prepared from acetic anhydride and morpholine. The principal absorption bands were identical, but the unknown curve contained a few additional bands. The authentic acetomorpholide gave a hydrobromide, m.p. 172–175°, which gave a mixed melting point of (sinter 156) 169–171° with the hydrobromide above. These results show the liquid product to be principally acetomorpholide.

The solid, fraction V, was recrystallized from 95% alcohol. The melting point was 89–91.2° (reported[4] for thioacetomorpholide, m.p. 88–90.3°). *Anal.* Calcd. for $C_6H_{11}NOS$: N, 9.65; S, 22.05. Found: N, 9.43; S, 22.80. The amount of acetomorpholide formed as calculated from the analyses of fractions III–V was about 16 g. or 0.124 mole, and the yield of thioacetomorpholide was about 12.6 g. or 0.087 mole. The theoretical yield from 0.4 mole of morpholine is 0.125 mole for each compound. The residue was extracted with alcohol, treated with Nuchar, filtered and cooled, but no crystalline solid separated.

The same experiment with benzene in place of cyclohexene gave 0.148 mole of hydrogen sulfide. The liquid and solids were washed out of the Carius tube with anhydrous acetone to obviate any hydrolysis. Distillation gave I (after removal of solvent), 10.9 g. of liquid, b.p. 88–100° (3–2 mm.), n^{25}D 1.4806; II, 9.3 g. liquid and 3.1 g. solid distilling at 113–135° (3–2 mm.). The residue weighed 12.0 g. and was a viscous black tar. The liquid fractions were redistilled to give 8.0 g. of acetomorpholide, b.p. 125–131.5° (24 mm.), n^{25}D 1.4777. The solid was crystallized from alcohol to give thioacetomorpholide, m.p. 89.8–93.1°. Found: N, 9.73; S, 22.5.

An exactly similar reaction was done with 11.2 g. of diisobutylene (commercial product redistilled, b.p. 100.5–102.0°, n^{25}D 1.4082), in place of cyclohexene. Distillation gave a small amount of unidentified C_8 mercaptans (1.1 g., b.p. 56–58° (25 mm.), n^{25}D 1.4510); and (1.2 g. b.p. 72–80° (25 mm.), n^{25}D 1.4565); 18 g. of acetomorpholide, mixed with thioacetomorpholide, b.p. 123–134° (26–28 mm.), n^{25}D 1.4752 and 1.4896; and 7.3 g. of thioacetomorpholide, b.p. 96–135° (1.0–1.5 mm.) and m.p. 88–90°. No crystalline product could be isolated from the alcohol extract of the pot residue.

A fairly clean-cut separation of acetomorpholide from the liquid fractions was made by washing with 50 cc. of water and extracting the insoluble oil with ether. The ether dissolved most of the thioacetomorpholide and the aqueous solution when evaporated down was extracted with chloroform. Distillation of the chloroform solution gave acetomorpholide, b.p. 128–135° (25 mm.), n^{25}D 1.4769. Found: C, 53.2; H, 8.3; S, 0.4; N, 10.8.

Morpholine and Sulfur Alone in Sealed Tube.—The reaction was done without any solvent present, but otherwise identical amounts and conditions as in previous experiments. There was obtained 0.16 mole of hydrogen sulfide, and working up as in the previous experiment gave I, 3.4 g. of liquid, b.p. 38–42° (120 mm.), n_D^{25} 1.4009, II, 10.2 g. liquid, b.p. 112–119° (14 mm.), n^{25}D 1.4800; III, 4.0 g. liquid, b.p. 92–100° (3–4 mm.), n^{25}D 1.4858; and IV, 3.6 g., solidifying in side-arm, b.p. 102–117° (1.5 mm.). The residue was extracted with boiling alcohol and then acetone and the alcohol solution, when cool, deposited needles, m.p. 260–265°, 0.01 g., which may be dithioöxalomorpholide. Analysis of the distilled fractions showed II and III to be mostly acetomorpholide and IV to be mostly thioacetomorpholide.

