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Oxidative Ring Closure of 1-Benzyloxy-3-arylureas to 1-Benzyloxybenzimidazolones[1]

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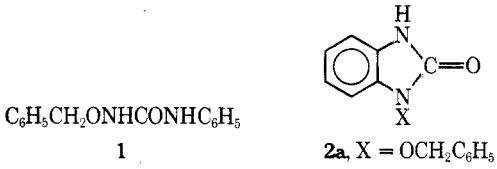
Lead tetraacetate oxidation of 1-benzyloxy-3-arylureas (1) results in intramolecular ring closure to form 1-benzyloxybenzimidazolone (2) or in intermolecular nitrogen to nitrogen coupling to form 1,2-dibenzyloxy-1,2-diphenylcarbamylhydrazines (7). Studies of the oxidation of structures related to 1 establish that the requirements for a ring closure are quite specific. Studies of the influence of substituents show that electron-withdrawing substituents on the aryl group inhibit the ring closure particularly when the substituents are ortho to the urea group. The decomposition of the hydrazines 7 occurs rapidly and aryl isocyanates and benzyl alcohol are first formed.

The finding that *N*-acyl-*O*-alkylhydroxylamines undergo oxidative coupling to *N,N*-diacyl-*N,N*-dialkoxyhydrazines[3] prompted us to study the lead tetraacetate oxidation of 1-benzyloxy-3-phenylurea[4] (1). Instead of the expected hydrazine product, oxidation of 1 with excess lead tetraacetate resulted in a single product, 1-benzyloxybenzimidazolone (**2a**), mp 159–160°, isolated in 85% yield and estimated in 97% yield by spectroscopic measurements. The structure of **2a** was established by catalytic hydrogenolysis to **2b** with palladium on carbon and to the known compound **2c** with Raney nickel. The properties of **2c** were identical with those of a sample of benzimidazolone prepared by the method of Kym.[5]



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2a, X = $OCH_2C_6H_5$
b, X = OH
c, X = H

Results and Discussion

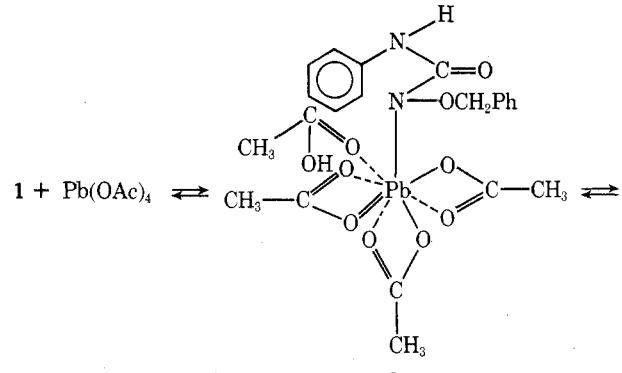
The proposed scheme for conversion of 1 to 2 is shown in Scheme I

Substituents on the Aryl Ring. The influence of substituents on the aryl ring of 1-benzyloxy-3-arylureas was studied first. Results are presented in Table I. Strongly electron-withdrawing groups decreased the yield of ring closure, and in these cases a competing reaction, nitrogen to nitrogen coupling, was observed (*vide infra*).

Groups in the ortho position markedly affect the ring closure. While a *p*- or *m*-chloro substituent appeared not to diminish the ring closure significantly below the unsubstituted case, no ring closure was observed with the *o*-chloro substituent. Even when 1-benzyloxy-3-*o*-chlorophenylurea was slowly added to lead tetraacetate to effect high dilution conditions only a 19% yield of benzimidazolone was realized. Under no conditions, high dilution or otherwise, were we able to affect a ring closure with 1-benzyloxy-3-*o*-nitrophenylurea.

