Use of Ketoxime Derivatives to Prepare α-Acetoxy Ketones[1a]

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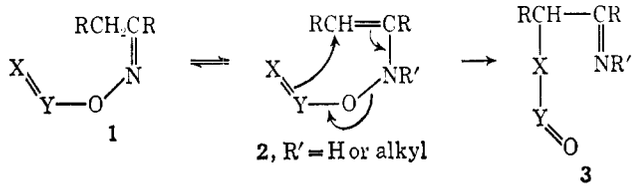
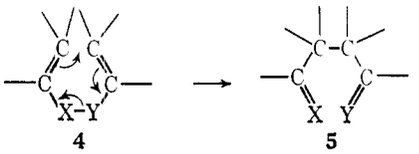
The O-acetyl derivatives of oximes from 4-heptanone (**10**), deoxybenzoin (**11**), dibenzyl ketone (**12**), cyclohexanone (**13**), 2-methylcyclohexanone (**38**), and *p*-nitrobenzyl *p*-methoxybenzyl ketone (**37**) have been prepared. Successive reactions of each of these oxime acetates with trimethyloxonium fluoroborate, triethylamine, and aqueous acid yielded an α-acetoxy ketone. Evidence is presented to support the idea that these transformations proceed *via* a facile Claisen-type rearrangement of an intermediate N-acetoxyenamine. In the cases of cyclohexanone and 2-methylcyclohexanone, a related rearrangement was effected by reaction of the ketones with the hydrochloride salt of O-acetyl-N-methylhydroxylamine (**28**). With unsymmetrical ketones, the proportions of structurally isomeric α-acetoxy ketones produced were not influenced by the stereochemistry of the starting oxime acetate.

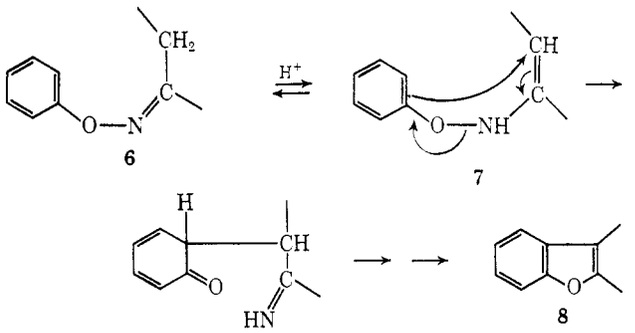
In earlier studies of the reactions of oxime arylsulfonates,[2] the formation of α-sulfonoxy ketones as by-products in several reactions suggested the possibility of a general rearrangement of O-substituted oximes **1** by way of the corresponding enamines **2** to form α-substituted imines **3**. Such rearrangements (**2** → **3**) would



be examples of the general rearrangement **4** → **5** of 1,5-dienes and analogous compounds of which the Claisen and Cope rearrangements are best known.[3] Studies[3] of



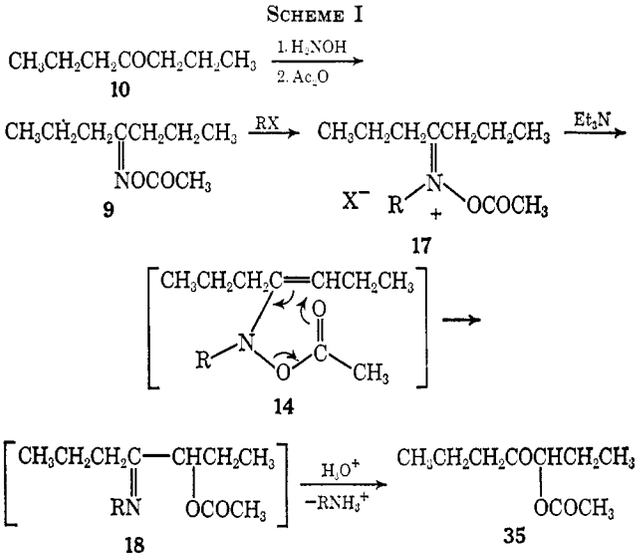
this concerted rearrangement **4** → **5** have indicated that any factors which will diminish the strength of the X–Y single bond in **4** will also facilitate rearrangement. Consideration of the average bond energy values[4] of pertinent single bonds [C–C (83 kcal/mol), C–N (70 kcal/mol), C–O (84 kcal/mol), N–N (38 kcal/mol), N–O (48 kcal/mol)] supports the idea that the rearrangement **4** → **5** will be especially favorable when the X–Y bond is either N–O or N–N. Examples of ready rearrangement involving N–N bond cleavage are presumably provided by the Fischer synthesis of indoles and by the related reaction of N,N′-divinylhydrazine derivatives.[5] Examples of rearrangement with concurrent N–O bond cleavage have been provided by recent studies of the acid-catalyzed



rearrangement of aryl ethers of oximes (*e.g.*, **6**) to form benzofurans **8**[6] in a reaction analogous to the Fischer indole synthesis.

We elected to study the reaction with O-acetyl derivatives of oximes (*e.g.*, **9**) since the anticipated reaction sequence (Scheme I) offered a potentially useful syn-

SCHEME I



thetic method for converting a ketone into the corresponding α-acetoxy ketone. Furthermore, the possibility existed the the configuration of an unsymmetrical ketone oxime could be used to determine the position of substitution by the acetoxyl group. For our initial studies we used ketones **10**–**13** which either were symmetrical or possessed only a single α-carbon atom capable of undergoing substitution.

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(2) (a) H. O. House and W. F. Berkowitz, *J. Org. Chem.*, **28**, 307, 2271 (1963); (b) for a recent review, see C. O'Brien, *Chem. Rev.*, **64**, 81 (1964).

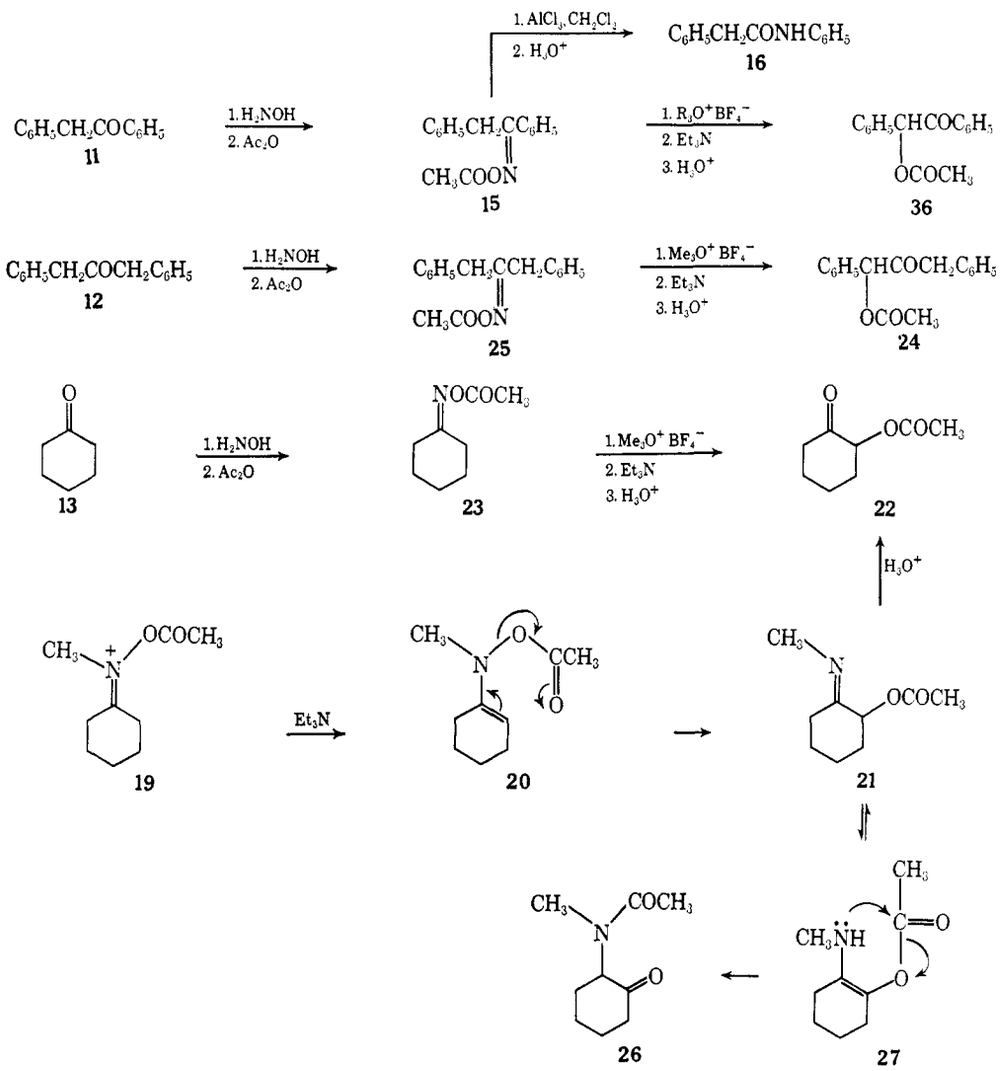
(3) For recent reviews, see (a) S. J. Rhoads, "Molecular Rearrangements," Vol. 1, P. de Mayo, Ed., Interscience Publishers, New York, N. Y., 1963, pp 655–706; (b) E. Vogel, *Angew. Chem, Intern. Ed. Engl.*, **2**, 1 (1963); (c) G. Schröder, J. F. M. Oth, and R. Merenyi, *ibid.*, **4**, 752 (1965).

(4) Data from F. A. Cotton and G. Wilkinson, "Advanced Inorganic Chemistry," Interscience Publishers, New York, N. Y., 1962, p 88.

(5) N. V. Sidgwick, I. T. Millar, and H. D. Springall, "The Organic Chemistry of Nitrogen," 3rd ed, Clarendon Press, Oxford, 1966, pp 623, 644–647.

(6) (a) T. Sheradsky, *Tetrahedron Lett.*, 5225 (1966); (b) A. Mooradian, *ibid.*, 407 (1967); (c) D. Kaminsky, J. Shavel, Jr., and R. I. Meltzer, *ibid.*, 859 (1967); (d) A. Mooradian and P. E. Dupont, *ibid.*, 2867 (1967).

Scheme II



To permit rearrangement, it was apparent that the starting oxime acetate (*e.g.*, **9**) must be converted into an enamine (*e.g.*, **14**). Although this conversion might in principle be accomplished by an acid- or base-catalyzed tautomerization of the oxime acetate to an enamine structure (*e.g.*, **14**, R = H), the use of aqueous or alcoholic solutions of acids or bases to accomplish this change would be complicated by the ready hydrolysis (or alcoholysis) of the oxime acetates to form the oximes. Treatment of oxime acetate **15** with aluminum chloride promoted not the desired rearrangement, but rather a Beckman rearrangement to form amide **16** (Scheme II). We therefore examined reactions of the oxime acetates **9** and **15** with alkylating agents to form the corresponding imminium salts (*e.g.*, **17**) since deprotonation of these salts should yield the enamines (*e.g.*, **14**). Although reactions of these oxime acetates with methyl iodide, methyl tosylate, and dimethyl sulfate were very slow even at elevated temperatures, the alkylation could be effected with the very reactive triethyloxonium and/or trimethyloxonium fluoroborate salts[7] in methylene chloride or nitromethane. The progress of the alkylation reaction could be followed in the infrared by observing the replacement of the band at 1760–1775 cm^{-1} (C=O of oxime acetate) by a new band at 1820 cm^{-1} which we attribute to the carbonyl stretching vibration of an acetoxyimminium salt.[8] From these measurements we concluded that the alkylations were accomplished most efficiently with solutions of trimethyloxonium fluoroborate in nitromethane, a reaction time of 2–3 hr at 25° being sufficient.

