hydrazine hydrate (ml) being 1:2. The reaction was assumed to be complete when the reaction mixture lost its color and/or metal oxide salt precipitated. By special experiments we showed that further heating of the reaction mixture leads to reduced yield. The structure and purity of the resulting pyrazoles were confirmed by the GC–MS and IR data, as well as by the melting points.

As follows from the time necessary for decomposition of unsubstituted acetylacetonates I-V, copper and aluminum chelates react 5–6 times more rapidly than do chromium and cobalt complexes (Table 1). Presumably, facile decomposition of the complexes is related to their kinetic stability, and aluminum and copper complexes turn out to be more labile than chromium and cobalt analogs [5]. The yield of the resulting dimethylpyrazole was higher in the case of labile complexes. Obviously, prolonged heating

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Chelate no.	М	п	$\mathbb{R}^1$	R <sup>2</sup>	R <sup>3</sup>	Reaction time, min	Pyrazole no.	Yield, %	mp, °C
I	Cr	3	Me	Me	Н	60	XXIV	51	107–109
П	Co	3	Me	Me	Н	60	XXIV	52	107-109
ш	Fe	3	Me	Me	Н	30	XXIV	59	107-109
IV	Al	3	Me	Me	Н	10	XXIV	68	107-109
V	Cu	2	Me	Me	Н	10	XXIV	70	107–109
VI	Cr	3	Me	Н	Н	50	XXV	31	Oil
VII	Cu	2	Me	<i>t</i> -Bu	Н	60	XXVI	64	_
VIII	Fe	3	Me	Ph	Н	210	XXVII	78	126–128
IX	Al	3	Me	Ph	Н	120	XXVII	89	126–128
Х	Cu	2	Me	Ph	Н	120	XXVII	93	126–128
XI	Fe	3	Ph	Ph	Н	240	XXVIII	80	112–116
XII	Al	3	Ph	Ph	Н	240	XXVIII	88	
XIII	Cu	2	Me	Me	Me	20	XXIX	54	134–136
XIV	Cu	2	Me	Me	Et	20	XXX	51	166–168
XV	Fe	3	Me	Me	Ph	40	XXXI	54	170–171
XVI	Cu	2	Me	Me	p-CH <sub>2</sub> C <sub>6</sub> H <sub>4</sub> SiMe <sub>3</sub>	30	XXXII	43	156–158
XVII	Cr	3	Me	Me	SEt	270	XXXIII	77	44-46 (decomp.)
XVIII	Cu	2	Me	Me	SEt	120	XXXIII	80	44-46 (decomp.)
XIX	Cr	3	Me	Me	SBu	300	XXXIV	65	Oil
XX	Fe	3	Me	Me	SBu	240	XXXIV	65	Oil
XXI	Fe	3	Me	Me	SPh	210	XXXV	57	134–136
XXII	Cu	2	Me	Me	SPh	120	XXXV	81	134–136
XXIII	Cr	3	Me	Me	SP(S)(OEt) <sub>2</sub>	120	XXXVI	41	Oil

Table 1. Reaction times, yields, and melting points<sup>a</sup> of pyrazoles XXIV–XXXIII obtained from chelates I–XVI (Scheme 1)

<sup>a</sup> Published data [4], mp, °C: **XXIV**, 106–107; **XXV**, oil; **XXVII**, 128; **XXIX**, 138; **XXX**, 176; **XXXI**, 172; **XXXIII**, 42–44; **XXXIV**, oil; **XXXV**, 134–136.

necessary for complete transformation of chromium and cobalt complexes favors partial decomposition of the product, so that its yield decreases.

Formylacetonate **VI** reacted with hydrazine at a higher rate as compared to analogous acetylacetonate complex **I**. Decomposition of pivaloylacetonate complex **VII** possessing one methyl and one *tert*-butyl group required a longer time than that necessary for decomposition of acetylacetonate analog **V**. Thus replacement of one  $\beta$ -methyl group by hydrogen accelerates decomposition, whereas replacement by *tert*butyl group hampers the process. 3-The yield of methylpyrazole from formylacetonate complex was as low as 30%, presumably due to its low stability and partial decomposition during the reaction.

