The observed features of the reaction of Pd(II) salts with the biradical ligands L^1 and L^2 are useful for explanation of the reaction chemistry of coinage metals with nitrogen-containing heterocyclic ligands which are interesting in bioinorganic chemistry.

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CONCLUSIONS

The first coordination compounds of stable nitroxyl biradical imidazolines have been synthesized. From the spectral data obtained, the paramagnetic ligand 4,4'-(ethyleneiminomethyl)di-2,2,5,5-tetramethyl-3-imidazoline-1-oxyl acts as a tetradentate bridge in a binuclear coordination compound with Pd(II), while the azine ligand 4-formyl-2,2,5,5-tetramethyl-3-imidazoline-1-oxyl acts as a bidentate bridge.

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SYNTHESIS OF ENAMINOTHIOCARBONYL COMPOUNDS (IMIDAZOLIDINE NITROXYL RADICALS) AND THEIR REACTIONS WITH SODIUM HYPOBROMITE

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Enaminocarbonyl compounds, especially enaminoketones, have been thoroughly investigated [1], but information on enaminothiocarbonyl compounds is scanty [1]. We have previously synthesized enaminoketones which are derivatives of imidazolidine nitroxyl radicals, and investigated some of their properties [2]. The aim of the present investigation was to synthesize enaminothiocarbonyl compounds which are derivatives of imidazolidine nitroxyl radicals, and to examine some of their properties. Enaminothioketones are known to be obtainable from the corresponding enaminoketones by treatment with sulfur-containing compounds such as hydrosulfides or hydrogen sulfide, phosphorus pentasulfide [1], or the Lawson reagent [3]. However, the use of these methods in the case of enaminoketones which are derivatives of imidazolidine nitroxyl radicals (I) did not give stationary results owing to the initial reduction of the nitroxyl group (cf. [4, 5]) followed by opening of the imidazolidine ring. It might be expected that enaminothiocarbonyl compounds would be obtainable by condensation of dithiocarboxylate esters with 1-hydroxy-2,2,4,5-5-pentamethyl-3-imidazoline (II) in the presence of phenyllithium, as we have previously reported for carboxylate esters [6]. In this case, ester condensation first gave diamagnetic 1-hydroxy-compounds, which afford the nitroxyl radicals on oxidation with manganese dioxide. It is, however, known that enaminothiocarbonyl compounds are higly sensitive to oxidation, and readily give the corresponding disulfides [1].

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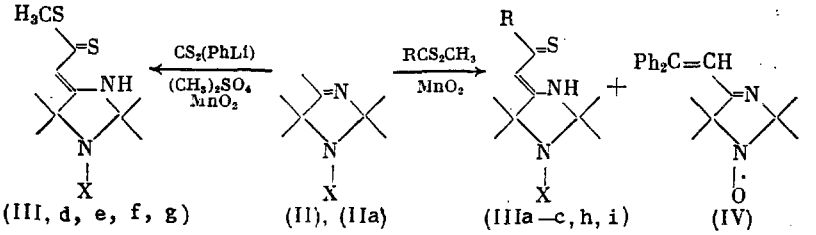
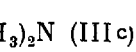
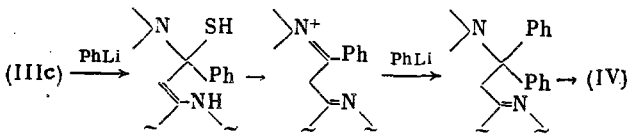
Reaction of the imidazoline (II) with methyl dithioacetate in the presence of phenyllithium, followed by oxidation of the reaction mixture with MnO_2, gives (IIIa),* which is the monomer, as shown by its EPR spectrum (a triplet with HFI a_N = 14.0 Oe, characteristic of nitroxyl monoradicals), and by its molecular mass. Compound (IIIa) exists in the conjugated enaminoketone tautomeric form, as shown by its UV spectrum and its IR spectrum, which did not show absorption for the SH, but which showed absorption at 2700-3000 cm^{-1} for a strong intramolecular hydrogen bond. In accordance with these findings, (IIIa) is assigned the structure 4-(2-thioxopropylidene)-2,2,5,5-tetramethylimidazolidine-1-oxyl:



R = CH_3(IIIa), C_6H_5 (IIIb), (IIIi), $(CH_3)_2N$ (IIIc),  (IIIh);

X = OH (II), (IIIf), OCH_3 (IIa), (IIIe), H (IIIi), (IIIg), O· (III a-d), (IIIh).