The direct addition of solutions of these imminium salts (*e.g.*, **17**) to water produced a small amount of rearranged α-acetoxy ketone; however, the major product was the starting ketone from competing hydrolysis rather than deprotonation of the imminium salt. This difficulty was overcome by adding the solution of imminium salt to anhydrous triethylamine and then hydrolyzing the reaction mixture with aqueous acid. By use of this procedure the desired enamine (*e.g.*, **14**) was apparently produced in the triethylamine solution and then underwent rapid rearrangement to form the intermediate α-acetoxyimine (*e.g.*, **18**). In an effort to learn how rapidly the rearrangement **20** → **21** occurred, solutions of imminium salt **19** were quenched in triethylamine at 0–10° and then hydrolyzed after relatively short reaction periods. As summarized in Table

(7) H. Meerwein in Houben-Weyl's "Methoden der organischen Chemie," Vol. 6, part 3, E. Muller, Ed., Georg Thieme Verlag, Stuttgart, Germany, 1965, p 329.

(8) The carbonyl stretching frequency for N-acetoxypyridinium salts is found at 1804–1830 cm^{-1}: V. J. Traynelis, A. I. Gallagher, and R. F. Martello, *J. Org. Chem.*, **26**, 4365 (1961); C. W. Muth and R. S. Darlak, *ibid.*, **30**, 1909 (965).

TABLE I

VARIATION IN PRODUCT YIELDS WITH REACTION CONDITIONS FOR DEPROTONATION AND SUBSEQUENT HYDROLYSIS OF THE PRODUCTS FROM IMMINIUM SALT 19

Reaction time and temperature before hydrolysis	Products, % yield[a]		
	Cyclohexanone	Acetoxy ketone 22	Amide 26
1 min at 5–10°	4	38	<1
10 min at 5–10°	4	30	<1
30 min at 5–10°	3	46	17
45 min at 5–25°	3	51	16
150 min at 25°	2	13	41
240 min at 25°	*b*	*b*	44[b]
Direct hydrolysis without Et_3N treatment	55	3	<1

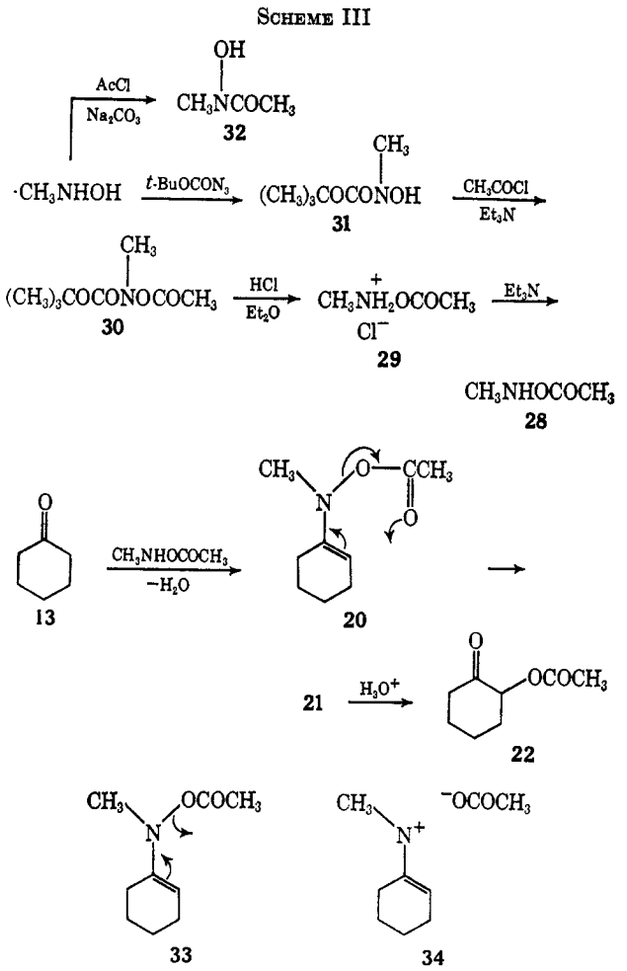
[a] Unless otherwise noted, the yields were determined by gas chromatographic analysis. [b] In this case the product was fractionally distilled to isolate keto amide **26** and the isolated yield is tabulated.

I, the half-life for rearrangement of the acetoxyenamine **20** at 5–10° is less than 30 sec. If the rearrangement is assumed to be a first-order process with a normal frequency factor, the maximum activation energy for rearrangement is approximately 20 kcal/mol. Of incidental interest was the observation that use of relatively long reaction periods prior to hydrolysis yielded significant amounts of a by-product, keto amide **26**. As indicated in Scheme II, we believe this by-product arises from an intramolecular O → N acetyl transfer (structure **27**) which becomes a serious side reaction if the initially formed acetoxyimine **21** is not hydrolyzed promptly. The formation of this by-product provides support for the intermediacy of acetoxyimine **21** in the formation of acetoxy ketone **22**.

Since it was not practical to follow the reaction of the imminium salts (*e.g.*, **19**) with triethylamine by spectrometric methods, we sought to obtain evidence for the intermediacy of acetoxyenamine **20** by generating this structure in a different way. For this purpose, O-acetyl-N-methylhydroxylamine (**28**) and the corresponding salt **29** were prepared as indicated in Scheme III.[9] Although O-acetyl derivative **28** underwent the characteristic[9] transacetylation to form N-acetyl derivative **32**, the corresponding hydrochloride salt **29** was relatively stable permitting a study of the reaction of O-acetyl salt **29** with cyclohexanone (**13**) in the presence of molecular sieves to remove water. The probable intermediate, enamine **20**, presumably rearranges as previously indicated (**20** → **21**) since acetoxy ketone **22** was formed upon hydrolysis. This combination of data therefore argues strongly that the rearrangement of acetoxyenamines (*e.g.*, **14** and **20**) occurs rapidly and can form the basis for the synthesis of α-acetoxy ketones. Our data, which do not include ^{18}O-labeling studies, do not provide compelling evidence that the rearrangement has occurred by a six-centered process (*e.g.*, **20**) rather than by a four-centered rearrangement (*e.g.*, **33**) or by an ionization–recombination sequence (*e.g.*, **34**). However, we regard these possibilities as distinctly less probable especially in view of the earlier cited behavior of O-aryl oximes **6** which apparently rearrange by a six-centered transition state **7** even at the expense of losing the resonance energy of a benzene ring.

(9) This preparative route is an adaptation of the route described by L. A. Carpino, C. A. Giza, and B. A. Carpino, *J. Amer. Chem. Soc.*, **81**, 955 (1959).

SCHEME III



To examine the selectivity of this acetoxylation procedure with unsymmetrical ketones, we chose ketones **37** and **38** (Scheme IV) for study. The stereoisomeric oximes **39a** and **40a** had been separated and characterized previously.[2a] Only one crystalline oxime of ketone **38** had been reported previously;[10] this material is believed to be the less-hindered isomer **41a** based on its Beckmann rearrangement to form lactam **46** when treated with concentrated H_2SO_4.[11] We have repeated this rearrangement (**41a** → **46**) under milder conditions (PCl_5 in methylene chloride) as additional support[12] for the stereochemistry **41a** assigned to this oxime, mp 43–44°, and to the derived oxime acetate **41b**. Following a procedure used earlier for the isomerization of the more stable stereoisomer of benzaldoxime to the less stable isomer,[13] oxime **41a** was converted into a mixture of the hydrochloride salts of oximes **41a** and **42a**. The mixture of oximes obtained from these salts was acetylated to yield a mixture of oxime acetates **41b** and **42b**. Although we were unsuccessful in efforts to isolate a sample of the oxime acetate **42b** from this mixture, its composition was readily determined from the nmr spectrum of the mixture.

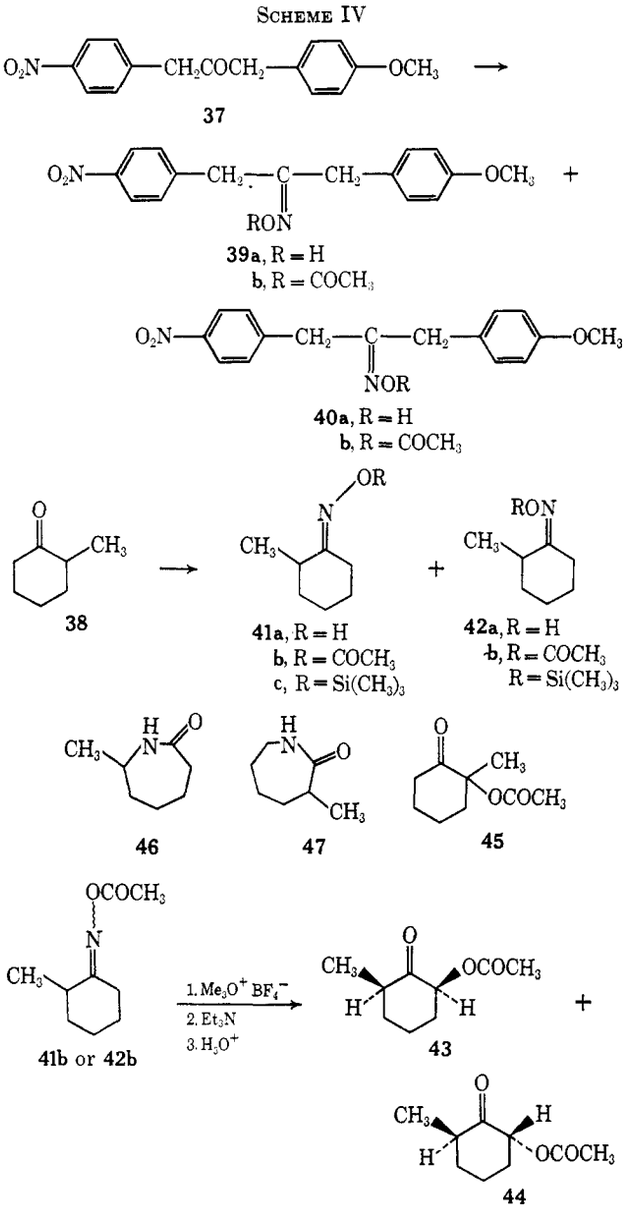
(10) (a) E. Müller, D. Fries, and H. Metzger, *Chem. Ber.*, **88**, 1891 (1955); (b) O. Wallach, *Ann.* **346**, 249 (1906); (c) A. J. N. Hope and S. Mitchell, *J. Chem. Soc.*, 4125 (1954).

(11) (a) J. von Braun and A. Heymans, *Ber.*, **63**, 502 (1930); (b) J. G. Hildebrand and M. T. Bogert, *J. Amer. Chem. Soc.*, **58**, 650 (1936); (c) A. Schaffler and W. Ziegenbein, *Chem. Ber.*, **88**, 1374 (1955).

(12) L. G. Donamura and W. Z. Heldt, *Org. Reactions*, **11**, 1 (1960).

(13) (a) E. Beckmann, *Ber.*, **22**, 429 (1889); (b) O. L. Brady and F. P. Dunn, *J. Chem. Soc.*, 1783 (1923).

