Structure and Reactivity. I. The Oximation Rates of Some Straight-Chain and Monomethyl-Substituted Alkanones

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The oximation rates have been determined for 65 straight-chain and monomethyl-substituted alkanones. The methyl ketones are the most reactive of the straight-chain ketones studied, followed by the ethyl ketones. The propyl and higher ketones have the same rate. A methyl group on the first carbon adjacent to the carbonyl group lowers the rate the most as compared to the corresponding straight-chain compounds. This decreased rate is observed to a smaller degree if the methyl group is on the second carbon, while a methyl group on the third carbon has no effect on the rate.

The rate of oxime formation of various alkanones has been the subject of a number of investigations.[1-8] However, no systematic or extended study has been reported. This paper reports the oximation rates of 65 alkanones at 20°. These compounds have been selected in such a manner that the oximation rate is defined with a high degree of probability for all of the theoretically possible structurally isomeric straight-chain and monomethyl-substituted alkanones up to and including fifteen carbon atoms.

The early investigators generally worked with equilibrium mixtures, as nothing was added to remove the hydrogen chloride liberated during the formation of the oxime. Bryant and Smith[5] found pyridine to be a satisfactory base for this purpose, thus driving the reaction to completion. These investigators used this fact to devise a generally useful method for the quantitative estimation of carbonyl groups.[5] Their method, slightly modified, has been found satisfactory for determining the oximation rates reported in this paper.

The results are shown in Table I. The methyl ketones (1–9) are the most reactive, followed by the ethyl ketones (10–16). In both series the rate becomes constant with the third and second member, respectively. The *n*-propyl and higher ketones (17–27) have the same rate. The above order of reactivity holds true for all of the branched homologous series shown in Table I, the isopropyl ketones (28–34) serving as an example. *sec*-Butyl (35–40), 1-methylbutyl (41–46), and higher 1-methylalkyl ketones have the same rate, as 1-methylheptyl ethyl ketone (47) has the same rate as the corresponding lower members (36 and 42). With the exception of their methyl ketones, the isobutyl (49–52) and the isopropyl ketones have the same rate. The identity of their rates was confirmed by testing several pairs of ketones simultaneously, 29 with 49, and 31 with 51. In both cases the color changes were identical. The 2-methylbutyl ketones (53–56) are slightly less reactive than the corresponding isobutyl ketones, the higher homolog (57) being of the same order of reactivity. The isopentyl[9] (58–60) and isohexyl ketones (62–64), as well as several of their homologs (61 and 65),

have the same rate as the corresponding straight-chain ketones.

The above results are in general agreement with previous studies on the oximation rate of ketones. From a consideration of the work of Petrenko-Kritschenko and co-workers[1,3] together with their own results, Ruzicka and Buijs[4] concluded that the *n*-alkyl methyl ketones have the same oximation rate while the symmetrical di-*n*-alkyl ketones have a lower but otherwise identical rate. Pringsheim and Gorgas[10] found that 2-pentanone forms the oxime more rapidly than 3-pentanone. Bryant and Smith[5] and Vavon and co-workers[7,8] found that a methyl group or groups adjacent to the carbonyl group results in a lower oximation rate.

The results are also compatible with a variety of rate studies on other groups.[11] As indicated above, in a given homologous series the methyl and ethyl ketones are the most reactive, followed by the propyl and higher ketones. This same order of reactivity has been observed with the *n*-alkyl halides in their reaction with sodium phenoxide,[12] sodium eugenoxide,[13] sodium guaiacoxide,[14] sodium *m*-4-xylyloxide,[15] sodium benzyloxide,[16] piperidine,[17] sodium thiocyanate,[18] and potassium iodide.[19] The observation that the thirty-carbon myricyl chloride[19] has the same order of reactivity as the lower chlorides suggests that the conclusions on oximation rates reported in this paper may be extended to higher ketones.[20] The isobutyl and isopentyl halides[12,13,17] have lower rates while isohexyl bromide[18] has the same rate as the normal bromide. Asinger and Eckoldt[21] determined the rate of reaction between cyclohexylamine and the 1-, 2-, 3-, 4-, 5-, 7-, and 8-bromohexadecanes. The 3- to 8- had the same rate; the 2-isomer had twice the rate while the 1-isomer had one-hundred times the rate of the 3- to 8-isomers. Asinger

(1) P. Petrenko-Kritschenko and S. Lordkipanidze, *Ber.*, **34**, 1702 (1901).

