RESEARCHES ON IMIDAZOLES

XXXI. 1, 2-Dialkyl-3-β-Ketoalkyl(aralkyl)-Imidazolinium Halides*

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Reaction of 1,2-dialkylimidazoles with α-halogenoketones gives a number of 1,2-dialkyl-3-[β-ketoalkyl(aralkyl)] imidazolinium halides. A study is made of the products of reaction of some imidazolinium halides with sodium hydroxide.

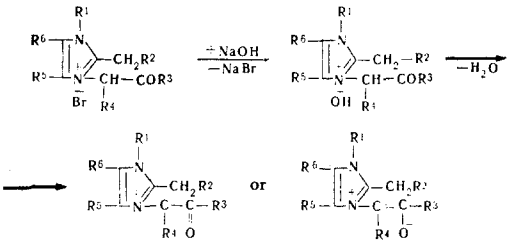
The literature does not describe 1, 2-dialkyl-3-[β-ketoalkyl(aralkyl)]-imidazolinium salts. Among other things, these compounds, by analogy with N-phenacylpicoline halides [1, 2], can be used as starting materials for synthesizing new pyrrolo-[1, 2-a]imidazole [3] heterocyclic systems.

We have now studied the reaction of various 1, 2-dialkylimidazoles with α-halogenoketones, whereby a number of 1, 2-dialkyl-3-[β-ketoalkyl-(aralkyl) imidazolinium halides (I–XXVI, Table 1) have been obtained. The quaternization reaction takes place readily in organic solvent: acetone, benzene, toluene, and alcohols. All the salts prepared, with the exception of 1-ethyl-2-methyl-3-(α-methylphenacyl)-5-chloroimidazolinium bromide (XXVI), are stable crystalline compounds.

1-Ethyl-2-methyl-4-nitro-5-chloroimidazole did not react with p-bromophenacylbromide, the starting materials being recovered, and apparently this is due to the low basicities of nitrochloroimidazoles [4]. It also proved impossible to prepare quaternary salts from 1, 2-dialkyl-5-chloroimidazoles and chloroacetaldehyde of bromoacetaldehyde diethylacetal.

By studying the properties of imidazolinium halides I–XXVI, it was established that the 3-(β-ketoaryl) derivatives give characteristic color reactions with picryl chloride and chloranil, ascribed by Kröhnke [5–7] to an enolbetaine structure of the analogous pyridine derivatives.

It was logical to consider that imidazolinium halides and sodium hydroxide give the corresponding quaternary imidazolinium bases. Actually, in the cases of salts XIII and XIV, it was possible to obtain crystalline compounds which, from their elementary analyses, and their not containing water of crystallization, were imidazolinium hydroxides (XXXVI, XXXVII). However, in the majority of the cases, these hydroxides were readily soluble in water, and they could be isolated and characterized only as their picrates (XXVII–XXXV, Table 2). The action of sodium hydroxide on nitrophenacyl derivatives of 1-ethyl-2-methyl-5-chloroimidazole (XI, XII), gave solids (XXXVIII, XXXIX), of a basic character, which analysis showed to contain one molecule of water less than the corresponding hydroxides. Possibly they are enolbetaines.



Treatment of hydroxides XXXVII and XXXIX with HCl and HBr gives the corresponding imidazolinium halides, XIV and XII respectively. We intend to make a more detailed study of the structures of the bases obtained from 1, 2-dialkyl-3-β-ketoalkyl(aralkyl) imidazolinium halides.

We prepared the starting 1, 2-dialkylimidazoles (XL–XLII) by alkylating 2-alkylimidazoles, not with alkyl halides [8, 9], but with esters of benzene sulfonic acid. 1-Benzyl-2-methylimidazole [10] (XLIII) was prepared by reacting 2-methylimidazole with benzyl chloride. 1, 2-Dimethyl-4, 5-dibromoimidazole XLIV was synthesized for the first time.

EXPERIMENTAL

1, 4, 5-Triphenyl-2-methylimidazole [11], 1, 2-dialkyl-5-chloro- and 1, 2-dialkyl-4-chloroimidazoles [12, 13] were prepared by known methods.