Benzoylacetonate and dibenzoylmethanate complexes VIII–XII having  $\beta$ -phenyl groups showed considerably higher stability toward hydrazine as

compared to analogous acetylacetonate chelates. The reactions were complete only with copper, aluminum, and iron complexes. Kinetically stable chromium and cobalt benzoylacetonates and dibenzoylmethanates reacted with hydrazine to a very small extent. Even after heating for 50 h under reflux, the main part of chromium and cobalt chelates **VIII–XII** remained unchanged, and the corresponding pyrazoles **XXVII** and **XXVIII** were detected only by chromatographic methods.

Thus  $\beta$ -substituents quite appreciably affect the reactivity of metal chelates toward hydrazine. Presumably, their effect originates primarily from steric factors: bulky  $\beta$ -substituents hamper access of hydrazine to the chelate entity.

Our previous studies on the reaction of hydrazine with acetylacetonates having various substituents at the central carbon atom showed that the formation of pyrazoles may be accompanied by side processes provided that the  $\alpha$ -substituent contains a functional group [1, 2]. In these cases several pyrazoles are formed, and subsequent separation of the products and their purification are necessary. Acetylacetonate complexes XIII-XXIII containing an alkyl, phenyl, benzyl, alkylsulfanyl, or arylsulfanyl group as  $\alpha$ substituent reacted with hydrazine regioselectively, and no by-products were formed. Pyrazoles obtained as a result of decomposition of complexes XIII-XXIII were isolated and identified. Decomposition of the alkyl-, phenyl- and benzyl-substituted acetylacetonate complexes was faster than decomposition of their unsubstituted analogs, whereas alkyl- and arylsulfanylsubstituted derivatives reacted with hydrazine at a lower rate.

The reaction of hydrazine with nitro-substituted acetylacetonates [Cu(acacNO<sub>2</sub>)<sub>2</sub>, Cr(acacNO<sub>2</sub>)<sub>3</sub>] gave 4-nitro-3,5-dimetylpyrazole (**XXXVII**), as was shown previously by GC–MS [1]. However, attempts to isolate this compound and determine its yield were unsuccessful. Presumably, pyrazole **XXXVII** undergoes decomposition with formation of tarry products.

As reported in [1], the reaction of hydrazine with halogen-substituted chromium(III) acetylacetonates, apart from expected 4-halo-3,5-dimethylpyrazoles, gave 3,5-dimethylpyrazole having no substituent on  $C^4$ . More detailed study on the reactions with  $Cr(acacCl)_3$ ,  $Cr(acacBr)_3$ , and  $Cr(acacI)_3$  showed that the presence of a halogen atom in the ligand almost does not affect the time of decomposition of chro-

mium(III) complexes. The fraction of 3,5-dimethylpyrazole among decomposition products of chloro- and iodo-substituted complexes was 20–25%, and 5–7% of 3,5-dimethylpyrazole was formed by decomposition of tris(3-bromopentane-2,4-dionato)chromium(III). Special experiments showed that 3,5-dimethylpyrazole is not formed in the reaction of 3-chloropentane-2,4dione with hydrazine. This means that dehalogenation precedes pyrazole ring closure. Most probably, hydrazine promotes partial reductive dehalogenation in the chelate ring, and the reaction of halogen-substituted acetylacetonates with hydrazine may be described by Scheme 2 including reactions (a)-(c).

# Scheme 2.

 $Cr(acacHlg)_3 \xrightarrow{N_2H_4 \cdot H_2O} 4-HlgPz$  (a)

 $Cr(acacHlg)_3 \xrightarrow{N_2H_4 \cdot H_2O} Cr(acacH)_3 (b)$ 

 $Cr(acacH)_3 \xrightarrow{N_2H_4 \cdot H_2O} 4-H-Pz$  (c)

We presumed that the contribution of reduction processes should be minimized in the reaction with bromo-substituted copper complex where the corresponding pyrazole is formed at a much higher rate [reaction (*a*)] than from chromium complexes and that 4-bromo-3,5-dimethylpyrazole should be obtained as the only product. However, only 3,5-dimethylpyrazole was formed in the reaction of Cu(acacBr)<sub>2</sub> with hydrazine hydrate. These findings suggest that dehalogenation [reaction (*b*)] of copper complexes is considerably faster than dehalogenation of chromium complexes.