(2) A. W. Stewart, *J. Chem. Soc.*, 410 (1905).

(3) P. Petrenko-Kritschenko and W. Kantscheff, *Ber.*, **39**, 1452 (1906).

(4) L. Ruzicka and J. B. Buijs, *Helv. Chim. Acta*, **15**, 8 (1932).

(5) W. M. D. Bryant and D. M. Smith, *J. Am. Chem. Soc.*, **57**, 57 (1935); S. Siggia, "Quantitative Organic Analysis *via* Functional Groups," 2nd Ed., John Wiley and Sons, Inc., New York, N. Y., 1954, pp. 28–30.

(6) A. R. Poggi, R. Biffoli, and C. Stella, *Gazz. chim. ital.*, **77**, 536 (1947); *Chem. Abstr.*, **42**, 3335 (1948).

(7) G. Vavon and P. Anziani, *Bull. soc. chim. France*, 2026 (1937).

(8) G. Vavon and D. Ivanoff, *Compt. rend.*, **177**, 453 (1923).

(9) The ketones were prepared from 4-methylpentanoic acid obtained from isobutyl bromide through the malonic ester synthesis. Ketones prepared from commercial isopentyl bromide always gave longer reaction times, presumably due to the presence of 2-methylbutyl bromide as an impurity.

(10) H. Pringsheim and A. Gorgas, *Ber.*, **57**, 1561 (1924).

(11) The following literature survey is not intended to be complete.

(12) D. Segaller, *J. Chem. Soc.*, 1154 (1913).

(13) S. S. Woolf, *ibid.*, 1172 (1937).

(14) J. A. Mitchell, *ibid.*, 1792 (1937).

(15) P. J. Hardwick, *ibid.*, 141 (1935).

(16) P. C. Haywood, *ibid.*, 1904 (1922); L. J. Goldsworthy [*ibid.*, 1102 (1926)] pointed out that sodium ethoxide is actually the reactive alkoxide present.

(17) S. M. McElvain and J. Semb, *J. Am. Chem. Soc.*, **53**, 690 (1931).

(18) T. I. Crowell, *ibid.*, **75**, 6046 (1953).

(19) J. B. Conant and R. E. Hussey, *ibid.*, **47**, 476 (1925).

(20) Attempts to determine the oximation rates of 12-tricosanone and 18-pentatriacontanone were unsuccessful owing to their insolubility in methanol.

(21) F. Asinger and H. Eckoldt, *Ber.*, **76**, 579 (1943).