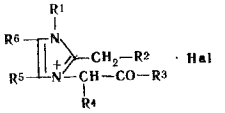
1, 2-Dimethylimidazole (XL). 76 g (0.42 mole) methyl benzenesulfonate was added in portions to 38.2 g (0.4 mole) 2-methylimidazole [14] at 170° C, with stirring, when the temperature of the mixture rose to 250° C. It quickly dropped to 235° C, where it was held for 30 min. The products were cooled to 70° C, 200 ml water added, the mixture cooled to 15° C, and with stirring, 50 ml 40% NaOH added dropwise till the solution was neutral to universal indicator. Then the precipitate was filtered off, yield of benzenesulfonate of 1, 2-dimethylimidazole 7.2 g. Colorless plates, mp 167°–169° C (ex dry EtOH). Found: N 11.06; S 12.06%. Calculated for $C_5H_8N_2 \cdot C_6H_5SO_3H$: N 11.01; S 12.61%.

After filtering off the solid, the brown mother liquors were extracted with $CHCl_3$, the extract dried over Na_2SO_4, the solvent evaporated off under vacuum, and the residue vacuum-distilled. Yield 15 g (39%)

*For Part XXX see [17].

Table 1

1, 2-Dialkyl-3-β-ketoalkyl(arlkyl)imidazolinium Halides*



Compound	R¹	R²	R³	R⁴	R⁵	R⁶	Hal	Mp, °C	Formula	Found, %				Calculated, %				Yield, %
										C	H	Hal	N	C	H	Hal	N	
I	CH_3	H	CH_3	CH_3	H	H	Cl	139—140	$C_9H_{15}ClN_2O$	53.27	7.43	17.51	14.05	53.33	7.46	17.49	13.87	91
II	CH_3	H	C_6H_5	H	H	H	Br	205—207	$C_{13}H_{15}BrN_2O$	52.92	5.29	26.84	9.40	52.89	5.12	27.07	9.49	88
III	CH_3	H	p-$O_2NC_6H_4$	H	H	H	Br	185—186	$C_{13}H_{14}BrN_3O_3$	45.44	4.52	23.03	11.93	45.89	4.15	23.49	12.35	65
IV	CH_3	H	p-BrC_6H_4	H	H	H	Br	225—226	$C_{13}H_{14}Br_2N_2O$	42.42	4.30	20.92	7.49	41.74	3.77	21.36	7.49	94
V	CH_3	H	p-C_6H_5—C_6H_4	CH_3	H	H	Br	232—234	$C_{20}H_{21}BrN_2O$	62.56	5.62	20.50	7.12	62.32	5.49	20.74	7.28	91
VI	C_2H_5	H	p-C_6H_5—C_6H_4	CH_3	H	H	Br	236—237	$C_{21}H_{23}BrN_2O$	63.04	5.77	20.08	6.90	63.16	5.80	20.01	7.02	44
VII	C_2H_5	H	CH_3	CH_3	H	Cl	Cl	110—113	$C_{10}H_{16}Cl_2N_2O$	—	—	13.98	10.80	—	—	14.11	11.15	—
VIII	C_2H_5	H	CH_3	C_2H_5	H	Cl	Br	140—145	$C_{11}H_{18}ClBrN_2O$	42.37	5.92	25.95	8.89	42.67	5.86	25.80	9.05	56
IX	C_2H_5	H	CH_3	H	H	Cl	Cl	98	$C_9H_{14}Cl_2N_2O \cdot H_2O$	42.74	6.58	13.62	10.95	42.37	6.28	13.89	10.98	51
X	C_2H_5	H	C_6H_5	H	H	Cl	Br	166—167	$C_{14}H_{16}BrClN_2O$	—	—	23.04	—	—	—	23.25	—	89
XI	C_2H_5	H	m-$O_2NC_6H_4$	H	H	Cl	Br	230—231	$C_{14}H_{15}BrClN_3O_3$	43.67	3.95	20.66	10.78	43.26	3.89	20.56	10.81	80