Similarly, reaction of (II) with methyl dithiobenzoate affords the enaminothione (IIIb), together with small amounts of the diamagnetic enaminothione (IIIi). When the condensation is carried out with O-methyl thiobenzoate, no (IIIi) is formed, only the enaminothioketone (IIIb) being obtained. This shows that reduction of the hydroxylamino-group in the imidazolidine heterocycle is apparently effected by the methanethiol liberated in the reaction. Reaction of (II) with N,N-dimethyldithiocarbamate gives the thioamide (IIIc) together with (IV). The formation of (IV) may be rationalized by postulating a mechanism involving successive double additions of phenyllithium to the enaminothioamide (IIIc):



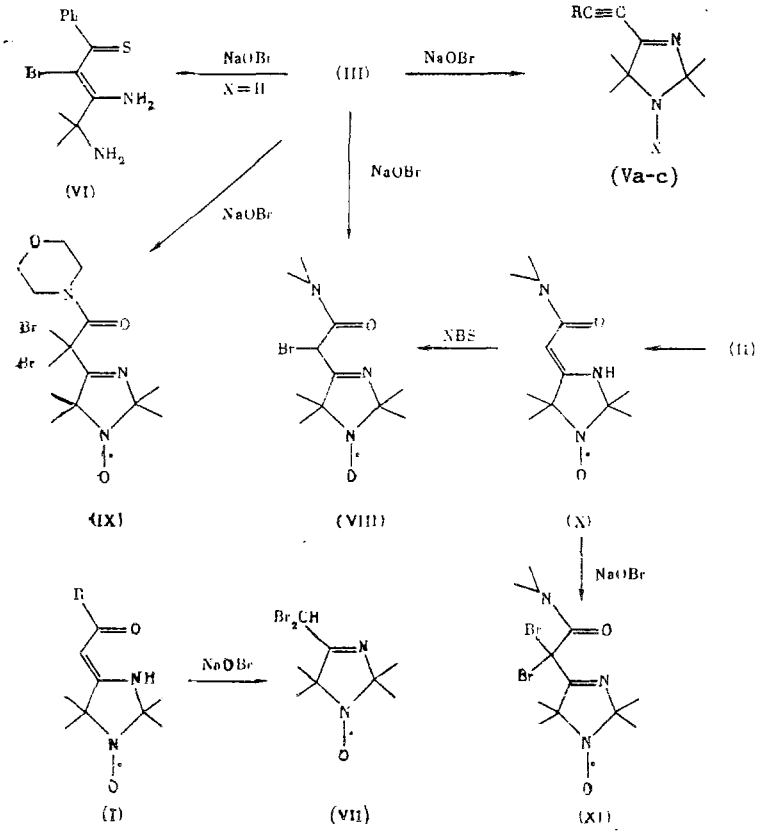
Reaction of (II) or its methoxy-derivative (IIa) with carbon disulfide in the presence of phenyllithium followed by treatment with dimethyl sulfate gave the corresponding enaminodithiocarboxylate esters (IIId) and (IIIe), respectively. It is noteworthy that it was not possible to isolate the dithiocarboxylic acid in the free state, since neutralization of solutions of the lithium salts of these acids resulted in cleavage of a molecule of carbon disulfide and the formation of the original imidazolines (II) and (IIa).

Attempts to hydrolyze the dithioester (IIId) by boiling in aqueous-alcoholic sodium hydroxide resulted in reduction of the nitroxyl group and formation of the 1-hydroxy-compound (IIIf) and the amino-compound (IIIg) only. This reduction clearly involves the liberation of methanethiol, but the hydrolysis product could not be isolated. In contrast, reaction with morpholine under quite severe conditions gave the thioamide, reduction of the nitroxyl group occurring only to an insignificant extent.