TABLE I

OXIMATION RATES OF SOME ALKANONES

Com-pound no.	Ketone	Preparation Method	R of R-MgBr	0.5 N NaOH required, ml.	25% reaction	50% reaction	90% reaction	k, av.
					Second-order velocity constants for			
1	2-Propanone[a]			15.0			250.0	250.0
2	2-Butanone[a]			15.0			107.4	107.4
3	2-Pentanone[a]			14.9			68.2	68.2
4	2-Hexanone	A	Butyl	15.0			68.2	68.2
5	2-Heptanone[a]			14.9			68.2	68.2
6	2-Octanone[a]			14.8			68.2	68.2
7	2-Nonanone	A	Heptyl	14.8			68.2	68.2
8	2-Decanone	A	Octyl	15.0			68.2	68.2
9	2-Heptadecanone[a, b]			14.8			68.2	68.2
10	3-Pentanone[a]			14.8		24.4	20.8	22.6
11	3-Hexanone	A	Propyl	15.0	15.74	15.50	15.65	15.6
12	3-Heptanone[a]			14.9	15.74	15.50	15.65	15.6
13	3-Octanone	A	Pentyl	14.8	15.74	15.50	15.65	15.6
14	3-Nonanone	A	Ethyl	15.0	15.74	15.50	15.65	15.6
15	3-Decanone	A	Heptyl	14.8	15.74	15.50	15.65	15.6
16	3-Pentadecanone	B	Dodecyl	13.8	15.74	15.50	15.65	15.6
17	4-Heptanone	A	Propyl	15.0	10.46	10.65	9.63	10.2
18	4-Octanone	A	Butyl	15.0	10.46	10.65	9.63	10.2
19	4-Nonanone	A	Pentyl	15.0	10.46	10.65	8.94	10.0
20	4-Decanone	A	Propyl	15.0	10.46	10.65	8.94	10.0
21	4-Pentadecanone	B	Propyl	14.7	10.46	10.65	8.94	10.0
22	5-Nonanone	A	Butyl	15.0	10.46	10.65	8.94	10.0
23	5-Decanone	A	Pentyl	15.1	10.46	10.65	8.94	10.0
24	5-Pentadecanone	A	Decyl	14.7	10.46	10.65	8.94	10.0
25	6-Pentadecanone	B	Pentyl	14.5	10.46	10.65	8.94	10.0
26	7-Pentadecanone	A	Octyl	14.8	10.46	10.65	8.94	10.0
27	8-Pentadecanone	B	Heptyl	14.6	10.46	10.65	8.94	10.0
28	3-Methyl-2-butanone[a]			14.8		24.4	25.0	24.7
29	2-Methyl-3-pentanone	A	Ethyl	15.1	1.74	1.67	1.42	1.61
30	2-Methyl-3-hexanone	A	Propyl	15.1	1.16	1.09	0.947	1.066
31	2-Methyl-3-heptanone	A	Butyl	15.1	1.16	1.09	0.977	1.076
32	2-Methyl-3-octanone	A	Pentyl	15.1	1.16	1.09	0.977	1.076
33	2-Methyl-3-nonanone	A	Hexyl	14.9	1.16	1.09	1.01	1.09
34	2-Methyl-3-tridecanone	A	Decyl	14.9	1.16	1.14	1.14	1.15
35	3-Methyl-2-pentanone	A	sec-Butyl	15.1	8.98	9.0	7.82	8.60
36	4-Methyl-3-hexanone	A	sec-Butyl	15.1	0.55	0.51	0.466	0.509
37	3-Methyl-4-heptanone	A	sec-Butyl	15.1	0.35	0.33	0.298	0.326
38	3-Methyl-4-octanone	A	sec-Butyl	15.1	0.35	0.33	0.298	0.326

and co-workers[22] studied the alkaline hydrolysis of the acetates and benzoates of 1-, 2-, 3-, and 4-octanol. The acetate rate ratios were 30:4:1.4:1 and the benzoate ratios 3.9:3.1:1:1. Similar results were obtained by Dorough and co-workers[23] in the acylation of the same octanols with acetic acid in sealed tubes and acetic anhydride in acetone. These same investigators also used the same reagents to determine the acylation rates of a number of methylheptanols. A methyl group adjacent to the hydroxyl group always resulted in a lower rate. Norris and Cortese[24] determined the reaction rate of a number of alkanols with p-nitrobenzoyl chloride in ether. Methanol was the most reactive, followed by ethanol. n-Propyl alcohol and higher normal alkanols had the same rate. The rates of the 2-, 3-, and 4-alkanols paralleled the oximation rates of the corresponding ketones shown in Table I. The 2-methyl-1-alkanols had the same rate, comparable to **49**, **54**, and **57** in Table I. The 3- and 4-methyl 1-alkanols had the same rate as the normal alkanols.

Experimental

Preparation of Ketones.—Unless otherwise indicated, the ketones were prepared by the following two methods.

Method A.—A Grignard reagent (see Table I) was treated with an aldehyde and the resulting carbinol was oxidized to the corresponding ketone with a sodium dichromate–sulfuric acid mixture according to Sandborn.[25] The carbinol yields were 50 to 72%, and the ketone yields were 61 to 83%.

Method B.—A Grignard reagent (see Table I) was converted to the cadmium dialkyl which was treated with an acid chloride according to the procedure of Cason and Prout.[26] Yields were 47 to 68%.

Ethyl 3-Hydroxy-3-Methylnonanoate.[27]—Seventy-three grams (3 g.-atoms) of magnesium metal turnings and 1 g. of U.S.P. mercuric chloride were placed in a 3-l. three-necked flask equipped with a stirrer, reflux condenser, and addition funnel. The flask was swept with dry nitrogen for 10 min. before covering the metal with 450 ml. of sodium-dried ether. The stirrer was started and 20 ml. of a mixture of 384 g. (3 moles) of 2-octanone and 380 g. (3.1 moles) of ethyl chloroacetate in 900 ml. of ether was added. The mixture was stirred and warmed until the reaction started. After the reaction became vigorous, the stirrer was stopped and

(22) F. Asinger, G. Geiseler, and G. Mueller, Ber., **93** 2491 (1960).