Morpholine and Sulfur under Reflux Conditions.—The experiment reported by Horton and Van Den Berghe was repeated exactly as described using 35.0 g. (0.4 mole) of morpholine and 12.8 g. (0.4 atom) of sulfur, and the amount of dithioöxalomorpholide isolated was 2.44 g., m.p. range 205–210°. This is a yield of 14% based on a theoretical yield of 0.066 mole, assuming that only thioacetomorpholide is the intermediate. Distillation of the filtrate through a 5-inch Vigreux column gave I, 2.0 g., b.p. 38° (25 mm.), n^{25}D 1.4520; II, b.p. 105° (2 mm.), 2.0 g. of liquid which was identified as principally acetomorpholide by its infrared spectrum; and finally III, b.p. 105–139° (2 mm.), 2.9 g. of liquid which solidified in the side-arm and when recrystallized melted at 89–92°. It was thioacetomorpholide. Found: N, 9.73; S, 22.10. The pot residue weighed 6.2 g. and was extracted with hot alcohol, treated with activated charcoal and filtered. The dark solution deposited 1.8 g. of solid of broad melting range which was not further examined.

WILMINGTON, DELAWARE

[CONTRIBUTION FROM THE WEIZMANN INSTITUTE OF SCIENCE AND THE SCIENTIFIC DEPARTMENT, ISRAELI MINISTRY OF DEFENCE]

The Structure of the Products of Condensation between Primary β-Hydroxyamines and Aliphatic Carbonyl Compounds

BY ERNST D. BERGMANN, E. GIL-AV[1] AND S. PINCHAS

RECEIVED JANUARY 7, 1952

The dependence of the structure of the condensation products between primary β-hydroxyamines and aliphatic ketones (oxazolidines or Schiff bases), on the structure of the ketones has been investigated. Molecular refraction and infrared spectrum of the products have been used as criteria. Whilst, generally speaking, 3-methyl-2-amino-3-butanol, $(CH_3)_2$-(OH)-CH(CH_3)-NH$_2$, gives oxazolidines, ethanolamine yields with highly shielded ketones larger amounts of the Schiff base than with straight-chain ketones. Moreover, the structure of some of the condensation products is dependent on the concentration, the system oxazolidine ⇄ Schiff base being in a state of mobile equilibrium.

The reaction between primary β-hydroxyamines and carbonyl compounds, which can lead either to Schiff bases (A) or oxazolidines (B), tends to give the former (A) if their C═N double bond is stabilized by resonance, otherwise the cyclic compound (B).[2] However, exceptions from this rule have already been observed by Cope and Hancock[3] for products derived from methyl isobutyl ketone and diisobutyl ketone, and by Bergmann, *et al.*,[4] for condensation products of aminoalcohols with pinacolone and 2-methyl-2-phenyl-4-pentanone and Daasch[5] has assigned a Schiff base structure to the condensation products of ethanolamine with methyl propyl and methyl amyl ketones, respectively, on the basis of a qualitative interpretation of their infrared spectra.

The structure of the condensation products of *aliphatic* ketones and primary β-hydroxyamines has, therefore, been reinvestigated to a better ap-

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(1) Part of a Thesis presented by E. Gil-Av to the Hebrew University, Jerusalem, in partial fulfillment of the requirements for the degree of Ph.D.

(2) E. Bergmann, E. Zimkin and S. Pinchas, *Rec. trav. chim.*, **71**, 168 (1952).

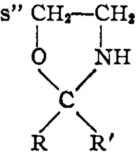
(3) A. C. Cope and E. M. Hancock, THIS JOURNAL, **64**, 1503 (1942).

(4) E. Bergmann, E. Fischer, E. Zimkin and S. Pinchas, *Rec. trav. chim.*, **71**, 213 (1952).

(5) L. W. Daasch, THIS JOURNAL, **73**, 4523 (1951).

