added 1.0 ml of 20% aqueous potassium hydroxide, and the reaction mixture was refluxed for 45 min under nitrogen. It was diluted with 200 ml of water and the product was extracted with chloroform. The extract was washed with water and dried over anhydrous sodium sulfate. The solvent was flash evaporated. The residue crystallized and triturated with aqueous methanol. The product, 0.174 g of needles, mp 223–228°, was purified by chromatography on 30 g of Florisil by gradient elution, 1.1 l. of benzene being used as the recipient and 200 ml of 3:7 acetone–benzene as the donor solvent. The eluent from 915 of 1185 ml gave 0.075 g of 17β-hydroxy-5α-androstane-3,6-dione (IIIb):[25] mp 232–235°; λ_{max} 2.76, 5.87 μ.

Acetylation of 30 mg of IIIb with acetic anhydride in pyridine yielded 21 mg of 17β-acetoxy-5α-androstane-3,6-dione (IIIa):[21] mp 186.5–188.5°; λ_{max} 5.80, 5.86 μ; RD (*c* 0.10), $[\alpha]_{700}$ −7°, $[\alpha]_{589}$ −6°, trough $[\alpha]_{350-420}$ −38°, peak $[\alpha]_{322}$ +152°, trough $[\alpha]_{314}$ +10°, peak $[\alpha]_{306}$ +120°, trough $[\alpha]_{302}$ +45°, peak $[\alpha]_{298}$ +106°, $[\alpha]_{290}$ −9°.

(B) To a solution of 2.8 mg of V, mp 216–218°, in 1.0 ml of methanol, was added 0.3 ml of 20% aqueous potassium hydroxide and the reaction mixture was refluxed for 15 min under nitrogen. It was diluted with 30 ml of water and the product was extracted with chloroform. The extracts were washed with water and dried over anhydrous sodium sulfate, and the solvent was evaporated to give 2.1 mg of needles, mp 223–227°. Recrystallization of the product from benzene–diethyl ether afforded 1.5 mg of colorless needles, mp 229–231°, undepressed on admixture with 17β-hydroxy-5α-androstane-3,6-dione (IIIb), mp 232–235°, obtained from IV as described above; the infrared spectra of both specimens were identical.

(25) F. Sondheimer, S. Kaufmann, J. Romo, H. Martinez, and G. Rosenkranz, *J. Am. Chem. Soc.*, **75**, 4712 (1953).

6β-Hydroxy-19-nortestosterone 17-Acetate.—A solution of 1.320 g of 19-nortestosterone enol diacetate[26] in 30 ml of 95% aqueous dioxane was treated with perchloryl fluoride, as described above for testosterone enol diacetate and worked up in the same manner, affording 1.272 g of a yellow syrup: λ_{max} 236 mμ; λ_{max} 2.75, 5.82, 5.96 μ. The product was chromatographed on a column of 50 g of Florisil by the gradient elution method using 2 l. of 1:2 × 10^3 acetone–benzene as the recipient and 300 ml of 3:17 acetone–benzene as the donor solvent. The first peak, eluted with 1800 ml of eluent, represented a mixture which could not be separated into identifiable products. The eluent from 1800 to 2200 ml gave a fraction, 0.340 g of solid, which was recrystallized from diethyl ether–*n*-hexane to afford 0.185 g (15% yield) of 6β-hydroxy-19-nortestosterone 17-acetate, mp 162–164°. Recrystallization from the same solvent mixture gave an analytical specimen: mp 166°; λ_{max} 237 mμ (log ε 4.17); λ_{max} 2.76, 5.82, 5.96 μ; RD (*c* 0.10), $[\alpha]_{700}$ −46°, $[\alpha]_{589}$ −62°; trough $[\alpha]_{371}$ −736°, peak $[\alpha]_{367}$ −705°, trough $[\alpha]_{357}$ −830°, shoulder $[\alpha]_{342-346}$ −391°, inflection $[\alpha]_{326-328}$ +225°, peak $[\alpha]_{307}$ +545°, $[\alpha]_{282}$ +39°.

Anal. Calcd for $C_{20}H_{28}O_4$: C, 72.26; H, 8.49. Found: C, 72.33; H, 8.52.

Registry No.—I, 2627-94-3; II, 855-55-0; IIIa, 745-43-7; IIIb, 899-39-8; IV, 13096-48-5; V, 13573-36-9; perchloryl fluoride, 7616-94-6; testosterone enol diacetate, 1778-93-4; 6β-hydroxy-19-nortestosterone 17-acetate, 13573-37-0.

(26) British Patent 755,129 (1956); *Chem. Abstr.*, **51**, 10601e (1957).