(23) G. L. Dorough, H. B. Glass, T. L. Gresham, G. B. Malone, and E. E. Reid, J. Am. Chem. Soc., **63**, 3100 (1941).

(24) J. F. Norris and F. Cortese, ibid., **49**, 2640 (1927).

(25) L. T. Sandborn, "Organic Syntheses," Coll. Vol. I, 2nd Ed., John Wiley and Sons, Inc., New York, N. Y., 1941, p. 340.

(26) J. Cason and F. S. Prout, Org. Syn., **28**, 75 (1948).

(27) This method is the procedure of J. Colonge and D. Joly [Ann. chim. (Paris), [11]**18**, 306 (1943)] for the preparation of ethyl 3-ethyl-3-hydroxy-pentanoate.

TABLE I (Continued)

Compound no.	Ketone	Preparation Method	Preparation R of R-MgBr	0.5 N NaOH required, ml.	Second-order velocity constants for 25% reaction	50% reaction	90% reaction	k, av.
39	3-Methyl-4-nonanone[c]	B	Pentyl	14.7	0.40	0.348		0.374
40	3-Methyl-4-decanone[d]	B	Hexyl	14.9	0.35	0.33		0.34
41	3-Methyl-2-hexanone	A	Methyl	15.1	8.98	9.0	7.82	8.60
42	4-Methyl-3-heptanone	A	Ethyl	15.1	0.55	0.51	0.453	0.504
43	5-Methyl-4-octanone	A	Propyl	15.1	0.35	0.33	0.28	0.321
44	4-Methyl-5-nonanone[e]	A	Butyl	15.1	0.35	0.33	0.298	0.326
45	4-Methyl-5-decanone[f]	B	Pentyl	14.6	0.35	0.32	0.274	0.315
46	4-Methyl-5-undecanone[g]	B	Hexyl	14.6	0.33	0.30	0.271	0.30
47	4-Methyl-3-decanone	B	Ethyl	14.7	0.55	0.51	0.496	0.519
48	4-Methyl-2-pentanone[a]			15.1	12.5	11.4	11.4	11.8
49	5-Methyl-3-hexanone	A	Isobutyl	15.1	1.74	1.67	1.65	1.69
50	2-Methyl-4-heptanone	A	Isobutyl	15.1	1.16	1.09	1.04	1.096
51	2-Methyl-4-octanone	A	Isobutyl	15.1	1.16	1.09	1.04	1.096
52	2-Methyl-4-undecanone[h]	B	Isobutyl	14.6	1.16	1.14	1.08	1.126
53	4-Methyl-2-hexanone	B	Methyl	14.9	10.4	10.0	10.4	10.3
54	5-Methyl-3-heptanone	B	Ethyl	14.7	1.49	1.35	1.36	1.40
55	6-Methyl-4-octanone	B	Propyl	14.8	0.87	0.835	0.79	0.832
56	3-Methyl-5-undecanone[i]	B	Hexyl	14.7	0.87	0.835	0.736	0.814
57	5-Methyl-3-undecanone[j]	B	Ethyl	14.6	1.49	1.35	1.33	1.39
58	5-Methyl-2-hexanone[a]			15.1			68.2	68.2
59	6-Methyl-3-heptanone	B	Ethyl	14.8	15.74	15.50	15.65	15.6
60	2-Methyl-5-dodecanone[k]	B	Heptyl	14.7	10.46	11.4	10.4	10.8
61	6-Methyl-3-dodecanone[l]	A	3-Methylnonyl	14.7	15.74	15.50	15.65	15.6
62	6-Methyl-2-heptanone	B	Methyl	15.1			68.2	68.2
63	7-Methyl-3-octanone	B	Ethyl	14.5	15.74	15.50	15.65	15.6
64	8-Methyl-4-nonanone[m]	B	Propyl	14.6	10.46	10.0	8.93	9.79
65	7-Methyl-3-tridecanone[n]	B	Ethyl	14.7	15.74	15.50	15.65	15.6

