SUBSTITUTED HYDROXYCARBOXYLIC HYDRAZIDES

LII. Disubstituted Glycolic Piperylhydrazides*

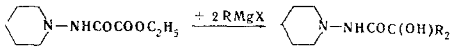
I. S. Berdinski and L. N. Machulenko

Khimiya Geterotsiklicheskikh Soedinenii, Vol. 5, No. 5, pp. 818–822, 1969

UDC 547.822.3'422: 542.957.2+541.651.7

The ethyl ester of oxalic acid piperylhydrazide has been synthesized, and its reactions with organomagnesium compounds investigated. The piperylhydrazides of diaryl-, dialkyl-, and dithienylglycolic acids have been obtained, and their properties examined. The IR and UV spectra of the compounds obtained, and the spectra of the halochromic salts and the basicity of the diaryl- and dithienylglycolic piperylhydrazides, were studied.

Piperylacetyl derivatives of diaryl- and dialkylglycolic phenylhydrazides have been investigated previously [2]. The present investigation was undertaken in order to study the effects of the piperyl group in hydrazides of these acids. The disubstituted glycolic piperylhydrazides were synthesized by reaction of the ethyl ester of oxalic acid piperylhydrazide with organomagnesium compounds [3], as follows:

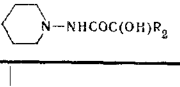


R = Ar, α-C$_4$H$_3$S, Alk

The ethyl ester of oxalic acid piperylhydrazide was obtained by reaction of piperylhydrazine with diethyl oxalate in alcoholic solution. The reaction of the ester with the organo-magnesium compounds proceeded smoothly to give the disubstituted glycolic piperylhydrazides in good yield. The reaction with α-thienylmagnesium iodide also gave the dithienylglycolic piperylhydrazides, as in the reaction of this magnesium derivative with the ethyl esters of unsymmetrically disubstituted oxalic acid hydrazides [4], but in contrast to the ethyl esters of oxalic acid hydrazides, which give only thienylglyoxylic acid hydrazides. The piperylhydrazides obtained are shown in Table 1. They are colorless, crystalline compounds, soluble in organic solvents; the dialkylglycolic piperylhydrazides are soluble in water.

The IR spectra (Fig. 1) of the piperylhydrazides in solution show bands at 3612–3617 cm^{-1}, corresponding to the free OH group, and bands at 3424–3431 cm^{-1} attributed to the valency stretching of the NH group. In the spectra of the diaryl- and dialkylglycolic piperylhydrazides, as also in the similar β-alkyl-β-arylhydrazides [5], bands are observed at 3312–3330 cm^{-1} as a result of the participation of the hydroxyl groups in hydrogen bonding. Bands of this frequency are seen in the compounds in question in the solid state also, their intensity being dependent on the nature of the substituent on the carbonyl carbon. In crystals, as a result of the formation of new hydrogen bonds, the frequency of the bands is reduced, and their positions change. The amide-I band occurs in solution at a frequency of 1695–1700 cm^{-1}, while in the crystalline form its frequency is reduced to 1655–1670 cm^{-1} as a result of the involvement of the carbonyl group in intermolecular hydrogen bonding. In the spectra of II, IV, VIII, and XII, the amide-II band is observed at 1536–1546 cm^{-1}. The amide-III band [6] in piperylhydrazides has a frequency of 1254–1270 cm^{-1}. The C—OH valency stretching band [7] in the piperylhydrazides has a frequency which is dependent on the nature of the substituent on the carbonyl carbon. In XII it is 1150 cm^{-1}, and on replacing an alkyl by an aryl group, the frequency falls [7] and, as we have found previously in a series of hydrazides, is dependent on the nature

