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Studies on Azole Compounds. III.¹⁾ Reactions of Oxazole N-Oxides with Phosphoryl Chloride and Acetic Anhydride²⁾

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Six kinds of 2-aryloxazole N-oxide derivatives were prepared, and their reactions with phosphoryl chloride and acetic anhydride were studied. Methyl group located on the 4-position of 2-aryloxazole N-oxide was easily subjective to nucleophilic attack as an active methyl group in the reaction with phosphoryl chloride or acetic anhydride, whereas 5-methyl group was inert to such an attack.

In early 1915, Diels and Riley⁴⁾ obtained a condensation product "oxidoöxazole" from the reaction of diacetyl monoxime and benzaldehyde in the presence of hydrochloric acid, and allotted an epoxide structure (I) to this compound. Later, Diltthey and Friedrichsen⁵⁾ pointed out that two another formulae II and III might be conceivable, but assumed the structure I was preferable to others. In 1947 Cornforth and Cornforth⁶⁾ assigned the oxazole N-oxide structure III to "oxidoöxazole" without providing any direct proof for it.

We have now prepared six kinds of the Diels' "oxidoöxazole" analogs and demonstrated that they are oxazole N-oxides by spectral examination and by their reductive conversion to the corresponding oxazoles. Further we examined the reaction with phosphoryl chloride and with acetic anhydride, and gained interesting results.

Preparation of the Diels' "oxidoöxazole" analogs was performed by the method of Diltthey and Friedrichsen⁵⁾; that is, treatment of monoximes of α -diketones with arylaldehydes in glacial acetic acid containing hydrogen chloride gave the expected products (III—VIII) in good yields (Table I).

All the compounds thus obtained have a strong absorption band around 1240 cm^{-1} indicative of an aromatic N-oxide group in infrared (IR) spectra. Their ultraviolet (UV) absorption spectra showed the hypsochromic shift in protic solvents compared with those in aprotic solvents, which observation is generally noticed as one of the characteristics of aromatic N-oxides; a typical example is shown in Figure 1. These observations apparently suggest that the Diels' "oxidoöxazoles," with which we are concerned, have the N-oxide structure (III). This assumption was further supported by the reduction of the products; they were readily reduced to the corresponding oxazoles by refluxing with zinc dust in water

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- 2) Abstracts of Papers, 88th Annual Meeting of the Pharmaceutical Society of Japan, Tokyo, April, 1968, p. 122.
- 3) Location: a) Nanakuma, Fukuoka; b) Katakasu, Fukuoka.
- 4) O. Diels and D. Riley, *Ber.*, **48**, 897 (1915).
- 5) W. Diltthey and J. Friedrichsen, *J. Prakt. Chem.*, **127**, 292 (1930).
- 6) J.W. Cornforth and R.H. Cornforth, *J. Chem. Soc.*, **1947**, 96.

TABLE I. Oxazole N-Oxides

$$\begin{array}{c} \text{R}^1 \\ \diagdown \\ \text{C}=\text{NOH} \\ \diagup \\ \text{R}^2 \\ \diagdown \\ \text{C}=\text{O} \end{array} + \text{ArCHO} \xrightarrow[\text{AcOH}]{\text{HCl}} \begin{array}{c} \text{R}^1 \\ \diagdown \\ \text{C}=\text{N} \rightarrow \text{O} \\ \diagup \\ \text{R}^2 \\ \diagdown \\ \text{C}=\text{O} \end{array} \text{Ar}$$

N-Oxide	R ¹	R ²	Ar	Yield (%)	mp(decomp.)(°C)
III ⁴⁾	CH ₃	CH ₃	C ₆ H ₅	84	101—102°
IV ⁴⁾	CH ₃	CH ₃	Anis ^{a)}	90	139—140°
V	CH ₃	C ₂ H ₅	C ₆ H ₅	65	75°
VI ⁷⁾	CH ₃	C ₆ H ₅	C ₆ H ₅	88	145—146°
VII	C ₆ H ₅	CH ₃	C ₆ H ₅	62	102—103°
VIII	C ₆ H ₅	CH ₃	Anis ^{a)}	55	120°

a) Anis=anisyl-

or by catalytic reduction in the presence of Raney Ni.⁷⁾ The reactions mentioned below also offer additional evidences.