TABLE I

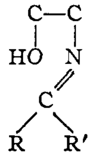
PHYSICAL CONSTANTS OF "OXAZOLIDINES"



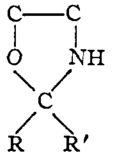
No.	R	R′	B.p., °C.	Mm.	n^{20}_D	d^{20}_4	M^{20}_D Obsd.	Calcd.[a]	C=N region	Infrared spectrum (cm.$^{-1}$) HO—C—N Region			
I	CH_3	CH_3	65	100	1.4553	0.9587	28.65	28.33	1662[b]	1035	1101	1139	1183
II	CH_3	C_2H_5	81.5–82	100	1.4448	.9341	32.84	32.95	.[c]		1103	1135	1161
III	CH_3	n-C_3H_7	77–78	22	1.4435	.9209	37.39	37.58	1660	1062	1105	1140	1165
IV	n-C_3H_7	n-C_3H_7	102–104	20	1.4458	.9017	46.50	46.82	1650	1076 (shoulder)	1107	1128	1179

For pure oxazolidine, without taking into account the specific depression of the oxazolidine ring. [b] Weak C=O absorption at 1712 cm.$^{-1}$. [c] Weak C=O absorption at 1718 cm.$^{-1}$.

proximation, using largely the experimental data obtained previously. The two criteria employed were, as in previous communications, the molecular refraction and the infrared absorption spectrum.



A



B

(1).—It has been shown[2,3] that the oxazolidine ring depresses the molecular refraction by about 0.5. This together with the fact that the molecular refraction of a Schiff base (A) is 1.50 higher than that calculated for the isomeric oxazolidine (B),[6] gives a total difference of 2.0 between the two forms and thus the possibility of an approximate numerical evaluation of the observed molecular refraction in terms of the contribution of the two forms.

(2).—The extinction coefficient in the infrared can be used in order to estimate the amount of Schiff base in the condensation products, if it is assumed that this coefficient is constant[7] in the series of compounds under investigation. An evaluation of the molecular extinction coefficient of the pure Schiff base can be made, for instance, taking as a basis the data of Daasch[5] for the diisobutyl ketone derivative V (ϵ 150), which contains about 80% of the open form (A), according to its molecular refraction.

It was first assumed that intermolecular forces did not influence the equilibrium between the two forms. In fact, a comparison of the results from the evaluation of the extinction coefficients of the compounds, determined in solution and listed in Table II, with the percentages of open structure, calculated from the molecular refraction, determined on the pure liquids, seemed on the whole to bear out this assumption.[8] The discrepancies observed were within the limits of the errors of the methods.

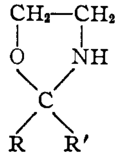
However, comparison of the absorption data found for the solution of the ethanolamine–methyl propyl ketone product (III) with the data of Daasch,[5] observed on the pure liquid, as well as the determination of the absorption of a number of compounds at different dilutions[9] showed that some of the compounds exhibit a change of the ratio oxazolidine : Schiff base with changes of the concentrations. These systems are in a state of mobile equilibrium. As this superposition of intermolecular forces obscures the effect of the substituents on the structure of the condensation products, conclusions drawn from the results must be of a very general nature (Table II).

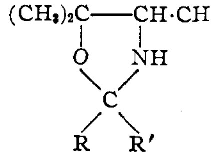
In the series of the compounds derived from ethanolamine, the measurements made confirm the view that ketones, in which the carbonyl group is

TABLE II

SCHIFF BASE (A) CONTENT IN "OXAZOLIDINES"

(a)



No.	R	R′	Concn., mole/l.	Infrared spectrum Molar extinction coefficient of C=N band	% Schiff base calculated from M^{20}_D
I	CH_3	CH_3	1.05	40	40
II	CH_3	C_2H_5	0.75	25	20
III	CH_3	n-C_3H_7	.6	35	20
IV	n-C_3H_7	n-C_3H_7	.45	30	10
V	i-C_4H_9	i-C_4H_9	.4	125	80
VI	CH_3	i-C_4H_9	.6	90	70
VII	CH_3	t-C_4H_9	.5	65	25
VIII	CH_3	2-Methyl-2-phenylpropyl	.55	70	35
		(b) 			
IX	CH_3	2-Methyl-2-phenylpropyl	0.35	80	50

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(6) As calculated from Eisenlohr's atomic refraction values.

(7) L. H. Cross and A. C. Rolfe, *Trans. Faraday Soc.*, **47**, 354 (1951); D. Barnard, *et al.*, *J. Chem. Soc.*, 915 (1950); Y. A. Anderson and W. D. Seyfried, *Anal. Chem.*, **20**, 998 (1948).

