TABLE I.—NMR ANALYSIS OF *O*-ALKYLAMIDOXIMES

$$R-C(=NOR')-NH_2$$

| R | R' | Peak in CPS TMS Standard | Description | No. of Protons | Assignment |
|---|---|---|---|---|---|
| Methyl | Benzyl | 106 | Sharp singlet | 3 | $CH_3$ |
| | | 275 | Broad band | 2 | $NH_2$ |
| | | 297 | Sharp singlet | 3 | $CH_2$ (benzyl) |
| | | 438 | Sharp singlet | 5 | Phenyl |
| Ethyl | Benzyl | 64 | Triplet | 3 | $CH_3$ |
| | | 121 | Quartet | 2 | $CH_2$ (ethyl) |
| | | 270 | Broad band | 2 | $NH_2$ |
| | | 296 | Sharp singlet | 2 | $CH_2$ (benzyl) |
| | | 437 | Sharp singlet | 5 | Phenyl |
| Pentyl | Benzyl | 42–162 | Series of three broad bands | 11 | Pentyl |
| | | 269 | Broad band | 2 | $NH_2$ |
| | | 299 | Broad-sharp singlet | 2 | $CH_2$ (benzyl) |
| | | 441 | Sharp singlet | 5 | Phenyl |
| Phenyl | Benzyl | 276 | Broad band | 2 | $NH_2$ |
| | | 299 | Sharp singlet | 2 | $CH_2$ (benzyl) |
| | | 440 | Multiple sharp bands | 10 | Phenyl (2) |
| Benzyl | Benzyl | 285 | Sharp singlet | 2 | $CH_2$ (benzyl attached to carbon) |
| | | 256 | Broad-sharp singlet | 2 | $NH_2$ |
| | | 290 | Sharp singlet | 2 | $CH_2$ (benzyl in ether linkage) |
| | | 422, 430 | Two sharp singlets with some overlapping | 10 | Phenyl (2) |

During the reaction time of 20 minutes the temperature went briefly to 92°. The mixture was cooled, allowed to stand overnight, extracted with ether: dried over $MgSO_4$, and distilled. A clear oil, 5.7 Gm. (45.7%), distilled at 81–82°/0.08 mm.

*Anal.*—Calcd. for $C_{10}H_{14}N_2O$; N, 15.73. Found N, 15.70.

***O*-Benzylhexanamidoxime.**—α-Benzyloximinoheptanoamide (9.2 Gm.) was reacted as described above with an appropriate amount of NaOBr. The resulting dark-red oil was distilled four times to obtain 0.5 Gm. (6%) of a yellowish oil boiling at 125–130°/0.3 mm.

*Anal.*—Calcd. for $C_{13}H_{20}N_2O$; N, 12.72. Found N, 12.74.

Nitrogen analyses were carried out on the Coleman nitrogen analyzer except for *O*-benzylhexanamidoxime which was analyzed by Micro-Tech Laboratories, Skokie, Ill. NMR spectra were run on the Varian A-60.

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# α-Alkyloximinonitriles by Pyrolysis of α-Alkyloximinocarboxamides with Phosphorus Pentoxide

By DOMINICK A. COVIELLO

**A preparation of α-alkyloximinonitriles is described in which the corresponding α-alkyloximinocarboxamides are heated with phosphorus pentoxide *in vacuo*. Structures were proven by infrared analysis and basic hydrolysis of the nitriles to the corresponding acids.**

IN A PREVIOUS COMMUNICATION (1), it was reported that attempts to cyclize β-phenethyl amides of α-alkyloximino acids to the corresponding 3,4-dihydroisoquinolines were fruitless. It was pointed out that experimental evidence indicated that the work-up of the reaction mixture apparently resulted in the hydrolysis of the amide to yield the amine moiety which could be isolated. There was no indication of the fate of the acid portion of the molecule, but it was assumed that under the conditions of the reaction, the oxime moiety decomposed thus accounting for the failure of the cyclization reaction.

In reconsidering the reaction, it was thought that it would be worthwhile to determine the fate of the acid portion of the molecule under similar conditions

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using unsubstituted α-alkyloximinocarboxamides as well as ascertain the feasibility of preparing the corresponding nitriles which would be interesting intermediates for further investigations.

