3,5-O-Benzylidene-6-[(2-chloroethyl)-ethylamino]-6-deoxy-1,2-O-isopropylidene-D-glucofuranose (XVIII).—A solution of 2.0 g. (5.26 mmoles) of 3,5-O-benzylidene-6-deoxy-6-[ethyl-(2-hydroxyethyl)-amino]-1,2-O-isopropylidene-D-glucofuranose (XV) in 50 ml. of dry dichloromethane was treated with 2.0 ml. (27.7 mmoles) of thionyl chloride at reflux temperature for 1.5 hours. The solution was cooled, diluted with 20 ml. of dry dichloromethane, then added dropwise with stirring to 200 ml. of saturated aqueous carbonate. The dichloromethane layer was separated, washed with 25 ml. of water, dried over magnesium sulfate, then evaporated to dryness *in vacuo* to yield 1.82 g. (86%) of a tan sirup. Recrystallization from absolute ethanol gave 1.26 g. (60%) of white crystals, m.p. 65–67°, $[\alpha]^{28}D$ +4.8° (0.5% in ethanol); λ_{max}^{KBr} no OH at 2.9, 7.25 (CH_3), 9.12, 9.26, 9.84 (C–O–C), 13.20, 14.30 μ (monosubstituted phenyl).

Anal. Calcd. for $C_{20}H_{28}ClNO_5$: C, 60.3; H, 7.04; Cl, 8.92; N, 3.52. Found: C, 60.3; H, 7.30; Cl, 8.86; N, 3.51.

6-[(2-Chloroethyl)-ethylamino]-6-deoxy-D-glucose hydrochloride (XXIV) was prepared from 3,5-O-benzylidene-6-[(2-chloroethyl)-ethylamino]-6-deoxy-1,2-O-isopropylidene-D-glucofuranose (XVIII) by the procedure used for the preparation of 6-[bis-(2-chloroethyl)-amino]-6-deoxy-D-glucose hydrochloride (XXIII). The "one-armed" mustard was obtained in quantitative yield as a pale brown sirup which was homogeneous on paper chromatography[17], with R_g 0.91.

Anal. Calcd. for $C_{10}H_{20}ClNO_5 \cdot HCl \cdot 1/3H_2O$: C, 38.5; H, 6.94; Cl, 22.8. Found: C, 38.7; H, 7.22; Cl, 22.3.

6-(2-Chloroethylamino)-6-deoxy-D-glucose Hydrochloride (XXV).—A solution of 2.53 g. (7.2 mmoles) of 3,5-O-benzylidene-6-deoxy-6-(2-hydroxyethyl-amino)-1,2-O-isopropylidene-D-glucofuranose (XVI) and 2.53 ml. (35.2 mmoles) of thionyl chloride in 20 ml. of dry dichloromethane was heated at reflux for 1 hour. The reaction mixture was allowed to cool to room temperature, then it was diluted with 10 ml. of dry dichloromethane and added dropwise with stirring to 75 ml. of saturated aqueous sodium carbonate. The dichloromethane layer was separated and the aqueous layer was extracted with 20 ml. of dichloromethane. The combined dichloromethane layers were dried over magnesium sulfate, then evaporated to dryness *in vacuo* to yield the blocked mustard XIX as an oil.

The crude blocked mustard XIX was heated on a steam-bath with 10 ml. of 6 *N* aqueous hydrochloric acid for 30 minutes. After being cooled to room temperature, the acid solution was extracted with two 10-ml. portions of chloroform, then the aqueous layer was lyophilized to give 0.96 g. of a brown foam which contained a major spot on paper chromatography,[17] with R_g 1.02 plus a trace component with R_g 0.60.

Anal. Calcd. for $C_8H_{16}ClNO_5 \cdot HCl$: C, 34.6; H, 6.12; Cl, 25.5; N, 5.03. Found: C, 35.2; H, 6.21; Cl, 25.2; N, 5.04.