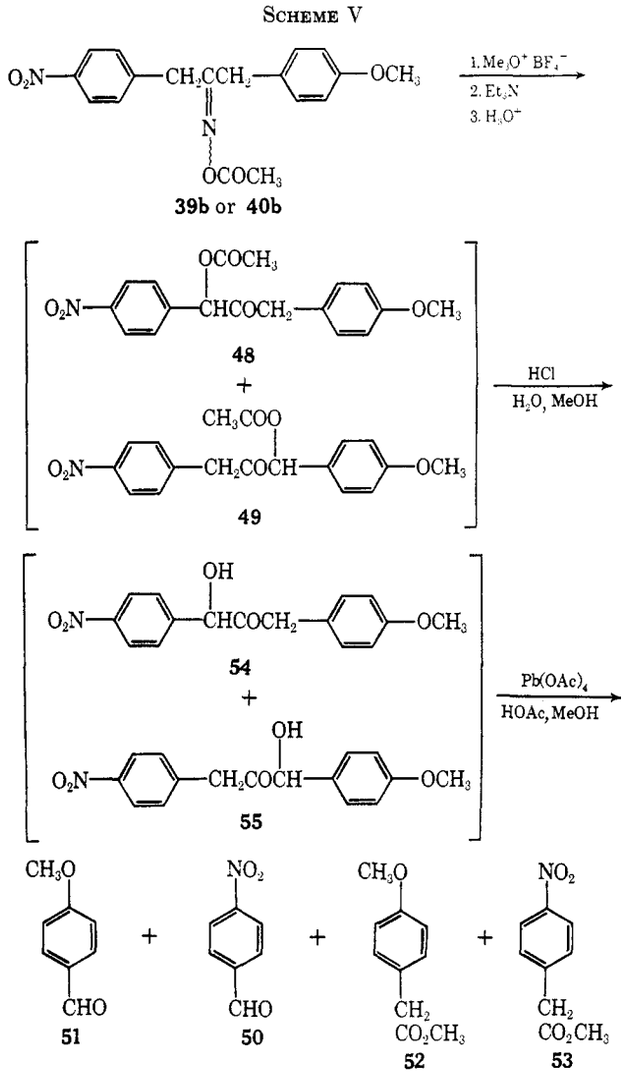
Scheme IV



Application of the usual alkylation–rearrangement sequence either to the pure oxime acetate **41b** or to the mixture of oxime acetates **41b** and **42b** produced, in 41–51% yield, mixtures of stereoisomeric secondary acetoxy ketones **43** and **44** which contained less than 1% of the tertiary acetate **45**. This result is to be contrasted with the acetoxylation of the ketone **38** by reaction with $Pb(OAc)_4$ in benzene[14] which produced a mixture containing 23% of the tertiary acetate **45** and 77% of the secondary acetates **43** and **44**. The reaction of 2-methylcyclohexanone (**38**) with the hydroxylamine salt **29** also produced (25% yield) a mixture containing 56% of the tertiary acetate **45** and 44% of the secondary acetates **43** and **44**.

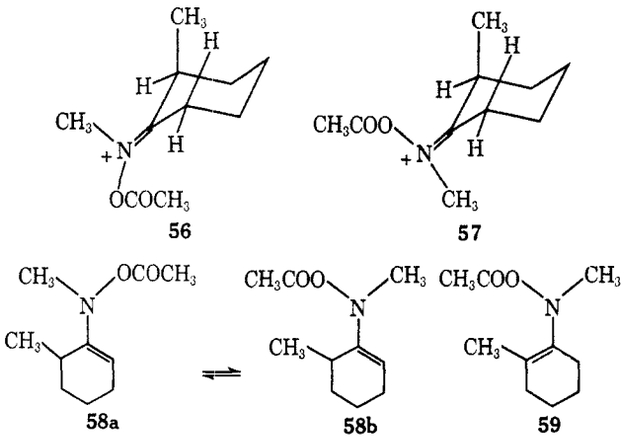
The oxime acetates **39b** and **40b**, obtained from the previously described[2a] oximes **39a** and **40a**, were also subjected to the usual alkylation–rearrangement sequence (Scheme V). Since we were unsuccessful in separating the initial products **48** and **49** from the relatively complex reaction mixture, a hydrolysis and cleavage procedure developed with the related acetoxy ketone **24** was applied to the reaction mixtures to produce mixtures of **50** and **52** from **48** and **54** and mixtures of **51** and **53** from **49** and **55**. Comparable mixtures of these four products, **50–53**, were obtained in low over-all yield (9–16%) irrespective of which oxime acetate isomer **39b** or **40b** served as the starting material.

Scheme V



These latter studies allow us to conclude that the stereochemistry of the starting oxime acetate does not control the position of acetoxylation of an unsymmetrical ketone in the reaction sequence studied here. Instead the position of attack is apparently determined by the position at which the enamine double bond is formed. For example, the addition of either of the salts **56** or **57** (from oxime acetates **41b** and **42b**) to an excess of the base, triethylamine, apparently resulted in the formation of the less highly substituted enamine **58**, which subsequently rearranged to the imine derivative of acetoxy ketones **43** and/or **44**. We attribute the selective formation of a single enamine (**58** not **59**) in this case to the kinetically controlled abstraction of the stereoelectronically favored axial proton from salts **56** and **57** by the relatively basic reaction medium. To minimize steric interactions between the nitrogen substituents and the 2-methyl group, salts **56** and **57** are

(14) The procedure of G. W. K. Cavill and D. H. Solomon, *J. Chem. Soc.*, 4426 (1955). Also see H. B. Henbest, D. N. Jones, and G. P. Slater, *ibid.*, 4472 (1961); J. D. Cocker, H. B. Henbest, G. H. Phillipps, G. P. Slater, and D. A. Thomas, *ibid.*, 6 (1965).



expected[15a] to exist very largely in the indicated conformations **56** and **57**.

Exposure of salts **56** and **57** to a weakly acidic medium where equilibration between enamines and immonium salts is rapid[15a,b] would be expected to produce an equilibrium mixture of enamines **58** and **59**. It seems likely that this equilibrium mixture would contain comparable amounts of the two structural isomers as is found with the dimethylaminoenamine of 2-methylcyclohexanone.[15c] In agreement with these expectations, the enamines generated from 2-methylcyclohexane (**38**) and the hydroxylamine salt **29** under weakly acidic conditions afforded the previously noted mixture of structurally isomeric acetates **45** (56% of mixture) and **43** and **44** (44% of mixture).

In the foregoing discussion, it has been assumed that the barrier to rotation about the enamine C–N bond is sufficiently low[16] to permit interconversion of conformations **58a** and **58b** prior to rearrangement of conformation **58a**.

Experimental Section[17]

Preparation of the Oxime Acetates 9, 15, 23, and 25.—The oximes were prepared by reaction of the ketones with a solution obtained from $HONH_3Cl$ and $NaHCO_3$, Na_2CO_3, or KOAc in aqueous MeOH or EtOH. 4-Heptanone oxime was isolated as a colorless liquid: bp 65–65.5° (1.0 mm) or 86–87° (9 mm); $n^{28}D$ 1.4468 [lit.[18] bp 93–94° (15 mm), $n^{20}D$ 1.4486]; ir (CCl_4) 3600, 3260 (free and associated OH), and 1645 cm^{-1} (C=N); nmr (CCl_4) δ 9.50 (1 H, br, OH), 1.9–2.6 (4 H, m, CH_2C=N), and 0.8–1.9 (10 H, m, aliphatic CH); mass spectrum, abundant fragments at *m/e* 98, 70, 57, and 43. 1,3-Diphenyl-2-propanone oxime crystallized from EtOH as white needles: mp 119–122° (lit.[19] mp 120–121°); ir ($CHCl_3$) 3580, 3260 (free and associated OH), and 1655 cm^{-1} (C=N); uv (95% EtOH) series of weak bands in the region 245–270 mμ (ϵ 305–455); nmr [$(CD_3)_2SO$] δ 6.8–7.5 (10 H, m, aryl CH), 3.56 (2 H, s, $ArCH_2$ *cis* to OH), and 3.38 (2 H, s, $ArCH_2$ *trans* to OH);[20] mass spectrum, weak molecular ion *m/e* 225, abundant fragments *m/e* 210, 182, 107, 106, 91, and 90.

Deoxybenzoin oxime (*syn* benzyl group)[2a,21] separated from EtOH as white needles: mp 94–96° (lit. mp 96–97°,[22] 98°[21]); ir ($CHCl_3$) 3580 and 3270 cm^{-1} (free and associated OH).

A solution of 8.926 g (69.5 mmol) of 4-heptanone oxime, 20.0 ml (21.7 g, 213 mmol) of Ac_2O, and 25 ml of Et_2O was refluxed for 1.4 hr, poured onto ice, and then neutralized with solid $NaHCO_3$. After Et_2O extraction, distillation afforded 10.38 g (87.5%) of the oxime acetate **9** as a colorless liquid, bp 46–47° (0.06 mm), $n^{26}D$ 1.4427, which exhibited only a single component on glpc[23] and tlc;[24] ir (CCl_4) 1775 (ester C=O) and 1640 cm^{-1} (C=N); nmr (CCl_4) δ 2.08 (*ca.* 3 H, s, CH_3CO) superimposed on a 2.0–2.5 m (*ca.* 4 H, CH_2C=N) and 0.7–2.0 (10 H, m, aliphatic CH); mass spectrum, abundant fragments at *m/e* 70, 45, 43, 41, 39, and 29.

Anal. Calcd for $C_9H_{17}NO_2$: C, 63.13; H, 10.00; N, 8.18. Found: C, 63.15; H, 10.00; N, 7.95.

The same procedure with 5.00 g (22.2 mmol) of 1,3-diphenyl-2-propanone oxime, 3.0 ml (3.3 g, 31 mmol) of Ac_2O, and 40 ml of Et_2O (reaction time 2.25 hr) afforded 5.74 g (95.5%) of a crude product, extracted with methylene chloride, which crystallized on standing, mp 34–37°. Recrystallization (Et_2O–pentane) separated 4.366 g (72%) of oxime acetate **25** as colorless prisms: mp 37–39.5°; mp 38–40 after sublimation under reduced pressure; ir ($CHCl_3$) 1765 (ester C=O) and 1635 cm^{-1} (C=N); uv (95% EtOH) series of weak peaks in the region 245–270 mμ (ϵ 270–485); nmr ($CDCl_3$) δ 7.2–8.0 (10 H, m, aryl CH), 3.80 (2 H, s, $ArCH_2$ *cis* to OAc), 3.74 (2 H, s, $ArCH_2$ *trans* to OAc),[20] and 2.27 (3 H, s, CH_3CO); mass spectrum, abundant fragments at *m/e* 209, 182, 117, 116, 91, 90, 60, 45, and 43.

Anal. Calcd for $C_{17}H_{17}NO_2$: C, 76.38; H, 6.41; N, 5.24. Found: C, 76.57; H, 6.40; N, 5.09.

A similar procedure with 8.992 g (79.3 mmol) of cyclohexanone oxime and 10.2 g (100 mmol) of Ac_2O in 50 ml of Et_2O for 16 hr at ambient temperature yielded oxime acetate **23** as 11.58 g (94%) of colorless liquid: bp 73.5–74° (0.25 mm) [lit.[25] bp 130° (20 mm)]; $n^{21}D$ 1.4824, $n^{25}D$ 1.4803; ir (liquid film) 1760 (ester C=O) and 1645 cm^{-1} (C=N); nmr (CCl_4) δ 2.08 (*ca.* 3 H, s, CH_3CO) superimposed on 1.3–2.8 (10 H, m, aliphatic CH).

Anal. Calcd for $C_8H_{13}NO_2$: C, 61.91; H, 8.44; N, 9.03. Found: C, 61.74; H, 8.39; N, 9.23.

After reaction of 5.00 g (23.6 mmol) of deoxybenzoin oxime with 7.93 g (75 mmol) of Ac_2O in 60 ml of refluxing Et_2O for 2 hr, distillation at 45–50° (0.1 mm) gave 5.727 g (95.5%) of crude acetate which solidified, mp 44–47°. Recrystallization (Et_2O–hexane) separated 5.457 g (91.5%) of oxime acetate **15** as white prisms: mp 48.5–50°; mp 51.5–52.5° after recrystallization [Et_2O–petroleum ether (bp 30–60°)],[26] ir (CCl_4) 1770 (ester C=O) and 1610 cm^{-1} (conjugated C=N); uv (95% EtOH) 246 mμ (ϵ 13,200); nmr ($CDCl_3$) δ 7.0–7.9 (10 H, m, aryl CH), 4.20 (2 H, s, CH_2C=N), and 2.17 (3 H, s, CH_3CO); mass spectrum, abundant fragments at *m/e* 103, 91, 77, 76, 60, 51, 50, 45, and 43.