As already pointed out, enaminothiocarbonyl compounds are readily oxidized to disulfides by a variety of oxidants, for example iodine in alkaline solution [1]. Treatment of the enaminothione (IIIb) with sodium hypobromite unexpectedly gave the nitroxyl radical (Va), which did not contain sulfur according to its elemental analysis. The IR spectrum of (Va) showed strong absorption at 2200 cm^{-1} attributed to the acetylenic C≡C bond, and in addition absorption at 1595 and 1605 cm^{-1} for conjugated C=N and benzene ring C=C bond vibrations. Accordingly, (Va) was assigned the structure 2,2,5,5-tetramethyl-4-phenylethynyl-3-imidazoline-1-oxyl. The reaction of dithioester (IIId) with NaOBr was similar, affording the ethynyl compound (Vb). The nitroxyl group does not participate in this reaction, and has no effect upon it. For instance, under similar conditions the methoxy-compound (IIIe) gave the ethynyl compound (Vc). The presence of the acetylenic grouping was confirmed by the ^{13}C NMR spectrum, in which signals for the carbons of the ethynyl group were present at 85.46 and 89.15 ppm.

*For preliminary communication, see [7].

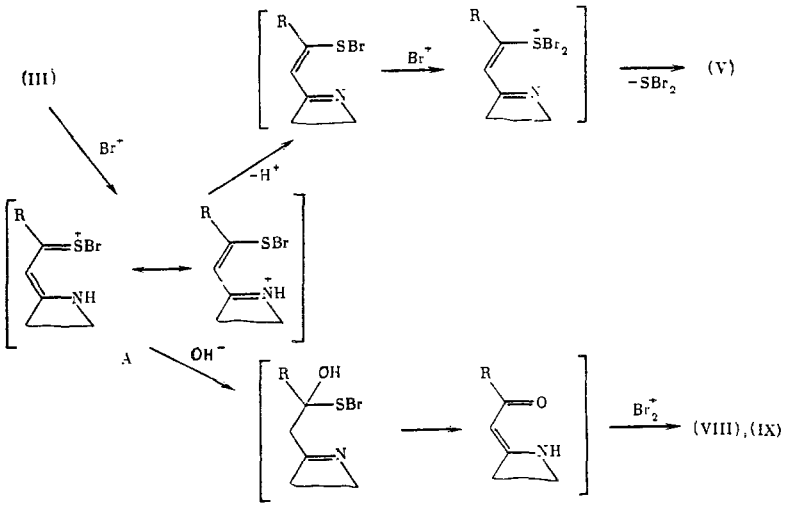
In contrast, treatment of the enaminothione (IIIi) with NaOBr resulted in fission of the imidazolidine ring with the formation of the aminoenaminothione (VI). It follows that enaminoketones (I) of similar structure react with NaOBr under these conditions with cleavage of the enaminoketone group to give bromomethyl-3-imidazolines (VII) [2]. The enaminothioamides (IIIc, h) react differently with NaOBr. In this instance, sulfur is replaced by oxygen, and further bromination gives the final reaction products, the monobromo-compound (VIII) or the dibromo-compound (IX).



$R = C_6H_5$ (Va), SCH_3 (Vb, c); $X = O$ (Va, b), OCH_3 (Vc).

The structure of (VIII) was confirmed by direct synthesis from the enaminoamide (X), obtained by condensing the imidazoline (II) with methyl N,N-dimethylcarbamate in the presence of phenyllithium. The IR spectrum of (VIII) (chloroform) showed complex absorption at 1675 cm^{-1} for the amide carbonyl group vibrations, and at 1620 cm^{-1} for the C=N bond, but no N–H or O–H absorption. In addition, the UV spectrum of (VIII) showed absorption with λ_{max} 226 nm, but no absorption characteristic of the enaminocarbonyl grouping. Hence, the spectral features show that (VIII) exists in the nonconjugated oxoimino tautomeric form, unlike other compounds of this type [2, 6]. It is also noteworthy that unlike the enaminoketones (I), treatment of the enaminoamide (X) with an excess of sodium hypobromite does not result in cleavage of the enaminocarbonyl grouping, but in the formation of the dibromo compound (XI). The monobromo compound (VIII) was obtained by reacting the enaminoamide (X) with an equimolar amount of N-bromosuccinimide.