Table 1



Compound	R	Mp, °C	Molecular formula	N, % found		N, % calculated	Yield, %
II	C_6H_5	182—183	$C_{19}H_{22}N_2O_2$	8.83:	8.90	9.03	98.1
III	m-$CH_3C_6H_4$	192—193	$C_{21}H_{26}N_2O_2$	7.99:	8.01	8.28	99.1
IV	p-$CH_3C_6H_4$	177—178	$C_{21}H_{26}N_2O_2$	7.97:	8.01	8.28	94.1
V	o-$CH_3OC_6H_4$	136—137	$C_{21}H_{26}N_2O_4$	7.29:	7.34	7.57	79.8
VI	m-$CH_3OC_6H_4$	149—150	$C_{21}H_{26}N_2O_4$	7.59:	7.64	7.57	94.7
VII	p-$CH_3OC_6H_4$	205—206	$C_{21}H_{26}N_2O_4$	7.59:	7.28	7.57	99.1
VIII	p-ClC_6H_4	199—200	$C_{19}H_{20}Cl_2N_2O_2$	7.19:	7.09	7.39	94.7
IX	α-C_4H_3S	152—153	$C_{15}H_{18}N_2O_2S_2$	8.46:	8.82	8.69	93.7
X	C_2H_5	133—134	$C_{11}H_{22}N_2O_2$	13.28:	12.81	13.08	91.9
XI	n-C_3H_7	141—142	$C_{13}H_{26}N_2O_2$	11.49:	11.67	11.57	96.1
XII	n-C_4H_9	82—83	$C_{15}H_{30}N_2O_2$	10.42:	10.08	10.37	88.8
XIII	n-C_5H_{11}	113—114	$C_{17}H_{34}N_2O_2$	9.22:	9.15	9.39	60.7
XIV	i-C_5H_{11}	138—139	$C_{17}H_{34}N_2O_2$	9.58:	9.68	9.39	90.8

Note: Compounds II, VI, and X were recrystallized from toluene, XII from benzene, and the remaining compounds from alcohol.

---

*For part LI, see [1].

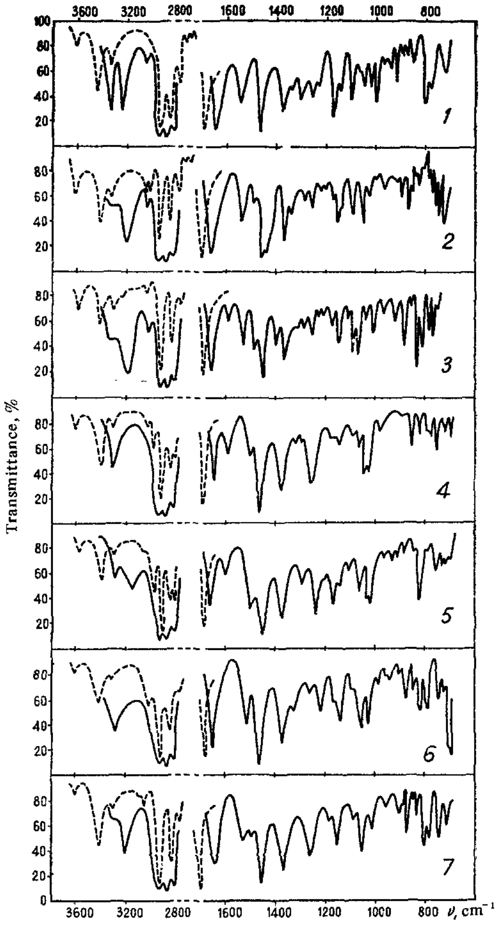


Fig. 1. IR spectra of disubstituted glycolic piperylhydrazides (the dashed lines show the spectra of 0.2% solutions in CCl_4, in 5 mm layers); 1) XII, 2) II, 3) VIII, 4) VI, 5) VII, 6) IX, 7) IV.

of the aryl group [1]. In the spectra of the diaryl- and dithienylglycolic piperylhydrazides, the frequency ν_{C-O} is variable within the limits 1045–1074 cm^{-1}. In IV, VII, and VIII, the presence of a p-substituent results in the appearance of a band at 820–830 cm^{-1}.