Acknowledgments.—The authors are indebted to Dr. Peter Lim and staff for the chromatograms and optical rotations, as well as the interpretation of the infrared spectra; and to Mr. O. P. Crews, Jr., and staff for large-scale preparations of intermediates.

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[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, FACULTY OF SCIENCE, CAIRO UNIVERSITY]

Action of Grignard Reagents. XVII.[1] Action of Organomagnesium Compounds on 5-Arylidene Derivatives of 3-Arylrhodanines, of 3-*p*-Tolyl-2,4-thiazolidinedione and on 2-Arylidene-3(2H)-4,5-benzthianaphthenone-1,1-dioxides

BY AHMED MUSTAFA, WAFIA ASKER, SAMIR KHATTAB, MOHAMED EZZ EL DIN SOBHY, ABDALLAH MOHAMED FLEIFEL AND KAMAL ABU-ELAZAYEM

RECEIVED AUGUST 14, 1959

Treatment of 5-arylidene derivatives of 3-arylrhodanines and of 3-*p*-tolyl-2,4-thiazolidinedione with Grignard reagents does not effect hetero-ring opening and only the double bond of the lateral chain of II and IV enters into reaction, yielding colorless products, believed to have structures III and V, respectively. 3-Phenylrhodanine and 3-*p*-tolyl-2,4-thiazolidinedione were proved to be stable when treated with phenylmagnesium bromide under similar conditions. When IIIa was treated with aqueous sodium hydroxide solution, α-mercapto-β,β-diphenylpropionic acid was obtained. Conjugate addition, without any indication of cleavage, now has been observed when the newly prepared 2-arylidene-3(2H)-4,5-benzthianaphthenone-1,1-dioxides (Xa-b) are allowed to react with organomagnesium halides, yielding colorless reaction products, believed to have structures XI.

Recently,[2] in conjunction with a study of the pharmacological and toxicological properties of rhodanine derivatives,[3] Mustafa and co-workers have prepared derivatives of 5-methylrhodanine and 5-methyl-3-phenyl-2,4-thiazolidinedione, through the action of Grignard reagents on 5-aralkylidene rhodanines and 5-aralkylidene-3-phenyl-2,4-thiazolidinediones, respectively.[4]

We now would like to report our extension of this investigation for the aim of preparation of a number of new derivatives needed for the pharmacological studies.

In this investigation, the action of Grignard reagents on 5-arylidene-3-arylrhodanines (IIa-h) and on 5-arylidene-3-*p*-tolyl-2,4-thiazolidinediones (IVa-e) has now been undertaken with the formation of the reaction products IIIa-l and Va-f, respectively (*cf.* Scheme A and B).

The Grignard reagents do not effect the hetero-ring opening and only addition of organomagnesium compounds to the conjugation created by attachment of an exocyclic double bond in the 5-position of a heterocyclic ring having a carbonyl function II and IV takes place.

The structure of IIIa, which is taken as an

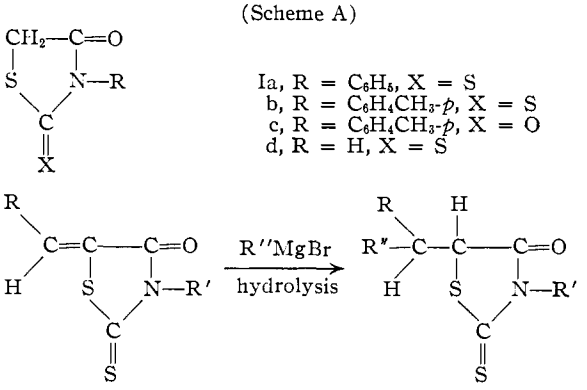
(1) A. Mustafa and M. M. Sallam, THIS JOURNAL, **81**, 1980 (1959).

(2) S. Tawab, A. Mustafa and A. F. A. Shalaby, *Nature*, **183**, 607 (1959).