Anal. Calcd for $C_{16}H_{15}NO_2$: C, 75.87; H, 5.97; N, 5.53. Found: C, 75.56; H, 6.01; N, 5.66.

After a solution of 2.00 g (3.95 mmol) of oxime acetate **15** and 4.0 g (30 mmol) of $AlCl_3$ in 45 ml of CH_2Cl_2 had been stirred under N_2 at 25–30° for 1 hr, the mixture was poured onto ice and then extracted with Et_2O. The crude brown oil (1.864 g) recovered, from the Et_2O extract crystallized from EtOH as 818 mg (48.5%) of phenylacetanilide (**16**), mp 114–116° (lit.[21] mp 117.5°),

(15) (a) F. Johnson, *Chem. Rev.*, **68**, 375 (1968); (b) see H. O. House, B. A. Tefertiller, and H. D. Olmstead, *J. Org. Chem.*, **33**, 935 (1968), and references cited therein; (c) W. D. Gurowitz and M. A. Joseph, *ibid.*, **32**, 3289 (1967).

(16) This rotation barrier is estimated to be in the range 12–21 kcal/mol. See (a) A. Mannschreck and U. Koelle, *Tetrahedron Lett.*, 863 (1967); (b) Y. Shvo, E. C. Taylor, and J. Bartulin, *ibid.*, 3259 (1967).

(17) All melting points are corrected and all boiling points are uncorrected. Unless otherwise stated magnesium sulfate was employed as a drying agent. The infrared spectra were determined with a Perkin-Elmer Model 237 infrared recording spectrophotometer fitted with a grating. The ultraviolet spectra were determined with a Cary recording spectrophotometer, model 14. The nmr spectra were determined at 60 mc with a Varian Model A-60 nmr spectrometer. The chemical shift values are expressed either in cycles per second or δ values (parts per million) relative to a tetramethylsilane internal standard. The mass spectra were obtained either with a CEC Model 21-130 or with a Hitachi (Perkin-Elmer) mass spectrometer. The microanalyses were performed by Dr. S. M. Nagy and his associates.

(18) (a) E. Muller and H. Metzger, *Chem. Ber.*, **88**, 165 (1955); (b) A. I. Vogel, W. T. Cresswell, G. H. Jeffery, and J. Leicester, *J. Chem. Soc.*, 514 (1952).

(19) C. H. DePuy and B. W. Ponder, *J. Amer. Chem. Soc.*, **81**, 4629 (1959).

(20) G. J. Karabatsos and R. A. Taller [*Tetrahedron*, **24**, 3347 (1968)] have noted that the *cis*-α-methylene protons of ketoximes normally have their nmr peaks about 0.2 ppm at lower field than the *trans*-α-methylene protons.

(21) S. S. Jenkins, *J. Amer. Chem. Soc.*, **55**, 703 (1933).

(22) G. Wittig, F. Bangert, and H. Kleiner, *Ber.*, **61**, 1140 (1928).

(23) A gas chromatography column packed with silicone gum, no. SE-30, suspended on Chromosorb P was employed for this analysis.

(24) A plate coated with silica gel was employed for this analysis.

(25) Z. Csuros, K. Zech, G. Dely, and E. Zalay, *Acta Chim. Hung.*, **1**, 66 (1951); *Chem. Abstr.*, **46**, 5003 (1952).

(26) The preparation and characterization of this substance was preformed by Dr. William F. Berkowitz [Ph.D. Dissertation, Massachusetts Institute of Technology, 1963].

identified with an authentic sample by a mixture melting point and comparison of ir spectra. Chromatography (SiO_2) of the residual oil (380 mg) from the mother liquid separated an additional 37 mg (2.5%) of amide **16** (eluted with EtOAc–PhH) and 90 mg of crude solid (eluted with PhH) with ir absorption suggesting the presence of the oxime acetate **15** and deoxybenzoin oxime. The crude product from a comparable experiment was analyzed by glpc[23] (diphenylmethane internal standard). The calculated yield of amide **16** (retention time 25 min) was 51% and no peak was observed corresponding to N-benzylbenzamide (retention time 26 min). The formation of primarily, if not exclusively, amide **16** as a Beckmann rearrangement[12] product is consistent with the formulation of the oxime acetate as **15** ($PhCH_2$ and OAc groups *cis*) corresponding to the known[21] stereochemistry of the starting oxime which was acetylated.

Preparation of O-Acetyl-N-methylhydroxylamine (28).—To a cold (0°) stirred mixture of 10.85 g (75.9 mmol) of *t*-butoxylcarbonyl azide and 6.95 g (83.5 mmol) of N-methylhydroxylamine hydrochloride was added, dropwise over 45 min, a solution of 11.4 g (285 mmol) of NaOH in 100 ml of H_2O. The cooling bath was removed and the resulting mixture was stirred for 3 hr and then partitioned between H_2O and Et_2O. The aqueous phase was acidified (pH 5) with aqueous HCl and extracted with Et_2O, and the extract was dried and concentrated. Distillation of the residual liquid (11.60 g) separated 9.104 g (80.5%) of the **N-hydroxy carbamate 31** as a colorless liquid: bp 50–50.5° (0.30 mm); $n^{28}D$ 1.4298; ir (liquid film) 3250 (br, associated OH) and 1702 cm^{-1} (carbamate C=O); nmr (CCl_4) δ 7.94 (1 H, br, OH), 3.08 (3 H, s, CH_3N), and 1.43 [9 H, s, $(CH_3)_3C$]; mass spectrum, abundant fragments at *m/e* 59, 56, 44, 41, and 39.

Anal. Calcd for $C_6H_{13}NO_3$: C, 48.96; H, 8.90. Found: C, 48.94; H, 8.88.

To a cold (0°) solution of 9.104 g (61.8 mmol) of carbamate **31** and 10.5 ml (7.6 g, 75 mmol) of anhydrous Et_3N in 300 ml of CH_2Cl_2 was added, dropwise and with stirring, 5.00 ml (5.80 g, 70.5 mmol) of AcCl. The resulting mixture was stirred for 50 min at 25–30° and then partioned between aqueous $NaHCO_3$ and CH_2Cl_2. The organic layer was dried (Na_2SO_4), concentrated, and distilled to separate 11.06 g (95% of the **N-acetoxy carbamate 30**, a colorless liquid: bp 47–48° (0.7 mm): $n^{28}D$ 1.4182; ir (liquid film) 1795 (acetate C=O) and 1725 cm^{-1} (carbamate C=O); nmr (CCl_4) δ 3.16 (3 H, s, CH_3N), 2.06 (3 H, s, CH_3CO), and 1.43 [9 H, s, $(CH_3)_3C$]; mass spectrum, abundant fragments at *m/e* 59, 57, 56, 44, 43, 41, and 39.

Anal. Calcd for $C_8H_{15}NO_4$: C, 50.78; H, 7.99; N, 7.40. Found: C, 50.62; H, 7.95; N, 7.60.

A solution of 2.066 g (10.6 mmol) of the N-acetoxy carbamate **30** in 10 ml of anhydrous Et_2O was treated with 124 mmol of anhydrous HCl in 40 ml of Et_2O. After the resulting solution stood under N_2 for 67 hr, the white needles which separated were collected, washed with anhydrous Et_2O, and dried under reduced pressure. **N-Acetoxyamine hydrochloride 29** amounted to 1.256 g (95%): mp 109–111° dec; ir (KBr pellet) 1805 cm^{-1} (acetate C=O); nmr (D_2O, partial hydrolysis probably occurred 3.18 (t, J = 10 Hz, Me group of $CH_3N^+H_2OR$) and 2.29 (s, CH_3CO).

A suspension of 164 mg (1.31 mmol) of hydrochloride **29** in 2 ml of CH_2Cl_2 was treated with 0.300 ml (0.217 g, 2.14 mmol) of Et_3N, which converted the initial suspension into a pale yellow solution from which a white solid (presumably $Et_3NH^+Cl^-$) separated. The resulting suspension was stirred at 25–30° and aliquots were removed periodically for ir analysis. After either 10 or 30 min the ir spectrum contained a strong peak at 1740 cm^{-1} (N-acetoxy C=O of **28**) and a very weak peak at 1635 cm^{-1} (C=O of hydroxamic acid **32**). After 16 hr the peaks were of comparable intensity and after 24 hr the peak at 1635 cm was more intense.

As described elsewhere,[27] a cold (0°) solution of 5.273 g (63.0 mmol) of N-methylhydroxylamine hydrochloride and 6.67 g (63.0 mmol) of Na_2CO_3 in 50 ml of MeOH was treated with 4.86 g (63.0 mmol) of AcCl to yield 2.44 g (43%) of **N-methylhydroxamic acid 32** as a colorless liquid: bp 60–62° (0.4 mm); $n^{27}D$ 1.4509 [lit.[27] bp 74–76° (0.8 mm), $n^{23}D$ 1.4512]; ir (liquid film) 3150, 2900 (br, associated OH), and 1620 cm^{-1} (amide C=O); nmr (CCl_4) δ 9.87 (1 H, s, OH), 3.20 (3 H, s, CH_3N), and 2.08 (3 H, CH_3CO).

(27) H. Ulrich and A. A. R. Sayigh, *J. Chem. Soc.*, 1098 (1963).

Conversion of 4-Heptanone Oxime Acetate (9) into the Acetoxy Ketone 35. A. Alkylation with Triethyloxonium Fluoroborate.—To 2.5 ml of a CH_2Cl_2 solution containing 2.48 g (13.0 mmol) of triethyloxonium fluoroborate[28] was added 1.71 g (10 mmol) of oxime acetate **9**. The initially heterogeneous mixture (two liquid phases) was stirred at 25–30° under N_2 for 2 hr at which time a single liquid phase was present. The ir spectrum (CH_2Cl_2) of an aliquot had absorptions of approximately equal intensity at 1760 (starting acetate **9**) and at 1820 cm^{-1} (alkylated acetate **17**).[8] From the ir spectra of aliquots, we concluded that the alkylation reaction (**9** → **17**) was complete after 21 hr at which time the solution was separated into three equal aliquots. The first aliquot was quenched with aqueous $NaHCO_3$ and the organic layer was dried, concentrated, and distilled in a short-path still (1.0 mm, 100° bath). The distillate, 357 mg of straw-colored liquid, was mixed with a known weight of anisole (internal standard) and analyzed by glpc.[29,30] The calculated yields of products were 11% 4-heptanone (**10**, eluted first), 4% acetoxy ketone **35** (eluted second), and *ca.* 10% a peak corresponding in retention time to the Beckmann product, N-propylbutyramide. Collected[29] samples of the ketones were identified with authentic samples by comparison of glpc retention times and ir spectra. The second aliquot of the original reaction mixture was cooled to 0°, treated with 2.0 ml of Et_3N, stirred for 15 min, and poured into H_2O. The crude product was partitioned between CH_2Cl_2 and aqueous HCl and the neutral organic phase was subjected to the previously described isolation and analytical procedure. The calculated[29,30] yields of products were <1% ketone **10**, 9% acetate **35**, and *ca.* 9% N-propylbutyramide. The third aliquot of the original reaction mixture was added to cold (0°) Et_3N and then subjected to the isolation procedure just described. The calculated[29,30] yields were 2% ketone **10**, 23% acetate **35**, and *ca.* 8% N-propylbutyramide.

The reaction was repeated with 36 mmol of triethyloxonium fluoroborate and 4.00 g (23.4 mmol) of oxime acetate **9** in 10 ml of CH_2Cl_2. After 16 hr the resulting mixture was added, dropwise and with vigorous stirring over 50-min, to 40 ml of cold, anhydrous Et_3N. The resulting mixture was stirred for 15 min, treated with excess aqueous 6 *M* HCl, stirred for 30 min, and then the crude product was isolated in the usual way. Analysis[29,30] of the distillate indicated the absence of 4-heptanone, a calculated yield of 60% acetate **35** and the presence of 1–2% a minor component with a retention time corresponding to N-propylbutyramide (the Beckmann rearrangement product expected from 4-heptanone oxime).