The formation of (V), (VIII), and (IX) may be represented by a reaction sequence involving electrophilic attack of the Br^+ cation of the sulfur atom, to give the resonance-stabilized cation A (cf. [8]). The subsequent course of the reaction is determined by the ratio of the rates of addition of the OH^- anion and cleavage of a proton in structure A, resulting, respectively, in replacement of sulfur by oxygen, or the formation of acetylenes:



EXPERIMENTAL

IR spectra were obtained on a UR-20 in KBr (concentration 0.25%) and in CCl_4 (concentration 5%), UV spectra on a Specord UV-VIS in ethanol, and the ^{13}C NMR spectrum on a Bruker WP-200SY in DMSO, concentration 15% (internal standard DMSO-d_6). The elemental analyses, melting points, yields, and spectral data of the products are given in Table 1.

4-(2-Thioxopropylidene)-2,2,5,5-tetramethylimidazolin-1-oxyl (IIIa). To a solution of phenyllithium, obtained from 6.85 g of bromobenzene and 0.61 g of lithium in 80 ml of dry ether, was added dropwise with stirring under argon a solution of 1.7 g of the imidazoline (II) in dry ether. After 15 min, the mixture was cooled to −5°C, and treated dropwise with stirring with a solution of 3.5 g of methyl dithioacetate in 5 ml of ether. Stirring was continued for 1 h at 0°C and 4 h at 20°C, following which the mixture was kept for 12 h and decomposed with 50 ml of water. The organic layer was separated, and the aqueous layer extracted with chloroform (3 × 50 ml). The combined extracts were dried over $MgSO_4$, and the solution treated with 5 g of MnO_2 and stirred for 1 h at 20°C. Excess oxidant was filtered off, the solution evaporated, and (IIIa) separated by column chromatography on a column of silica, eluent a mixture of hexane and chloroform (1:1).

Similarly, treatment of the imidazoline (II) with methyl dithiobenzoate gave 2,2,5,5-tetramethyl-4-(2-thioxo-2-phenylethylidene)imidazolidine-1-oxyl (IIIb) and 2,2,5,5-tetramethyl-4-(2-thioxo-2-phenylethylidene)imidazolidine (IIIi), and treatment with O-methyl thiobenzoate afforded the enaminothione (IIIb). Reaction with methyl N,N-dimethyldithiocarbamate gave 4-(N,N,-dimethylaminothiocarbonylmethylene)-2,2,5,5-tetramethylimidazolidine-1-oxyl (IIIc) and 4-(2,2-diphenylvinyl)-2,2,5,5-tetramethyl-3-imidazoline-1-oxyl (IV). Reaction with methyl N,N-dimethylcarbamate afforded 4-(N,N-dimethylaminocarbonylmethylene)-2,2,5,5-tetramethylimidazolidine-1-oxyl (X).

4-(Methyldithiocarbonylmethylene)-2,2,5,5-tetramethylimidazolidine-1-oxide (IIId). To a solution of phenyllithium, obtained from 63 g of bromobenzene and 5.6 g of lithium in 300 ml of dry ether, was added dropwise with stirring under argon a solution of 15,6 g of the imidazoline (II) in dry ether. The mixture was stirred for 15 min at 20°C, cooled to −5°C, and 20 ml of carbon disulfide added dropwise over 20 min. The mixture was stirred for 1 h at 0°C and 4 h at 20°C, then decomposed with 150 ml of water. The aqueous layer was separated, and the ether layer extracted with 30 ml of water. The combined aqueous solutions were washed with ether (3 × 50 ml), then 28 ml of dimethyl sulfate was added dropwise with cooling at 10°C under argon. After 1 h, the mixture was extracted with ether (2 × 100 ml) and chloroform (2 × 50 ml), and the combined extracts dried over $MgSO_4$. The solution was treated with 25 g of MnO_2, and stirred for 1 h at 20°C. Excess oxidant was filtered off, and the solution evaporated. (IIId) was isolated by chromatography on a column of silica, eluent chloroform.

Similarly, from the imidazoline (IIa), excluding the oxidation step, there was obtained 4-(methyldithiocarbonylmethylene)-1-methoxy-2,2,5,5-tetramethylimidazolidine (IIIe).