(3) In view of the marked interest in many derivatives of thiazolidone which proved to be useful as anesthetics (A. R. Surrey, THIS JOURNAL, **71**, 3354 (1949)), anti-convulsants (H. D. Troutman and L. M. Long, *ibid.*, **70**, 3436 (1948)) and amebacidal agents (A. R. Surrey and R. A. Cutler, *ibid.*, **76**, 578 (1954)), the presence of a thiazolidine moiety in penicillin, the fungi-toxic or bacteria-toxic activity shown by many derivatives of rhodanines (H. K. Pujari and M. K. Rout, *J. Sci. Ind. Res. (India)*, **14B**, 398 (1955)); F. C. Brown and C. K. Bradsher, *Nature*, **168**, 171 (1951); F. C. Brown, C. K. Bradsher, E. C. Morgan, M. Tetenbaum and P. Wilder, THIS JOURNAL, **78**, 384 (1956).

(4) A. Mustafa, W. Asker, A. F. A. Shalaby and M. E. Sobhy, *J. Org. Chem.*, **23**, 1992 (1958).

(Scheme A)

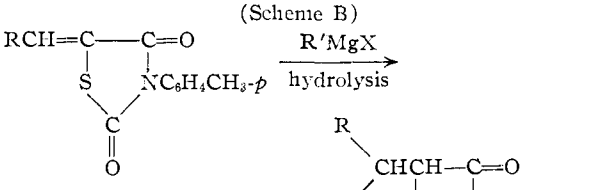


Ia, R = C_6H_5, X = S
b, R = $C_6H_4CH_3$-*p*, X = S
c, R = $C_6H_4CH_3$-*p*, X = O
d, R = H, X = S

IIa, R = R′ = C_6H_5
b, R = $C_6H_4OCH_3$-*p*, R′ = C_6H_5
c, R = C_6H_4Cl-*p*, R′ = C_6H_5
d, R = $C_6H_3:O_2CH_2(3:4)$, R′ = C_6H_5
e, R = C_6H_5, R′ = $C_6H_4CH_3$-*p*
f, R = $C_6H_4OCH_3$-*p*, R′ = $C_6H_4CH_3$-*p*
g, R = C_6H_4Cl-*p*, R′ = $C_6H_4CH_3$-*p*
h, R = $C_6H_3:O_2CH_2(3:4)$, R′ = $C_6H_4CH_3$-*p*
i, R = C_6H_5, R′ = **H**

IIIa, R = R′ = R″ = C_6H_5
b, R = $C_6H_4OCH_3$-*p*, R′ = R″ = C_6H_5
c, R = C_6H_4Cl-*p*, R′ = R″ = C_6H_5
d, R = C_6H_4Cl-*p*, R′ = C_6H_5, R″ = $C_6H_4CH_3$-*p*
e, R = $C_6H_3:O_2CH_2(3:4)$, R′ = R″ = C_6H_5
f, R = $C_6H_3:O_2CH_2(3:4)$, R′ = C_6H_5, R″ = $C_6H_4CH_3$-*p*
g, R = R″ = C_6H_5, R′ = $C_6H_4CH_3$-*p*
h, R = C_6H_5, R′ = R″ = $C_6H_4CH_3$-*p*
i, R = $C_6H_4OCH_3$-*p*, R′ = $C_6H_4CH_3$-*p*, R″ = C_6H_5
j, R = $C_6H_4OCH_3$-*p*, R′ = R″ = $C_6H_4CH_3$-*p*
k, R = C_6H_4Cl-*p*, R′ = $C_6H_4CH_3$-*p*, R″ = C_6H_5
l, R = $C_6H_3:O_2CH_2(3:4)$, R′ = $C_6H_4CH_3$-*p*, R″ = C_6H_5
m, R = R″ = C_6H_5, R′ = H

(Scheme B)



IVa, R = C_6H_5
b, R = $C_6H_4CH_3$-*p*
c, R = $C_6H_4OC_2H_5$-*o*
d, R = $C_6H_4OCH_3$-*p*
e, R = $C_6H_3:O_2CH_2(3:4)$