An authentic sample of **N-propylbutyramide**, prepared from propylamine and butyryl chloride, was isolated as a colorless liquid: bp 125–126° (15 mm); $n^{25}D$ 1.4399 [lit.[31] bp 127–132° (20 mm)]; ir (CCl_4) 1645 (amide C=O) and 1540 cm^{-1} (NH bending); nmr (CCl_4) δ 8.1 (1 H, br, NH), 3.22 (2 H, m, CH_2N), and 0.7–2.5 (12 H, m, aliphatic CH); mass spectrum, molecular ion at *m/e* 129, abundant fragments at *m/e* 71, 44, 43, 41, 30, and 27. Previously described procedures[32] were followed to prepare 3-bromo-4-heptanone, bp 68.5–71° (7 mm) [lit.[32] bp 82–83° (17 mm)], which exhibited a single major component on glpc[23] and had the following spectral properties: ir (CCl_4) 1720 cm^{-1} (C=O); nmr (CCl_4) δ 4.09 (1 H, t, J = 6.5 Hz, BrCHCO), 2.4–2.9 (2 H, m, CH_2CO), and 0.8–2.4 (10 H, m, aliphatic CH); mass spectrum, molecular ion at *m/e* 194 (^{81}Br isotope), abundant fragments at *m/e* 71 ($CH_3CH_2CH_2C{\equiv}O^+$), 43, and 41 with pairs of weak peaks at 121 and 123 ($CH_3CH_2C^+HBr$) and at 149 and 151 ($CH_3CH_2CHBrC{\equiv}O^+$). Solvolysis[32] of this bromo ketone in a solution of NaOAc in HOAc afforded an authentic sample of the **acetoxy ketone 35**: bp 68.5–69.5° (2.3 mm), $n^{24}D$ 1.4252 [lit.[32] bp 98–100° (16 mm), $n^{25}D$ 1.4240]. Analysis by tlc[24] and glpc[23] indicated the product to be homogeneous: ir (CCl_4) 1745 (ester C=O), 1735, and 1720 cm^{-1} (C=O in two conformations of acetoxy ketone); nmr (CCl_4) δ 4.94 (1 H, m, COCHOAc), 2.3–2.8 (2 H, m, CH_2CO), 2.13 (3 H, s, CH_3CO), and 0.7–2.0 (10 H, m, aliphatic CH); nass spectrum, abundant

(28) Prepared by the procedure of H. Meerwein, *Org. Syn.*, **46**, 113 (1966).

(29) A gas chromatography column packed with Apiezon L suspended on Chromosorb G was employed for this analysis.

(30) A programmed increase in column temperature was used in this analysis.

(31) S. I. Gertler and A. P. Yerington, U. S. Department of Agriculture U. S. Government Printing Office, Washington, D. C., ARS-33-31; *Chem. Abstr.*, **50**, 17297 (1956).

(32) J. Colonge and J. C. Dubin, *Bull. Soc. Chim. Fr.*, 1180 (1960).

fragments at *m/e* 129 [$CH_3CH_2CH(OCOCH_3)C{\equiv}O^+$], 101 ($CH_3CH_2CH{=}O^+COCH_3$), 71 ($CH_3CH_2CH_2C{\equiv}O^+$), 43, and 41. Acid-catalyzed hydrolysis (HCl in H_2O–MeOH at 25°) of acetoxy ketone **35** afforded **3-hydroxy-4-heptanone** as a colorless liquid: $n^{24}D$ 1.4301 (lit.[32] $n^{25}D$ 1.4275) which was homogeneous by tlc[24] and glpc[23] analyses: ir (liquid film) 3475 (br, assoc OH) and 1710 cm^{-1} (C=O); nmr (CCl_4) δ 4.13 (1 H, m, OCHCO), 3.47 (1 H, s, OH), 2.3–2.9 (2 H, m, CH_2CO), and 0.8–2.3 (10 H, m, aliphatic CH); mass spectrum, molecular ion at *m/e* 130, abundant fragments at *m/e* 73, 71 ($CH_3CH_2CH_2C{\equiv}O^+$), 59 ($CH_3CH_2CH{=}^+OH$), 57, 55, 43, 41, and 31.[33]

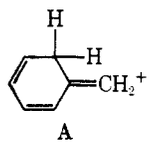
B. Alkylation with Trimethyloxonium Fluoroborate.—A solution of 13.20 g (97 mmol) of trimethyloxonium fluoroborate[34] and 10.59 g (62 mmol) of oxime acetate **9** in 25 ml of CH_3NO_2 was prepared at 0° and then stirred at 25–30° for 1.25 hr. (Preliminary experiments employing the previously described ir analysis established that the reaction was complete in various solvents after the following times: 1.8–3.2 hr for the suspension in CH_2Cl_2; 1 hr for the suspension in 1,2-dimethoxyethane; 20–30 min for the solution in CH_3NO_2.) Gas evolution (presumably Me_2O) was noted as the solution warmed to 25–30°. The resulting solution was added to 40 ml of cold (0°) Et_3N under N_2, and then hydrolyzed and worked up in the usual way. Fractional distillation of the crude liquid product separated 4.295 g (40.3%) of the pure[29,30] acetoxy ketone **35** [bp 87–89° (12 mm), $n^{26}D$ 1.4217], and 0.872 g of a fraction [bp 89–92°, $n^{26}D$ 1.4249] which contained[29,30] 92% acetoxy ketone **35** (total yield 48%) and several minor higher boiling impurities. In comparable small-scale reactions with other solvents used for the alkylation, anisole was added (internal standard) and the crude products were analyzed;[29,30] the calculated yields of acetoxy ketone **35** were 59% with CH_2Cl_2 and 40% with 1,2-dimethoxyethane.

Conversion of Deoxybenzoin Oxime Acetate (15) into Acetoxy Ketone 36.—Attempts to methylate oxime acetate **15** with CH_3I were unsuccessful and reactions with methyl tosylate or with dimethyl sulfate at elevated temperatures (100–160°) produced complex reaction mixtures from which various amounts of deoxybenzoin, benzoin, benzil, and phenylacetanilide were ultimately isolated.

After a solution of 2.895 g (19.3 mmol) of trimethyloxonium fluoroborate and 2.850 g (11.3 mmol) of oxime acetate **15** in 12.5 ml of CH_3NO_2 had been allowed to react for 4 hr (alkylation complete by ir analysis), the reaction solution was added to 12 ml of cold (0°) Et_3N and then stirred at 25–30° for 20 min. After following the previously described hydrolysis and isolation experiments, the crude neutral product was obtained as 3.928 g of brown oil which showed one major spot on tlc[24] corresponding to acetoxy ketone **36**. After chromatography (200 g of SiO_2), the fractions eluted with PhH–Et_2O were recrystallized (hexane–CH_2Cl_2) to separate 922 mg (33.6%) of benzoin acetate (**36**) as tan prisms, mp 79–83°. Recrystallization (EtOH) gave pure benzoin acetate, mp 80–81.5° (lit.[35] mp 81.5–82.5°), identified with an authentic sample by a mixture melting point and by comparison of ir spectra, ir ($CHCl_3$) 1735 (acetate C=O) and 1695 cm^{-1} (conjugated C=O).

Conversion of Diphenylacetone Oxime Acetate (25) into Acetoxy Ketone 24.—After reaction of 7.999 g (53.3 mmol) of trimethyloxonium fluoroborate with 7.152 g (26.8 mmol) of oxime acetate **25** in 25 ml of CH_3NO_2 for 2.1 hr, the mixture was quenched in 80 ml of cold (0°) Et_3N and then stirred at 25–30° for 30 min. The usual hydrolysis and isolation procedure separated the crude product (a brown liquid) which was divided into two equal portions for purification. One aliquot was chromatographed (SiO_2) to separate 2.4 g (68%) of crude acetoxy ketone **24** (identified by ir absorption) in fractions eluted with PhH and with PhH–Et_2O. This material was added to a solution of 5 ml of aqueous 2 *M* HCl in 25 ml of MeOH and allowed to stand at 25–30° for 62 hr. After dilution with water, 1.744 g (57.5%) of 1,3-diphenyl-1-hydroxy-2-propanone was collected as tan needles, mp 112–114°. The second aliquot was distilled in a short-path still (0.02 mm, 150° bath) and the distillate (2.00 g or 56% of crude acetoxy ketone **24**, identified by ir absorption) was hydrolyzed as described above to yield 1.203 g (50.5%) of hydroxy ketone, mp 113–114.5°. After recrystallization (cyclohexane–MeOH) each of these hydroxy ketone samples melted at 114.5–115.5° and was identified with an authentic sample by a mixture melting point.

To obtain authentic samples 1,3-diphenyl-2-propanone (**12**) was brominated according to a published procedure[36] to yield crude 1-bromo-1,3-diphenyl-2-propanone as white needles, mp 44–47° (lit.[37] 47–48°), from pentane–Et_2O followed by sublimation: ir (CCl_4) 1735 cm^{-1} (C=O); nmr ($CDCl_3$) δ 6.9–7.7 (10 H, m, aryl CH), 5.57 (1 H, s, BrCHCO), and *ca.* 3.75 1nd 3.97 (2 H, AB pattern, J = 16 Hz, CH_2CO); mass spectrum, molecular ion at *m/e* 290 (^{81}Br isotope), abundant fragments at *m/e* 119 ($C_6H_5CH_2C{\equiv}O^+$) and 91 ($C_7H_7^+$) as well as weak peaks at *m/e* 169 and 171 ($C_7H_6Br^+$). 1,3-Dibromo-1,3-diphenyl-2-propanone (a mixture of diastereoisomers) was isolated as white needles: mp 71–97° (lit.[36] mp 79–97°); ir (CCl_4) 1740 cm^{-1} (C=O of α,α′-dibromo ketone); nmr ($CDCl_3$) δ 7.0–7.7 (10 H, m, aryl CH) and 5.65–5.85 (2 H, m, BrCHCO); mass spectrum, abundant fragments at *m/e* 208, 180, 179, 178, 141, 91, 82, 80, 44, and 40. Reaction of the dibromo ketone with NaI in aqueous acetone[38] yielded 89.5% **1-hydroxy-1,3-diphenyl-2-propanone**, mp 115–116° (lit.[38] mp 114.5–116.5°), or white needles, mp 117–117.5°, after recrystallization (cyclohexane–MeOH): ir ($CHCl_3$) 3470 (associated OH) and 1725 cm^{-1} (C=O); uv (95% EtOH) 253 mμ (ε 405), 259 (473), 264 (422), and 293 (365); nmr [$(CD_3)_2SO$ + D_2O)] δ 6.8–7.8 (10 H, m, aryl CH), 5.23 (1 H s, OCHCO), and 3.83 (2 H, s, CH_2CO); mass spectrum, molecular ion at *m/e* 226 with abundant fragments at *m/e* 208, 121, 107 ($C_7H_6OH^+$), 105, 92 (fragment A),