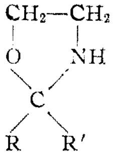
(8) It has also been shown (E. Gil-Av and Y. Hirshberg, unpublished results) that the ultraviolet absorption spectra of 2-phenyl-4,5,5-trimethyl-, 2-phenyl-2,4,5,5-tetramethyl- and 2-(m-nitrophenyl)-2,4,5,5-tetramethyloxazolidine are practically independent of the solvent (n-heptane and ethyl alcohol).

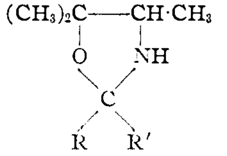
(9) The ethanolamine derivative of acetone (I) showed a drop in extinction coefficient of 60% when the concentration was reduced from 1.2 to 0.6 mole/l. and the derivative of methyl ethyl ketone (II) a decrease by 40% as its concentration was decreased from 1.05 to 0.1 mole/l.

TABLE III

TEMPERATURE DEPENDENCE OF THE MOLECULAR REFRACTION OF SOME "OXAZOLIDINES"

(a)



No.	R	R′	n^{30}_D	d^{30}_4	M^{30}_D	n^{60}_D	d^{60}_4	M^{60}_D	Δ
III	CH_3	n-C_3H_7	1.4453	0.9209	37.39	1.4352	0.8920	37.82	0.43
IV	n-C_3H_7	n-C_3H_7	1.4458	.9017	46.50	1.4370	.8756	47.00	.56
		(b)							
IX	CH_3	2-Methyl-2-phenylpropyl	1.5024	0.9581	80.57	1.4912	0.9359	81.04	0.47
X	CH_3	t-C_4H_9	1.4372	.8799	55.34	1.4264	.8546	55.61	.27

highly shielded, show a pronounced tendency to form Schiff bases. As, however, pinacolone (VII) gives more of the cyclic product than methyl isobutyl ketone (VI), both according to the molecular refraction and the extinction coefficient, other than simply steric factors must play a part in determining the structure of the condensation products.

Ethanolamine derivatives of straight-chain aliphatic ketones, (I) to (IV), contain usually less of the open structure,[10] especially if examined in dilute solutions.

As shown before[2] compounds derived from 3-methyl-2-amino-3-butanol, on the other hand, tend much more to give oxazolidines, perhaps because of the influence of the substitution on the valency angles in the aminoalcohol. Thus, even the condensation products with methyl isobutyl ketone, pinacolone and diisobutyl ketone[2,4] do not contain any appreciable amount of Schiff base. The derivative IX of 2-methyl-2-phenyl-4-pentanone, however, consists of about 50% of the open form, and its structure seems to be only little influenced by dilution.

Metzger[11] has investigated the temperature dependence of the equilibrium (A) $\rightleftarrows$ (B), in a number of cases. He considered a change of the molecular refraction with temperature equal to or smaller than 0.22 for the interval 30–60° as the "normal" effect[12]; greater changes were ascribed to a shift of the equilibrium from the cyclic to the open form. This method has been applied to the substances listed in Table III. They all show increases larger than 0.22 in the temperature range from 30–60°. At least for substances (III), (IV) and (IX) (increase: 0.43, 0.56, 0.47) there appears, therefore, to exist also a thermal shift of the equilibrium toward the open form.

Experimental

The condensation products of ethanolamine and diisobutyl ketone (V), methyl isobutyl ketone (VI), pinacolone (VII) and 2-methyl-2-phenyl-4-pentanone (VIII) as well as those of 3-methyl-2-amino-3-butanol and 2-methyl-2-phenyl-4-pentanone (IX) and pinacolone (X) have been described before.[2]

2,2-Dimethyloxazolidine (I).[9]—A mixture of 0.25 mole each of acetone and ethanolamine was condensed azeotropically in boiling benzene[2]; the theoretical amount of water collected in a trap within 4.5 hours. The resulting solution was fractionated in a Todd column, first at atmospheric pressure, then *in vacuo*. The oxazolidine distilled at 64–65° (100 mm.), yield 14 g. (65%).

Anal. Calcd. for $C_5H_{11}NO$: N, 13.8. Found: N, 13.6.