Va, R = R′ = C_6H_5
b, R = C_6H_5, R′ = $C_6H_4CH_3$-*p*
c, R = C_6H_5, R′ = $CH_2C_6H_5$
d, R = $C_6H_4OC_2H_5$-*o*, R′ = C_6H_5
e, R = $C_6H_4OCH_3$-*p*, R′ = $C_6H_4CH_3$-*p*
f, R = $C_6H_3:O_2CH_2(3:4)$, R′ = C_6H_5

VIa, R = H
b, R = COC_6H_5
c, R = C_2H_5

VII

example of compounds IIIa-l, is inferred from the fact that it is colorless, readily transformed by the action of hot aqueous sodium hydroxide (10%) into a colorless substance believed to have structure VIa.[5]

(5) *Cf.* the easy opening of the hetero-ring in 5-aralkylidenerhodanines by the action of aqueous sodium hydroxide (E. Campaigne and R. E. Cline, *ibid.*, **21**, 32 (1956)).

The structure of VIa is inferred from the fact that it has an acidic character, forms S-benzoyl derivative VIb[4] and its alcoholic solution gives intense blue color with alcoholic ferric chloride solution. Treatment of solution of VIa in glacial acetic acid with hydrogen peroxide gives a sulfur-free compound believed to be identical with VII. Oxidation of an acetone solution of VII with potassium permanganate yielded benzophenone.

Similarly, a colorless product is obtained by the action of alcoholic potassium hydroxide on Va, which proved to be identical with VII, obtained by the action of hydrogen peroxide on VIa as described above.

The finding that Vb is obtained by the action of phenylmagnesium bromide on IVb and by the action of *p*-tolylmagnesium iodide on IVa may be taken in favor of the assigned structure for the Grignard products (*cf.* V).

Both 3-phenylrhodanine (Ia) and 3-*p*-tolyl-2,4-thiazolidinedione (Ic), having less tendency for tautomerism,[6] proved to be stable toward the action of phenylmagnesium bromide under similar conditions, thus showing the stability of the hetero-ring toward the action of Grignard reagent.

The absorption spectra for the model compound rhodanine (Id), for 5-benzylidenerhodanine (IIi) and for 5-diphenylmethylrhodanine (IIIm) give evidence for the assigned structure for the products by the action of Grignard reagents on 5-arylidene rhodanines.

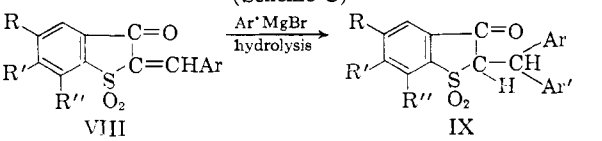
The ultraviolet absorption curves of Id and of IIIm are essentially identical, showing absorption with the main bands at λ_{294} and λ_{298}, respectively. It is significant that the benzylidene compound IIi which would be expected to have longer conjugation and absorb at a longer wave length does indeed absorb with the main band at λ_{274}.

Study of the infrared curves of the above-mentioned compounds shows that compound IIi has a fairly heavy absorption at 6.3 μ which band is missing in curves for Id and IIIm.

One reasonable interpretation is that this band at 6.3 μ is attributed to the >C=C< double bond in conjugation with the carbonyl as well as the phenyl groups. The heavy band at 6.9 μ in all of these curves is probably associated with the C to N bond.

Reactions of Grignard Reagents with 2-Arylidene-3(2H)-4,5-benzthianaphthenone-1,1-dioxides. —Recently, Mustafa and Sallam,[1] in conjunction with a study of the pharmacological action of sulfur-containing compounds against Bilhariazis snails, have shown that conjugate addition, without any indication of cleavage reaction, takes place when 2-arylidine-3(2H)-thianaphthenone-1,1-dioxides (VIII) are treated with arylmagnesium halides, yielding reaction products of structure IX (*cf.* Scheme C).