Bodendorf and Towliati⁷⁾ have described that treatment of 4-methyl-2,5-diphenyloxazole N-oxide (VI) with an excess of phosphorus trichloride in chloroform resulted in the formation of 4-chloromethyl-2,5-diphenyloxazole (XXIII) in 70% yield accompanied by recovery of VI in 20%, the normally deoxygenated product (XXII) being noticed only in a small amount.

Fig. 1. UV Spectra of 4,5-Dimethyl-2-phenyloxazole N-Oxide (III)

—: dioxane
 ----: dioxane: EtOH (1:1)

This unexpected result prompts us to re-examine the reaction of the oxazole N-oxides with phosphorus trichloride. At first VI was treated with phosphorus trichloride under the same condition as that reported by Bodendorf and Towliati.⁷⁾ After purification by column chromatography on alumina, the all products were analyzed by gas liquid chromatography, and it was shown that the normally deoxygenated product, 4-methyl-2,5-diphenyloxazole (XXII), was produced as the preponderant product in 67.5% yield, 4-chloromethyl derivative (XXIII) being also isolated as a minor product in 26.6% yield. The conclusive evidence for the structure of XXIII will be offered below.

The failure of isolating XXII by Bodendorf and Towliati may be due to the inadequate separating procedure and also to the fact that XXII is not only more soluble but also has a lower melting point compared with XXIII.

Similarly the reaction of 4,5-dimethyl-2-phenyloxazole N-oxide (III) with one equivalent of phosphorus trichloride resulted in the formation of 4,5-dimethyl-2-phenyloxazole (IX) (64%) and 4-chloromethyl-5-methyl-2-phenyloxazole (X) (16%).

It seems well reasonable that the formation of 4-chloromethyl compounds (X and XXIII) is due to the action of phosphoryl chloride formed during the course of deoxygenation reaction on the unchanged N-oxide. In order to confirm this assumption, the reaction of III with phosphoryl chloride was subsequently carried out under the same condition as that

7) K. Bodendorf and H. Towliati, *Arch. Pharm.*, **298**, 293 (1965).

8) E. Hayashi, H. Yamanaka and K. Shimizu, *Chem. Pharm. Bull. (Tokyo)*, **7**, 141 (1959).

Chart 1

with phosphorus trichloride, and the same 4-chloromethyl-5-methyl-2-phenyloxazole (X) was isolated in 77% yield.

It is well known that the methyl group located on the 2-position of azole ring is an active methyl closely similar to the methyl group of α - or γ -picoline, whereas the 4- or 5-methyl group of azole ring resembles rather to the unreactive methyl of β -picoline. Therefore, the formation of 4-chloromethyl derivative X from the N-oxide III seems apparently inconsistent with the generally accepted behavior of 4-methyl group of oxazole ring, and it is interesting to explore the scope of this type of reaction and to gain some insight into the reaction mechanism. With such aims, the following studies were carried out.

When a solution of III in acetic anhydride was heated on a water-bath for three hours, an acetoxymethyl derivative (XI) was obtained in 31% yield accompanied by benzoic acid (XII) (29%) and diacetyl (XIII) which was detected as the osazone only in a small amount. The latter two products apparently resulted from the ring rupture reaction. This acetoxymethyl compound (XI) was proved identical with the product prepared from X and potassium acetate in boiling acetic acid.

In order to further affirm the structure of XI, the alternative acetoxymethyl compound, 5-acetoxymethyl-4-methyl-2-phenyloxazole (XVII) was prepared from diacetyl monoxime by the reaction sequence shown in Chart 1. The monobromide (XIV) formed from diacetyl monoxime and bromine afforded acetonitrile on treatment with phosphorus pentachloride by the second-order Beckmann rearrangement,⁹ and its mass spectrum showed a peak corresponding to $\text{BrCH}_2\text{C}\equiv\text{O}^+$. Accordingly XIV is 1-bromo-3-oximinobutan-2-one and the final product of this reaction sequence is obviously 5-acetoxymethyl-4-methyl-2-phenyloxazole (XVII).