XII	C_2H_5	H	p-$O_2NC_6H_4$	H	H	Cl	Br	212—214	$C_{14}H_{15}BrClN_3O_3$	43.09	3.42	20.77	10.70	43.26	3.89	20.56	10.81	94
XIII	C_2H_5	H	p-BrC_6H_4	H	H	Cl	Br	215—216	$C_{14}H_{15}Br_2ClN_2O$	39.43	3.48	17.93	6.66	39.79	3.58	18.91	6.63	98
XIV	C_2H_5	H	C_6H_5	C_6H_5	H	Cl	Cl	200—201	$C_{20}H_{20}Cl_2N_2O$**	64.24	5.20	19.15	7.73	64.01	5.37	18.88	7.46	37
XV***	C_2H_5	H	p-C_6H_5—C_6H_4	CH_3	H	Cl	Br	224—225	$C_{21}H_{22}BrClN_2O$	57.79	4.84	26.22	6.31	58.14	5.11	26.59	6.44	58
XVI	C_3H_7	CH_3	p-BrC_6H_4	H	Cl	H	Br	213—215	$C_{16}H_{19}Br_2ClN_2O$	42.19	4.40	17.87	6.27	42.65	4.25	17.73	6.22	47
XVII	C_3H_7	CH_3	C_6H_5	H	H	Cl	Br	161—163	$C_{16}H_{20}BrClN_2O$	52.01	5.40	21.89	7.56	51.69	5.42	21.49	7.53	75
XVIII	C_3H_7	CH_3	p-BrC_6H_4	H	H	Cl	Br	194—196	$C_{16}H_{19}Br_2ClN_2O$	42.36	4.08	17.88	6.90	42.62	4.25	17.73	6.21	88
XIX	C_4H_9	C_2H_5	p-BrC_6H_4	H	Cl	H	Br	166—168	$C_{18}H_{23}Br_2ClN_2O$	44.99	4.78	16.04	6.12	45.17	4.84	16.69	5.85	62
XX	C_3H_7	CH_3	p-$O_2NC_6H_4$	H	H	Cl	Br	197—198	$C_{16}H_{19}BrClN_3O_3$	45.97	4.60	19.48	10.43	46.11	4.59	19.18	10.08	85
XXI	C_3H_7	CH_3	p-C_6H_5—C_6H_4	CH_3	H	Cl	Br	164—165	$C_{23}H_{26}BrClN_2O$	59.95	5.71	24.59	5.85	59.81	5.67	24.91	6.07	48
XXII	$CH_2C_6H_5$	H	p-C_6H_5—C_6H_4	CH_3	H	H	Br	180—182	$C_{26}H_{25}BrN_2O$	67.22	5.18	17.29	6.01	67.68	5.46	17.32	6.07	59
XXIII	CH_3	H	p-BrC_6H_4	H	Br	Br	Br	196—198	$C_{13}H_{12}BrN_2O$	—	—	59.63	—	—	—	60.09	—	31
XXIV	C_2H_5	H	p-BrC_6H_4	H	C_6H_5	C_6H_5	Br	209—210	$C_{26}H_{24}Br_2N_2O$	58.20	4.40	29.72	5.08	57.79	4.48	29.58	5.19	65
XXV	C_6H_5	H	p-BrC_6H_4	H	C_6H_5	C_6H_5	Br	152—154	$C_{30}H_{24}Br_2N_2O$	60.86	4.58	—	4.55	61.24	4.11	—	4.76	50
XXVI	C_2H_5	H	C_6H_5	CH_3	H	Cl	Br	—	$C_{15}H_{18}BrClN_2O$	—	—	—	—	—	—	—	—	—

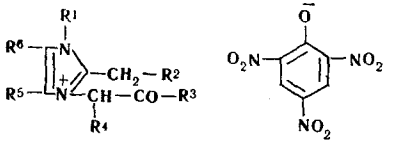
*For analysis the compounds were purified by recrystallization: II–VI, XI–XIII, XV–XVIII, XX and XXII ex dry EtOH, X ex Me_2CO, XIX from EtOH–Me_2CO (1:10); I and IX precipitated by Me_2CO ex dry EtOH; XXI and XXIV precipitated by ether ex Me_2CO; VIII precipitated by ether from EtOH–Me_2CO. Salt XXVI was a hygroscopic viscous liquid, which was not analyzed.

**For compounds XIV, XV, XXI, and XXIII, the analyses give total halogen, while for the rest of the compounds it is ionic halogen.