Photolytic Reaction of Ethyl Azidoformate with Enol Acetates

JOHN F. W. KEANA, SUE B. KEANA, AND DENNIS BEETHAM

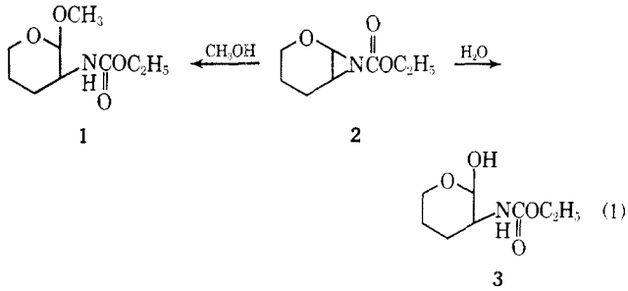
Department of Chemistry, University of Oregon, Eugene, Oregon 97403

Received April 13, 1967

Irradiation of a dilute dichloromethane solution of ethyl azidoformate and isopropenyl acetate or 1-acetoxycyclohexene leads to the corresponding very reactive N-carbethoxyaziridine which upon water treatment affords an α-carbethoxyamino ketone in modest yield. Products derived from C–H insertion of the likely intermediate, carbethoxynitrene, are also observed to a lesser extent.

Our interest in the photolysis of ethyl azidoformate[1] in the presence of enol acetates stems from a search for a new general synthesis of N-protected α-aminocarbonyl groupings (Scheme I) which could be used in connection with the synthesis of some natural products.

Brown and Edwards[2] have studied the related photochemical reaction of ethyl azidoformate with dihydropyran and have isolated in good yield the reactive aziridine **2**. Subsequent reaction of this substance with water produced urethan **3**, while with methanol urethan **1** was obtained along with some **3** (eq 1).



1 2 3 (1)

(1) W. Lwowski, T. J. Maricich, and T. W. Mattingly, Jr., *J. Am. Chem. Soc.*, **85**, 1200 (1963); W. Lwowski and T. W. Mattingly, Jr., *ibid.*, **87**, 1947 (1965); W. Lwowski and T. J. Maricich, *ibid.*, **87**, 3630 (1965); K. Hafner, W. Kaiser, and R. Puttner, *Tetrahedron Letters*, 3953 (1964).

We wish to report the results of our studies on the photodecomposition of ethyl azidoformate in the presence of somewhat less than 1 equiv of either isopropenyl acetate or 1-acetoxycyclohexene in dichloromethane solution.[3,4]

Results and Discussion

Removal of the solvent at 25° under vacuum after photolysis of a solution of ethyl azidoformate and isopropenyl acetate in dichloromethane afforded a clear pale yellow oil. The nmr and infrared spectra of this oil[5] were consistent with the presence of a large pre-

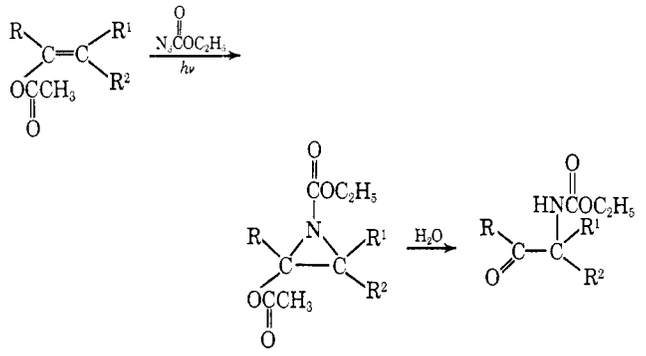
(2) I. Brown and O. E. Edwards, *Can. J. Chem.*, **43**, 1266 (1965).

(3) The photodecomposition of isopropenyl acetate and 1-acetoxycyclohexene could in principle be a serious side reaction. However, Mazur[4] has shown that ultraviolet irradiation of a dilute solution of isopropenyl acetate or 1-acetoxycyclohexene in cyclohexane for 24 hr or longer resulted in recovery of much starting enol acetate, accompanied by less than a 30% yield of rearranged products. While we have not directly observed such rearranged products in our experiments, they may well be present in minor amounts.

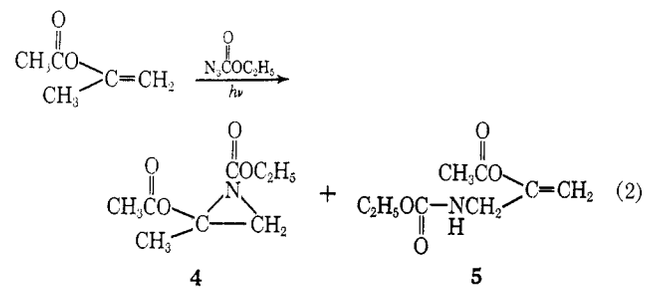
(4) A. Yogev, M. Gorodetsky, and Y. Mazur, *J. Am. Chem. Soc.*, **86**, 5208 (1964).