The IR spectra of the isomeric acetoxymethyloxazoles, XI and XVII, are definitely different from each other in the finger print region, in spite of the similarity in the shorter wave length region. They are also able to be effectively separated by gas-liquid chromatography.

Gas liquid chromatography of the crude products from the reaction of III and acetic anhydride demonstrated clearly the presence of XI but not the isomer XVII.

Furthermore, it was shown that the reaction of both 2-anisyl-4,5-dimethyloxazole N-oxide (IV) and 4-methyl-2,5-diphenyloxazole N-oxide (VI) progressed in the same way, and the corresponding 4-chloromethyloxazoles, XVIII and XXIII, were obtained from the reactions with phosphoryl chloride and 4-acetoxymethyloxazoles, XIX and XXIV, from those with acetic anhydride. From the reaction of IV and acetic anhydride, *p*-methoxybenzamide (XXI) was also isolated besides XIX, XIII and *p*-methoxybenzoic acid (XX). Acetylbenzoyl (XXV), one of the ring cleavage product obtained from the reaction of VI and acetic anhydride, was characterized as the dioxime.¹⁰ Transformation of 4-chloromethyl compounds, XVIII and XXIII to the corresponding 4-acetoxymethyl compounds, XIX and XXIV, was effected similarly by means of potassium acetate in acetic acid.

The reactions mentioned above are shown in Chart 1.

On the contrary, the reaction of 5-methyl-4-phenyloxazole N-oxides, VII and VIII, with acetic anhydride gave no acetoxymethyl derivative, and only the ring cleavage products, acetylbenzoyl (XXV), carboxamide (XXI and XXVI) and carboxylic acid (XX and XII), were isolated besides a large amount of resinous substances. The reaction with phosphoryl chloride gave essentially the same results (Chart 2).

From the results described above, it is now apparent that 4-methyl group of 2-aryloxazole N-oxide may be subjective to nucleophilic attack as an active methyl group in the reaction with phosphoryl chloride or acetic anhydride, but 5-methyl group is inert to such an

9) L.G. Donaruma and W.Z. Heldt, "Org. Reactions," Vol. 11, John Wiley & Sons. Inc., New York, N.Y., 1960, p. 38.

10) H. Rheinboldt and O. Schmitz-Dumont, *Ann.*, **444**, 130 (1925).

Chart 2

attack. Such a reactivity of 4-methyl group is significantly interesting as an characteristic of 2-aryl-4-methyloxazole N-oxide.

The ring cleavage reaction with acetic anhydride may be assumed to stem from the nucleophilic attack of acetoxy anion at the 2-position of the initially formed acetyl-adduct of N-oxide (A) to give 1,2-dihydro derivative (B), and then follows the course a and a' (Chart 3). On the other hand, the formation of 4-acetoxymethyl-2-aryloxazole cannot be rationalized by any course originated from the intermediate B. We wish to propose tentatively the following pathway in which the 2-aryl group acts as an electron-acceptor and the anhydrobase (C) is essential as an intermediate. Although the transformation of C to D seems very likely to proceed by a concerted mechanism, it is not clear yet whether it is an intramolecular reaction (course b) or an intermolecular one (course b'). The mechanisms of the reactions with phosphoryl chloride may be similar to these ones.

Further studies are in progress in order to explore the reactivities of oxazole N-oxides.

Chart 3

Experimental¹¹⁾

Preparation of Oxazole N-Oxides

General Procedure—Into a solution or a suspension of α -diketone monoxime (0.1 mole) and arylaldehyde (0.11 mole) in glacial acetic acid (20 ml), dry hydrogen chloride was bubbled for 30 min under ice-cooling. Addition of ether brought about precipitation of a crystalline product, which was filtered and washed with ether. This was dispersed in H_2O and the aqueous solution was basified with conc. NH_4OH , and extracted with $CHCl_3$. After drying over anhyd. Na_2SO_4 , the $CHCl_3$ was removed *in vacuo* and the residue was recrystallized from ether or benzene to afford oxazole N-oxides.

