SUBSTITUTED HYDROXYCARBOHYDRAZIDES

XXXV. Tolylhydrazides of α-Aryl-α-(2-thienyl)- and α-Butyl-α-(2-thienyl)-glycolic Acids*

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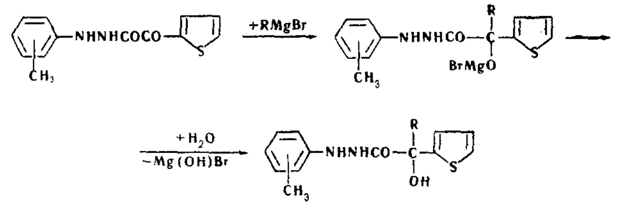
Tolylhydrazides of α-thienylglyoxylic acid are reacted with Grignard reagents, to give a series of hitherto undescribed tolylhydrazides of α-aryl-α-(2-thienyl)- and α-butyl-α-(2-thienyl)glycolic acid and their benzoyl derivatives. UV spectra data of the tolylhydrazides given are synthesized. A study is made of the IR spectra of a number of arylhydrazides of α-phenyl-α-(2-thienyl)glycolic acid.

Phenylhydrazides of α-aryl-α-(2-thienyl)- and α-alkyl-α-(2-thienyl)glycolic acids have previously been synthesized [2], and found to have high antispasmodic activity [3]. To ascertain the effect of a methyl group at the ring nitrogen atom on the properties of these compounds, the tolylhydrazides of the above-mentioned acids (Table 1) were synthesized from the tolylhydrazides of α-thienylglyoxylic acid [4], the equation being



R = C_6H_5, p-$CH_3C_6H_4$, o-$CH_3OC_6H_4$, C_4H_9

They were colorless crystalline substances, soluble in organic solvents. Heating the tolylhydrazides with benzoyl chloride in benzene gave the N-benzoyl derivatives shown in Table 1.

The UV absorption spectra of the synthesized tolylhydrazides, and of previously prepared [2] phenylhydrazides of α-thienyl-, α-aryl-, and α-alkylglycolic-acids, were examined. Figure 1 and Table 2 give the results of the spectroscopic investigations. The results show that when one aryl or alkyl group at the carbinol carbon atom is replaced by a thienyl residue, two maxima are retained in the 230 and 280 nm regions, which are also observed with arylhydrazides of diaryl- and dialkylglycolic acids [5, 6]. However, the thienyl group does affect the spectrum. The thiophene ring shows absorption at 235 nm [7]. In connection with the superposition of the thiophene absorption there is an increase in the intensity of absorption for the K band at 234 nm as compared with aryl hydrazides of diaryl- and dialkylglycolic acids [5]. The extinction of this band also depends on the nature of the aryl group at the nitrogen.

Insertion of a methyl group into this ring increases the extinction, particularly when it enters at the para position. For p-tolylhydrazides the B band, due to the transition $A_{1g} \rightarrow B_{2u}$ [8], is shifted towards the longer wavelength region. For phenyl- and tolylhydrazides of α-thienyl-, α-o-anisylglycolic acids, this maximum is higher than for the other compounds, but lower than for the corresponding tolylhydrazides of α,α-di(o-anisyl)glycolic acid [6], which is connected with the presence of only one anisyl group.

Figure 2 and Table 3 give data for the IR spectra of the arylhydrazides of α-phenyl-α-(2-thienyl)glycolic acid and the N-benzoyl derivative of the phenylhydrazide [2].

In the 3000 cm^{-1} region, the compounds studied have, in the solid state, two bands each, corresponding to OH and NH groups involved in hydrogen bonding. In solution there is separation of the bands and increase in the vibration frequencies due to disappearance of the hydrogen bonds. The band at 3600 cm^{-1} belongs to the OH group, the one at 3400–3450 cm^{-1} to the NH group linked to carbonyl [9], and the 3345–3360 cm^{-1} band to the NH group joined to the aromatic ring. The 1661 cm^{-1} and the 1685 cm^{-1} bands for, respectively, the phenylhydrazide and the tolylhydrazides of phenyl-α-(2-thienyl)glycolic acid belong to a type amide-I; in solution the frequency of this band is raised to 1700 cm^{-1}, indicating participation of the carbonyl in hydrogen bonding. With the benzoyl derivative of the phenylhydrazide of phenylthienylglycolic acid, the amide-I band is split into two (1711 and 1617 cm^{-1}). The splitting of this band, also found with the acetyl derivative of the phenylhydrazide of benzilic acid [9], is due to interaction between vibrations of the two carbonyls in the group —CO NH NHCO— [10]. The band at 1524–1542 cm^{-1} is of the amide-II type, with the benzyl derivative the amide-II band frequency is 1572 cm^{-1}. The 1323–1351 cm^{-1} band, absent from the spectrum of the phenylhydrazide of thienylglyoxylic acid [4], corresponds to vibration of the group