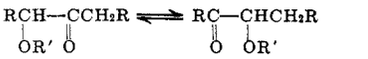


A

91 ($C_7H_7^+$), 79, and 77. Acetylation of this hydroxy ketone with NaOAc and Ac_2O in refluxing Et_2O for 45 hr followed by distillation of the crude neutral product in a short-path still (0.02 mm, 140° bath) formed acetoxy ketone **24** as a pale yellow liquid, $n^{28}D$ 1.5516 [(lit.[39] bp 195° (5 mm)], in 88.6% yield: ir (liquid film) 1745 (ester C=O) and 1735 cm^{-1} (C=O); uv (95% EtOH) 253 mμ (ε 636), 258 (679), 264 (622), and 289 (478); nmr (CCl_4) δ 6.8–7.6 (10 H, m, aryl CH), 5.96 (1 H s, OCHCO), 3.58 (2 H, s, CH_2CO), and 2.03 (3 H, s, CH_3CO); mass spectrum, molecular ion at *m/e* 268 with abundant fragments, *m/e* 177 [$C_6H_5CH(OCOCH_3)C{\equiv}O^+$], 149 ($C_7H_6OC^+CH_3$), 107 ($C_7H_6OH^+$), 91 ($C_7H_7^+$), and 43. After a solution of 690 mg (2.57 mmol) of acetoxy ketone **24** in a mixture of 1.25 ml of aqueous 2 *M* HCl and 6 ml of MeOH had been stirred at 25–30° for 62 hr, dilution with H_2O precipitated 533 mg (92%) of the crude 1-hydroxy-1,3-diphenyl-2-propanone. After recrystallization from cyclohexane–MeOH, the α-hydroxy ketone (433 mg or 74%) was obtained as needles, mp 115.2–116.4°, which was identified with the previously described sample by a mixture melting point and comparison of ir spectra.[32]

In an adaptation of a previously described general procedure,[40] a solution of 1.988 g (4.49 mmol) of anhydrous $Pb(OAc)_4$ and 605 mg (2.67 mmol) of 1-hydroxy-1,3-diphenyl-2-propanone in MeOH–HOAc (1:1 v/v) was heated at 50–55° with stirring under N_2 for 2.1 hr and then treated with 10 ml of H_2O, 0.35 ml (0.63 g, 6.4 mmol) of concentrated H_2SO_4, and 406 mg of *n*-butylbenzene and extracted with CH_2Cl_2. After the organic extract had been washed with aqueous $NaHCO_3$, analysis by glpc[29] indicated the presence of benzaldehyde (yield 82%, retention time 17.0 min), *n*-butylbenzene (36.5 min), and methyl phenylacetate (86%, 54.5 min). Methyl benzoate (38.5 min)

(33) From the mass spectra of the α-bromo ketone, the α-acetoxy ketone, and the α-hydroxy ketone, and from the similarities in the nmr spectra of these three compounds, we conclude that the potential problem with isomerization i ⇌ ii (R′ = H or $COCH_3$) has not complicated the products we have isolated.



(34) Prepared by the procedure of H. Meerwein, *Org. Syn.*, **46**, 120 (1966).

(35) B. B. Corson and N. A. Saliani, "Organic Syntheses," Coll. Vol. II, John Wiley & Sons, Inc., New York, N. Y., 1943, p 69.

(36) R. Breslow, T. Eicher, A. Krebs, R. A. Peterson, and J. Posner, *J. Amer. Chem. Soc.*, **87**, 1320 (1965).

(37) A. C. B. Smith and W. Wilson, *J. Chem. Soc.*, 1342 (1955).

(38) A. W. Fort, *J. Amer. Chem. Soc.*, **84**, 2620 (1962).

(39) V. I. Veksler, *Zh. Obsch. Khim.*, **20**, 1289 (1950); *Chem. Abstr.*, **45** 1540 (1951).

(40) E. Baer, *J. Amer. Chem. Soc.*, **62**, 1597 (1940).

and phenylacetaldehyde (24.5 min) were not detected. Collected samples of the benzaldehyde and methyl phenylacetate were identified by comparison of ir spectra and glpc retention times.

Conversion of Cyclohexanone Oxime Acetate (23) into 2-Acetoxycyclohexanone (22).—A mixture of 1.637 g (10.9 mmol) of trimethyloxonium fluoroborate, 833 mg (5.37 mmol) of oxime acetate **23**, and 10 ml of CH_2Cl_2 was stirred at 25–30° for 2 hr (alkylation complete by ir analysis) and then added to 7.5 ml of cold (0°) Et_3N and stirred for 45 min. After the usual hydrolysis and isolation procedures, 304 mg of *n*-butylbenzene was added and the CH_2Cl_2 solution of products was analyzed by glpc.[29,30] The calculated yields were 3% cyclohexanone (**13**, euted first), 51% 2-acetoxycyclohexanone (**27**, eluted second), and 15.5% keto amide **26** (eluted third). Cyclohexanone was identified by its glpc retention time and a collected[29] sample of acetoxy ketone **22** was identified with an authentic sample by comparison of ir spectra and glpc retention times. Reaction of cyclohexanone with $Pb(OAc)_4$ as previously described[14] yielded an authentic sample of the pure[29] acetoxy ketone **22**: bp 99–103° (5 mm); $n^{25}D$ 1.4587 [lit.[14] bp 123–126° (16 mm)]; ir (CCl_4) 1760 (ester C=O) and 1735 cm^{-1} (C=O); nmr (CCl_4) δ 4.8–5.3 (1 H, m, OCHCO) and 2.03 (*ca.* 3 H, s, CH_3CO) superimposed on 1.3–2.7 (*ca.* 8 H, m, aliphatic CH); mass spectrum, molecular ion at *m/e* 156, abundant fragments at *m/e* 113, 67, and 43. A collected[29] sample of keto amide **26** was identified with a subsequently described sample by comparison of ir spectra and glpc retention times.

To examine the effect of reaction time after the alkylated product has been treated with Et_3N, the alkylation reaction was repeated (reaction time 2–4 hr) and the resulting suspension was added to cold (0°) Et_3N. Aliquots of the resulting mixture were removed, hydrolyzed, and analyzed[29,30] periodically. The results of this study are summarized in Table I. In one case the triethylamine solution was allowed to stir for 240 min and then the crude product was fractionally distilled. Keto amide **26** was isolated in 44% yield as a colorless liquid, bp 103–106° (0.20 mm), $n^{25}D$ 1.4923, which contained a single component by glpc:[29] ir (CCl_4) lacks absorption in the 3- or 6-μ regions attributable to NH and has peaks at 1725 (ketone C=O) and 1650 cm^{-1} (amide C=O); nmr (C_6D_6) δ 5.0–5.5 (1 H, m, NCHCO), with *ca.* 3 H singlets at 2.57 (CH_3N) and 1.85 (CH_3CO) superimposed on a multiplet at 1.0–3.0 (*ca.* 8 H, aliphatic CH); mass spectrum, molecular ion at *m/e* 169, abundant fragments at *m/e* 126, 98, 74, 70, 43, 42, and 41.

Anal. Calcd for $C_9H_{15}NO_2$: C, 63.88; H, 8.94; N, 8.28. Found: C, 63.63; H, 8.92; N, 8.11.

Reaction of Cyclohexanone with O-Acetyl-N-methylhydroxylamine Hydrochloride (29).—A mixture of 1.9 g of Linde Molecular Sieve No. 5A, 318 mg (2.53 mmol) of hydroxylamine salt **29**, 501 mg (5.11 mmol) of cyclohexanone, and 10 ml of CH_2Cl_2 was stirred at 25–30° for 36 hr. Then 258 mg of *n*-butylbenzene (internal standard) was added and an aliquot of the mixture was washed with water and analyzed by glpc[29,30] indicating a 44% yield of acetoxy ketone **22**. A comparable hydrolysis and analysis after a 64-hr reaction period indicated the yield of acetoxy ketone **22** to be 46% with cyclohexanone as the only other volatile product detected. A collected[29] sample of acetoxy ketone **22** was identified with an authentic sample by comparison of glpc retention times and ir spectra.

Attempts to accomplish the conversion by reaction of cyclohexanone in CH_2Cl_2 with hydroxylamine salt **29** in the presence of excess Et_3N with or without $CaCl_2$[41] resulted in the formation of only small amounts of the acetoxy ketone.

Preparation of the Ketone 37.—Published[2a] procedures were followed to prepare 1-(4-methoxyphenyl)-3-(4-nitrophenyl)-1-propanol. However, the previously noted[2a] difficulty in dehydrating this alcohol to the corresponding olefin led us to use the following procedure. A solution of 17.332 g (59.8 mmol) of 1-(4-methoxyphenyl)-3-(4-nitrophenyl)-1-propanol, 11.71 g (117 mmol) of KOAc, and 50 ml of Ac_2O was heated to 85–95° for 6 hr and then diluted with 150 ml of water. Solid $NaHCO_3$ was added and the mixture was extracted with CH_2Cl_2. After the organic extract had been dried and concentrated, the residual pale yellow solid (19.5 g) was recrystallized (Et_2O) to separate 16.73 g (88.5%) of **1-acetoxy-1-(4-methoxyphenyl)-3-(4-nitrophenyl)propane** as pale yellow prisms: mp 61–63.5°; ir (CCl_4) 1740 cm^{-1} (ester C=O); uv (CH_3CN) 222 mμ (ε 16,100), 276 (12,500), and 280 (12,300); nmr ($CDCl_3$) δ 6.7–8.3 (8 H, m, aryl CH), 5.71 (1 H, t, J = 7 Hz, AcOCHAr), 3.79 (3 H, s, OCH_3), 2.04 (3 H, s, CH_3CO), and 1.7–3.0 (4 H, m, aliphatic CH); mass spectrum, abundant fragments at *m/e* 117, 91, 60, 58, 45, 44, and 43.

Anal. Calcd for $C_{18}H_{19}NO_5$: C, 65.64; H, 5.82; N, 4.25. Found: C, 65.67; H, 5.54; N, 4.03.

A solution of 5.01 g (15.2 mmol) of this acetate and 80 mg of TsOH in 100 ml of PhH was refluxed for 20 min and then cooled, washed with aqueous $NaHCO_3$, dried, and concentrated. The residual oil, 4.067 g (99%) of **1-(4-methoxyphenyl)-3-(4-nitrophenyl)propene**, crystallized as pale yellow prisms, mp 84–87° (lit.[2a] mp 89.8–90.6°), identified with the previously described[2a] material by comparison of ir spectra. This olefin was converted into ketone **37**, mp 94–95° (lit.[2a] 94–94.5°), by the published[2a] procedure. The reported[2a] nmr data for ketone **37** in $CDCl_3$ solution were complicated by partial overlap of the methoxy peak with the peak for one benzylic methylene group. A more satisfactory spectrum was obtained in $(CD_3)_2CO$ with peaks at 6.7–8.3 (8 H, m, aryl CH), 3.99 (2 H, s, benzylic protons of $-CH_2C_6H_4NO_2$–4), 3.79 (2 H, s, benzylic protons of $-CH_2C_6H_4OCH_3$–4), and 3.74 (3 H, s, OCH_3). When a solution of 62 mg of ketone **37** in 0.300 ml of acetone-d_6 was treated with 2 drops of 2% DCl in D_2O the respective times for exchange of one-half of the benzylic protons for deuterons were approximately 15 min for the δ 3.99 peak and 45 min for the δ 3.79 peak. When a comparable solution was treated with 2 drops of 20% DCl in D_2O, the approximate times for half-exchange were 2 min for the δ 3.99 peak and 10 min for the δ 3.79 peak. Similar treatment of a solution with 2 drops of 2% NaOD in D_2O resulted in the immediate formation of a deep purple color and essentially complete exchange in 20 sec for the δ 3.99 peak; the approximate time for half-exchange for the δ 3.79 peak was 8 min. Thus, with both acidic and basic catalysts, the benzylic protons adjacent to the *p*-nitrophenyl ring are removed more rapidly than protons at the other benzylic position. It was also of interest to note that, except for the loss of benzylic CH absorption, the nmr spectrum of ketone **37** in the alkaline acetone-d_6 solution was unaltered for at least 15 min indicating the absence of rapid degradation in the basic solution.