(Scheme C)



VIII IX

(6) F. C. Brown, C. K. Bradsher, E. C. Morgan, M. Tetenbaum and P. Wilder, THIS JOURNAL, **78**, 384 (1956).

TABLE I

GRIONARD PRODUCTS (III, V, XI) FROM ARYLIDENE DERIVATIVES OF 3-ARYLRHODANINE (II), 3-*p*-TOLYL-2,4-THIAZOLIDINEDIONE (IV) AND 3(2H)-4,5-BENZTHIANAPHTHENONE-1,1-DIOXIDE (X)

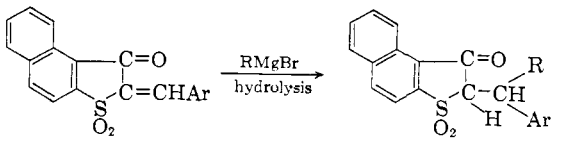
Arylidene derivative	Product	Solvent of crystn.[d]	M.p.,[a] °C.	Yield, %	Color with H_2SO_4	Formula	Carbon, % Calcd.	Carbon, % Found	Hydrogen, % Calcd.	Hydrogen, % Found	Nitrogen, % Calcd.	Nitrogen, % Found	Sulfur, % Calcd.	Sulfur, % Found
IIa	IIIa	A	150	60	No color	$C_{22}H_{17}NOS_2$	70.40	70.14	4.53	4.52	3.73	3.44	17.06	16.82
b	b	A	145	65	Yellow	$C_{23}H_{19}NO_2S_2$	68.14	67.86	4.69	4.42	3.45	3.30	15.80	16.05
c	c	A	119	65	Yellow	$C_{23}H_{16}ClNOS_2$[b]	64.46	64.36	3.90	3.53	3.41	3.18	15.62	15.37
c	d	A	141	70	Yellow	$C_{23}H_{16}ClNOS_2$	65.17	65.35	4.25	4.17				
d	e	A	185	65	Yellowish-red	$C_{23}H_{17}NO_3S_2$	65.87	65.78	4.05	3.91				
d	f	A	165	70	Intense red	$C_{24}H_{19}NO_3S_2$	66.51	66.42	4.38	4.66	3.23	3.66		
e	g	A	135	65	No color	$C_{23}H_{19}NOS_2$	70.95	71.15	4.88	4.96	3.59	3.66	16.45	16.19
e	h	B	147	75	Yellow	$C_{24}H_{21}NOS_2$	71.46	71.75	5.21	5.28				
f	i	A	127	70	Yellow	$C_{24}H_{21}NO_2S_2$	68.71	68.41	5.01	4.76	3.34	3.31	15.27	15.03
f	j	C	148	75	Yellowish-brown	$C_{25}H_{23}NO_2S_2$	69.28	69.28	5.31	5.50				
g	k	A	137	60	Yellowish-brown	$C_{23}H_{18}ClNOS_2$[c]	65.17	64.90	4.25	4.28	3.30	2.97	15.11	14.84
h	l	A	139	70	Orange-red	$C_{24}H_{19}NO_3S_2$	66.51	66.18	4.38	4.52	3.23	2.93	14.75	14.38
IVa	Va	A	164	77	No color	$C_{23}H_{19}NO_2S$	73.99	73.67	5.09	4.97	3.75	3.52	8.58	8.18
a	b	A	156	60	Yellow	$C_{24}H_{21}NO_2S$	74.42	74.14	5.43	5.29	3.62	3.45	8.27	8.10
a	c	A	166	57	Yellow	$C_{24}H_{21}NO_2S$	74.42	74.38	5.43	5.28	3.62	3.46	8.27	8.05
c	d	A	142	59	Yellow	$C_{23}H_{20}NO_2S$	71.94	71.88	5.51	5.46	3.36	3.24	7.67	7.35
d	e	A	143	61	Yellowish-red	$C_{23}H_{20}NO_3S$	71.94	71.82	5.51	5.48	3.36	3.21	7.67	7.59
b	b	A	156	73	Yellow	$C_{24}H_{21}NO_2S$	74.42	74.19	5.43	5.29	3.62	3.51	8.27	8.22
e	f	D	172	67	Brownish-red	$C_{24}H_{19}NO_4S$	69.06	68.92	4.56	4.27	3.36	3.18	7.67	7.54
Xa	XIa	B	191	58	Yellowish-green	$C_{23}H_{18}O_3S$	75.37	75.65	4.52	4.55			8.04	7.78
b	b	D	209	70	Greenish-yellow	$C_{27}H_{22}O_4S$	73.30	73.50	4.97	4.87			7.24	7.37
b	c	D	178	70	Green	$C_{21}H_{18}O_4S$	68.85	68.92	4.91	4.89			8.74	8.53