The inhibition of ring closure with the *o*-fluoro, *o*-chloro, and *o*-nitro compounds is probably a combination of inductive and steric effects. In cases where both electron withdrawal and steric repression are important (*e.g.*, the nitro and chloro compounds), the ring closure reaction is strongly inhibited. In cases where steric repulsion is small and the

Scheme I



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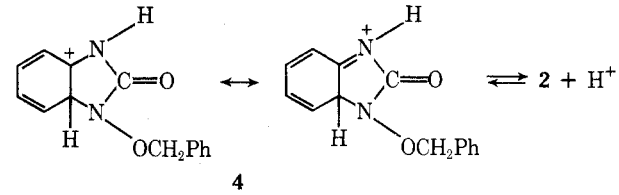

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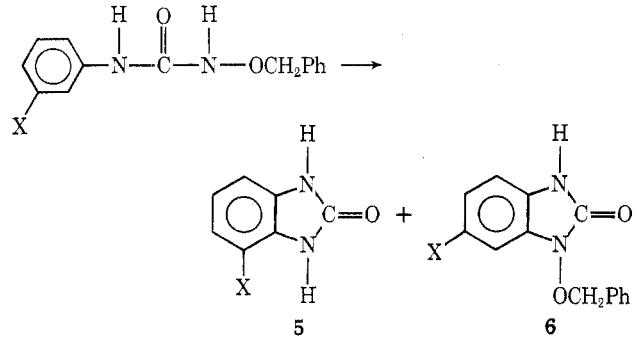
Table I
Products from Lead Tetraacetate Oxidation of 1-Benzyloxy-3-arylureas in Chloroform Solution[a]

Reaction no.	Aromatic substituent	Registry no.	% benzimidazolone[b]	% carbamate
1	*p*-CH_3O	51457-93-3	95	0
2	*p*-CH_3	51457-92-2	100	0
3	*p*-H	33026-77-6	97	0
4	*p*-Cl	51457-91-1	94	0
5	*p*-NO_2	51457-90-0	12	88
6	*m*-CH_3	51457-96-6	97	0
7	*m*-Cl	51457-94-4	99	0
8	*m*-NO_2	51457-95-5	15	84
9	*o*-CH_3O	51458-01-6	98	0
10	*o*-CH_3	51458-00-5	96	0
11	*o*-F	51457-99-9	41	50
12	*o*-Cl	51457-98-8	0	98
13	*o*-NO_2	51457-97-7	0	96

[a] All reactions were run with an initial concentration of 5.82×10^{-2} *M* solutions of 1-benzyloxy-3-arylureas in chloroform containing 5.94×10^{-2} *M* concentration of lead tetraacetate. [b] Values reported are actual percentage yields of isolated product.

Table II
Ratio of Isomeric Benzimidazolone Products from Lead Tetraacetate Oxidation of Meta-Substituted 1-Benzyloxy-3-arylureas



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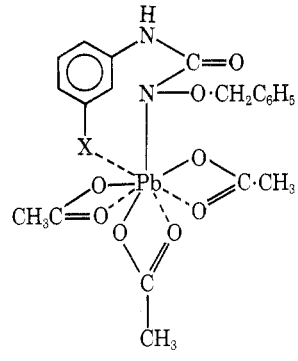
	%	Position of NH in nmr	%	Position of NH in nmr	of/pf
m-Cl	51	11.41	49	11.24	1.04
m-CH_3	45	10.54	55	10.68	0.82
m-NO_2	60	11.86	40	11.68	1.50

inductive influence is large (*e.g.*, fluorine), the ring closure is moderately inhibited. And in the case where the inductive influence is still smaller and the steric interaction is also small (*e.g.*, methoxyl), ring closure is quantitative.

In the case of meta-substituted 1-benzyloxy-3-arylureas two isomeric products are possible depending upon whether ring closure occurs ortho or para to the substituent. The presence of these isomeric products were established by nmr spectra, and they were isolated from the reaction mixture either by fractional crystallization or thin layer chromatography. Structure **6** was established for the higher melting isomer from oxidation of 1-benzyloxy-3-*m*-chlorophenylurea by hydrogenolysis to 5-chlorobenzimidazolone. The same product was obtained by hydrogenolysis of 1-benzyloxy-6-chlorobenzimidazolone obtained as the only product from the lead tetraacetate oxidation of 1-benzyloxy-3-*p*-chlorophenylurea. Similar evidence established that the higher melting isomer from oxidation of 1-benzyloxy-3-*m*-methylphenylurea has structure **6**. Attempts to hydrogenate the products from 1-benzyloxy-3-*m*-nitrophenylurea were not successful and assignment of **6** as the higher melting isomer was made on the basis of the position of the NH absorption in the nmr spectra.