Chromium and Cobalt chelates with thiocyanatosubstituted acetylacetone reacted with hydrazine to produce 4–6 compounds whose yield and ratio depended on the conditions, in particular concentration of the initial reactants and their ratio, reaction time, and acidity of the medium. By GC–MS we identified among the products bis(3,5-dimethyl-1*H*-pyrazol-4-yl)disulfide and 3,5-dimethyl-1*H*-pyrazole-4-thiol. We failed to identify the other products on the basis of the GC–MS data, but 4-thiocyanato-3,5-dimethyl-1*H*pyrazole was clearly absent.

Selenium-containing analog behaved similarly. We had at our disposal a mixture of incompletely substituted selenocyanates with the composition Cr (acacSeCN)<sub>x</sub>(acacH)<sub>3-x</sub>. It was treated with hydrazine, and GC–MS analysis of the products revealed 3,5-

dimethylpyrazole (which can be formed from unsubstituted precursor), 3,5-dimethyl-1H-pyrazole-4selenol (major product), and 4-ethoxyselanyl-3,5dimethyl-1*H*-pyrazole bis(3,5-dimethyl-1Hand pyrazol-4-yl) diselenide as minor product. No detected selenocyanato-substituted pyrazole was among the products.

Treatment of acetoxy-substituted acetylacetonate complexes XXXVIII-XL with hydrazine gave pyrazole XLI as the only product (Scheme 3). Metal-free acetoxy-substituted acetylacetone reacted with hydrazine in a similar way [6].







M = Cr, n = 3 (**XXXVIII**); M = Al, n = 3 (**XXXIX**); M = Cu, n = 2 (XL).

The reactions of hydrazine with metal acetylacetonates containing a phenylsulfonyloxy group, namely Cu[acacOS(O)<sub>2</sub>Ph]<sub>2</sub>, Ni[acacOS(O)<sub>2</sub>Ph]<sub>2</sub>, and  $Fe[acacOS(O)_2Ph]_3$ , led to the formation of 3-6 products whose ratio depended on the conditions and the nature of the central metal ion. Unfortunately, we failed to identify these products by their mass spectra.

Complex XLII containing an aldehyde group reacted with hydrazine according to Scheme 4. We



failed to improve the yield of acetal XLIII by increasing the reaction time, and the ratio of compounds XLIII and XLIV did not change.

Metal acetylacetonates were also brought into reactions with other nucleophiles, which could give rise to heterocyclic compounds. We found that phenylhydrazine, o-phenylenediamine, urea, and thiourea were almost inactive toward the examined complexes. Such reactions occurred only with kinetically labile (Table 2) aluminum and copper complexes and only in the presence of an acid (Scheme 5).







XLVIII, XLIX, L, LI

R = H (IV, XLVIII), Me (XLV, XLIX), Ph (XLVI, L), SPh (XLVII, LI).

Analogous reactions with acetylacetonate complexes having more complex  $\alpha$ -substituents [NO<sub>2</sub>, Br, PhS, (EtO)<sub>2</sub>P(O)S] were accompanied by a number of side processes. As a rule, they resulted in the formation of complex mixtures of products, and only a few of them were identified. The main side processes are illustrated by Scheme 6.

As a rule, the corresponding free ligands reacted in a similar way [6]. Taking into account that the above reactions are possible only with kinetically labile complexes under acid catalysis, we presume that the reactions with phenylhydrazine, o-phenylenediamine, urea, and thiourea involve the free diketones liberated as a result of decomposition of the complexes by the action of acid.

## **EXPERIMENTAL**

The IR spectra were recorded in the range from 4000 to 400 cm<sup>-1</sup> on a Perkin–Elmer Spectrum 100 BX-II spectrometer from samples prepared as KBr





pellets. Gas chromatographic–mass spectrometric analysis was performed using an Agilent 6890N gas chromatograph coupled with an Agilent 5973N massselective detector; HP-5MS column,  $30 \text{ m} \times 0.25 \text{ µm}$ ; carrier gas helium, continuous flow at a volume rate of 0.7 ml/min; oven temperature programming from 50°C (1 min) at a rate of 10 deg/ min to 280°C (20 min); electron impact, 70 eV, total ion scanning in the a.m.u. range from 50 to 410; delay 2 min. The mass spectra of compounds LII–LVII were obtained using an HP 1100 liquid chromatograph coupled with a mass-selective detector (atmospheric pressure chemical ionization, positive ion detection, a.m.u. range 100–600, nebulizer pressure 413.7 kPa, drying gas flow rate 6 l/min, temperature 200°C, vaporizer temperature 350°C).

