RESEARCH ON IMIDAZOLES

XXXIV. Derivatives of Imidazo[2,1-b]Thiazolid-2,3-Ones*

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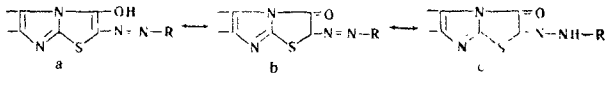
The reactivity of the methylene group of 5-phenyl- and 5,6-diphenylimidazo[2,1-b]thiazolid-3-ones is investigated. The corresponding alkylidene, arylidene, and azomethine derivatives are prepared by reaction with, respectively, aldehydes, isatin, and nitro compounds. Diazonium salts give azo coupling products whose IR spectra show them to be 2-arylhydrazines of imidazo[2,1-b]thiazolid-2,3-diones.

The literature describes the preparation of various methylene group derivatives of imidazolino[2,1-b]thiazolid-3-one [1–3] and thiazolino[3,2-a]benzimidazol-3-one [1,2,4–15]. Some of these derivatives have antispasmodic and hypotensive actions [2], while others are of interest as cyanine and merocyanine dyes [4–12].

Continuing a study of the mobility of hydrogen atoms of methylene between sulfur and carbonyl (carboxyl) [16,17], a study has now been made of the reactions of the previously synthesized imidazo[2,1,-b]thiazolid-3-ones [17] with carbonyl compounds (aldehydes, isatin), nitro compounds, and diazonium salts.

It has been found that 5-phenyl-, and 5,6-diphenylimidazol[2,1-b]thiazolid-3-ones, when boiled in ethanol plus piperidine, or in glacial acetic acid, react readily with aliphatic, aliphatic-aromatic, aromatic and heterocyclic aldehydes, as well as with isatin, to give the corresponding ylidene derivatives (I-XXI, table).

Reaction of 5-phenyl(5,6-diphenyl)imidazo[2,1-b]-thiazolid-3-ones with aromatic nitro compounds in ethanol gives azomethine derivatives, (XXII-XXIV). Diazonium salts (best aryldiazonium fluoroborates) give azo coupling products (XXV–XXIX), which can exist in three tautomeric forms (a, b, and c).



The IR spectra of compounds XXV-XXIX have sharp absorption bands characteristic of valence vibrations of the CO group of amides of acids (1705–1735 cm^{-1}) and the NH group (3230–3270 cm^{-1}). These results can be taken as proving that in the solid state compounds XXV–XXIX have the structure of hydrazones of imidazo[2,1-b]thiazolidin-2,3-diones (c). The products of reaction of diazonium salts with β-dicarbonyl compounds [19] and nitroacetic ester [20] have a similar structure (arylhydrazones and not azo compounds).

The IR spectra of ylidene and azomethine derivatives of imidazo[2,1-b]thiazolid-3-ones, were also investigated, and found to confirm the structures assigned to them. When the spectra of the azomethine derivatives (XXII-XXIV) are compared with those of the starting 5-phenyl-(5,6-diphenyl)imidazo[2,1-b]-thiazolid-3-ones (ν_{CO} near 1750 cm^{-1}), it is evident that the band of the CO group valence vibrations is appreciably shifted towards the high frequency region (e.g. by 30 cm^{-1}), which indicates conjugation of the C=O group with the C=N double bond.

EXPERIMENTAL

Alkylidene (arylidene) derivatives of imidazo[2,1-b]thiazolid-3-ones (I–XX, table). a) 0.0105 mole aldehyde (liquid aldehydes were freshly distilled) and 3–4 drops of piperidine were added to a hot solution of 0.01 mole 5-phenyl- or 5,6-diphenylimidazo[2,1-b]thiazolid-3-one [17], and the whole boiled for 3 1/2–4 hr, cooled, and the solid filtered off and washed with EtOH. Evaporation of the mother liquor gave more of the compound. I-IX, XIII, and XIV were prepared in this way.

b) 0.0105 mole aldehyde or isatin was added to a hot solution of 0.01 mole imidazo[2,1-b]thiazolid-3-one in 20–30 ml glacial AcOH, and the mixture boiled for 1–2 hr. The product was worked up as described above. X-XII and XV-XXI were prepared in that way. A catalyst, fused NaOAc (0.006 mole), was used when synthesizing X and XIX, refluxing time 15 min. The compounds were yellow (I, III–IV, VII, IX, XII–XV, XVIII), orange (II, VIII, XVI), reddish-orange (VI, X, XVII), red (XI, XIX, XX), or reddish violet (XXI) crystals, soluble with difficulty in cold ethanol and most organic solvents, insoluble in water.