The ratio of **5** to **6** was estimated by integrating the two NH peaks in the nmr for each compound, the CH_3 peaks for the methyl compounds, and the CH_2 peaks for the nitro compounds. The results are in Table II.

From the percentage yields the ratios of ortho to para partial rate factors (of/pf) have been calculated.[6] The value for the methyl compound, 0.82, lies between the value 0.60 for the deuteration (D_2SO_4) of toluene[7] and 1.0 for the detritiation (H_2SO_4) of toluene.[8] In contrast, of/pf for the chloro compound is 1.04 and for nitration[6] and detritiation of chlorobenz of/pf are 0.21 and 0.22, respectively. Possibly a lead-containing intermediate **7** in which the lead is coordinating with nonbonding electrons on either the chloro or nitro groups could explain the unexpectedly large amount of ortho direction.[10]



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Oxidative cyclization of 1-benzyloxy-3-(α-naphthyl)urea led exclusively to attack at the β position of the naphthalene ring rather than the peri position.

Hydrazines. In those cases where oxidative ring closure failed to occur a nitrogen to nitrogen coupling reaction was observed. In most cases the hydrazines **8** formed by the oxidative coupling of the 1-benzyloxy-3-arylureas were too unstable to isolate and nitrogen gas, which was evolved almost as fast as the reagents were combined, and the carbamates were found as reaction products. Only in the case of 1-benzyloxy-3-*o*-nitrophenylurea was the hydrazine relatively stable. This hydrazine, which was isolated as a viscous oil, slowly decomposed with the evolution of nitrogen over a period of 32 hr in bromoform or chloroform solutions and benzyl *o*-nitrophenylcarbamate was isolated as the sole reaction product.

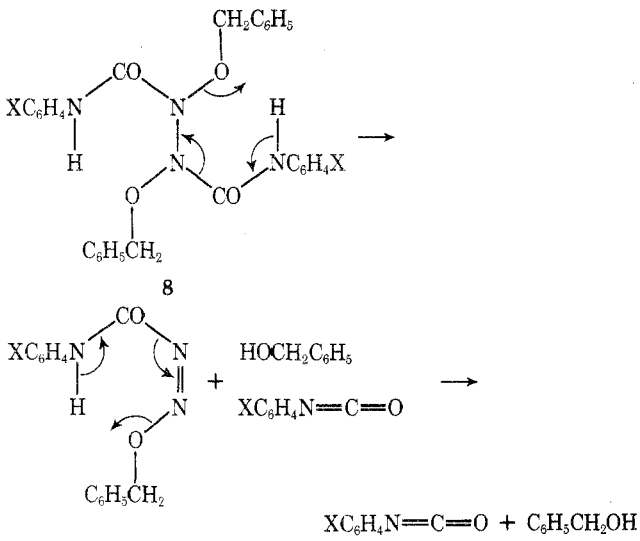
Isocyanates and alcohols were identified as the first reaction products from decompositions of hydrazines. An infrared spectrum of chloroform solution of 1-benzyloxy-3-*p*-nitrophenylurea, determined 90 sec after addition of lead tetraacetate, showed a strong absorption at 2260 cm^{-1} which was found to be identical, both in position and shape, to the N=C=O absorption of *p*-nitrophenyl isocyanate. The intensity of this absorption increased for the first 5 min after initiation of the oxidation reaction and then slowly decreased for the next hour. In a subsequent work-up of the reaction solution only benzyl *p*-nitrophenylcarbamate, the reaction product from *p*-nitrophenyl isocyanate and benzyl alcohol, was obtained as the major reaction product.