(5) Aziridines **4** and **9** were not stable to vapor phase chromatography or column chromatography. Vacuum distillation was accompanied by ta r formation. Nmr spectra of the distillates indicated that only slight enrichment of the aziridines had been effected. Consequently, the oily mixture rich in aziridine as obtained directly from the photolysis experiments was used for spectral determinations and chemical transformations.

SCHEME I



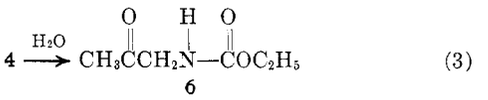
ponderance of the expected aziridine **4**, together with lesser amounts of unreacted ethyl azidoformate (weak absorption at 2135 and 2170 cm^{-1}) and possibly some enol acetate **5** (very weak N–H absorption at 3400 cm^{-1}) (eq 2) presumably derived from an insertion reaction of the likely intermediate carbethoxynitrene[1] into the C–H bond of the methyl group of isopropenyl acetate.



4 **5** (2)

The nmr spectrum of aziridine **4**[5] consisted of a triplet and a quartet centered at 1.28 and 4.17 ppm, respectively, due to the protons of the ethoxy group, a sharp singlet at 1.60 ppm due to the C-methyl group, and a sharp singlet at 2.00 ppm due to the acetoxy protons. The ring protons appeared as a broad singlet at 2.33 ppm; however, in benzene solution[6] the ring protons appeared as two broad singlets at 2.32 and 2.38 ppm downfield from internal TMS.[7-9] Moreover, the nmr spectrum of the oil clearly demonstrated the absence of a significant amount of starting isopropenyl acetate (no peak at 1.87 ppm), carbethoxyaminoacetone (**6**) (no peak at 2.13 ppm), or the oxazoline **8** (no peak at 2.49 ppm).

Aziridine **4**[5] could be selectively hydrolyzed to **6** by stirring a dichloromethane solution of aziridine **4** with water present as a second phase for several minutes (eq 3). Isopropenyl acetate was shown to be stable to these conditions. It was assumed that the enol acetate **5** was likewise stable. Vapor phase chromatography of the water-treated material revealed the presence of **6** (retention time, 9.5 min) (47% yield, based on starting isopropenyl acetate) together with a peak of retention time 13.7 min (6% yield, based on starting isopropenyl acetate), which was attributed to enol acetate **5**. Consistent with this formulation, the nmr spectrum of the water-treated material demonstrated absorption due to ketone **6** along with lesser amounts of other acetoxy-containing material. The relatively small yield of enol acetate **5** precluded its isolation and complete characterization. Ketone **6** was identified by elemental analysis and spectral and vpc comparisons with authentic material prepared by chromium trioxide oxidation of the known carbethoxyaminopropan-2-ol.[10]



6 (3)

Vapor phase chromatography of aziridine **4**[5] at 188° resulted in decomposition to **6** and a second substance with the same retention time as that of enol acetate **5** (13.7 min) in a ratio of 1:1. This second substance was collected on a preparative scale and identified as the oxazoline **8** on the basis of spectral data and elemental analysis. Material collected was probably contaminated with some of the isomeric enol acetate **5** thought to be present in the original photolysis mixture. Consistent with this contention was the weak N–H absorption at 3400 cm^{-1}, the small shoulder at 1800 cm^{-1}, and the weak absorption at 870 cm^{-1} in the infrared spectrum of the collected material. Broad intense absorption was observed at 1760 and 1710 cm^{-1} attributed to the oxazoline **8**. The absence of intense absorption in the 960–800-cm^{-1} region was consistent with the absence of hydrogens on a carbon–carbon double bond in oxazoline **8**.

The nmr spectrum of this last substance was also consistent with the oxazoline structure, exhibiting a two-proton singlet at 4.45 ppm (ring protons), a two-proton quartet centered at 4.20 ppm and a three-proton triplet centered at 1.28 ppm (ethoxy group), a three-proton singlet at 2.49 ppm (C-methyl group), and a three-proton singlet at 2.10 ppm (acetoxy protons). Moreover, the substance could be converted to **6** by treatment with aqueous methanolic hydrogen chloride.

Ketone **6** and oxazoline **8** were also formed in about a 1:3 relative ratio as judged by vpc and nmr analysis when a sample of aziridine **4**[5] was warmed in the steam bath for 1 hr. The oxazoline **8** could be envisaged as resulting from thermally induced ring opening of aziridine **4** to the ion pair **7**, followed by ring closure to give a five-membered ring (eq 4). A concerted rearrangement would also explain the transformation. The rearrangement is analogous to the well-known thermal rearrangement of certain N-acylaziridines to oxazolines.[11]

(6) N. S. Bhacca and D. H. Williams, "Applications of NMR Spectroscopy in Organic Chemistry," Holden-Day, Inc., San Francisco, Calif., 1964, Chapter 7.