$\gtrdot$C—OH, the band at 1302–1320 cm^{-1} to the ArN=

group. As was previously established [9], the 1126–1140 cm^{-1} band is to be assigned to vibration of the group —N—N—, and when there is a benzoyl group on one of the nitrogen atoms, the vibration frequency shifts to 1156 cm^{-1}. Valence vibrations of the C—O— bond in hydroxyl, absent with the phenylhydrazide thienylglyoxylic acid [4], appear at 1036 cm^{-1}. This frequency is lowered in accordance with the general

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*For part XXXIV see [1].

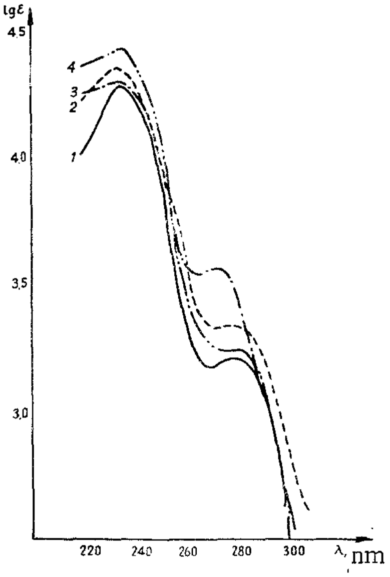


Fig. 1. UV spectra of m-tolylhydrazides of substituted glycolic acids: 1) α-butyl-α-(2-thienyl)-; 2) α-phenyl-α-(2-thienyl) 3) α-(o-anisyl)-α-(2-thienyl)-; 4) α-(p-tolyl)-α-(2-thienyl)-.

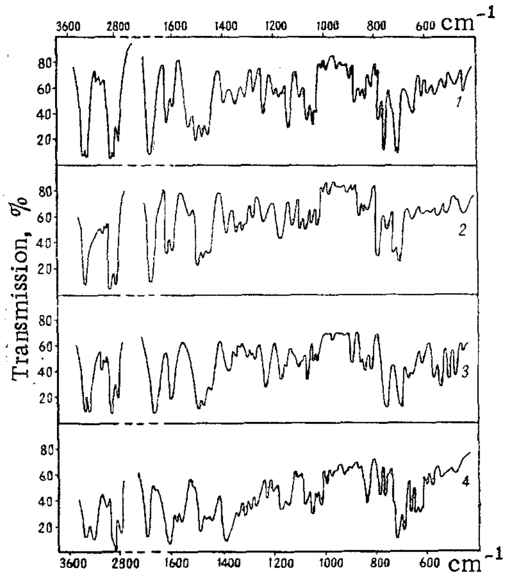
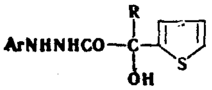


Fig. 2. IR spectra of arylhydrazides of α-phenyl-α-(2-thienyl)glycolic acid: 1) o-tolyl; 2) m-tolyl-; 3) phenyl-; 4) N-benzoylphenyl hydrazide.

Table 1



Ar	R	Mp, ° C	Formula	Found, %	
				N	S
o-$CH_3C_6H_4$	C_6H_5	170—171	$C_{19}H_{18}N_2O_2S$	8.21. 8.23	9.31
	p-$CH_3C_6H_4$	134—135	$C_{20}H_{20}N_2O_2S$	7.79. 7.67	8.82
	o-$CH_3OC_6H_4$	123—124	$C_{20}H_{20}N_2O_3S$	7.51. 7.38	8.71
	C_4H_9	132—133[a]	$C_{17}H_{22}N_2O_2S$	8.62. 8.51	10.09
m-$CH_3C_6H_4$	C_6H_5	132—133[b]	$C_{19}H_{18}N_2O_2S$	8.54. 8.36	9.23
	p-$CH_3C_6H_4$	120—120.5	$C_{20}H_{20}N_2O_2S$	7.76. 7.54	9.43
	o-$CH_3OC_6H_4$	125—126	$C_{20}H_{20}N_2O_3S$	7.40. 7.36	8.66
	C_4H_9	117—117.5	$C_{17}H_{22}N_2O_2S$	8.63. 8.44	9.82
p-$CH_3C_6H_4$	C_6H_5	150—151	$C_{19}H_{18}N_2O_2S$	8.41. 8.32	9.37
	o-$CH_3OC_6H_4$	171—172	$C_{20}H_{20}N_2O_3S$	7.74. 7.50	8.55
	C_4H_9	138—139	$C_{17}H_{22}N_2O_2S$	8.61. 8.53	9.71

Table 1 (cont'd.)