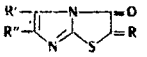
Azomethine derivatives of imidazo[2,1-b]thiazolid-3-ones (XXII–XXIV, table). 0.01 mole nitro compound was added to a hot solution of 0.01 mole imidazo[2,1-b]thiazolid-3-one in 50–100 ml absolute EtOH, and the whole refluxed for 1 1/2 hr. The precipitate was filtered off and washed with EtOH. Red prisms, readily soluble in $CHCl_3$, soluble with difficulty in EtOH, insoluble in ether and water.

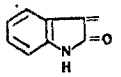
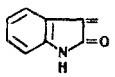
2-Arylhydrazones of imidazo[2,1-b]thiazolidin-2,3-diones (XXV–XXIX). 0.01 mole imidazo[2,1-b]thiazolid-3-one was warmed with 50–100 ml glacial AcOH to dissolve it, the solution cooled to 10–15°, and a suspension of 0.01 mole aryldiazonium fluoroborate in 50 ml MeOH added, when solution took place rapidly. The solution was left in a dark place for 36–48 hr at 18–20°, and the precipitate filtered off. Evaporation of the mother liquor gave a further quantity of the substance. XXV and XXVIII were prepared in this way.

b) 0.01 mole of imidazo[2,1-b]thiazolid-3-one and 2 g fused NaOAc were dissolved in 45 ml glacial AcOH plus 10 ml Ac_2O by warming, then the solution cooled to 10–15°, and a suspension of 0.01 mole aryldiazonium fluoroborate in 50 ml dry MeOH plus 5 ml Ac_2O added. The fluoroboride dissolved, and after 10–15 min, a precipitate started to form. The mixture was left in a dark place for 6–12 hr at 18–20°, then worked up as described in (a) above. XXVI, XXVII, and XXIX were prepared in this way. Yellow crystals, soluble with difficulty in most cold organic solvents, insoluble in water.

*For Part XXXIII see [18].