In the UV region (Fig. 2), the absorption of the piperylhydrazides is dependent to a large extent on the nature of the radical on the carbonyl carbon atom. In contrast to dibutylglycolic phenylhydrazide [8], XII does not exhibit a maximum, and absorbs very weakly. Compound II shows similar behavior in comparison with the corresponding hydrazide [8]. The absorption observed in the dianisylglycolic piperylhydrazides depends on the anisyl residue, and the spectra are reminiscent of those of the corresponding phenylhydrazides [8, 9]. The spectrum of IX resembles that of thiophene [10].

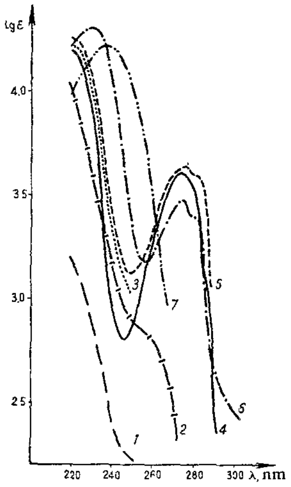


Fig. 2. UV spectra of disubstituted glycolic hydrazides: 1) XII, 2) II, 3) IV, 4) V, 5) VI, 6) VII, 7) IX.

The diaryl- and dithienylglycolic piperylhydrazides give colored solutions in concentrated sulfuric acid. In order to characterize the resulting halochromic salts, their absorption spectra in the visible region (Fig. 3), and their basicity constants, were determined. As is also the case with the diarylglycolic arylhydrazides [11], the nature of the halochromic absorption of the salts of these acids depends on the nature of the aryl substituent on the carbonyl carbon atom, and the absorption maximum occurs at the same wavelength as in the corresponding phenylhydrazides [9, 11]. However, in comparison with the latter, in the case of the piperylhydrazides the extinction is higher. The halochromic salt of IX has two maxima, at 415 nm (lg ε 4.10) and 520 nm (lg ε 4.50). Its wavelength maximum occurs at the same wavelength as that of the salt of IV, but its extinction is lower.

The basicity constants pK_{R^+} were determined spectrophotometrically, by the method [12] previously used by one of us and Kostareva [13] to determine this value for the arylhydrazides of a series of diarylglycolic acids. The following equation was used to calculate the basicity constants:

$$C = pK_{R^+} - lg\frac{C_{R^+}}{C_{ROH}}$$

The ionic concentration C_{R^+} was determined by measuring the optical density at maximum absorption. The value of pK_{R^+} was determined graphically from the relationship of $lg(C_{R^+}/C_{ROH})$ to C_0 when $lg(C_{R^+}/C_{ROH}) = 0$. The value of the function C_0 was taken from the literature [12] for triarylcarbinols, in view of the close relationship between the latter and the compounds under investigation. The results are shown in Fig. 4 and given in Table 2. The results show that the hydrazides described here are somewhat more basic than the corresponding phenylhydrazides [13]. The basicity is dependent on the nature of the substituent on the carbonyl carbon, and is reduced when the thienyl is replaced by the p-chlorophenyl radical.

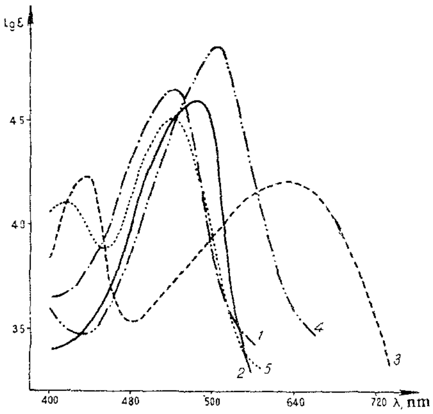


Fig. 3. Spectra of halochromic salts of diaryl- and dithienylglycolic piperylhydrazides: 1) Di-p-tolyl-, 2) Di-(p-chlorophenyl)-, 3). Di-(o-anisyl)-, 4) Di-(p-anisyl)-, 5) Dithienylglycolic piperylhydrazide.