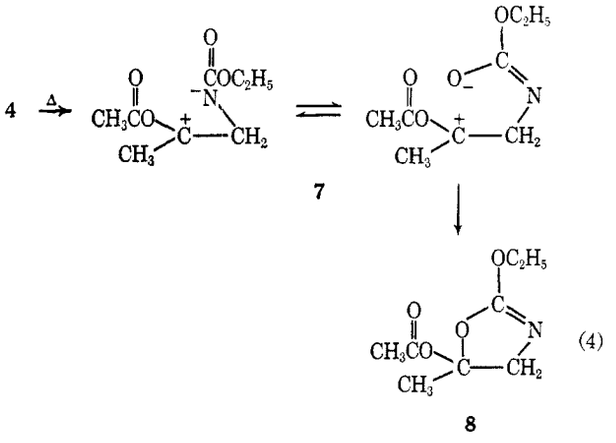
(7) The broad singlet in carbon tetrachloride must have resulted from accidental magnetic equivalence of the two ring protons. Since an AB or AX pattern for the ring protons was not observed in benzene, the geminal coupling constant must be of the order of less than 1 cps. Consistent with this contention, the geminal coupling constant for the pair of aziridine ring protons in 2-phenylaziridine is 0.87 cps.[8] It has also been estimated that the geminal coupling constant for the ring protons in 1-carbomethoxyaziridine is 1–2 cps.[9]

(8) S. L. Manatt, D. D. Elleman, and S. J. Brois, *J. Am. Chem. Soc.*, **87**, 2220 (1965).

(9) F. A. L. Anet and J. M. Osyany, *ibid.*, **89**, 352 (1967).

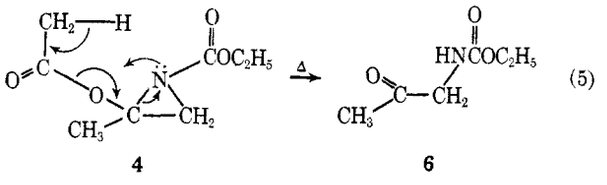
(10) Laboratoires Dausse S. A., French Patent 1,340,810 (1963); *Chem. Abstr.*, **60**, 4152*h* (1964).

(11) P. E. Fanta and E. N. Walsh, *J. Org. Chem.*, **31**, 59 (1966), and earlier papers.



(4)

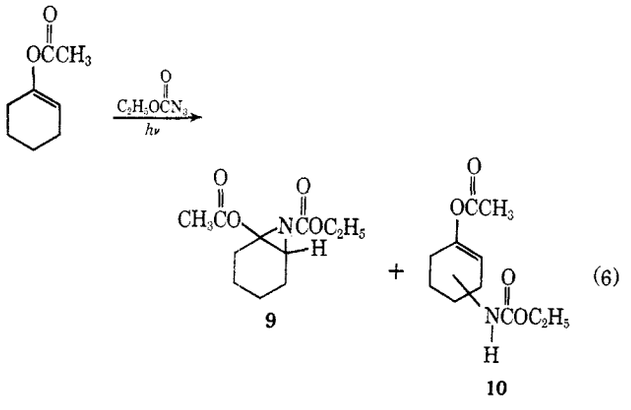
The formation of ketone **6** from aziridine **4** upon heat treatment probably results from thermal elimination of ketene (eq 5). The nitrogen atom of aziridinyl carba-



(5)

mates should be unusually basic since contributing resonance structures involving the lone pair of electrons and the carbonyl carbon atom are presumably higher in energy than their acyclic counterparts owing to the strain energy involved with introducing a double bond *exo* to a three-membered ring.[12,13]

The products of the photolysis of ethyl azidoformate in the presence of 1-acetoxycyclohexene in dichloromethane were analogous to those derived from isopropenyl acetate. The predominant product after removal of the solvent at 25° was the unstable aziridine **9**[5] as deduced from the nmr spectrum of the oil. The presence of lesser amounts of enol acetates **10** was apparent from weak N–H absorption at 3400 cm^{-1} in the infrared spectrum and the extra peaks in the nmr spectrum due to magnetically nonequivalent sets of ethoxy groups and acetoxy groups (eq 6).



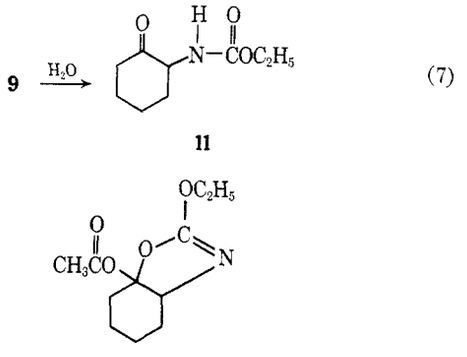
(6)

The nmr spectrum of aziridine **9**[5] consisted of a quartet and triplet centered at 4.15 and 1.28 ppm, respectively, due to the ethoxy group, a sharp singlet at 1.98 ppm due to the acetoxy group, a slightly broadened triplet centered at 2.65 ppm due to the aziridine ring proton, and broad absorption at 2.5–1.3 ppm due to the cyclohexane ring protons.