[a] Commercially available. [b] Ketone was dissolved in 100 ml. of pyridine-indicator solution with warming and cooled, and 25 ml. of hydroxylamine hydrochloride solution was added. [c] New compound, b.p. 94–96° (20 mm.). Calcd. for $C_{10}H_{20}O$: CO, 17.9. Found: CO, 17.4. [d] New compound, b.p. 113–115° (25 mm.). Calcd. for $C_{11}H_{22}O$: CO, 16.4. Found: CO, 16.2. [e] New compound, b.p. 189–190° (745 mm.). Calcd. for $C_{10}H_{20}O$: CO, 17.9. Found: CO, 17.9. [f] New compound, b.p. 110–112° (23 mm.). Calcd. for $C_{11}H_{22}O$: CO, 16.4. Found: CO, 15.9. [g] New compound, b.p. 133–135° (34 mm.). Calcd. for $C_{12}H_{24}O$: CO, 15.2. Found: CO, 14.7. [h] New compound, b.p. 122–124° (20 mm.). Calcd. for $C_{12}H_{24}O$: CO, 15.2. Found: CO, 14.7. [i] New compound, b.p. 123–125° (20 mm.). Calcd. for $C_{12}H_{24}O$: CO, 15.2. Found: CO, 14.8. [j] New compound, b.p. 123–125° (24 mm.). Calcd. for $C_{12}H_{24}O$: CO, 15.2. Found: CO, 14.7. [k] New compound, b.p. 144–146° (28 mm.). Calcd. for $C_{13}H_{26}O$: CO, 14.1. Found: CO, 13.7. [l] New compound, b.p. 137–139° (22 mm.). Calcd. for $C_{13}H_{26}O$: CO, 14.1. Found: CO, 13.7. [m] New compound, b.p. 85–87° (12 mm.). Calcd. for $C_{10}H_{20}O$: CO, 17.9. Found: CO, 17.3. [n] New compound, b.p. 154–156° (22 mm.). Calcd. for $C_{14}H_{28}O$: CO, 13.2. Found: CO, 12.8.

the reaction was moderated with a bath of cold water. After the initial reaction was over, the remainder of the mixture was added with stirring as rapidly as possible with external cooling. About 45 min. was required. After the addition was complete, the cooling bath slowly was removed and the mixture finally was refluxed for 1 hr. on the steam bath. The mixture was allowed to cool and was poured onto a mixture of 1800 g. of cracked ice, 600 ml. of water, and 90 ml. of concentrated sulfuric acid. The ether layer was separated, washed once with dilute sulfuric acid, once with dilute aqueous potassium bicarbonate, dried with anhydrous potassium carbonate, and distilled. A fraction boiling at 136–138° (14 mm.) was collected. Two runs gave yields of 538 g. (83%) and 555 g. (83.5%).

Ethyl 3-Methyl-2-nonenoate.—Phosphorus pentoxide (1170 g.) was placed in a 5-l. three-necked flask equipped with a stirrer and reflux condenser. Dry, thiophene-free benzene (2 l.) was added and the mixture was heated to boiling with stirring. Ethyl 3-hydroxy-3-methylnonanoate (1 kg.) was added in 250-g. lots at 0.5-hr. intervals. As the dehydration proceeded, the mixture became viscous and stirring became impossible. The mixture was gently refluxed for a total of 4 hr., the stirrer being turned by hand at frequent intervals. The flask was allowed to cool and the benzene solution was decanted and distilled. A fraction, b.p. 122–128° (14 mm.), was collected. Most of the material boiled at 122–123° (14 mm.); yield was 747 g. (81.5%).

Ethyl 3-Methylnonanoate.[28]—The ethyl 3-methyl-2-nonenoate was reduced over platinum oxide (Engelhard Industries) in methanol at 40–50-lb. pressure. The ester boiled at 123–125° (26 mm.), yielding 95%.

(28) J. Cymerman, I. M. Heilbron, and E. R. H. Jones, J. Chem. Soc., 144 (1944).

3-Methylnonanoic Acid.—Ethyl 3-methylnonanoate (100 g., 0.5 mole) and 60 g. of sodium hydroxide dissolved in 250 ml. water were placed in a 2-l. three-necked flask equipped with a stirrer and reflux condenser. The mixture was refluxed with stirring for 2 hr. Water (250 ml.) was added and the alcohol was distilled, finally, under reduced pressure. The residue was allowed to cool, acidified with dilute sulfuric acid, extracted with ether, and distilled. A fraction boiling at 155–157° (21 mm.) was collected; yield was 75 g. (87%).