The presence of *p*-nitrophenyl isocyanate as a reaction intermediate in the lead tetraacetate oxidation of 1-benzyloxy-3-*p*-nitrophenylurea in chloroform solution was further established by the addition of *n*-butylamine to the reaction solution. In this case the major reaction products were 1-*n*-butyl-3-*p*-nitrophenylurea and benzyl alcohol. Presumably the *n*-butylamine, which is much more reac-

tive toward isocyanates than benzyl alcohol, reacted with the *p*-nitrophenyl isocyanate from the decomposition of the hydrazine compound 8 to yield the 1-*n*-butyl-3-*p*-nitrophenylurea, along with the unreacted benzyl alcohol. Compounds 1 and 2 do not react with *n*-butylamine under these conditions. In chloroform solutions containing no *n*-butylamine the *p*-nitrophenyl isocyanate slowly reacts with the benzyl alcohol to give the benzyl *p*-nitrophenylcarbamate as the reaction product.

A mechanism of decompositon of 8 by which it is possible to explain the observations is shown in Scheme II. First,

Scheme II



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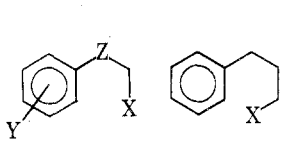
$XC_6H_4N{=}C{=}O + C_6H_5CH_2OH$

the mechanism provides an explanation of the observed products. Second, intramolecular hydrogen transfer occurs in this system in a similar way as acid catalysis was shown to occur with the 1,2-diacyl-1,2-dialkoxyhydrazines.[3] Such internal protonation would provide an explanation for the much more rapid decomposition of 8 than of 1,2-diacyl-1,2-dialkoxyhydrazines.[3,11] Third, the NH proton in 1,2-dibenzyloxy-1,2-di-*o*-nitrophenylhydrazine is expected to form a stable hydrogen bond to the nitro group, and thus the hydrogen would not be available for the internal protonation suggested in the mechanism. The *o*-nitro compound is the most stable that has been encountered in this series. Fourth, as was found earlier[3] 1,2-dialkoxy-1,2-diacylhydrazines decompose in two consecutive steps. Similarly, here it is found that the plot of volume of nitrogen evolved as time was an "S" shaped curve. These four observations support the proposed mechanism.

Oxidation of Related Structures. The supposition that a ring closure might be expected by oxidation of other systems 9,10 containing a readily oxidizable group situated γ with respect to an aromatic ring was tested.

Oxidation of 4-phenyl-1-butanols, 3-phenyl-1-propanols,[13] and 2-phenoxyethanol[13] with lead tetraacetate has been reported to give ring closures analogous to I. Similarly lead tetraacetate oxidation of 5-(*p*-nitrophenyl)valeric acids and 3-(*o*-biphenyl)propionic acid resulted in intramolecular cyclization to 6-nitro-1,2,3,4-tetrahydronaphthalene and 9,10-dihydrophenanthrene, respectively.[14] Because of these reports and our finding with 1-benzyloxy-3-phenylurea other compounds with a readily oxidizable group situated γ or δ to an aromatic ring activated by an amido or ether function were studied.

We have reported the fact that ring closure failed in the lead tetraacetate oxidation of malonic anilide, phenoxyacetone oxime, and 1,2,4-triphenylsemicarbazide. Also with 1,1-dimethyl-4-phenylsemicarbazide which is more like I, oxidative dimerization occurred resulting in a very different type of ring closure product, 1,4-dimethyl-2,5-di(phenylcarbamyl)hexahydrotetrazine (11).[15] In a continued



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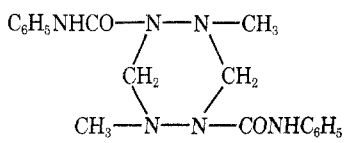

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attempt to establish the limitations of the ring closure reaction, oxidations of several structures like 8 with a hydroxylamino group (–NHO–) at X were studied. In all cases the ring was activated by a methoxyl group at Y or an oxygen or nitrogen at Z. *N*-Acetyl-*O*-*p*-methoxybenzylhydroxylamine, *N*-*p*-methoxyphenylacetyl-*O*-benzylhydroxylamine, *N*-phenoxyacetyl-*O*-benzylhydroxylamine, *N*-phenoxyacetyl-*O*-benzylhydroxylamine, and phenyl benzyloxycarbamate all gave the oxidative nitrogen to nitrogen coupling and not ring closure. In the case of 1,1-diphenyl-3-benzyloxyurea a 99% yield of 1-benzyloxy-3-phenylbenzimidazolone, the ring closed product, was obtained. Thus it is established that the ring closure 1 to 2 has a narrow specific requirement in structure. The hydroxylamino group cannot be replaced by a hydrazine, oximino, or methylene group, and the unoxidized NH group of 1 can only be replaced by *N*-aryl but not by oxygen or methylene. In general, oxidations of 3-substituted 1-phenylpropanes do not give ring closures under the conditions used for cyclization of 1.