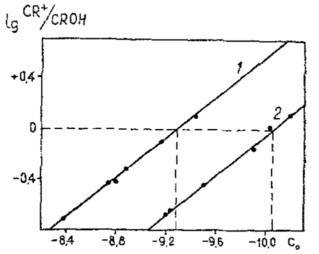


Fig. 4. Graph for the determination of pK_{R^+} for the piperylhydrazides. 1) Dithienyl-, 2) Di-(p-anisyl)glycolic piperylhydrazides.

EXPERIMENTAL

Ethyl ester of oxalic piperylhydrazide (I). A solution of 22.5 g of piperylhydrazine (obtained according to [14], by reduction of N-nitrosopiperidine with zinc dust in acetic acid, in 89.6% yield) in 25 ml of alcohol was kept for one day with 39 g of diethyl oxalate. The precipitate of oxalic piperylhydrazide which separated was filtered off, and

I was isolated from the filtrate in 25.0 g (55.5%) yield. It was soluble in benzene, toluene, alcohol, and light petroleum. Plates from light petroleum, mp 70–71° C. Found, %: N 13.82, 14.27. Calculated for $C_9H_{16}N_2O_3$, %: N 14.01.

Table 2

pK_{R^+} Values for Diaryl- and Dithienylglycolic Piperylhydrazides

R	pK_{R^+}
α-C_4H_3S	—9.28
p-$CH_3OC_6H_4$	—10.05
o-$CH_3OC_6H_4$	—13.48
p-$CH_3C_6H_4$	—13.87
p-ClC_6H_4	—17.41

Benzilic piperylhydrazide (II). To the Grignard reagent (from 7.9 g of bromobenzene and 1.2 g of magnesium) was added 2.0 g of compound I. The reaction mixture was heated on the water bath for 30 min, and decomposed with a saturated solution of ammonium chloride. Compounds III–XIV were obtained similarly.

The IR spectra were taken (as pastes in vaseline oil, and solutions in CCl_4) on an IKS-14 spectrophotometer with LiF and NaCl prisms, and the UV spectra were recorded on an SF-4 spectrophotometer, in alcoholic solution. The halochromic solutions were prepared by adding 1 ml of an acetic acid solution of the piperylhydrazide, of known concentration, to 9 ml of H_2SO_4 of varying percentage content. The spectra of the halochromic solutions were recorded on an SF-10 recording spectrophotometer.

REFERENCES

1. I. S. Berdinskii, N. A. Asanova, and N. A. Kostareva, collection: Biologically Active Compounds [in Russian], 237, 1968.
2. I. S. Berdinskii, ZhOKh, **34**, 762, 1964.
3. I. S. Berdinskii and P. A. Petyunin, ZhOKh, **26**, 2592, 1956.
4. I. S. Berdinskii, ZhOKh, **34**, 1773, 1964.
5. I. S. Berdinskii, E. Yu. Posyagina, G. S. Posyagin, and V. F. Ust-Kachkintsev, ZhOrKh, **4**, 91, 1968.
6. Miyazawa, T. Shimanauchi, and S. Mizushima, J. Chem. Phys., **29**, 611, 1958.
7. H. H. Zeiss and M. Tsutsui, J. Am. Chem. Soc., **75**, 897, 1953.
8. I. S. Berdinskii, ZhOKh, **33**, 1214, 1963.
9. I. S. Berdinskii and N. A. Kostareva, ZhOrKh, **2**, 1392, 1966.
10. S. Menczel, Z. phys. Chem., **125**, 161, 1927.
11. I. S. Berdinskii and N. A. Kostareva, ZhOKh, **35**, 876, 1965.
12. N. C. Deno, J. J. Jaruzelsky, and A. Schriesheim, J. Am. Chem. Soc., **77**, 3044, 1955.
13. I. S. Berdinskii and N. A. Kostareva, ZhOKh, **37**, 1776, 1967.
14. L. Knorr, Ann., **221**, 297, 1883.

30 May 1967

Gor'kii Perm State University