[a] Melting points are uncorrected. [b] Calcd.: Cl, 8.66. Found: Cl, 8.99. [c] Calcd.: Cl, 8.38. Found: Cl, 8.62. [d] A, ethyl alcohol; B, benzene–light petroleum ether; C, petroleum ether (90–120°); D, benzene.

We now would like to report, in extension of this investigation, the reaction of Grignard reagents with 2-arylidene-3-(2H)-4,5-benzthianaphthenone-1,1-dioxides (Xa-b). Thus, when Xa-b are treated with organomagnesium halides, similar conjugate addition, without any indication of cleavage reaction, takes place (*cf.* scheme D) yielding reaction products believed, by analogy, to have structures XI.

The 3(2H)-4,5-benzthianaphthenone-1,1-dioxide, having less tendency for enolization,[7] proved to be stable toward the action of phenylmagnesium bromide under similar conditions, illustrating the stability of the hetero-ring toward the action of Grignard reagents. The activity of the vinyl group in X may be compared with the activity of the exocylic double bond in II.

(Scheme D)



Xa, Ar = C_6H_5
b, Ar = $C_8H_4OCH_3$-*p*

XIa, Ar = R = C_6H_5
b, Ar = $C_6H_4OCH_3$-*p*, R = $C_6H_4CH_3$-*p*
c, Ar = $C_8H_4OCH_3$-*p*, R = CH_3

The condensation of 3(2H)-4,5-benzthianaphthenone-1,1-dioxide with aromatic aldehydes has not been reported. We now have studied this condensation reaction[8] and have obtained the new arylidene derivatives Xa-b needed in this investigation.

Experimental

Preparation of 2-Arylidene-3(2H)-4,5-benzthianaphthenone-1,1-dioxides (Xa-b).—A mixture of 1.0 g. of the 3(2H)-4,5-benzthianaphthenone-1,1-dioxide[9] and 2 ml. of the appropriate aldehydes was heated, after the procedure described for the preparation of VIII.[8]

2-Benzylidene-3(2H)-4,5-benzthianaphthenone-1,1-dioxide (Xa) forms pale yellow crystals from a mixture of benzene–light petroleum ether[10]; m.p. 245°, yield 85%. It gives red color when treated with concentrated sulfuric acid.

Anal. Calcd. for $C_{19}H_{12}O_3S$: C, 71.25; H, 3.75. Found: C, 71.10; H, 4.10.

2-*p*-Methoxybenzylidene-3(2H)-4,5-benzthianaphthenone-1,1-dioxide Xb gives yellow needles from benzene–benzine (50–70°); m.p. 267–268°, yield 65%. It gives purple-red color with concentrated sulfuric acid.

Anal. Calcd. for $C_{20}H_{14}O_4S$: C, 68.28; H, 4.00; S, 9.14. Found: C, 68.54; H, 3.95; S, 8.99.

Action of Grignard Reagents on 5-Arylidene-3-arylrhodanines (IIa-h), on 5-Arylidene-3-*p*-tolyl-2,4-thiazolidinedione (IVa-e) and on 2-Arylidene-3(2H)-4,5-benzthianaphthenone-1,1-dioxides (Xa-b).—The following illustrates the procedure. To a Grignard solution (prepared from 0.9 g. of magnesium and 9.0 g. of bromobenzene in 50 ml. of dry ether) was added a solution or suspension of 1.0 g. of each of IIa–h, IVa–e and Xa–b in dry benzene (50 ml.).