4,5-Dimethyl-2-phenyloxazole N-Oxide (III)—Colorless columns (ether), mp 101–102° (decomp.), (lit.⁴⁾ mp 100–101°, 84% yield. *Anal.* Calcd. for $C_{11}H_{11}O_2N$: C, 69.82; H, 5.86; N, 7.40. Found: C, 70.02; H, 5.98; N, 7.33. UV $\lambda_{max}^{dioxane}$ m μ (log ϵ): 267.5 (4.12), 278 (4.07), 317 (4.43), 332 (4.29); λ_{max} (dioxane: EtOH=1:1) m μ (log ϵ): 260 (4.06), 303 (4.47), 316 (4.36). IR ν_{max}^{KBr} cm^{-1} : 1238 (N→O). NMR ($CDCl_3$) τ : 7.81 (3H, quartet, $J \sim 1$ cps, CH_3), 7.69 (3H, quartet, $J \sim 1$ cps, CH_3), 2.57 (3H, multiplet, phenyl 3,4,5-H), 1.60 (2H, multiplet, phenyl 2,6-H).

2-Anisyl-4,5-dimethyloxazole N-Oxide (IV)—Colorless prisms (benzene), mp 139–140° (decomp.), (lit.⁴⁾ mp 140–141°, 90% yield. UV $\lambda_{max}^{dioxane}$ m μ (log ϵ): 266.5 (3.96), 321 (4.34), 337 (4.18); λ_{max} (dioxane: EtOH=1:1) m μ (log ϵ): 260 (3.79), 312 (4.40), 328 (4.21). IR ν_{max}^{KBr} cm^{-1} : 1238 (N→O). NMR ($CDCl_3$) τ : 7.82 (3H, quartet, $J \sim 1$ cps, CH_3), 7.68 (3H, quartet, $J \sim 1$ cps, CH_3), 6.13 (3H, singlet, CH_3O), 3.01 (2H, doublet, $J_{ortho} = 9$ cps, anisyl 3,5-H), 1.58 (2H, doublet, $J_{ortho} = 9$ cps, anisyl 2,6-H).

5-Ethyl-4-methyl-2-phenyloxazole N-Oxide (V)—Colorless prisms (ether), mp 75° (decomp.), 65% yield. *Anal.* Calcd. for $C_{12}H_{13}O_2N$: C, 70.91; H, 6.45; N, 6.89. Found: C, 70.88; H, 6.48; N, 7.18. UV $\lambda_{max}^{dioxane}$ m μ (log ϵ): 267 (3.95), 279 (3.90), 317 (4.25), 332 (4.12); λ_{max} (dioxane: EtOH=1:1) m μ (log ϵ): 306 (4.24), 320 (4.12). IR ν_{max}^{KBr} cm^{-1} : 1232 (N→O).

4-Methyl-2,5-diphenyloxazole N-Oxide (VI)—Colorless needles (benzene), mp 145–146° (decomp.), 88% yield. *Anal.* Calcd. for $C_{16}H_{13}O_2N$: C, 76.47; H, 5.22; N, 5.57. Found: C, 76.23; H, 5.03; N, 5.46. UV $\lambda_{max}^{dioxane}$ m μ (log ϵ): 272 (4.34), 342 (4.25); (dioxane: EtOH=1:1) m μ (log ϵ): 261 (4.26), 326 (4.30). IR ν_{max}^{KBr} cm^{-1} : 1240 (N→O).

5-Methyl-2,4-diphenyloxazole N-Oxide (VII)—Colorless needles (ether), mp 102–103° (decomp.), 62% yield. *Anal.* Calcd. for $C_{16}H_{13}O_2N$: C, 76.47; H, 5.22; N, 5.57. Found: C, 76.60; H, 5.14; N, 5.38. UV $\lambda_{max}^{dioxane}$ m μ (log ϵ): 318 (4.26), 334 (4.13); λ_{max} (dioxane: EtOH=1:1) m μ (log ϵ): 307 (4.31), 322 (4.15). IR ν_{max}^{KBr} cm^{-1} : 1240 (N→O).

2-Anisyl-5-methyl-4-phenyloxazole N-Oxide (VIII)—Colorless needles (ether), mp 120° (decomp.), 55% yield. *Anal.* Calcd. for $C_{17}H_{15}O_3N$: C, 72.58; H, 5.37; N, 4.98. Found: C, 72.09; H, 5.20; N, 4.72. UV $\lambda_{max}^{dioxane}$ m μ (log ϵ): 321 (4.38), 338 (4.24); λ_{max} (dioxane: EtOH=1:1) m μ (log ϵ): 314 (4.47), 329 (4.29). IR ν_{max}^{KBr} cm^{-1} : 1239 (N→O).