***IR spectrum of XV (UR-10, vaseline mull): ν_{CO} 1700 cm^{-1}.

Table 2

Picrates of 1,2-Dialkyl-3-β-ketoalkyl(aralkyl)imidazolinium Compounds*



Compound	R¹	R²	R³	R⁴	R⁵	R⁶	Mp, °C	Formula	Found, %				Calculated, %			
									C	H	Hal	N	C	H	Hal	N
XXVII	CH_3	H	p-BrC_6H_4	H	H	H	140—142	$C_{19}H_{16}BrN_5O_8$	43.19	3.24	15.02	12.79	43.69	3.09	15.30	13.40
XXVIII	C_2H_5	H	CH_3	H	H	Cl	177—179	$C_{15}H_{16}ClN_5O_8$	42.02	3.88	8.87	16.38	41.92	3.75	8.24	16.55
XXIX	C_2H_5	H	C_6H_5	H	H	Cl	153—154	$C_{20}H_{18}ClN_5O_8$	48.93	3.56	7.20	14.19	48.83	3.69	7.29	14.24
XXX	C_2H_5	H	p-BrC_6H_4	H	H	Cl	177—179	$C_{20}H_{17}BrClN_5O_8$	42.06	3.10	—	12.90	42.08	3.00	—	12.27
XXXI	C_2H_5	H	C_6H_5	C_6H_5	H	Cl	200—201,5	$C_{26}H_{22}ClN_5O_8$	55.00	3.83	6.30	12.13	54.98	3.90	6.24	12.33
XXXII	C_3H_7	CH_3	p-BrC_6H_4	H	Cl	H	157—158	$C_{22}H_{21}BrClN_5O_8$	44.16	3.60	—	11.72	44.13	3.54	—	11.69
XXXIII	C_3H_7	CH_3	C_6H_7	H	H	Cl	77— 78	$C_{22}H_{22}ClN_5O_8$	50.98	4.28	6.89	13.67	50.82	4.26	6.82	13.47
XXXIV	C_3H_7	CH_3	p-BrC_6H_4	H	H	Cl	109—110	$C_{22}H_{21}BrClN_5O_8$	43.74	3.56	—	12.18	44.13	3.54	—	11.69
XXXV	C_4H_9	C_2H_5	p-BrC_6H_4	H	Cl	H	126—128	$C_{24}H_{25}BrClN_5O_8$	46.00	3.90	—	11.10	45.98	4.02	—	11.17

*For analysis XXIX was purified by recrystallization from water, XXXIII from aqueous EtOH, and the rest from EtOH.

colorless liquid, bp 86°–90° C (8 mm), which crystallized on cooling, mp 37°. Picrate mp 177°–178° C. According to the literature [8], compound XL is a liquid bp 205°–206°, picrate mp 179°.

1-Ethyl-2-methylimidazole (XLI). Prepared by the method used for XL, by alkylating 2-methylimidazole with ethyl benzenesulfonate. Yield 32% bp 84°–86° C (6 mm), picrate mp 168°–169°C. The literature [8] gives bp 212°–213°, picrate mp 168°–169° C.

1-Ethyl-2-methyl-4, 5-diphenylimidazole (XLII). Prepared by the above method, by alkylating 2-methyl-4, 5-diphenylimidazole [15]. Yield 50%, mp 124° C (ex petrol ether). The literature [9] gives mp 125° C.

1-Benzyl-2-methylimidazole (XLIII). 32.8 g (0.4 mole) 2-methylimidazole and 55 g (0.435 mole) benzyl chloride were added to a NaOEt solution made from 9.2 g (0.4 g at) Na and 200 ml dry EtOH. The mixture was refluxed for 3 hr, filtered, the solvent distilled off, the residue dissolved in $CHCl_3$, the solution washed with water, dried over $MgSO_4$, and the solvent distilled off. Vacuum-distillation then gave 32 g (46.6%) XLIII, bp 120°–121° C (1 mm), n_D^{20} 1.5615. The literature [10] gives bp 125°–127° C (3 mm).

1, 2-Dimethyl-4, 5-dibromoimidazole (XLIV). Prepared by the method used for preparing 2-methyl 4, 5-dibromoimidazole [16], by brominating XL. Yield 42%, colorless needles, mp 88°–90° C (ex water), solubility in most organic solvents low. Found: C 23.61; H 2.64; Br 63.34; N 11.03%. Calculated for $C_5H_6Br_2N_2$: C 23.65; H 2.38; Br 62.94; N 11.03%.