The product has to be used immediately, as it changes upon standing. The molecular weight (theory, 101), which was found to be correct (found, 104) after the fractionation, changed considerably with time (after one week, found, 160), and also the refractive index changed with time.

2-Methyl-2-ethyloxazolidine (II).—When 0.2 mole each of methyl ethyl ketone and ethanolamine were condensed as above, 13.7 g. of crude product was obtained. Fractionation gave 11.2 g. (50%) of the pure substance, b.p. 81.5–82° (100 mm.).

Anal. Calcd. for $C_6H_{13}NO$: N, 12.2; mol. wt., 115. Found: N, 11.9; mol. wt., 119.

2-Methyl-2-*n*-propyloxazolidine (III).—This product which has been described before[2] is best obtained when 6.0 g. of methyl propyl ketone and 4.0 g. of ethanolamine are azeotropically condensed in boiling benzene in presence of a small quantity of iodine; the reaction is complete after two hours. From the crude product (8.9 g.), a yield of 3.4 g. (40%) of the oxazolidine was obtained by fractionation; b.p. 77–78° (22 mm.). This product, however, was only 95.6% pure, as the last traces of ethanolamine (b.p. 74° (22 mm.)) could not be eliminated by fractionation.

Anal. Calcd. for $C_7H_{15}NO$: N, 10.8. Found: N, 11.3.

2,2-Di-*n*-propyloxazolidine (IV).—The condensation of 0.1 mole each of di-*n*-propyl ketone and ethanolamine was carried out as in the preceding example. The product is distilled at 102–104° (20 mm.), yield 9.0 g. (57%).

Anal. Calcd. for $C_9H_{19}NO$: N, 8.9. Found: N, 8.8.

An attempt was also made to prepare in the same manner oxazolidines from ethanolamine and the simplest aliphatic aldehydes.[13] The product obtained with propionaldehyde resinified upon distillation; that from butyraldehyde could not be separated from ethanolamine. In the latter case,

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(10) J. B. Doughty, *et al.*, THIS JOURNAL, **72**, 2866 (1950), have prepared a number of oxazolidines from ethylenimine and carbonyl compounds. The molecular refractions of the 2-ethyl-, 2-propyl-, 2-isopropyl- and 2,2-dimethyl derivatives point to the presence of certain amounts of Schiff base in the products. See also ref. 1 (Table III).

(11) J. Metzger, *Rec. trav. chim.*, **71**, 243 ff. (1952).

(12) In contradistinction with current belief, the molecular refraction has a slight temperature coefficient (Weissberger, "Physical Methods of Organic Chemistry," Vol. I, Interscience Publishers, Inc., New York, N. Y., 1949, p. 1177).

(13) The condensation product of ethanolamine and formaldehyde described by A. M. Paquin (*Ber.*, **82**, 316 (1949)) is not the unsubstituted oxazolidine, as already evident from its high boiling point (100° (6–7 mm.)).

the infrared spectrum of the crude product showed the band characteristic of the C═N double bond.

The physical constants of the above four products are given in Table I.

The infrared spectra were measured in approximately 10% solutions in carbon tetrachloride using a Perkin-Elmer infrared spectrometer model 12C, equipped with a rock salt prism. The refractive indices were determined with a Bausch and Lomb precision refractometer.

REHOVOTH AND TEL-AVIV, ISRAEL

[CONTRIBUTION FROM THE CALIFORNIA RESEARCH CORPORATION]

t-Alkyl Groups. I. Orientation of *t*-Alkylation Products of Toluene and Ethylbenzene

BY MAURICE J. SCHLATTER AND ROBERT D. CLARK

RECEIVED JULY 28, 1952

t-Butyltoluenes obtained by alkylation ranged in composition from the 67% meta, 33% para equilibrium ratio to 7% meta, 93% para. Recurrence of this latter composition strongly suggests that it is a true limiting value. *o*-*t*-Butyl or *o*-*t*-amyl derivatives of toluene and ethylbenzene were not found in any of the *t*-alkylation products investigated, but ortho derivatives were found when *n*- and *s*-alkyl groups were introduced. Controversial *t*-alkylations were repeated and the products analyzed by infrared spectrometric methods.