(7) *Cf.* A. Kohen and S. Smiles, *J. Chem. Soc.*, 408 (1930); A. A. Lier and S. Smiles, *ibid.*, 523 (1931); A. W. Weston and C. M. Suter, THIS JOURNAL, **61**, 389 (1939); F. Arndt, A. Kirsch and P. Nachtwey, *Ber.*, **59**, 1074 (1926); H. D. Hartough and S. L. Meisel, "Compounds with Condensed Thiophene Rings," Interscience Publishers, Inc., New York, N. Y., 1954, p. 157.

(8) *Cf.* A. Mustafa and S. M. A. Zayed, THIS JOURNAL, **79**, 3500 (1957).

(9) W. E. Truce and G. A. Toren, *ibid.*, **76**, 697 (1954).

(10) Light petroleum is the fraction boiling at 40–60° and petroleum ether at 60–100°; the boiling ranges of other fractions are specified.

After evaporation of the ether, the mixture was heated for 3 hours on a steam-bath. After standing overnight at 25° it was poured slowly into 100 ml. of saturated aqueous ammonium chloride solution to which 3 ml. of concentrated hydrochloric acid was added, and extracted with ether. The ethereal layer was dried over anhydrous sodium sulfate, filtered, and evaporated. The solidified residues, after washing with light petroleum were crystallized from the appropriate solvents.

The Grignard products listed in Table I were prepared similarly. They are all colorless, insoluble in cold aqueous sodium hydroxide (10%), give no color with alcoholic ferric chloride and are generally soluble in hot benzene and/or alcohol but are difficultly soluble in light petroleum.

Action of Aqueous Sodium Hydroxide Solution on IIIa.—Two grams of IIIa and 20 ml. of aqueous sodium hydroxide solution (10%) were heated on a steam-bath for one hour until all the solid was dissolved. The reaction mixture was cooled, poured onto crushed ice and acidified with dilute hydrochloric acid. The solid so obtained was filtered off and crystallized from aqueous ethyl alcohol (50%) as colorless crystals, yield *ca.* 1.2 g., m.p. 146°, identified as VIa (m.p. and mixed m.p.[4]).

Reaction of VIa with (a) Ethyl Iodide.—One gram of VIa was dissolved in 10 ml. of ethyl alcohol, treated with 4 ml. of aqueous sodium hydroxide (10%) and with 3 ml. of freshly distilled ethyl iodide. The reaction mixture was refluxed on a water-bath for 0.5 hour, set aside to cool, and then poured into 100 ml. of cold water. It was filtered off and the filtrate was acidified with cold dilute hydrochloric acid. The solid so obtained was crystallized from petroleum ether as colorless crystals (*ca.* 0.8 g.), m.p. 136°, identified as VIc (m.p. and mixed m.p.[4]).

(b) **Benzoyl Chloride.**—A solution of 1 g. of VIa in 10 ml. of aqueous sodium hydroxide solution was treated gradually with 2 ml. of benzoyl chloride. The reaction mixture was vigorously shaken for 20 minutes, then poured onto 200 ml. of cold water and acidified with dilute hydrochloric acid. The solid so obtained was collected and crystallized from dilute ethyl alcohol as colorless crystals (*ca.* 0.5 g.), m.p. 178°, identified as VIb (m.p. and mixed m.p.[4]).