Reaction of VI with Phosphorus Trichloride—The reaction of VI (1.25 g, 0.005 mole) and phosphorus trichloride (2.5 g, 0.018 mole) in $CHCl_3$ (15 ml) was carried out by the same procedure of Bodendorf and Towliati.⁸⁾ The mixture of products was chromatographed on alumina with $CHCl_3$, and all eluted products were collected, weighed, and analyzed by gas liquid chromatography. The analysis was carried out in a Shimadzu gas chromatograph GC-2C provided with a 1.5 m stainless steel column filled with 1.5% SE-30 on Chromosorb W (60–80 mesh) which was kept at 190°, hydrogen being used as carrier gas (gas products 1.5 kg/cm²). The relative retention time (min) and the results of the calculation of the yields were as follows: 4-methyl-2,5-diphenyloxazole (XXII) (4.9, 67.5%), 4-chloromethyl-2,5-diphenyloxazole (XXIII) (8.8, 26.6%).

Reaction of III with Phosphorus Trichloride—To a solution of III (1.89 g, 0.01 mole) in $CHCl_3$ (10 ml) was added phosphorus trichloride (1.52 g, 0.011 mole) in $CHCl_3$ (10 ml) and the mixture was refluxed for 30 min. After cooling, the reaction mixture was made slightly alkaline with conc. NH_4OH under ice-cooling. The organic layer was separated, washed with water, dried over anhyd. Na_2SO_4 , and the solvent was removed. The residue was recrystallized from petroleum ether to yield 0.23 g of 4-chloromethyl-5-methyl-2-phenyloxazole (X), colorless fine needles, mp 83–84°. *Anal.* Calcd. for $C_{11}H_{10}ONCl$: C, 63.61; H, 4.82; N, 6.74. Found: C, 63.43; H, 4.66; N, 6.84. UV λ_{max}^{EtOH} m μ (log ϵ): 276 (4.27). The mother liquor was distilled under reduced pressure to give 0.65 g of 4,5-dimethyl-2-phenyloxazole (IX), bp 109° (3 mmHg), mp 50–51°.

The products obtained from another run was chromatographed on alumina with $CHCl_3$, and all eluted products were collected, weighed, and analyzed by gas liquid chromatography. The analysis was carried

11) All melting points are uncorrected. UV spectra were measured on a Shimadzu SV-50A Spectrophotometer, IR spectra on a NihonBunko DS-301 Spectrophotometer, NMR spectra on a Japan Electron Optics Model JNM 3H-60 and JNM C-60-H Spectrometer at 60 Mc. with tetramethylsilane as an internal standard. Mass spectra were kindly taken on a JMS-OLSG Mass Spectrometer in Akishima Factory, JEOL, Ltd.

out in a Shimadzu gas chromatograph GC-1C provided with a 2 m copper column filled with 1.5% SE-30 on Chromosorb W (60—80 mesh) which was kept at 125°, nitrogen being used as carrier gas (flow rate 90 ml/min). The relative retention time (min), and the results of the calculation of the yields were as follows: IX (3.1, 64%), X (8.8, 16.3%).

Reaction of III with Phosphoryl Chloride—The reaction of III (0.95 g, 0.005 mole) with POCl₃ (0.84 g, 0.0055 mole) was carried out under a similar condition to that with PCl₃. The solvent was removed and the residue was recrystallized from petroleum ether to give 0.85 g (77% yield) of X.