The object of this research was to obtain accurate analyses of *t*-alkylation products of toluene and ethylbenzene in preparation for study of the factors controlling orientation in these alkylations. For completeness a number of cases were reinvestigated which were the subject of controversy or which were in apparent disagreement with our findings. These studies were greatly facilitated by the use of infrared spectrometry in the analysis of the hydrocarbon mixtures. This technique is rapid, accurate and not subject to the errors inherent in most of the methods formerly available for solving this otherwise very difficult analytical problem.

A series of alkylations of toluene with a variety of *t*-butylating agents and catalysts are summarized in Table I, along with several *t*-amylations of toluene and *t*-butylations of ethylbenzene. Alkylations of toluene with other than *t*-alkylating agents are presented in Table II. A clear cut difference between *t*-alkyl groups and other alkyl groups in the ortho-alkylation of alkylbenzenes is evident on comparing the isomer analyses in Table I with those in Table II. No appreciable amount of ortho-isomer was detected in the products from the *t*-butylation or *t*-amylation of toluene or ethylbenzene.[1] On the other hand, all three isomers were obtained in all cases where other than *t*-alkylating agents were used. It is of interest that even the diisopropylbenzene fraction from the alkylation of benzene with propylene over a "solid phosphoric acid" catalyst has been shown to contain an appreciable amount of ortho isomer.[2]

t-Butylation of toluene (Table I) gave *t*-butyltoluene fractions ranging in composition from 67 ± 3% meta, 33 ± 3% para to 7 ± 3% meta, 93 ± 3% para with several cases at each extreme. Isomerization experiments (Table IV) showed the former composition to be the equilibrium ratio. Recurrence of the latter composition strongly suggests that it too is a true limiting value. In the intermediate region between the composition limits indicated above, the meta–para ratio appears to be quite sensitive to small variations in the amount of catalyst and in the alkylation procedure.

The recurrence of the 7% meta, 93% para *t*-butyltoluene ratio under mild alkylating conditions suggests that this is the initial product and that other product compositions result from isomerization of this. The data in this paper, however, do not exclude the possibility that different meta–para ratios may result from alkylation in the very different environments existing in the catalyst and hydrocarbon phases or at the interface between hydrocarbon and catalyst phase. Likewise, the data do not preclude the possibility that the meta component in this initial product may result entirely or in part from attack of the alkylating agent on the ortho position followed either by rearrangement of the *o*-*t*-butyltoluene or of the alkylation intermediate.

Several *t*-alkylations which had been reported to give only the meta or the para isomer were repeated (expts. 8, 9, 10, 15) and were found to give mixtures of meta and para isomers falling in the range defined above.[3] Similarly, although selective *p*-alkylation has been claimed in alkylations with other than *t*-alkylating agents, those repeated here (Table II) gave considerable quantities of all three isomers. This result is in essential agreement with reports of recent studies in which spectrometric analytical methods were used.[4]

The *t*-amylations of toluene and *t*-butylations of ethylbenzene reported in Table I are not adequate to establish the limiting compositions of the alkylates in these systems. However, these limits must fall outside of the 72–20% meta and 28–80% para ranges in the former case and the 45–15% meta and 55–85% para ranges in the latter.

Several isomerization experiments were carried out in order to obtain information on the relative ease of isomerization of the *t*-butyltoluene isomers and to determine the equilibrium composition for comparison with the isomer ratios in the alkylation products. These are summarized in Tables III

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(1) This result is consistent with reports of similar alkylations by (a) E. Noelting, *Chimie & industrie*, **6**, 719 (1921); (b) K. T. Serijan, H. F. Hipsher and L. C. Gibbons, THIS JOURNAL, **71**, 873 (1949).

(2) F. W. Melpolder, J. E. Woodbridge and C. E. Headington, *ibid.*, **70**, 935 (1948).

(3) This general result is in accordance with J. H. Simons and H. Hart, *ibid.*, **69**, 979 (1947), and Serijan, *et al.*, reference 1b.

(4) (a) F. E. Condon, *ibid.*, **71**, 3544 (1949); (b) W. M. Kutz, J. E. Nickels, J. J. McGovern and B. B. Corson, *J. Org. Chem.*, **16**, 699 (1951).