**Table 2.** Yields of pyrazoles **XLVIII–LI** in the reactions of chelates **IV** and **XLV–XLVII** with phenylhydrazine (reaction time 60 min)

Chelate	$\mathbf{R}^1$	$\mathbb{R}^2$	R <sup>3</sup>	Pyrazole	Yield, %
IV	Me	Me	Н	XLVIII	72
XLV	Me	Me	Me	XLIX	73
XLVI	Me	Me	Ph	L	69
XLVII	Me	Me	SPh	LI	75

Thin-layer chromatography was performed on Sorbfil PTSKh-P-V plates using benzene or benzene– acetone (10:1) as eluent. The analytical data for the isolated compounds are collected in Table 1.

Acetylacetonates **I–V** and **VII–XV** were synthesized by standard procedures in aqueous alcohol in the presence of sodium acetate and were purified by recrystallization from appropriate solvent (alcohol or benzene–petroleum ether). 2,4-Dioxopentane-3-carbaldehyde (**VI**) was synthesized according to the procedure described in [7], complexes **XVII–XXII** were prepared as reported in [8], and compound **XXIII** was obtained as described in [9].

Tris(3-selenocyanatopentane-2,4-dionato)chromium(III) [Cr(acac)<sub>x</sub>(acacSeCN)<sub>3-x</sub>]. Triselenium dicyanide was prepared according to the procedure described in [10]. Selenium dioxide, 6.75 mmol, was added to a solution of 4.5 mmol of malononitrile in 1 ml of DMF. After 2 min. the mixture turned turbid and gradually warmed up, and gas evolution was observed. After cooling, a solution of 2 mmol of tris(acetylacetonato)chromium(III) in 2 ml of DMF was added in small portions. The mixture was stirred until the reaction was complete (TLC) and diluted with a saturated aqueous solution of sodium chloride, the precipitate was filtered off, dried under reduced pressure over phosphoric anhydride, and dissolved in chloroform, the solution was filtered, and the product was precipitated with hexane and purified by recrystallization from benzene-hexane.

**Reaction of metal diketonates I–XXIII with hydrazine hydrate (***general procedure***).** A mixture of 0.5 g of complex **I–XXIII**, 10 ml of alcohol, and 1 ml of hydrazine hydrate was heated under reflux until it became colorless and hydroxo metal salt separated (for reaction time, see Table 1). After cooling, the mixture was diluted with a tenfold volume of water and extracted with chloroform  $(3 \times 5 \text{ ml})$ . The extract was dried over magnesium sulfate and evaporated under reduced pressure, and the residue was recrystallized from a minimal amount of alcohol. According to the GC–MS data, all isolated compounds contained only one volatile component whose mass spectrum matched pyrazole **XXIV–XXXVI** with a probability of 80–95% (NIST05 library). Their IR spectra matched pyrazoles **XXIV–XXXVI** with a probability of 70–95% (Aldrich Condensed Phase library). The yields and melting points of the isolated compounds are given in Table 1 [4].

Reactions of diketonates IV, XLV, XLVI, XLVII, Al(acacBr)<sub>3</sub>, and Al(acacNO<sub>2</sub>)<sub>3</sub> with phenylhydrazine hydrochloride, urea, and thiourea (general procedure). A mixture of 1 mmol of aluminum complex and 3 mmol of the corresponding nitrogencontaining nucleophile in ethanol was heated until it became homogeneous, 0.3 ml of concentrated hydrochloric acid was added, and the mixture was heated for 3 h more. The solution was filtered while hot and was left to stand in the cold for crystallization. The precipitate was filtered off, dried, and dissolved in 5 ml of water, 1 ml of 25% aqueous ammonia was added, and the mixture was extracted with chloroform. The extract was evaporated, and the residue was analyzed by LC-MS (HP 1100 LC). The yields of pyrazoles formed in the reactions with phenylhydrazine and reaction times are given in Table 2.

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