Experimental Section

Melting points were corrected and were determined in capillary tubes using an A. H. Thomas Unimelt apparatus. Infrared spectra were obtained using a Perkin-Elmer grating infrared spectrophotometer, Model 621. The nuclear magnetic resonance spectra (nmr) were taken on a Varian A60 instrument. Mass spectra were run on a Hitachi Perkin-Elmer RMU-6E mass spectrometer. Microanaylses were determined at the University of Idaho on a Perkin-Elmer, Model 240, elemental analyzer. Osmotic molecular weight determinations were run on a Hitachi Perkin-Elmer molecular weight apparatus, Model 115.

1-Benzyloxy-3-arylureas. These preparations were carried out by reaction of benzyloxyamine[16] with an equimolar quantity of aryl isocyanate. The details of these preparations are described elsewhere.[17]

Solvent. Chloroform was purified by shaking several times with concentrated sulfuric acid, drying with anhydrous calcium chloride, passing through a column of alumina, and distilling. All lead tetraacetate oxidations run in chloroform were run within 24 hr of the completion of this purification procedure.

Lead Tetraacetate Oxidation of 1-Benzyloxy-3-phenylurea. Method I. To 1.00 g (4.13 mmol) of 1-benzyloxy-3-phenylurea dissolved in 50 ml of dry chloroform was added with stirring a 10-ml solution of chloroform containing 2.01 g (4.53 mmol) of lead tetraacetate analyzed by Arapahoe Chemical Co. as 95% lead tetraacetate and 5% acetic acid. Upon mixing the reaction solutions a precipitate having the same melting point and infrared spectrum as lead diacetate was formed. The solution was filtered, and the precipitate was washed with chloroform until 250 ml of filtrate was obtained. The filtrate was washed twice with 50-ml aliquots of water and dried with anhydrous calcium chloride. On removing the chloroform, 0.96 g (96%) of white solid remained which on recrystallization from ethanol–water gave 0.85 g of pure 1-benzyloxybenzimidazolone: mp 159–160°; ir (Nujol) 1705 (C=O); nmr (DMSO-d_6) δ 5.22 (s, 2), 6.80–7.70 (m, 9), broad 11.10 ppm (s, 1). Major peaks in the mass spectrum at 70 eV include *m/e* (relative intensities) 240 (26), 134 (100), 108 (60), 105 (95), 91 (52). *Anal.* Calcd for $C_{14}H_{12}N_2O_2$: C, 70.00; H, 5.01; N, 11.67. Found: C, 69.87; H, 5.13; N, 11.93.

Lead Tetraacetate Oxidation of Other 1-Benzyloxy-3-Para-Substituted Arylureas. Physical data and analyses for the oxidation products of other 1-benzyloxy-3-para-substituted arylureas are given in Table III.

Table III
Summary of Physical Data and Analyses for Substituted 1-Benzyloxybenzimidazolone (2) Products Obtained as Sole Reaction Products in High Yields[a] from Oxidation of 1-Benzyloxy-3-Para-Substituted Ureas

Substituent on 2	Registry no.	Mp, °C	Analysis, %	
			Calcd	Found
6-Methoxy	53820-90-9	149–150	C 66.65	66.63
			H 5.22	5.34
			N 10.37	10.32
6-Methyl	53820-91-0	162–163	C 70.85	70.87
			H 5.55	5.56
			N 11.02	10.88
6-Chloro	53820-92-1	153–154	C 61.21	61.22
			H 4.04	4.13
			N 10.20	10.16

[a] All reactions were run in chloroform solutions with an initial concentration of 5.82×10^{-2} *M* 1-benzyloxy-3-arylurea and 6.10×10^{-2} *M* lead tetraacetate. Products from top to bottom of table were obtained in 95, 100, and 94% yield, respectively.