Reaction of Dithioester (IIId) with Sodium Hydroxide. A solution of 0.5 g of (IIId) and 3 ml of 10% aqueous NaOH in 15 ml of methanol was boiled for 10 h, the alcohol removed,

TABLE 1. Constants, Yields, and Spectra of Compounds Obtained

Compound*	Yield, %	Mp, °C	Found/Calculated, %				Empirical formula	IR spectrum, ν, cm^{-1}	UV spectrum, λ_{max} (log ε)
			C	H	N	S			
(IIIa)	35	120–121	56.4/56.4	8.0/8.0	12.8/13.2	15.4/15.0	$C_{10}H_{17}N_2OS$	1580 (NC=CC=S)	245 (3,77), 380 (4,2)
(IIIb)	35	162–163	65.6/65.6	6.8/6.9	10.3/10.2	11.5/11.4	$C_{15}H_{19}N_2OS$	1590 (NC=CC=S)	243 (3,84), 304 (3,96), 398 (4,13)
(IIIc)	20	144–146	54.4/54.5	8.3/8.3	17.3/17.4	13.1/13.2	$C_{11}H_{20}N_3OS$	1610 (NC=CC=S)	302 (4,19), 327 (4,25)
(IIId)	45	170–172	48.9/49.0	7.0/6.9	11.5/11.4	26.4/26.1	$C_{10}H_{17}N_2OS_2$	1585 (NC=CC=S)	323 (3,93), 374 (4,35)
(IIIe)	55	83–84	50.4/50.7	7.7/7.7	10.7/10.8	25.1/24.6	$C_{11}H_{20}N_2OS_2$	1580 (NC=CC=S)	315 (3,84), 373 (4,33)
(IIIf)	20	161–163	48.9/48.9	7.3/7.3	11.4/11.4	26.1/26.0	$C_{10}H_{18}N_2OS_2$	1590 (NC=CC=S)	315 (4,25), 370 (4,53)
(IIIg)	20	165–168	52.2/52.2	7.9/7.9	12.4/12.2	27.5/27.8	$C_{10}H_{18}N_2S_2$	1585 (NC=CC=S), 3300, 3330 (NH)	316 (4,0), 370 (4,48)
(IIIh)	67	130–132	55.0/55.0	7.7/7.7	14.5/14.8	11.2/11.3	$C_{13}H_{22}N_3O_2S$	1605 (NC=CC=S)	306 (4,23), 329 (4,29)
(IIIi)	5	123–125	69.1/69.2	7.7/7.7	10.6/10.7	12.5/12.3	$C_{15}H_{20}N_2S$	1590 (NC=CC=S), 3330 (NH)	297 (3,83), 396 (4,04)
(IV)	20	98–99	79.5/79.3	7.4/7.2	8.6/8.8	–	$C_{21}H_{23}N_2O$	1595, 1610, 1615 (C=C, C=N)	227 (4,22), 275 (4,12)
(Va)	80	95–96	74.8/74.8	7.1/7.1	11.4/11.6	–	$C_{15}H_{17}N_2O$	2220 (C≡C), 1595, 1605 (C=C, C=N)	274 (4,33)
(Vb)	75	68–69	56.6/56.9	6.9/7.1	13.1/13.3	15.2/15.2	$C_{10}H_{15}N_2OS$	2160 (C≡C), 1590 (C=N)	263 (4,15)
(Vc)	75	Oil	58.5/58.3	8.0/8.0	12.4/12.4	13.9/14.2	$C_{11}H_{18}N_2OS$	2170 (C≡C), 1595 (C=N)	220 (3,96), 267 (4,01)
(VI)	20	232–233	48.4/48.3	5.1/5.1	9.6/9.4	10.7/10.2	$C_{12}H_{15}BrN_2S$ †		272 (KBr)
(VIII)	90	133–134	43.7/43.4	6.2/6.2	13.8/13.7	–	$C_{11}H_{19}BrN_3O_2$†	1675 (C=O), 1620 (C=N)	226 (4,14)
(IX)	60	115–116	36.8/36.6	4.8/4.7	9.9/9.9	–	$C_{13}H_{20}Br_2N_2O_3$ †	1605 (C=N), 1670 (C=O)	–
(X)	55	111–112	58.4/58.4	9.0/8.8	18.3/18.6	–	$C_{11}H_{20}N_3O_2$	1650 (NC=CC=O)	280 (4,39)
(XI)	90	101–102	34.4/34.4	4.7/4.7	11.2/10.9	–	$C_{11}H_{18}Br_2N_3O_2$ †	1605 (C=N), 1680 (C=O)	–

*Compounds (IIIe), (IV), and (Va, b) were recrystallized from hexane, (III) and (VIII)-(XI) from a mixture of ethyl acetate and hexane, and (Vc) was purified by sublimation.
†Found/Calculated for Br, %: 26.3/26.7 (VI); 25.9/26.3 (VIII); 37.6/37.6 (IX); 41.2/41.7 (XI).

the residue diluted with 15 ml of water, and the solid which separated was filtered off and dried. Chromatography on a column of silica (eluent, chloroform) gave 0.1 g of starting material (IIId), 4-(methyldithiocarbonylmethylene)-1-hydroxy-2,2,5,5-tetramethylimidazolidine (IIIa) and 4-methyldithiocarbonylmethylene-2,2,5,5-tetramethylimidazolidine (IIIg).