Vpc analysis of aziridine **9**[5] at 184° led to thermal decomposition of the sample and production of four major peaks with retention times of 1.0, 9.2 15.3, and 18.0 min in a relative ratio of 10:7:5:5. The 1-min peak corresponded in retention time to that of solvent and starting enol acetate. The 9.2-min peak was collected and identified as 2-carbethoxyaminocyclohexanone (**11**) on the basis of spectral and vpc comparisons with an authentic sample of ketone **11** prepared by chromium trioxide oxidation of the known[14] 2-carbethoxyaminocyclohexanol.

The 15.3- and 18.0-min peaks were collected together and tentatively identified as a mixture of C–H insertion products **10** and oxazoline **12** on the basis of spectral and elemental analysis. The constitution of these peaks was not examined further.

Treatment of a dichloromethane solution of aziridine **9** with water afforded a new mixture, nmr analysis of which revealed the complete absence of aziridine **9**, accompanied by new absorption attributed to ketone **11** (eq 7). The stability of 1-acetoxycyclohexene to the



(7)

above conditions for extended periods of time was established in another experiment. It was therefore assumed that the enol acetates **10** were likewise stable to the water treatment. The ratio of ketone **11** to insertion products **10** could then be estimated by vpc to be 23:5, corresponding to a 44% yield of ketone **11**, based on starting enol acetate.

Finally, methanol–sodium methoxide treatment of the original photolysis mixture afforded an oil, the vapor phase chromatogram of which consisted solely of a solvent peak (1.0 min) and one other peak with the retention time of ketone **11**. The latter peak must have been a mixture of 2-, 3-, and 4-carbethoxyaminocyclohexanone derived by partial methanolysis of both aziridine **9** and the insertion products **10**. The nmr spectrum was in complete accord with this interpretation.

It is pertinent that the photolysis reactions were carried out in *dilute* dichloromethane solution, thus solid as well as liquid enol acetates should be suitable substrates in the photolysis reaction.

Experimental Section

Infrared spectra were recorded with a Beckman IR-7 spectrophotometer. The small letters in parentheses found after infrared maxima refer to the relative intensities of the peaks.

(12) H. C. Brown and A. Tsukamoto, *J. Am. Chem. Soc.*, **83**, 2016 (1961).
(13) A. Hassner and C. Heathcock, *J. Org. Chem.*, **29**, 3640 (1964).
(14) M. Rona and D. Ben-Ishai, *J. Org. Chem.*, **26**, 1446 (1961).

Very weak, weak, moderate, and strong are referred to as vw, w, m, and s, respectively. Nmr spectra were determined on a Varian Associates Model A-60 high-resolution spectrometer using carbon tetrachloride as the solvent unless otherwise stated. Chemical shifts are recorded in parts per million downfield from internal TMS. Vapor phase chromatography was done on a Wilkins Aerograph instrument employing helium as the carrier gas. Analyses in the isopropenyl acetate series were performed on a 10 ft × $^3/_{16}$ in. 5% Dow 710 on firebrick (60–80 mesh) column at a temperature of 188° and a gas pressure of 10 psi. Analyses in the 1-acetoxycyclohexene series were performed on a 5 ft. × 0.25 in. 5% Dow 710 on firebrick (60–80 mesh) column at a temperature of 184° and a gas pressure of 10 psi. Elemental analyses were performed by Micro-Tech Laboratories, Skokie, Ill. Irradiations were carried out in a cylindrical glass vessel fitted with a quartz immersion well containing a Vycor filter. A Dry Ice condenser was used to prevent escape of the dichloromethane during the reaction. Agitation was provided by nitrogen which was bubbled up through the solution during photolysis. A 200-w Hanovia high-pressure mercury lamp constituted the light source.