(c) **Hydrogen Peroxide.**—A mixture of 0.5 g. of VIa and 10 ml. of glacial acetic acid and 2 ml. of hydrogen peroxide was kept aside at room temperature for 2 days. It was poured onto crushed ice, and the solid thus separated was collected and crystallized from dilute acetic acid as colorless crystals (*ca.* 0.20 g.), m.p. 155°, not depressed with an authentic sample of VII.[11]

Action of Potassium Hydroxide Solution on Va.—Treatment of Va with an alcoholic potassium hydroxide solution (10%), as described in the case of IIIa, and extending the heating period for 3 hours gave, after acidification, an impure colorless substance having a wide range of m.p. The reaction was repeated using 0.5 g. of Va and 20 ml. of an alcoholic potassium hydroxide solution (20%) and was refluxed for 10 hours. The solid that separated during refluxing was collected, dissolved in water and acidified with cold dilute hydrochloric acid. The solid that separated was crystallized from aqueous alcohol as colorless crystals (*ca.* 0.25 g.), m.p. 155° (not depressed when mixed with a sample of VII prepared as above).

Action of Potassium Permanganate on VII.—A solution of 0.5 g. of VII in 30 ml. of acetone was treated portionwise with 40 ml. of 5% aqueous potassium permanganate solution. The reaction mixture was refluxed for 2 hours, cooled and poured onto ice-cold water. It was extracted with ether, dried and evaporated. A solution of the oily residue in 4 ml. of absolute alcohol was treated with a concentrated alcoholic solution of 2,4-dinitrophenylhydrazine containing a few drops of concentrated hydrochloric acid. The reaction mixture was refluxed for 10 minutes and the separated crystals, upon cooling, were collected and identified as benzophenone 2,4-dinitrophenylhydrazone (m.p. and mixed m.p.).

Acknowledgment.—The authors are indebted to Professor C. L. Stevens of Wayne State University for the determination of the infrared and ultraviolet absorption spectra.

(11) Prepared after E. P. Kohler and C. Heritage, *Am. Chem. J.*, **33**, 21 (1905); E. P. Kohler and R. M. Johnstin, *ibid.*, **33**, 35 (1905).

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Cyclization of Acylaminoalkanols to 2-Oxazolines[1]

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RECEIVED AUGUST 21, 1959

Through the use of *o*-toluenesulfonyl chloride and pyridine it has been found possible to form 2-oxazolines from acylaminoalkanols in which the amido group is attached to primary, secondary or tertiary carbon, and the alcohol is primary or secondary. The yield of oxazoline ranged from 21–85% depending upon the structure of the acylaminoalkanol. Sulfonic acid esters are suggested as intermediates.

In earlier work in this Laboratory[2] it was found that the treatment of various N-aroyl derivatives of 2-methyl-2-amino-1-propanol (I) with *p*-toluenesulfonyl chloride in pyridine gave excellent yields of the corresponding 2-aryl-4,4-dimethyl-2-oxazolines. This work has been extended to other amides of (I), and to the preparation of 2-oxazolines from N-aroyl derivatives of 2-aminoethanol (II), 2-amino-1-butanol (III) and 1-amino-2-propanol (IV). The amides and oxazolines which were prepared are listed in Tables I and II.

(1) Abstracted from a thesis submitted by Robert C. Rittner in partial fulfillment of the requirements for the degree of Doctor of Philosophy, New York University, February, 1954, and presented at the 124th Meeting of the American Chemical Society, Chicago, Ill., September, 1953.

(2) R. N. Boyd and R. H. Hansen, THIS JOURNAL, **75**, 5896 (1953).

The oxazolines from I were prepared in the manner previously outlined,[2] at temperatures below 20° but with the use of *o*-toluenesulfonyl chloride (b.p. 129–131° (14 mm.)). When the same procedure was followed with the *p*-chloro- and *p*-ethoxybenzamides of II, the chief products were the corresponding chloroamides, $ArCONHCH_2CH_2Cl$, rather than the oxazolines. Since it was possible that a chloro compound might have arisen from the action of hydrochloric acid in the course of attempted isolation of an oxazoline (see Experimental section), one isolation sequence was run (with Ar = *p*-chlorophenyl) in the absence of hydrochloric acid, and in another hydrobromic acid was substituted for hydrochloric acid. In both cases, the chloroamide was the product. Thus, it appeared likely that the chloroamide was