Catalytic Hydrogenation of 1-Benzyloxybenzimidazolone with Palladium on Carbon. In a microhydrogenation apparatus was placed 0.210 g (0.875 mmol) of 1-benzyloxybenzimidazolone in 20 ml of 95% ethanol and 0.1 g of 5% palladium on carbon. The mixture was stirred for 40 min, and 23 ml of hydrogen corrected to STP (1.02 mmol) was absorbed. The catalyst was removed by filtration, and the solution was analyzed for toluene using glc and the internal standard technique. The estimated yield of toluene was 0.070 g, 87%. The solvent was removed and the solid product (0.121 g, 92%, mp 228–232°) was obtained. This product was recrystallized from a mixture of acetone and carbon tetrachloride and was observed to decompose sharply at 230° and produce a green color with a ferric chloride solution: ir (Nujol) broad 3115, 1680 cm^{-1}. *Anal.* Calcd for $C_7H_6N_2O_2$: C, 55.99; H, 4.03; N, 18.66. Found: C, 56.14; H, 4.19; N, 18.82.

Catalytic Hydrogenation of 1-Benzyloxybenzimidazolone with Raney Nickel. Hydrogenation of 0.247 g (1.03 mmol) of 1-benzyloxybenzimidazolone with Raney nickel catalyst occurred in about 8 hr with an observed uptake of 48.5 ml (0.216 mmol) of hydrogen. The solution was filtered and 0.069 g, 73%, of toluene was estimated to be present using glc and the internal standard technique. Upon evaporation 0.130 g, 94%, of white solid (mp 309–313°) was obtained. Purification was achieved by recrystallization from acetone: mp 313–315°; mmp with benzimidazolone[5] 313–315°. *Anal.* Calcd for $C_7H_6N_2O$: C, 62.67; H, 4.51; N, 20.89. Found: C, 62.52; H, 4.64; N, 20.77.

Lead Tetraacetate Oxidation of 1-Benzyloxy-3-*p*-nitrophenylurea. In a closed system connected to a gas buret, a 1.00-g (3.49 mmol) sample of 1-benzyloxy-3-*p*-nitrophenylurea dissolved in 50 ml of chloroform was added with stirring to a 10-ml chloroform solution containing 1.70 g (3.84 mmol) of lead tetraacetate. Upon mixing the reaction solutions 34.0 ml (STP) or 1.518 mmol of a gas was evolved which gave no infrared spectrum and had the same glc retention time as nitrogen. The evolution of gas was complete within 2 min of the initial mixing time. The mixture was filtered, and 0.93 g of solid was obtained when the chloroform was evaporated A 0.75-g sample of this was dissolved in ethyl acetate and placed on 50 g of a neutral alumina column. Upon eluting the column with 50 ml of ethyl acetate, 0.60 g (80%) of a solid product, mp 157–158°, was obtained. This compound had identical ir and nmr spectra with benzyl *p*-nitrophenylcarbamate prepared by the reaction of benzyl alcohol with *p*-nitrophenyl isocyanate: ir (Nujol) 3333 (N–H), 1740 cm^{-1} (C=O); nmr (DMSO-d_6) δ 5.23 (s, 2), 7.31–8.32 (m, 9), 10.46 ppm (broad s, 1). *Anal.* Calcd for $C_{14}H_{12}N_2O_4$: C, 61.76; H, 4.44; N, 10.29. Found: C, 61.94; H, 4.37; N, 10.32.

Further elution of the column with 75 ml of methanol afforded 0.072 g (9.6%) of a solid product, mp 200–201°, which was identified as 1-benzyloxy-6-nitrobenzimidazolone: ir (Nujol) 1720 (C=O), 1080, 835, 700 cm^{-1}; nmr (DMSO-d_6) δ 5.28 (s, 2), 7.05–8.06 (m, 8), 11.84 ppm (broad s, 1). *Anal.* Calcd for $C_{14}H_{11}N_3O_4$: C, 58.94; H, 3.89; N, 14.73. Found: C, 58.86; H, 3.92; N, 14.68. A comparison of the integration of the N–H protons in the nmr spectrum of the original reaction mixture showed the benzyl *p*-nitrophenylcarbamate and 1-benzyloxy-6-nitrobenzimidazolone to be present in a molar ratio of 88 to 12%, respectively. The volume of nitrogen evolved corresponds to 87% of the urea to hydrazine 8 and on to *p*-nitrophenylcarbamate.