Irradiation of Ethyl Azidoformate in the Presence of Isopropenyl Acetate.—A solution of 1.141 g (0.0114 mole) of freshly distilled isopropenyl acetate, 1.564 g (0.0136 mole) of ethyl azidoformate, and 75 ml of dichloromethane was irradiated until the characteristic azide bands at 2135 and 2170 cm^{-1} were no longer present in the infrared spectrum of the solution (*ca.* 7 hr). The solvent was removed at 25° and 22 mm, affording 2.203 g (103% of theory) of a pale yellow oil: $\lambda_{max}^{CCl_4}$ 3400 (vw), 2990 (m), 1750 (s), 1738 (s), 1370 (m), 1240 (s), 1205 cm^{-1} (s). The nmr spectrum is described above. The oil is referred to below as "crude aziridine **4**." The material decomposed within hours at 25° but could be stored for weeks without decomposition (by nmr) at −20°. Distillation of 107 mg of crude aziridine **4** at 81° and 0.07 mm afforded 63 mg of clear colorless oil, the nmr spectrum of which was the same as that of crude aziridine **4**, and 44 mg of a dark tarry residue. Chromatography of crude aziridine **4** over Florisil effected partial hydrolysis to **6**. Vapor phase chromatography of crude aziridine **4** revealed three predominant peaks of retention times 2.5, 9.5, and 13.7 min. The 2.5-min peak corresponded in retention time to mixtures of solvent, starting enol acetate, and other low molecular weight material. The 9.5-min peak was collected and identified as **6**. The nmr spectrum of **6** exhibited broad absorption centered at 5.8 ppm corresponding to a proton on nitrogen, a four-proton multiplet centered at 4.0 ppm which was taken to be the quartet of the ethoxy group superimposed on a doublet corresponding to the other methylene protons of ketone **6** as split by the adjacent proton on nitrogen, a three-proton singlet at 2.13 ppm (acetoxy group), and a three-proton triplet at 1.22 ppm (methyl protons of the ethoxy group). This substance was identical by spectral comparisons with an authentic sample of ketone **6**, the preparation of which is described in the next experiment.

Anal. Calcd for $C_6H_{11}NO_3$: C, 49.66; H, 7.60; N, 9.66. Found: C, 49.56; H, 7.69; N, 9.41.

Carbethoxyaminoacetone (6).—A solution of 0.986 g of carbethoxyaminopropan-2-ol[10] and 10 ml of acetone was treated at 0° with a slight excess of chromium trioxide in sulfuric acid[15] and stirred for 30 min. After addition of 1 ml of isopropyl alcohol and neutralization with saturated sodium bicarbonate solution, the solution was extracted with chloroform. The extract was dried over sodium sulfate and concentrated, affording 0.625 g of a clear oil. Preparative vpc afforded the pure specimen which was identical by spectral comparisons with that derived from crude aziridine **4**.

Oxazoline 8.—The 13.7-min peak derived from vpc of crude aziridine **4** was collected on a preparative scale. Spectral details are reported above. Treatment of an 11-mg sample of pure oxazoline **8** with 0.5 ml of methanol and 0.02 ml of 10% hydrochloric acid under reflux for 10 min followed by evaporation of the solvent afforded a pale orange oil which was shown by nmr and vpc analysis to consist mainly of carbethoxyaminoacetone **6**, together with a small amount of starting material.

Anal. Calcd for $C_8H_{13}NO_4$: C, 51.34; H, 6.95; N, 7.49. Found: C, 51.33; H, 7.08; N, 7.34.

Hydrolysis of Crude Aziridine 4.—A solution of 154 mg of crude aziridine **4** and 2 ml of dichloromethane was treated with 0.2 ml of water and vigorously stirred at 25° for 2 hr. The organic phase was separated, dried over sodium sulfate, and evaporated, affording 138 mg of pale yellow oil. The nmr spectrum of the oil demonstrated the absence of aziridine **4** and prominent new absorption due to **6**. Based on vpc analysis of the oil, **6** was produced in an over-all yield of 47% from isopropenyl acetate.

Thermolytic Decompostion of Aziridine 4.—An 89-mg sample of crude aziridine **4** was heated under nitrogen in the steam bath for 1 hr. There was obtained 80 mg of a yellow oil, nmr and vpc analysis of which showed **6** and oxazoline **8** to be present in a ratio of about 1:3, together with other impurities.

Irradiation of Ethyl Azidoformate in the Presence of 1-Acetoxycyclohexene.—A solution of 1.303 g (0.0093 mole) of freshly distilled 1-acetoxycyclohexene, 1.223 g (0.011 mole) of ethyl azidoformate, and 75 ml of dichloromethane was irradiated until the characteristic azide bands at 2135 and 2170 cm^{-1} were no longer present in the infrared spectrum of the solution (*ca.* 7 hr). The solvent was removed at 25° and 22 mm, affording 2.298 g (106% of theory) of a pale yellow oil: $\lambda_{max}^{CCl_4}$ 3400 (vw), 2940 (m), 1760 (s), 1720 (s), 1370 (m), 1180 cm^{-1} (s). The nmr spectrum is described above. The oil is referred to below as "crude aziridine **9**." The instability of aziridine **9** to purification procedures was analogous to that of aziridine **4** described above. Vapor phase chromatography of crude aziridine **9** was accompanied by themal decomposition of the sample and production of four major peaks with retention times of 1.0, 9.2, 15.3, and 18.0 min. The 9.2-min peak was collected and identified as 2-carbethoxyaminocyclohexanone (**11**). The nmr spectrum exhibited broad absorption centered at 5.7 ppm corresponding to a proton on nitrogen, a three-proton multiplet centered at 4.1 ppm corresponding to the methylene protons of the ethoxy groups and the methine proton attached to the carbon atom bearing the nitrogen atom, broad absorption at 2.8 to 1.6 ppm corresponding to the eight methylene protons of the cyclohexane ring, and, lastly, a three-proton triplet centered at 1.22 ppm corresponding to the methyl protons of the ethoxy group. This substance was identical by spectral comparisons with an authentic sample of **11**, the preparation of which is described in the next experiment. In earlier experiments peaks of retention time 15.3 and 18.0 min were unresolved. In a preliminary experiment this mixture was collected and tentatively identified as a mixture of C–H insertion products **10**, probably containing some oxazoline **12**. Analytical results are in agreement with this assignment, with the exception of the somewhat high C value found. The nmr spectrum of this mixture showed absorption in the vinyl region and at least two sets of magnetically nonequivalent acetoxy and ethoxy groups. The infrared spectrum showed N–H as well as multiple C=O absorption. The mixture was not examined further.