Preparation of the Oxime Derivatives 41 and 42 of 2-Methylcyclohexanone (38).—Reaction of 35.2 g (0.314 mol) of ketone **38** with an aqueous solution of $HONH_3Cl$ and NaOAc yielded, after distillation, 32.00 g (80%) of a liquid, bp 66.5° (0.3 mm), which partially crystallized on standing. Successive recrystallizations (Et_2O–hexane and hexane) at Dry Ice temperatures separated 20.74 g (52%) of the **oxime stereoisomer 41a** as white needles, mp 43–44° [lit. mp 42–43°,[10a] 43–44,[10b] bp 104° (15 mm),[10a] 114–115° (16 mm)[10c]]. This isomer, believed to have the configuration indicated in structure **41a**,[11,42] has the following spectral properties: ir ($CHCl_3$) 3570, 3265 (free and associated OH), and 1660 cm^{-1} (C=N); nmr ($CDCl_3$) δ 14.20 (1 H, s, OH), 3.0–3.5 (1 H, m, CHC=N), 1.0–2.7 (8 H, m, aliphatic CH), and 1.13 (3 H, d, J = 6.5 Hz, CCH_3); mass spectrum, molecular ion at *m/e* 127, abundant fragments at *m/e* 110, 95, 67, 55, 41, 39, and 27. The crude liquid oxime (believed to be a mixture of **41a** and **42a**) recovered from the recrystallization mother liquors had ir and nmr absorption very similar to that of the pure crystalline isomer.

To a solution of 3.71 g (17.8 mmol) of PCl_5 in 40 ml of CH_2Cl_2 was added, portionwise with stirring, 2.135 g (16.8 mmol) of oxime **41a** (mp 43–44°). The reaction mixture was stirred for 5 min, then poured with stirring into 100 ml of boiling H_2O, neutralized (pH 8) with $NaHCO_3$, and concentrated, and the residual solid was extracted with CH_2Cl_2. Drsing and concentration of the organic extract left 1.621 g (76%) of crude lactam **46**, mp 60–77°. Recrystallization from hexane gave 1.074 g (50%) of lactam **46** as white needles melting within the range 82–88°: mp 89–91° after recrystallization [lit. mp 90–91°,[11b] 91–92°[11c,42a]]; ir (CCl_4) 3390, 3280, 3190 (free and associated NH), and 1665 cm^{-1} (amide C=O); nmr ($CDCl_3$) δ 3.50 (1 H, m, >NCH<), 2.44 (2 H, m, CH_2CO), 1.0–2.2 (8 H, m, aliphatic CH), and 1.24 (2 H, d, J = 6.8 Hz, CH_3C); mass spectrum, molecular ion at *m/e* 127, abundant fragments at *m/e* 112, 85, 55, 44, and 41.

A solution of 13.88 g (0.109 mol) of oxime **41a** and 16.35 g (0.151 mol) of Ac_2O in 25 ml of CH_2Cl_2 was refluxed for 3 hr and

(41) E. P. Blanchard, Jr., *J. Org. Chem.*, **28**, 1397 (1963).

(42) The melting points reported for the isomeric lactams are 90–91° and 91–92° for **46** [see ref 11 and (a) F. F. Blicke and N. J. Doorenbos, *J. Amer. Chem. Soc.*, **76**, 2317 (1954); (b) B. Philips, S. W. Tinsley, and P. S. Starcher, U. S. Patent 3,000,878; *Chem. Abstr.*, **56**, 1355 (1962)] and 97–98° for **47** (ref 11c).

then cooled and worked up (aqueous $NaHCO_3$ and CH_2Cl_2). Distillation of the residual liquid separated 17.06 g (93%) of **oxime acetate 41b** as a colorless liquid: bp 74–74.5° (0.16 mm); $n^{25}D$ 1.4768; ir (liquid film) 1765 (ester C=O) and 1635 cm^{-1} (C=N); nmr (CCl_4) δ 1.3–3.5 (9 H, m, aliphatic CH), 2.09 (3 H, s, CH_3CO), and 1.15 (3 H, d, J = 6.5 Hz, CCH_3); mass spectrum, molecular ion at m/e 169, abundant fragments at m/e 95, 81, 55, 43, 41, 39, and 27.

Anal. Calcd for $C_9H_{15}NO_2$: C, 63.88; H, 8.94; N, 8.28. Found: C, 63.59; H, 8.93; N, 8.44.

A solution of 2.24 g (17.6 mmol) of oxime **41a** and 1.55 g (9.64 mmol) of 1,1,1,3,3,3-hexamethyldisilazane in 5 ml of CH_2Cl_2 was allowed to stand at 25–30° for 8 days and then concentrated and distilled to separate 3.184 g (91%) of **silyl ether 41c** as a colorless liquid: bp 78–79.5° (10 mm); $n^{25}D$ 1.4480. The product exhibited a single peak on glpc:[29] ir (liquid film) 1630 cm^{-1} (weak, C=N); nmr (CCl_4) δ 1.2–2.3 (9 H, m, aliphatic CH), 1.07 (3 H, d, J = 6.5 Hz, CCH_3), and 0.15 (9 H, s, $SiCH_3$); mass spectrum, molecular ion at m/e 199 (^{28}Si isotope), abundant fragments at m/e 184, 75, 73, 55, 45, 41, 29, and 27.

Anal. Calcd for $C_{10}H_{21}NOSi$: C, 60.24; H, 10.62; N, 7.03. Found: C, 60.06; H, 10.50; N, 6.88.

A similar reaction of 10.88 g (111 mmol) of cyclohexanone oxime with 9.374 g (58.1 mmol) of 1,1,1,3,3,3-hexamethyldisilazane in 75 ml of CH_2Cl for 83 hr yielded 14.81 g (77%) of the **trimethylsilyl ether of cyclohexanone oxime**, bp 73–75° (20 mm), $n^{25}D$ 1.4551, which contained on major component (>99%) by glpc.[43] A sample of the product was collected[43] for characterization: ir (CCl_4) 1630 cm^{-1} (C=N); nmr (CCl_4) δ 1.4–2.8 (10 H, m, aliphatic CH) and 0.15 (9 H, s, $SiCH_3$); mass spectrum, molecular ion at m/e 185 (^{28}Si isotope), abundant fragments at m/e 170, 96, 75, 45, 41, and 27.

Anal. Calcd for $C_9H_{19}NOSi$: C, 58.32; H, 10.33; N, 7.56. Found: C, 58.46; H, 10.36; N, 7.86.

Following a general procedure used previously for the isomerization of benzaldoxime,[13] a solution of 2.179 g (17.2 mmol) of oxime **41a** in 40 ml of anhydrous Et_2O was saturated with HCl gas at 25–30°. The crude hydrochloride salt which separated was washed with Et_2O and then added to a cold (0°), rapidly stirred solution of 1.85 g (17.4 mmol) of Na_2CO_3 in 150 ml of H_2O. The mixture (pH 9) was extracted with Et_2O and the extract was dried and concentrated. The ir and nmr absorption of the residual liquid (1.749 g or 80%) were similar to the spectra of the starting crystalline oxime **41a**. However, reaction of a 101-mg (0.795 mmol) sample of this crude oxime product with 180 μl of O,N-bis(trimethylsilyl)acetamide in 2.0 ml of hexane for 24 hr afforded a mixture of silyl ethers containing[29] both the previously described silyl ether **41c** and a component, believed to be the isomeric silyl ether **42c**, which was eluted slightly more rapidly. A cold (0°) solution of 1.277 g (10 mmol) of the mixture of oximes **41a** and **42a** in 4 ml of pyridine was treated with 2.127 g (20.8 mmol) of Ac_2O. After the resulting mixture had been allowed to stand at 0° for 22 hr, 4 ml of MeOH was added and the mixture was concentrated under reduced pressure to leave 1.643 g (97%) of a mixture of oxime acetates **41b** and **42b**. A portion of this product was distilled in a short-path still (0.1 mm and 60° bath). Although the ir spectra of these samples (distilled and undistilled) are similar to the spectrum of the previously described acetate **41b**, the nmr spectrum (C_6D_6) of the distilled mixture shows, in addition to an aliphatic CH multiplet (δ 1.0–3.4) and an acetyl singlet (δ 1.88), two doublets of approximately equal intensity at δ 1.11 (J = 6.5 Hz) and 0.91 (J = 7.2 Hz) attributable to the C-methyl doublets of **41b** and **42b**, respectively. In $CDCl_3$ solution these doublets are located at δ 1.12 and 1.14. Since complications from isomerization and thermal instability prevented us from isolating the pure oxime acetate **42b**, this mixture of oxime acetates **41b** and **42b** was employed in our subsequent studies.

Conversion of 2-Methylcyclohexanone Oxime Acetate (41b and 42b) into the Acetoxy Ketones 43 and 44.—After a solution of 13.22 g (78.1 mmol) of oxime acetate **41b** and 13.16 g (89.0 mmol) of trimethyloxonium fluoroborate in 30 ml of CH_2Cl_2 had been stirred for 3 hr, the alkylation was complete (ir analysis) and the mixture was added to 75 ml of cold (0°) Et_3N, and then subjected to the usual hydrolysis and isolation procedure. Distillation separated 5.510 g (41%) of a mixture of acetoxy ketones, bp 62–64° (0.12 mm), which contained[29] 46% ketone **44** (eluted first) and 54% ketone **43** (eluted second). Less than 1% of the tertiary acetoxy ketone **45** was present. Collected[29] samples of ketones **43** and **44** were identified with subsequently described samples by comparison of ir spectra and glpc retention times. In a comparable experiment where an internal standard (*n*-butylbenzene) was added to the crude product, the calculated[29] yields were 0.5% **45** (retention time 45.3 min), 17% **44** (52.9 min), and 31% **43** (61.2 min). The same experiment was repeated employing the previously described mixture of oxime acetates **41b** and **42b**. The calculated[29] yields of products were 17% ketone **44** and 34% ketone **43** with less than 1% tertiary acetate **45**.

To obtain authentic samples of acetoxy ketones **43–45**, a solution of 68.28 g (0.608 mol) of 2-methylcyclohexanone (**38**) and 139.5 g (0.315 mol) of $Pb(OAc)_4$ in 500 ml of PhH was refluxed for 12 hr at which time no Pb(IV) salt remained. The reaction mixture was partioned between H_2O and CH_2Cl_2 and the organic layer was washed with aqueous $NaHCO_3$, dried, and concentrated Fractional distillation of the residue (75 g of yellow liquid) separated 20.1 g of crude starting ketone **38**, bp <40° (5.2 mm), 13.45 g of fractions, bp 40–60.5° (5.2–0.2 mm), containing[29,43] starting material and acetoxy ketones **43–45**, 22.16 g of fractions, bp 60.5–64.2° (0.2 mm), containing[29,43] acetoxy ketones **43–45**, and 5.00 g of fractions, bp 64–105° (0.2 mm), containing[43] the three acetoxy ketones and higher boiling materials. The composition of the acetoxy ketone mixture in this reaction was 23% **45** (first eluted), 54% **44** (eluted second), and 23% **43** (eluted third). Further distillation (50-cm Teflon spinning-band column) afforded fractions enriched in each of the acetoxy ketones from which pure samples were collected.[43] The tertiary **acetoxy ketone 45**[44] has the following spectral propertes: ir (CCl_4) 1745 (ester C=O) and 1730 cm^{-1} (C=O); nmr ($CDCl_3$) δ 1.2–2.8 (8 H, m, aliphatic CH), 2.09 (3 H, s, CH_3CO), and 1.42 (3 H, s, CCH_3); mass spectrum, molecular ion at m/e 170, abundant fragments at m/e 127, 81, 71, 58, and 43.

The second acetate eluted is believed to be the less stable *trans* **isomer 44**: ir (CCl_4) 1750 (ester C=O) and 1730 cm^{-1} (C=O); nmr (CCl_4) δ 5.05 (1 H, m, AcOCHCO), 1.0–3.0 (7 H, m, aliphatc CH), 2.07 (3 H, s, CH_3CO), and 1.12 (3 H, d, J = 7.0 Hz, CCH_3); mass spectrum, molecular ion at m/e 170, abundant fragments at m/e 128, 81, 55, 43, and 41.

Anal. Calcd for $C_9H_{14}O_3$: C, 63.51; H, 8.29. Found: C, 63.44; H, 8.31.