Detection of *p*-Nitrophenyl Isocyanate during Lead Tetraacetate Oxidation of 1-Benzyloxy-3-*p*-nitrophenylurea. To a 1.00-g (3.5 mmol) sample of 1-benzyloxy-3-*p*-nitrophenylurea in 40 ml of chloroform was added 1.40 g (3.15 mmol) of lead tetraacetate, and the mixture was stirred for 30 sec at room temperature. A sample of the reaction mixture was placed in a 464-μ path length liquid infrared cell and the infrared spectrum of the solution was run between 2350 and 2200 cm^{-1}. The first infrared spectrum was run 90 sec after the initial addition of the lead tetraacetate to the reaction solution and showed a strong infrared absorption at 2260 cm^{-1}. The intensity of this band increased for the first 5 min and then slowly decreased for the next hour until it disappeared. A solution of *p*-nitrophenyl isocyanate in chloroform showed a strong infrared absorption at the same wave number (2260 cm^{-1}) and the intensity of this absorption also slowly decreased when benzyl alcohol was added to the solution. Both of these bands had the same characteristic shape being rather broad with the maximum intensity occurring at the lower wavelength side of the band.

Lead Tetraacetate Oxidation of 1-Benzyloxy-3-*m*-nitrophenylurea. When this oxidation was carried out using method I, a 99% yield of solid was obtained. From the nmr it was estimated that this solid was a mixture of 15% of two isomeric 1-benzyloxynitrobenzimidazolones and 85% benzyl *m*-nitrophenylcarbamate. Only this latter compound was isolated from this reaction mixture using column chromatography (alumina and ethyl acetate) and was shown to be identical to the product from *m*-nitrophenyl isocyanate with benzyl alcohol: ir (Nujol) 3306, 1690, 1530, 725 cm^{-1}; nmr (DMSO-d_6) δ 5.27 (s, 2), 7.25–9.67 (m, 9), 10.30 ppm s, 1). *Anal.* Calcd for $C_{14}H_{12}N_2O_4$: C, 61.76, H, 4.44, N, 10.29. Found: C, 61.75, H, 4.42, H, 10.40. From the column chromatograph the 1-benzyloxynitrobenzimidazolones were obtained by elution with methanol. From the nmr spectra of the mixture the yields were estimated to be 87% for the carbamate and 13% for the isomeric benzimidazolones, while the ratio of the latter compounds was estimated to be 60:40.

Lead Tetraacetate Oxidation of 1-Benzyloxy-3-*m*-nitrophenylurea Using High Dilution Conditions. Method II. Isolation of the benzimidazolones was undertaken from a high dilution experiment where 1.00 g (3.49 mmol) of 1-benzyloxy-3-*m*-nitrophenylurea in 500 ml of chloroform was added slowly (100 min) to 1.70 g (3.84 mmol) of lead tetraacetate in 100 ml of chloroform. From this oxidation 0.92 g of solid product which was estimated to be 93% 1-benzyloxynitrobenzimidazolones and 7% benzyl *m*-nitrophenylcarbamate by nmr was obtained. One isomeric benzimidazolone was isolated by fractional crystallization from chloroform: mp 220–221°; ir (Nujol) 1722, 1517, 1337, 693 cm^{-1}; nmr (DMSO-d_6) δ 5.30 (s, 2), 6.93–8.05 (m, 8), 11.68 ppm (s, 1). *Anal.* Calcd for $C_{14}H_{11}N_3O_4$: C, 58.94, H, 3.89, N, 14.73. Found: C, 58.70, H, 3.90, N, 14.72. From chloroform–carbon tetrachloride solution a second isomer precipitated: mp 173–174°; ir (Nujol) 1730, 1532, 1350, 854, 710 cm^{-1}; nmr δ 5.32 (s, 2), 7.02–7.76 (m, 8), 11.86 (s, 1). *Anal.* Calcd for $C_{14}H_{11}N_3O_4$: C, 58.94, H, 3.89, N. 14.73. Found: C, 58.82, H, 3.90, N, 14.93. The ratio of these two isomeric 1-benzyloxynitrobenzimidazolones was estimated to be 40 to 60%, respectively.