Anal. Calcd for $C_{11}H_{17}NO_4$: C, 58.15; H, 7.49; N, 6.17. Found: C, 59.05; H, 7.76; N, 6.08.

2-Carbethoxyaminocyclohexanone (11).—A solution of 1.74 g (0.0095 mole) of 2-carbethoxyaminocyclohexanol[14] as a mixture of *cis–trans* isomers and 20 ml of acetone was treated at 0° with a slight excess of chromium trioxide in sulfuric acid[15] and stirred for 2 hr. After addition of 1 ml of isopropyl alcohol and neutralization with saturated sodium bicarbonate solution, the solution was extracted with chloroform. The extract was dried over sodium sulfate and concentrated, affording 1.42 g of yellow oil, which was purified by preparative vapor phase chromatography, affording the analytical specimen as a colorless oil. This material was identical by spectral comparisons with that derived from crude aziridine **9**.

Anal. Calcd for $C_9H_{15}NO_3$: C, 58.38; H, 8.11; N, 7.57. Found: C, 58.81; H, 8.17; N, 7.72.

Treatment of 1-Acetoxycyclohexene with Water.—A solution of 0.198 g of 1-acetoxycyclohexene and 5 ml of dichloromethane was stirred vigorously for 14 hr at 25°. The organic layer was separated, dried over sodium sulfate, and concentrated, affording 190 mg of starting enol acetate, containing by vpc less than 1% cyclohexanone. Isopropenyl acetate was similarly stable.

Hydrolysis of Crude Aziridine 9.—A solution of 0.239 g of crude aziridine **9** and 2 ml of dichloromethane was treated with 0.2 ml of water and stirred vigorously at 25° for 7 hr. The organic layer was separated, dried over sodium sulfate, and concentrated, affording 0.199 g of a pale yellow oil. The nmr spectrum of this material revealed the complete disappearance of aziridine **9**, accompanied by new absorption due to ketone **11**. Clearly discernible were at least four magnetically nonequivalent acetoxy groups, attributable perhaps to the four positional isomers possible for the insertion products **10**. These same

(15) K. Bowden, I. M. Heilbron, E. R. H. Jones, and B. C. L. Weedon, *J. Chem. Soc.*, 39 (1946).

acetoxy peaks were present in crude aziridine **9**. The yield of **11** was 44%, while that of the insertion products **10** was 11%, based on starting enol acetate, as determined from the vapor phase chromatogram of the hydrolysis product. The oxazoline **12** should not have been formed under these conditions, based on the assumption that this substance is derived from heat treatment of aziridine **9**. Supporting this contention the vpc trace above contained no 18.0-min peak.

Methanol–Sodium Methoxide Treatment of Crude Aziridine 9.—A solution of 142 mg (0.625 mmole) of crude aziridine and 1.5 ml of absolute methanol was treated with 37 mg (0.685 mmole) of sodium methoxide and allowed to stand at 25° for 5.5 hr. The reaction mixture was poured into 4 ml of water and thoroughly extracted with dichloromethane. The extract was dried over sodium sulfate and concentrated, affording 92 mg (79% yield) of a yellow oil. The nmr spectrum of this substance contained no absorption due to acetoxy protons. The spectrum was almost identical with that of ketone **11**, except that the quartet–triplet due to the ethoxy group was slightly broadened and weak absorption appeared at about 3 ppm, attributable to the proton on the carbon bearing the nitrogen atom in the 3- and 4-carbethoxyaminocyclohexanone isomers. The vapor phase chromatogram consisted of minor amounts of material corresponding in retention time to that of solvent together with one symmetrial peak with retention time exactly that of 2-carbethoxyaminocyclohexanone.

Registry No.—**4**, 13640-73-8; **6**, 13640-74-9; **8**, 13640-75-0; **9**, 13640-76-1; **11**, 13640-77-2; ethyl azidoformate, 817-87-8.

Acknowledgment.—We thank the National Science Foundation, Grant GP5805, for financial support of this work.