3-Methyl-1-nonanol.—Lithium aluminum hydride (35 g.) was dissolved in 1000 ml. of sodium-dried ether in a 5-l. three-necked flask equipped with a stirrer, reflux condenser, and addition funnel. Ethyl 3-methylnonanoate (294 g., 1.47 moles) dissolved in 500 ml. of ether was added drop by drop with stirring, and the mixture was stirred for 1 hr. after the addition was complete. Water (200 ml.) was then added drop by drop and the mixture was stirred for 15 min. after the addition was complete. The mixture was poured onto crushed ice and acidified with dilute sulfuric acid. The ether layer was separated, dried over anhydrous potassium carbonate, and distilled. A fraction boiling at 121–123° (20 mm.) was collected; yield was 211 g. (91%).

3-Methyl-1-bromononane.—3-Methyl-1-nonanol (211 g., 1.3 moles) was placed in a 1-l. three-necked flask equipped with a stirrer, reflux condenser, and dropping funnel. The flask was cooled to −5° with a Dry Ice–acetone bath and 400 g. of phosphorus tribromide was added drop by drop with stirring, the temperature being kept at −5 to 5°. After the addition was complete, the mixture was stirred for 1 hr. at 0–5° and then allowed to stand overnight. The mixture was poured into ice water, extracted with ether, dried over anhydrous potassium carbonate, and distilled. A fraction boiling at 109–111° (18 mm.) was collected; yield was 230 g. (78%).

5-Methylundecanoic Acid.—3-Methyl-1-bromononane (110 g., 0.5 mole) and 120 g. (0.75 mole) of diethyl malonate were placed in a 2-l. three-necked flask equipped with a stirrer and reflux condenser; t-butyl alcohol[29] (250 ml.) was added. The equivalent of 0.5 mole of a sodium hydride–mineral oil dispersion was added with stirring as rapidly as the refluxing allowed. The mixture was refluxed with stirring for 15 hr. The t-butyl alcohol was removed by distilling under reduced pressure on the water bath with stirring. Water was added to the cooled residue to dissolve the sodium bromide. The ester layer was separated and distilled· to 110° (20 mm.) to remove low boiling material. The residue was hydrolyzed according to Vliet, Marvel, and Hsueh.[30] After the 3-hr. heating period with sulfuric acid was completed, the mixture was allowed to cool and the top layer was taken up in ether. The ether was distilled and the decarboxylation was completed. The cooled residue was dissolved in a solution of 20 g. of sodium hydroxide dissolved in 750 ml. of water and extracted twice with ether; the ether extracts were discarded. The aqueous solution was acidified with dilute sulfuric acid, the top layer was separated, and the water layer was extracted twice with ether. The top layer and ether extracts were combined and distilled. A fraction boiling at 174–175° (16 mm.) was collected; yield was 74 g. (74%).

Analysis and Rate Determinations—A modified method[3] of Bryant and Smith[5] was used. A Fisher constant temperature water bath was used. Temperature was controlled with a "JUMO" thermoregulator with a rated sensitivity of 0.005°, purchased from the Scientific Glass Apparatus Co., Bloomfield, N. J. The bath thermometer had a range of 0–100°, graduated in 0.1°. Mallinckrodt Analytical Reagent chemicals were used.

Preparation of Reagents.—The pyridine-indicator solution was prepared by placing 0.25 ml. of a 4% solution of bromophenol blue in methanol in a 1-l. volumetric flask. Pyridine (20 ml.) was added and the mixture was diluted with methanol. Final volume adjustment was made in the constant temperature bath at 20°.

The hydroxylamine hydrochloride solution was prepared by dissolving 42.000 g. of hydroxylamine hydrochloride in 160 ml. of distilled water in a 1-l. volumetric flask, and the solution was diluted with methanol. Final volume adjustment was made at 20°.

The 0.5 N sodium hydroxide was prepared by dissolving 20.5 g. of sodium hydroxide pellets in 100 ml. of distilled water. The solution was cooled and diluted with 900 ml. of methanol. The cloudy solution was allowed to stand overnight and the clear solution was decanted. The solution was standardized against 0.5 N hydrochloric acid using phenolphthalein as indicator. The normality was always adjusted to within 0.25% of 0.5 N.