The third acetoxy ketone eluted is believed to be the more stable *cis* **isomer 43**: ir (CCl_4) 1755 (ester C=O) and 1735 cm^{-1} (C=O); nmr (CCl_4), δ 5.06 (1 H, m, AcOCHCO), 1.2–2.8 (7 H, m, aliphatic CH), 2.06 (3 H, s, CH_3CO), and 1.00 (3 H, d, J = 6.5 Hz, CCH_3); mass spectrum, molecular ion at m/e 170, abundant fragments at m/e 128, 127, 81, 55, 43, and 41.

Anal. Calcd for $C_9H_{14}O_3$: C, 63.51; H, 8.29. Found: C, 63.66; H, 8.37.

The nmr spectra of the two secondary acetoxy ketones **43** and **44** were also determined in C_6D_6 solution. *cis* isomer **43** (presumably with both acetoxy and methyl groups in equatorial positions) has peaks at δ 1.94 (3 H, s, CH_3CO) and 0.93 (3 H, d, J = 6.2 Hz) whereas the corresponding peaks for *trans* isomer **44** (presumably a mixture of conformers in which either the AcO group or the Me group is axial) are found at δ 1.90 and 0.99 (J = 7.0 cps). Because of the small differences in chemical shifts and coupling constants observed for the two isomers, it seemed inadvisable to use the various empirical relationships[45] to assign stereochemistry to the two acetoxy ketones. Consequently, mixtures containing various proportions of acetoxy ketones **43–45** were heated to 150° in quinoline solution until the proportions of compounds **43** and **44** became constant. The approximate equilibrium concentrations of the two secondary

(43) A gas chromatography column packed with silicone fluid, no. 710, suspended on Chromosorb P was employed for this analysis.

(44) E. W. Warnhoff and W. S. Johnson [*J. Amer. Chem. Soc.*, **75**, 494 (1953)] reported by 105–107° (6 mm); J. Colonge and J. C. Dubin reported[32] bp 89° (4.5 mm).

(45) Usually an axial C-methyl group is found at higher field and, when α to a ketone, this group undergoes a larger upfield shift when the solvent is changed from CCl_4 to C_6D_6: (a) N. S. Bhacca, and D. H. Williams, "Applications of Nmr Spectroscopy in Organic Chemistry," Holden-Day, Inc., San Francisco, Calif., 1964; (b) M. Fetizon, J. Gore, P. Laszlo, and B. Waegell, *J. Org. Chem.*, **31**, 4047 (1966). (c) It has also been noted [T. M. Moynehan, K. Schofield, R. A. Y. Jones, and A. R. Katritzky, *J. Chem. Soc.*, 2637 (1962)] that the vicinal coupling constant is usually larger for an equatorial H–axial CH_3 arrangement than for an equatorial CH_3–axial H. This latter coupling constant correlation is consistent with our assignment. The chemical shift differences ($\Delta_{CCl_4}^{C_6D_6}$ values of 0.07 ppm for **43** and 0.13 ppm for **44**) are also in the predicted direction.

acetates were 75–80% **43** and 20–25% **44** leading to the assignment of the *cis* stereochemistry **43** (two equatorial substituents) to the more stable epimer.

Reaction of 2-Methylcyclohexanone (38) with O-Acetyl-N-methylhydroxylamine Hydrochloride (29).—A mixture of 306 mg (2.73 mmol) of ketone **38**, 257 mg (2.06 mmol) of hydroxylamine salt **29**, 1.15 g of Linde Molecular Sieves No. 5A, and 2.5 ml of CH_2Cl_2 was stirred at 25–30° for 44 hr. The resulting mixture was mixed with *n*-butylbenzene (internal standard), washed with H_2O, and analyzed.[29] The calculated yield of the acetoxy ketone mixture was 25% containing 56% **45**, 30% **44**, and 14% **43**. The same mixture of acetoxy ketones was obtained in a duplicate experiment. Collected[29] samples of the three acetoxy ketones were identified with previously described samples by comparison of ir spectra and glpc retention times.

Preparation of the Oxime Derivatives 39 and 40 of Ketone 37.—Reaction of 10.01 g (35.6 mmol) of ketone **37** with a mixture of $NaHCO_3$ and $HONH_3Cl$ in H_2O–MeOH yielded 10.07 g (95.7%) of a mixture of oximes **39a** and **40a** as tan needles, mp 100–110°. Application of the subsequently described nmr analysis indicated that this crude product contained 41% *syn-p*-methoxybenzyl isomer **40a** and 59% *syn-p*-nitrobenzyl isomer **39a**. Application of the previously described[2a] fractional crystallization with 1,2-dimethoxyethane–Et_2O (1:1 v/v) as a solvent separated 1.439 g of the less-soluble *syn-p*-nitrobenzyl isomer **39a** as pale yellow prisms, mp 138–144.5° (lit.[2a] mp 141.3–143.2°), estimated (nmr analysis) to contain more than 95% isomer **39a**. A series of fractional crystallizations separated 273 mg of a sample of the more-soluble oxime isomer **40a** as pale yellow needles, mp 130–133 (lit.[2a] mp 133–134.2°), estimated (nmr analysis) to contain 95% isomer **40a**. The nmr absorptions of the two oxime isomers were effectively resolved by use of CD_3COCD_3 as a solvent. In this medium the *syn-p*-nitrobenzyl isomer **39a** has absorption at δ 6.7–8.3 (8 H, m, aryl CH), 3.74 (5 H, superimposed signals for OCH_3 and *p*-nitrobenzyl CH_2), and 3.42 (2 H, s, *p*-methoxybenzyl CH_2) while the *syn-p*-methoxybenzyl isomer **40a** has absorption at δ 6.7–8.3 (8 H, m, aryl CH), with singlets at δ 3.74 (3 H, OCH_3), 3.63 (2 H, *p*-nitrobenzyl CH_2), and 3.55 (2 H, *p*-methoxybenzyl CH_2). These chemical shift values are consistent with the empirical correlation[20] which noted that α-methylene protons *cis* to an oxime hydroxy function are found at lower field than the corresponding *trans*-α-methylene protons (*e.g.*, the *p*-methoxybenzylic protons are at lower field for isomer **40a** than for isomer **39a**). Consequently, these nmr data are consistent with the configuration assigned previously[2a] to the oximes **39a** and **40a** as a result of Beckmann rearrangements.

A cold (0°) solution of 273 mg (0.91 mmol) of the more-soluble oxime isomer **40a** (mp 130–133°) in 2 ml of pyridine was treated with 205 mg (2.0 mmol) of Ac_2O and allowed to stand in the cold for 20 hr. After dilution with MeOH and concentration, the residual crude acetate **40b** (290 mg or 93%, mp 93–98°) was recrystallized from MeOH to separate 175 mg (56%) of **oxime acetate 40b** as pale yellow needles: mp 102–103°; ir ($CHCl_3$) 1765 (ester C=O) and 1630 cm^{-1} (C=N); uv (CH_3CN) 215 mμ (ε 15,400) and 273 (11,800); nmr (CD_3COCD_3) δ 6.7–8.3 (8 H, m, aryl CH) with three closely spaced singlets (total 7 H) at δ 3.76 (OCH_3), 3.72 (benzylic CH_2), and 3.70 (benzylic CH_2) as well as a singlet at δ 2.17 (3 H, CH_3CO).

Anal. Calcd for $C_{18}H_{18}N_2O_5$: C, 63.15; H, 5.30; N, 8.18. Found: C, 63.03; H, 5.39; N, 8.15.

Crystalline oxime acetate **40b** was more efficiently prepared by direct actylation of the crude mixture of oximes **39a** and **40a** either before or after removal of the less-soluble oxime **39a** by fractional crystallization.

Following the previously described procedure, 1.222 g (4.075 mmol) of the less-soluble oxime isomer **39a** (mp 138–144.5°) was acetylated to yield 1.495 g of he crude oxime acetate **39b** as a yellow oil. Since attempts to recrystallize this material were unsuccessful, a sample was chromatographed (SiO_2). The pure **oxime acetate 39b** was eluted with hexane–Et_2O as a pale yellow liquid: ir ($CHCl_3$) 1765 (ester C=O) and 1630 cm^{-1} (C=N); uv (CH_3CN) 274 mμ (ε 10,900); nmr (CD_3COCD_3) δ 6.7–8.3 (8 H, m, aryl CH), 3.85 (2 H, s, *p*-nitrobenzyl CH_2), 3.75 (3 H, s, OCH_3), 3.59 (2 H, s, *p*-methoxybenzyl CH_2), and 2.13 (3, H, s, CH_3CO).

Anal. Calcd for $C_{18}H_{18}N_2O_5$: C, 63.15; H, 5.30; N, 8.18. Found: C, 63.30; H, 5.38; N, 8.09.

Alkylation and Rearrangement of Oxime Acetates 39b and 40b.—A solution of 927 mg (6.17 mmol) of trimethyloxonium fluoroborate and 321 mg (0.938 mmol) of the *syn-p*-nitrobenzyl isomer **39b** in 3 ml of CH_3NO_2 was stirred at 25–30° for 2 hr and subjected to the usual hydrolysis and isolation procedure. Since we were unsuccessful in attempts to isolate the pure acetoxy ketones **48** and **49** from the crude reaction product, the following analytical procedure was followed. The crude product was chromatographed (SiO_2) and 96 mg of fractions containing acetoxy ketones **48** and **49** [ir ($CHCl_3$) 1750–1700 (broad, ester and ketone C=O) and 1235 cm^{-1} (ester COC)] were eluted with PhH and with PhH–Et_2O. Other fractions eluted from the column were identified as follows: (1) 18 mg of crude *p*-nitrophenylacetonitrile which melted at 113–114° after recrystallization from methanol and was identified with an authentic sample by a mixture melting point and comparison of ir spectra; (2) 35 mg of crude ketone **37** which melted at 91.5–94° after recrystallization and was identified by a mixture melting point and comparison of ir spectra. A solution of the acetoxy ketone fractions and 2 ml of 2 *M* aqueous HCl in 8 ml of MeOH was stirred at 25–30° for 91 hr and then diluted with H_2O and extracted with CH_2Cl_2. The resulting crude neutral product (85 mg of hydroxy ketones as a brown liquid) had ir absorption at 3450 (OH) and 1720 cm^{-1} (C=O) but lacked absorption in the 1200–1240-cm^{-1} region attributable to unchanged acetoxy ketone. Following the cleavage procedure previously described for 1-hydroxy-1,3-diphenyl-2-propanone, a solution of the crude hydroxy ketones was treated with 270 mg (0.59 mmol) of $Pb(OAc)_4$ in a mixture of 5 ml of anhydrous MeOH and 5 ml of anhydrous HOAc for 2.1 hr. The resulting crude neutral product was mixed with a known weight of biphenyl (internal standard) and analyzed by glpc.[29,30] The calculated[29,30] yields of cleavage products, in order of increasing retention times, were **51**, 5.1%; **50**, 4.3%, **52**, 5.1%; and **53**, 3.7%. From a second comparable experiment, the calculated yields were **51**, 4.8%; **50**, 5.9%; **52**, 5.6%; and **53**, 3.7%. A collected sample[29] of each product was identified with an authentic sample by comparison of ir spectra and glpc retention times.

Comparable reaction sequences were performed on 499-mg (1.46 mmol) and 507-mg (1.48 mmol) samples of the *syn-p*-methoxybenzyl isomer **40b**. The calculated[29,30] yields of products from the two experiments were **51**, 7.0%, 6.5%; **50**, 2.0%, 12%; **52**, 9.8%, 12%; and **53**, 6.0%, 4.0%. Collected[29] samples of these products were identified as previously described. In one experiment 27 mg of ketone **37**, mp 92–94°, was also isolated. As a blank experiment, a sample of ketone **37** was treated with $Pb(OAc)_4$ under the conditions employed to cleave the corresponing hydroxy ketones. None of the cleavage products **50–53** was detected[29,30] in the crude neutral product from this blank experiment.

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