Reaction of III with Acetic Anhydride—A solution of III (1.89 g, 0.01 mole) in Ac₂O (5 ml) was heated on a water-bath (90°) for 2 hr and the solvent was distilled under reduced pressure. From the distillate, a small amount of diacetyl osazone was isolated by the addition of phenylhydrazine. To the residue was added water and made alkaline with K₂CO₃. The alkaline solution was extracted with ether. The aqueous solution was made acid to give 0.35 g (29%) of benzoic acid. The ether solution was dried and the solvent removed, and the residue was distilled under reduced pressure to afford 0.71 g (31%) of 4-acetoxymethyl-5-methyl-2-phenyloxazole (XI), bp 170—180° (bath temp., 2 mmHg), colorless prisms, mp 51—52° (petroleum ether). *Anal.* Calcd. for C₁₃H₁₃O₃N: C, 67.52; H, 5.67; N, 6.06. Found: C, 67.98; H, 5.79; N, 6.26. UV $\lambda_{\text{max}}^{\text{EtOH}}$ m μ (log ϵ): 274 (4.22). IR KBr disc, cm⁻¹: 1735 (>C=O), 1240 (=C-O-C), 1018, 953, 836, 806, 775, 715, 696. NMR (CDCl₃) τ : 7.96 (3H, singlet, CH₃-CO-O-), 7.58 (3H, singlet, CH₃-C=), 5.07 (2H, singlet, -CH₂-O-), 2.58 (3H, multiplet, phenyl 3,4,5-H), 2.0 (2H, multiplet, phenyl 2,6-H).

Preparation of 5-Acetoxymethyl-4-methyl-2-phenyloxazole (XVII)—Into a solution of 1-acetoxy-2-oxo-3-oximinobutane (XV)¹² (1.59 g, 0.01 mole) and benzaldehyde (1.17 g, 0.011 mole) in glacial acetic acid, dry hydrogen chloride was bubbled for 30 min and the resulting solution was allowed to stand for 3 hr under ice-cooling. Addition of ether brought about precipitation of a crystalline product which was washed with ether by decantation, and then water was added, and the solution was made alkaline with conc. NH₄OH, extracted with CHCl₃, and the CHCl₃ extract was dried over Na₂SO₄. The solvent was removed under reduced pressure, and the residue was recrystallized from ether to afford 0.34 g (14%) of 5-acetoxy-4-methyl-2-phenyloxazole N-oxide (XVI), colorless fine needles, mp 99—100°. *Anal.* Calcd. for C₁₃H₁₃O₄N: C, 63.15; H, 5.30; N, 5.67. Found: C, 63.24; H, 5.21; N, 6.02.

A solution of XVI (0.13 g) in MeOH (20 ml) was shaken with Raney Ni (from Ni-Al Alloy 0.5 g) in the stream of hydrogen at atmospheric pressure. After the absorption of hydrogen stopped, the catalyst was removed by filtration. The filtrate was evaporated to dryness and the colorless oily residue was taken up in ether. After drying over anhyd. Na₂SO₄, ether was evaporated and the residue was distilled under reduced pressure to give 0.10 g (83%) of XVII, bp 150—160° (bath temp., 2 mmHg), colorless prisms, mp 38—39° (petroleum ether). *Anal.* Calcd. for C₁₃H₁₃O₃N: C, 67.52; H, 5.67; N, 6.06. Found: C, 67.70; H, 5.76; N, 5.84. UV $\lambda_{\text{max}}^{\text{EtOH}}$ m μ (log ϵ): 276 (4.29). IR KBr disc, cm⁻¹: 1739 (>C=O), 1238 (=C-O-C-), 1027, 974, 791, 783, 719, 694. NMR (CDCl₃) τ : 7.86 (3H, singlet, CH₃-CO-O-), 7.68 (3H, singlet, CH₃-C=), 4.82 (2H, singlet, -CH₂-O-), 2.43 (3H, multiplet, phenyl 3,4,5-H), 1.84 (2H, multiplet, phenyl 2,6-H).

Conversion of X to XI—To a solution of X (0.07 g, 0.33 mmole) in AcOH (5 ml) was added finely ground KOAc (0.07 g, 0.71 mmole) and the mixture was refluxed for 10 hr, and the solvent was removed under reduced pressure. To the residue was added a small amount of water, and the solution was made alkaline with K₂CO₃, and extracted with ether. The ether solution was dried over anhyd. Na₂SO₄, filtered, and ether was removed, the residue was recrystallized from petroleum ether to give 0.04 g (53%) of XI, colorless prisms, mp 51—52°.