Concerning the Hydrolysis and Aminolysis of Phenyl N-Methylacetimidate[1]

MARJORIE KANDEL AND E. H. CORDES[2]

Contribution No. 1496 from the Department of Chemistry, Indiana University, Bloomington, Indiana

Received March 24, 1967

The pH-rate profiles for hydrolysis and methylaminolysis of phenyl N-methylacetimidate exhibit maxima which cannot be accounted for in terms of ionization of the reactants. In both instances, a transition from rate-determining attack of the nucleophilic reagent on the alkaline side of the pH-rate maximum to rate-determining decomposition of a tetrahedral intermediate on the acid side may account for these observations. Over the pH range from 4 to 13, the hydrolysis and methylaminolysis of phenyl N-methylacetimidate yields phenol (or phenolate) as a product. At room temperature, the thermodynamically stable mixture of the two isomers of phenyl N-methylacetimidate consists of about one-third *syn* and two-thirds *anti*, as was determined from appropriate proton resonance spectra.

Studies of nucleophilic reactions of imido esters have provided considerable information and insight into a central question relevant to such reactions for acyl substrates in general: the problem of the existence, modes of formation, and modes of decomposition of tetrahedral intermediates. Two points are of particular note. In the first place, the hydrolysis of benzimidates,[3] oxazolines,[4] and imino lactones,[5] and the aminolysis of benzimidates[6] occur with rate-determining decomposition of the tetrahedral intermediate under sufficiently acidic conditions but with rate-determining attack of nucleophilic reagent in more basic situations. In the second place, the tetrahedral intermediates formed from these substrates and water or amines may decompose with expulsion of the resident amine moiety and formation of the corresponding oxygen ester or new imidate or, in contrast, with expulsion of alcohol and formation of amides or amidines. The tetrahedral intermediates formed in the course of hydrolysis of imino lactones exhibit more than one mode of decomposition depending on the pH and the nature and concentration of buffers;[5,7] similarly aminolysis of imidates yields either amidines or new imidates depending on reaction conditions.[6,8–12]

In view of the significance of the above results for understanding of nucleophilic reactions at acyl carbon, we were prompted to extend these studies to a novel substrate, phenyl N-methylacetimidate. This substrate is of interest since, in the first place, the phenoxide function is a much better leaving group than the alcoholates of most other substrates studied thus far and the tetrahedral intermediates derived from this substrate may decompose preferentially with its expulsion. Such behavior might provide the basis for an extended study of those factors which influence the modes of decomposition of these intermediates. In the second place, the tetrahedral intermediate generated from this substrate and water is similar to that generated from phenyl acetates and amines. Phenyl acetate aminolysis is a particularly well studied, but not a completely understood, reaction.[13] Examination of the former reaction might shed light on the latter.

Experimental Section

Materials.—Phenyl N-methylacetimidate [bp 79° (5 mm), lit.[14] 65° (1.2 mm)] was prepared by refluxing distilled phenol and acetoxime benzene sulfonate in toluene dried by distillation, according to the procedure of Oxley and Short.[14] Acetoxime benzene sulfonate (mp 52°, lit.[15] mp 53°) was prepared according to the procedure of Kenner, Todd, and Webb,[15] and was dried *in vacuo* for 2 days prior to use.

The position of the C=N stretching frequency of phenyl N-methylacetimidate in the infrared region is 5.88 μ. Table I gives the features of the nuclear magnetic resonance (nmr)

(1) Supported by Grant No. AM 08232 from the National Institutes of Health.

(2) Career Development Awardee of the National Institutes of Health.

(3) R. H. DeWolfe and F. B. Augustine, *J. Org. Chem.*, **30**, 699 (1965).

(4) R. B. Martin and A. Parcell, *J. Am. Chem. Soc.*, **83**, 4835 (1961).

(5) G. L. Schmir and B. A. Cunningham, *ibid.*, **87**, 5692 (1965).

(6) E. S. Hand and W. P. Jencks, *ibid.*, **84**, 3505 (1962).

(7) B. A. Cunningham and G. L. Schmir, *ibid.*, **88**, 551 (1966).

(8) A. Pinner, "Die Imidoather und ihre Derivate," Berlin, 1892.

(9) R. M. Roberts, *J. Am. Chem. Soc.*, **72**, 3603 (1950).

(10) R. M. Roberts and R. H. DeWolfe, *ibid.*, **76**, 2411 (1954).

(11) E. Schmidt, *Ber.*, **47**, 2545 (1914).

(12) R. Roger and D. G. Neilson, *Chem. Rev.*, **61**, 179 (1961).

(13) For a thorough review, see T. G. Bruice and S. J. Benkovic, "Bioorganic Mechanisms," Vol. 1, W. A. Benjamin Inc., New York, N. Y., 1966, p 27 ff.

(14) P. Oxley and W. F. Short, *J. Chem. Soc.*, 1514 (1948).

(15) G. W. Kenner, A. R. Todd, and R. F. Webb, *ibid.*, 1231 (1956).