Powdered α-alkyloximinocarboxamides were mixed thoroughly with a slight excess of phosphorus pentoxide and then heated with a Bunsen flame under reduced pressure. In all cases a vigorous reaction ensued during which oils were collected in reasonable yields and characterized as α-alkyloximinonitriles by infrared analysis. The characteristic nitrile peak showed up as a medium sharp band at 2235 cm.$^{-1}$ for α-benzyloximinobutyronitrile, and a medium sharp band at 2236 cm.$^{-1}$ for α-benzyloximinopropionitrile. The values are well within the reported range (2). Alkaline hydrolysis of the nitriles produced the corresponding α-alkyloximino acids.

The success of the dehydration reaction would then indicate that the failure of the Bischler-Napieralski reaction in the instance cited must be attributed to factors other than the stability of the alkyloximino group.

## EXPERIMENTAL

Amides prepared according to the procedure of Woolley and co-workers (3) have been reported (4).

**α-Benzyloximinobutyronitrile.**—A 30.9-Gm. quantity (0.15 mole) of α-benzyloximinobutyramide was ground in a mortar and transferred to a round-bottom flask. Then 28.4 Gm. (0.2 mole) of phosphorus pentoxide was added, the flask was stoppered and manually shaken until the mixture was homogeneous. The flask was connected to a vacuum system set for downward distillation. The system was evacuated to 0.35 mm. and heating was started. Frothing and discoloration ensued as a brown oil distilled. Heating was discontinued when the temperature of the vapors fell from 129° to 50°. The reaction mixture was cooled and exhaustively extracted with benzene. The benzene extract was combined with the distillate, the benzene removed, and the residue distilled under reduced pressure. Five grams (17.3%) of an oil was collected at 102–105°/0.5 mm. The procedure followed was that outlined in the literature (5). A small amount of the oil was heated with 10% NaOH, cooled, and acidified. The solid obtained was filtered off, crystallized from alcohol-water. The melting point was 88–90°, as compared to the reported value of 86° (6). A mixed melting point showed no depression.

**α-Benzyloximinopropionitrile.**—In like manner, α-benzyloximinopropionamide was converted to the nitrile. In this case, in an effort to reduce mechanical losses, smaller vessels were used to run smaller amounts. Only the reaction vessel was changed for each run and in this way the yield was increased to 32%. The observed boiling point of α-benzyloximinopropionitrile was 74–76°/0.2 mm. Basic hydrolysis of the oil produced a solid melting at 85°. The melting point was consistent with that obtained when the acid was prepared in this laboratory by standard procedures (6). The melting point was not in agreement with the reported value of 73–75° (6), but nitrogen analysis of the amide did check (4). A mixed melting point showed no depression.

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# Phosphorus-Nitrogen Compounds II. Some *p*-Toluidine Derivatives

By LINDLEY A. CATES and NOEL M. FERGUSON

**Certain organophosphorus compounds containing substituted *p*-toluidine moieties were prepared for evaluation as cancer chemotherapeutic agents. The compounds that were synthesized include phosphoramidochloridic acids, phosphoramidates, phosphoramidothionates, a phosphorodiamidate, and a phosphorodiamidic chloride. The *S*-*p*-chlorobenzylthiuronium salt of a phosphoramidochloridic acid is also reported.**

THE FIRST paper in this series (1) reported the synthesis of some carboxy- and carbethoxy-substituted aryl derivatives containing phosphorus-nitrogen bonds. This series has been extended to include some related *P–N* compounds involving substituted *p*-toluidine moieties.

Phosphoramidochloridic acids (I) constitute a relatively new class of organophosphorus compounds, of which there are few examples in the literature. Most of these compounds are arylsulfonamide derivatives (2–6), one of which was included in a group of derivatives said to possess tumor-inhibiting activities (6). All reported phosphoramidochloridic acids were prepared by treating phosphorimidic trichlorides or phosphoramidic dichlorides with formic acid (2–8). The use of an acidic reagent is not necessary in this type of synthesis, however, since the *p*-toluidine derivatives were prepared by aqueous hydrolysis of the corresponding phosphoramidic dichlorides. In either case, the acid chloride character of phosphor-

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