Reaction of IV with Phosphoryl Chloride—The reaction was carried out in the same way as that of III with POCl₃. 2-Anisyl-4-chloromethyl-5-methyloxazole (XVIII) was obtained in 84% yield, mp 85—86° (petroleum ether-ether). *Anal.* Calcd. for C₁₂H₁₂ONCl: C, 60.63; H, 5.05; N, 5.89. Found: C, 60.55; H, 5.03; N, 5.68.

Reaction of IV with Acetic Anhydride—The reaction was carried out in the same way as that of III with Ac₂O. 2-Anisyl-4-acetoxymethyl-5-methyloxazole (XIX) and anisic acid (XX) were obtained in yields of 45% and 25% respectively. Very small amounts of anisamide and diacetyl were also obtained. XIX: bp 195—205° (bath temp., 2 mmHg), mp 66—67°, (petroleum ether-ether). *Anal.* Calcd. for C₁₄H₁₅O₄N: C, 64.36; H, 5.79; N, 5.36. Found: C, 64.63; H, 5.83; N, 5.72. UV $\lambda_{\text{max}}^{\text{EtOH}}$ m μ (log ϵ): 282 (4.40). IR $\nu_{\text{max}}^{\text{KBr}}$ cm⁻¹: 1739 (>C=O), 1240 (-CH₂-O-C=). NMR (CDCl₃) τ : 7.90 (3H, singlet, CH₃-CO-O-), 7.59 (3H, singlet, CH₃-C=), 6.14 (3H, singlet, CH₃-O-), 4.94 (2H, singlet, >-CH₂-O-), 2.98 (2H, doublet, *J*_{ortho}=9 cps, anisyl 3,5-H), 1.96 (2H, doublet, *J*_{ortho}=9 cps, anisyl 2,6-H).

Conversion of XVIII to XIX—This conversion was carried out in the same way as the preparation of XI from X. Yield of XIX: 49%.

Reaction of VI with Phosphoryl Chloride—The reaction was carried out in the same way as that of III with POCl₃. 4-Chloromethyl-2,5-diphenyloxazole (XXIII) was obtained in 59% yield, mp 139° (EtOH). *Anal.* Calcd. for C₁₆H₁₂ONCl: C, 71.24; H, 4.45; N, 5.19. Found: C, 71.66; H, 4.74; N, 5.32. UV $\lambda_{\text{max}}^{\text{EtOH}}$ m μ (log ϵ): 221 (4.26), 303 (4.43).

12) O. Diels and M. Farkas, *Ber.*, **43**, 1957 (1910).

Reaction of VI with Acetic Anhydride—The reaction was carried out in the same way as that of III with Ac_2O . 4-Acetoxymethyl-2,5-diphenyloxazole (XXIV) and benzoic acid (XII) were obtained in yields of 58% and 15% respectively. Very small amounts of acetylbenzoyl (XXV) was isolated as dioxime.¹⁰ XXIV: mp 96–97° (ether). *Anal.* Calcd. for $\text{C}_{18}\text{H}_{15}\text{O}_3\text{N}$: C, 73.70; H, 5.15; N, 4.78. Found: C, 73.47; H, 4.86; N, 4.59.

Conversion of XXIII to XXIV—The reaction was carried out in the same way as the conversion of X to XI. Yield of XXIV: 56%.

Reaction of VII with Phosphoryl Chloride—The reaction was carried out in the same way as that of III with POCl_3 . No expected chlorinated product could be isolated and a large amount of resinous oil was formed, besides only very small amounts of acetylbenzoyl (XXV) and benzamide (XXVI) were obtained.

Reaction of VII with Acetic Anhydride—The reaction was carried out in the same way as that of III with Ac_2O . Acetylbenzoyl (XXV), benzamide (XXVI) and benzoic acid (XII) were obtained in yields of 10%, 37% and 26% respectively.

Reaction of VIII with Phosphoryl Chloride—The reaction was carried out in the same way as that of III with POCl_3 . The result was the same as the reaction of VII with POCl_3 . Besides a large amount of resinous oil, the formation of trace amount of acetylbenzoyl (XXV), anisamide (XXI) and anisic acid (XX) were noticed.

Reaction of VIII with Acetic Anhydride—The reaction was carried out in the same way as that of III with Ac_2O . Acetylbenzoyl (XXV), anisamide (XXI) and anisic acid (XX) were obtained in yields of 7%, 35% and 30% respectively.

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