Derivatives of Imidazo[2,1-b]thiazolid-3-one*



Compound	R	R′	R″	Mp (decomp.), °C	Formula	Found, %				Calculated, %				Yield, %
						C	H	N	S	C	H	N	S	
I**	C_4H_9CH	C_6H_5	H	118—119	$C_{16}H_{16}N_2OS$	67.44	5.99	9.75	11.09	67.51	5.67	9.85	11.28	35.2
II	$C_6H_5CH{=}CHCH$	C_6H_5	H	218—219	$C_{20}H_{14}N_2OS$	72.80	4.10	8.49	9.98	72.70	4.27	8.48	9.71	25.8
III	C_6H_5CH	C_6H_5	H	178—179	$C_{18}H_{12}N_2OS$	71.50	3.95	9.43	10.59	71.03	4.01	9.21	10.54	42.7
IV	p-$CH_3OC_6H_4CH$	C_6H_5	H	183—184	$C_{19}H_{14}N_2O_2S$	68.63	4.18	8.52	9.72	68.24	4.22	8.38	9.59	33.5
V	p-$(CH_3)_2CHC_6H_4CH$	C_6H_5	H	143—145	$C_{21}H_{18}N_2OS$	72.49	4.92	8.35	9.11	72.83	5.24	8.09	9.26	31.8
VI	o-$O_2NC_6H_4CH$	C_6H_5	H	206—208	$C_{18}H_{11}N_3O_3S$	61.90	3.47	11.94	8.98	61.88	3.17	12.03	9.18	35.8
VII	m-$O_2NC_6H_4CH$	C_6H_5	H	242—244	$C_{18}H_{11}N_3O_3S$	61.56	3.15	11.75	9.15	61.88	3.17	12.03	9.18	44.4
VIII	p-$O_2NC_6H_4CH$	C_6H_5	H	261.5—263.5	$C_{18}H_{11}N_3O_3S$	62.01	3.03	11.85	9.19	61.88	3.17	12.03	9.18	46.9
IX	2-Nitrofurfurylidene	C_6H_5	H	192—193	$C_{16}H_{10}N_2O_2S$	64.98	3.35	9.70	10.79	65.29	3.42	9.52	10.89	62.6
X	5-Nitro-2-furfurylidene	C_6H_5	H	257—258.5	$C_{16}H_9N_3O_4S$	56.77	2.56	12.25	9.53	56.63	2.67	12.38	9.45	63.4
XI	$C_6H_5CH{=}CHCH$	C_6H_5	C_6H_5	201—202.5	$C_{26}H_{18}N_2OS$	76.71	4.21	6.95	8.01	76.82	4.46	6.89	7.89	97.5
XII	C_6H_5CH	C_6H_5	C_6H_5	195—196	$C_{24}H_{16}N_2OS$	76.15	4.35	7.11	8.68	75.77	4.24	7.36	8.43	77.6
XIII	p-$CH_3OC_6H_4CH$	C_6H_5	C_6H_5	200—201	$C_{25}H_{18}N_2O_2S$	73.35	4.21	6.62	7.89	73.15	4.42	6.82	7.81	37.0
XIV	p-$(CH_3)_2CHC_6H_4CH$	C_6H_5	C_6H_5	169.5—171	$C_{27}H_{22}N_2OS$	76.98	5.04	6.74	7.53	76.75	5 25	6.63	7.59	35.8
XV	o-$O_2NC_6H_4CH$	C_6H_5	C_6H_5	195—197	$C_{24}H_{15}N_3O_3S$	67.10	3.42	10.18	7.53	67.75	3.55	9.88	7.54	73.6
XVI	m-$O_2NC_6H_4CH$	C_6H_5	C_6H_5	235.5—237	$C_{24}H_{15}N_3O_3S$	67.63	3.50	9.87	7.56	67.75	3.55	9.88	7.54	49.4
XVII	p-$O_2NC_6H_4CH$	C_6H_5	C_6H_5	242—244	$C_{24}H_{15}N_3O_3S$	68.11	3.67	9.68	7.43	67.75	3.55	9.88	7.54	63.5
XVIII	2-Nitrofurfurylidene	C_6H_5	C_6H_5	235—236	$C_{22}H_{14}N_2O_2S$	71.19	3.84	7.47	8.45	71.33	3.81	7.56	8.66	41.9
XIX	5-Nitro-2-furfurylidene	C_6H_5	C_6H_5	270	$C_{22}H_{13}N_3O_4S$	63.62	3.14	10.24	7.86	63.60	3.16	10.12	7.72	71.4
XX		C_6H_5	H	334—336	$C_{19}H_{11}N_3O_2S$	66.59	3.31	12.12	9.45	66.07	3.21	12.17	9.28	78.4
XXI		C_6H_5	C_6H_5	340	$C_{25}H_{15}N_3O_2S$	—	—	10.35	7.21	—	—	9.97	7.61	70.1
XXII	p-$(CH_3)_2NC_6H_4$—N	C_6H_5	H	180.5—181	$C_{19}H_{16}N_4OS$	—	—	15.53	8.91	—	—	16.08	9.20	35.9
XXIII	p-$(CH_3)_2NC_6H_4$—N	C_6H_5	C_6H_5	205—205.5	$C_{25}H_{20}N_4OS$	—	—	13.00	7.14	—	—	13.20	7.55	29.5
XXIV	p-$(C_2H_5)_2NC_6H_4$—N	C_6H_5	C_6H_5	207—207.5	$C_{27}H_{24}N_4OS$	—	—	12.46	7.06	—	—	12.38	7.08	25.2
XXV	C_6H_5NHN	C_6H_5	H	252.5—253 5	$C_{17}H_{12}N_4OS$	63.86	3.72	17.52	10.02	63.73	3.78	17.49	10.01	57.8
XXVI	p-$CH_3OC_6H_4NHN$	C_6H_5	H	236.5—238	$C_{18}H_{14}N_4O_2S$	61.49	3.91	16.07	9.18	61.70	4.03	15.99	9.15	71.0
XXVII	p-BrC_6H_4NHN	C_6H_5	H	252—253	$C_{17}H_{11}BrN_4OS$	51.52	2.85	13.88	8.14	51.12	2.78	14.03	8.03	83.4
XXVIII	C_6H_5NHN	C_6H_5	C_6H_5	227.5—229.5	$C_{23}H_{16}N_4OS$	70.06	4.35	13.95	7.58	69.68	4.07	14.13	8.09	69.4
XXIX	p-$CH_3OC_6H_4NHN$	C_6H_5	C_6H_5	220—222	$C_{24}H_{18}N_4O_2S$	67.36	4.24	13.25	7.57	67.59	4.25	13.14	7.52	70.1

*Crystallization was used to purify the compounds I, III-V, IX, XII ex EtOH; II ex BuOH-dichloroethane (4:1); **VI, XI, XIV, XV, XVIII, XXVIII, XXIX** ex BuOH; **VII, VIII, X, XVI, XIX** ex dichloroethane; **XVII** ex AcOH; **XX, XXI** ex dimethylformamide; **XXV-XXVI** ex dioxane; **XXVII**, ex hexanol-dimethylformamide (4:1); **XXII** precipitated with ether from $CHCl_3$; **XXIV** precipitated with EtOH from $CHCl_3$; **XXIII** ex EtOH–$CHCl_3$ (2:1).

**IR spectra, cm^{-1}: I 1725 (CO); III 1722 (CO); XX 1695, 1735 (CO), 3170, 3200 (NH); XXII 1720 (CO); XXIII 1720 (CO); XXIV 1718 (CO); XXV 1712 (CO), 3270 (NH); XXVI 1705 (CO), 3260 (NH); XXVII 1710 (CO), 3270 (NH); XXVIII 1725 (CO), 3270 (NH); XXIX 1735 (CO), 3230 (NH). The spectra were determined with solids (in vaseline mulls), with a UR-10 instrument, by E. M. Peresleni and Yu. I. Pomerantsev, and we take the opportunity of thanking them.

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