Determination of the Volume of 0.5 N Sodium Hydroxide Required for Complete Reaction.—One-hundred milliliters of pyridine-indicator solution (cooled to 20° in the water bath) and 25 ml. of hydroxylamine hydrochloride solution (cooled to 20°) were pipeted into nine 250-ml. erlenmeyer flasks. One of the flasks was set aside as a blank. The calculated amount of ketone required to react with one-half of the hydroxylamine hydrochloride present was weighed out in a 12 × 35 mm. shell vial to the nearest milligram. The vial was transferred to the flask with forceps; the flask was stoppered, shaken, and allowed to stand 24 hr. or longer at room temperature. The yellow solution was

titrated with 0.5 N sodium hydroxide to a color match with the blank against a white background illuminated with a 30-watt double tube fluorescent desk lamp.[32] As the end point was approached, the alkali was added in 0.1-ml. portions until the sample displayed a distinctly darker blue color than the blank. The buret reading less 0.1 ml. was taken as the end point. Results are shown in Table I. The results of this titration may be used to calculate the per cent purity of the ketones[5] and also may serve as a method of analysis for the twelve new ketones recorded in Table I.

Determination of the Time Required for 25, 50, and 90% Oximation—The water bath was equipped with a readily removable 9.5 × 18.5 cm. tray made of wire screen. This tray supported a 9 × 18 cm. piece of white glass (milk glass). The tray was illuminated with a 30-watt double tube fluorescent desk lamp.[32] The volume (25, 50, or 90%) of 0.5 N sodium hydroxide found necessary for complete reaction was added from a buret to a 250-ml. erlenmeyer flask containing the pyridine-indicator and hydroxylamine hydrochloride solutions. The solution became a deep blue. The flask was placed on the tray in the water bath together with another flask containing only the pyridine indicator and hydroxylamine hydrochloride solutions, the latter flask serving as a color blank. While the flasks were cooling to bath temperature, the calculated amount of ketone required to react with one-half of the hydroxylamine hydrochloride present was weighed out in a small crucible to the nearest milligram. The crucible was transferred to the flask with forceps and the time was noted while swirling the flask to mix the contents. As the end point was approached, the tray was momentarily lifted from the water bath to make color comparisons. As the color change is gradual, a time interval was taken. The first value of the interval was the time the solution was a slightly darker blue color than the blank, while the second value was the time the solution was a slightly paler blue color than the blank. The midpoint of the interval was the time used for calculating the reaction velocity constants. The number of identical rate constants recorded in Table I indicates only that the end points occurred within the same time interval.

The sodium chloride present in the above test solutions did not have an appreciable effect on the rate. Two ketones, 2-methyl-3-heptanone and 3-methyl-4-heptanone, were tested for 90% reaction as described above, while in comparison runs the alkali was added just before the end point. Good color matches were always observed.

The test solutions to which alkali has been added are stable. An alkaline test solution that was allowed to stand for 14 hr. at room temperature before the ketone was added gave the same results as the solutions treated as above.

Calculation of the Second-Order Reaction Velocity Constants.—The calculated hydroxylamine hydrochloride concentrations are 0.11738, 0.11410, and 0.109238 M for 25, 50, and 90% reaction, respectively. The corresponding ketone concentrations are one-half the above amounts or 0.05869, 0.05705, and 0.054619 M. Time is expressed in minutes.

Comparative Oximation Rates of Pairs of Ketones.—The required volumes of 0.5 N sodium hydroxide were added to two flasks containing the pyridine-indicator–hydroxylamine hydrochloride solution and the flasks placed on the tray in the water bath. The ketones were weighed out in separate crucibles and simultaneously added to the flasks. The color changes in the two flasks were compared with each other to and past the end point.

(29) The t-butyl alcohol was used without further treatment.

(30) E. B. Vliet, C. S. Marvel, and C. M. Hsueh, "Organic Syntheses," Coll. Vol. II, John Wiley and Sons, Inc., New York, N. Y., 1943, p. 416.

(31) Methanol was used as the solvent instead of ethanol; 42 g. of hydroxylamine hydrochloride per liter was used instead of 35 g. per liter.

(32) A white background and uniform illumination was found necessary for obtaining reproducible results.