Calculated, %		Yield, %	Benzoyl derivatives				Yield, %
N	S		Mp, ° C	Formula	N, %		
					Found	Calculated	
8.28	9.47	74.2	129—131[c]	$C_{26}H_{22}N_2O_3S$	6.15. 6.15	6.33	90.6
7.96	9.09	81.7	—	—	—	—	—
7.60	8.70	89.6	229—230[d]	$C_{27}H_{24}N_2O_4S$	5.66. 5.89	5.93	63.8
8.80	10.05	78.3	149—150[a]	$C_{24}H_{26}N_2O_3S$	6.51. 6.39	6.63	91.0
8.28	9.47	88.7	178—179	$C_{26}H_{22}N_2O_3S$	6.12. 6.53	6.33	68.2
7.96	9.09	71.0	181—182[a]	$C_{27}H_{24}N_2O_3S$	6.06. 6.43	6.14	77.7
7.60	8.70	70.6	179—180	$C_{27}H_{24}N_2O_4S$	5.56. 5.45	5.93	74.4
8.80	10.06	94.3	138—139	$C_{24}H_{26}N_2O_3S$	6.90. 6.66	6.63	88.8
8.28	9.47	89.6	208—209[a]	$C_{26}H_{22}N_2O_3S$	6.10. 6.05	6.33	90.4
7.60	8.70	95.1	187—188	$C_{27}H_{24}N_2O_4S$	6.37. 5.85	5.93	93.6
8.80	10.06	97.5	178—179[a]	$C_{24}H_{26}N_2O_3S$	6.77. 6.38	6.63	89.7

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a) ex EtOH; b) ex benzene; c) ex xylene; d) ex glacial AcOH; the rest of the compounds ex toluene.

Table 2

UV spectra of Arylhydrazides of α-Aryl-α-(2-thienyl)- and α-Butyl-α-(2-thienyl)-glycolic Acids

Ar	R	K Band		Band	
		λ_{max}, nm	lg ε	λ_{max}, nm	lg ε
C_6H_5	C_4H_9	236	4.28	280	3.21
o-$CH_3C_6H_4$	"	234	4.30	278	3.24
m-$CH_3C_6H_4$	"	234	4.29	280	3.23
p-$CH_3C_6H_4$	"	234	4.33	286	3.22
C_6H_5	C_6H_5	236	4.31	278	3.17
o-$CH_3C_6H_4$	"	234	4.36	276	3.31
m-$CH_3C_6H_4$	"	234	4.36	276	3.35
p-$CH_3C_6H_4$	"	236	4.37	284	3.27
C_6H_5	o-$CH_3OC_6H_4$	232	4.30	274	3.59
o-$CH_3C_6H_4$	"	230	4.30	276	3.57
m-$CH_3C_6H_4$	"	234	4.30	274	3.57
p-$CH_3C_6H_4$	"	236	4.35	272	3.56

Table 3

IR Spectra of Arylhydrazides of α-Phenyl-α-(2-thienyl)glycolic Acid in the 3000 cm^{-1} Region

Ar	Positions of absorption maxima, cm^{-1}	
	Vaseline mull	CCl_4 solution
C_6H_5	3386, 3340	3600, 3440, 3345
o-$CH_3C_6H_4$	3370, 3330	3612, 3450, 3360
m-$CH_3C_6H_4$	3350	3610, 3450, 3360

tendency to lowering with tertiary alcohols when there is an unsaturated group at the carbinol carbon [11]. The 890 and 610 cm^{-1} bands correspond to vibrations of the thiophene ring.

EXPERIMENTAL

o-Tolylhydrazide of α-phenyl-α-(2-thienyl)glycolic acid. The Grignard reagent was prepared from 7.9 g bromobenzene and 1.2 g Mg, and 2.6 g o-tolylhydrazide of 2-thienylglyoxylic acid [4] was added to it. The whole was heated for 40 min, then decomposed with dilute HCl. Yield 2.5 g (74%), soluble in benzene, toluene, ethanol. Tolylhydrazides of substituted thienylglycolic acids were prepared similarly from the corresponding tolylhydrazides of 2-thienylglyoxylic acid. The UV spectra were determined by means of a SF-4 spectrophotometer, and the IR spectra with a UR-10 spectrometer.

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