4-Morpholinothiocarbonylmethylene-2,2,5,5-tetramethylimidazolidine-1-oxyl (IIIh). A solution of 1 g of the dithioester (IIId) and 1.5 ml of morpholine in 15 ml of methanol was

boiled for 24 h, then evaporated. (IIIh) was isolated by chromatography on a column of silica (eluent, chloroform).

Reaction of Enaminothiocarbonyl Compounds with Sodium Hypobromite. To a solution of NaOBr, prepared from 1 g of sodium hydroxide and 0.5 ml of bromine in 10 ml of water, was added dropwise with stirring at 0°C a solution of 2 mmoles of the enaminothiocarbonyl compound in 5 ml of THF. The mixture was stirred for 10 min, diluted with 10 ml of water, extracted with chloroform (3 × 15 ml), the extracts dried over $MgSO_4$, and the solution evaporated. In the case of the enaminothione (IIIi), the residue was diluted with dry ether, and the precipitate 3,4-diamino-2-bromo-4-methyl-1-phenyl-2-pentene-1-thione (VI) isolated. In the case of the enaminothioamide (IIIc), the monobromo compound (VIII) was purified by recrystallization. The ethynyl compounds 4-phenylethynyl- (Va) and 4-methylthioethynyl-2,2,5,5-tetramethyl-3-imidazoline-1-oxyl (Vb), and 4-methylthioethynyl-2,2,5,5-tetramethyl-1-methoxy-3-imidazoline (Vc) were isolated by chromatography on a column of silica, eluent ether–hexane (1:1). 4-(1,1-Dibromo-2-morpholino-2-oxoethyl)-2,2,5,5-tetramethyl-3-imidazoline-1-oxyl (IX) was isolated by chromatography.

The ^{13}C NMR spectrum of (Vc) (δ, ppm) was: 157.98 (C=N), 90.75 (C^2 of the heterocycle), 89.15 and 85.46 (C≡C), 71.8 (C^4 of the heterocycle), 62.82 (O–CH_3), 17.87 (SCH_3), and a broad band centered at 23 ppm (gem-dimethyl groups in the heterocycle) (cf. [9]).

4-(1,1-Dibromo-2-N,N-dimethylamino-2-oxoethyl)-2,2,5,5-tetramethyl-3-imidazoline-1-oxyl (XI). To a solution of NaOBr, obtained from 1 g of NaOH and 0.5 ml of bromine in 10 ml of water, was added dropwise with stirring a solution of 0.5 g of the enaminoamide (X) in 5 ml of THF at 0°C. The solid which separated after 5 min was filtered off, washed with water, and dried.

4-(1-Bromo-2-N,N-dimethylamino-2-oxoethyl)-2,2,5,5-tetramethyl-3-imidazoline-1-oxyl(VIII). A mixture of 0.5 g of the enaminoamide (X) and 0.39 g of N-bromosuccinimide in 10 ml of dry CCl_4 was stirred for 3 h at 20°C. The precipitated succinimide was filtered off, and the solution evaporated. (VIII) was isolated by chromatography in a column of silica, eluent a mixture of ethyl acetate and hexane (1:1), yield 60%.

CONCLUSIONS

1. Reaction of 1-hydroxy-2,2,4,5,5-pentamethyl-3-imidazoline with thiocarboxylic acid derivatives in the presence of phenyllithium followed by oxidation affords enaminothiocarbonyl derivatives of imidazoline nitroxyl radicals.

2. Treatment of the enaminothiocarbonyl compounds with sodium hypobromite affords, depending on the substituent at the thiocarbonyl carbon atom, either acetylenic derivatives, or bromo-derivatives of the enaminocarbonyl compounds.

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