Hydrobromide, colorless crystals, mp 243°–245° C (ex water), slightly soluble in EtOH, acetone, and dichloroethane. Found: C 17.89; H 2.11; Br 70.86; N 8.48%. Calculated for $C_5H_7Br_3N_2$: C 17.93; H 2.10; Br 71.59; N 8.37%.

1,2-Dialkyl-3-[β-ketoalkyl(aralkyl) imidazolinium halides (I–XXVI; Table 1). 0.02 mole 1, 2-dialkylimidazole was added to a hot solution of 0.02 mole α-halogenoketone in 15–25 ml benzene or toluene (for liquid or low-melting halogenoketones), or 40–50 ml of the same solvent (in the case of nitro(bromo) phenacyl bromide). The mixture was refluxed for 2–6 hr, when a precipitate of solid quaternary salt soon formed. The products were cooled, the solid filtered off, washed with the same solvent, then with acetone, and dried. Compounds **I–VI, IX–XIV, XVII–XXII** and **XXVI** were obtained by running the in benzene. In preparing **XXII**, reaction reactants were refluxed together for 24 hr. VII was prepared in acetone (5 hr refluxing), XXIV in EtOH (3 hr refluxing). Colorless or pale-yellow crystalline compounds (except XXVI) readly soluble in water and EtOH.

Action of NaOH on 1, 2-dialkyl-3-[β-ketoalkyl (aralkyl)] imidazolinium halides. Excess aqueous NaOH was added to an aqueous solution of 0.01 mole imidazolinium halide in 10–100 ml water. In most of the experiments the resultant imidazolium hydroxide was readily soluble in water, and no precipitate formed. After acidifying to pH 5–6 with AcOH, an aqueous solution of picric acid was added, the precipitate was filtered off, and washed with water. Table 2 gives physical constants and elementary analyses of the 1, 2-dialkyl-3-[β-ketoalkyl(aralkyl)] imidazolinium picrates prepared.

From bromide XIII an oily base was obtained XXXVI, which crystallized on drying in a vacuum-desiccator over NaOH. Yellow crystals mp 83°–85° C ex acetone, readily soluble in water and EtOH, decomposed on keeping. The analytical data show that XXXVI is 1-ethyl-2-methyl-3-(p-bromophenacyl)-5-chloroimidazolinium hydroxide. Found: C 46.74; H 4.24; Hal total 32.18; N 8.07%. Calculated for $C_{14}H_{16}BrClN_2O_2$: C 46.75; H 4.48; Hal total 32.08; N 7.79%. IR spectrum (tabletted with KBr) 1710 cm^{-1} (ν_{CO}).

From chloride XIV a white crystalline compound XXXVII was obtained mp 158°–159° C (ex MePrCO), very slightly soluble in water, readily soluble in EtOH. It did not lose weight when dried (100° C), and a titration with the Karl Fischer reagent did not show any water of crystallization. With HCl gas it gave the starting quaternary salt XIV. Analytical data and properties show XXXVII to be 1-ethyl-2-methyl-3-desyl-5-chloroimidazolinium hydroxide. Found: C 67.32; H 5.82; Cl 9.92; N 7.81%. Calculated for $C_{20}H_{21}ClN_2O_2$: C 67.31; H 5.93; Cl 9.93; N 7.85%.

From bromide XI base XXXVIII was obtained, for analysis recrystallized from acetone, and dried at 40°–50° C. Dark-red crystals mp 120°–122° C, readily soluble in water, to give an almost colorless solution. The analytical results show XXXVIII to probably be an enolbetaine. Found: C 54.30; H 4.50; Cl 11.60; N 14.20%. Calculated for $C_{14}H_{14}ClN_3O_3$: C 5.64; H 4.59; Cl 11.52; N 13.66%.

From bromide XII base XXXIX was obtained, purified for analysis by precipitating from EtOH-ether with petrol ether, then dried over NaOH in a vacuum-desiccator. Dark-brown crystals, mp 107°–108° C (became moist at 90°), soluble in water, giving an almost colorless solution, HBr converts it to the starting salt XII. Found: C 54.20; H 4.55; Cl 10.80; N 14.20%. Calculated for $C_{14}H_{14}ClN_3O_3$: C 54.64; H 4.59; Cl 11.52; N 13.66%.

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