Lead Tetraacetate Oxidation of Other 1-Benzyloxy-3-Meta-Substituted Arylureas. Physical data and analyses for the oxidation products of other 1-benzyloxy-3-meta-substituted arylureas are given in Table IV.

Lead Tetraacetate Oxidation of 1-Benzyloxy-3-*o*-nitrophenylurea. From the oxidation of 1.00 g (3.49 mmol) of 1-benzyloxy-3-*o*-nitrophenylurea with 1 g (2.26 mmol) of lead tetraacetate was isolated 0.950 g of an oily product: ir (neat) 3318, 1725, 735, 693 cm^{-1}; nmr ($CDCl_3$) δ 5.27 (s, 2), 6.90–8.75 (m, 9), 11.11 ppm (s, 1).

A 0.600-g (1.05 mmol) sample of this product was dissolved in 30 ml of bromoform and connected to a gas buret. The temperature of solution was held at 23.0° and Table V shows the observed evolution of nitrogen gas. Upon removal of the bromoform under reduced pressure a solid product was obtained. A pure sample, mp 65–66°, was obtained upon recrystallization of this product from a hexane–carbon tetrachloride mixture. This product was identified as benzyl *o*-nitrophenylcarbamate by comparison of the nmr and infrared spectra with a sample of benzyl *o*-nitrophenylcarbamate prepared by the reaction of benzyl alcohol with *o*-nitrophenyl iso-

Table IV
Summary of Physical Data and Analyses for Isomeric Aryl-Substituted 1-Benzyloxybenzimidazolones (2) from 1-Benzyloxy-3-Meta-Substituted Arylureas

Substituent on 2	Registry no.	Mp, °C	Ratio of products estimated by nmr, %	Analysis, % Calcd	Found
5-Methyl[b]	53820-93-2	153–154	55	C 70.85	71.13
				H 5.55	5.67
				N 11.02	11.02
7-Methyl	53820-94-3	139–140	45	C 70.85	70.99
				H 5.55	5.66
				N 11.02	11.04
5-Chloro[b]	53820-95-4	204–205	49	C 61.21	61.12
				H 4.04	4.13
				N 10.20	10.31
7-Chloro	53820-96-5	160–161	51	C 61.21	61.00
				H 4.04	3.95
				N 10.20	10.19

[a] Overall yields were 96% for the two methyl compounds and 98% for the two chloro compounds. [b] Structures were identified by conversion of these compounds to 5-methylbenzimidazolone and 5-chlorobenzimidazolone by hydrogenolysis. The same compounds were obtained by hydrogenolysis of 1-benzyloxy-6-methylbenzimidazolone and 1-benzyloxy-6-chlorobenzimidozolone, respectively.

cyanate: ir (Nujol) 3340, 1733, 750, 691, cm^{-1}; nmr ($CDCl_3$) 5.20 (s, 2), 6.85–8.65 (m, 9), 9.86 ppm (s, 1). *Anal.* Calcd for $C_{14}H_{12}N_2O_4$: C, 61.76; H, 4.44, N, 10.29. Found: C, 61.88, H, 4.46, N, 10.29.

The decomposition of the oil in $CDCl_3$ was followed by nmr. The nmr absorption due to the oil slowly disappeared while that due to benzyl *o*-nitrophenylcarbamate slowly increased until the latter absorption was all that was present in the spectrum after 24 hr.

Lead Tetraacetate Oxidation of Other 1-Benzyloxy-3-Ortho-Substituted Arylureas. Physical data and analyses for the oxidation products of other 1-benzyloxy-3-ortho-substituted arylureas are given in Table VI.

Lead Tetraacetate Oxidation of 1-Benzyloxy-3-α-naphthylurea. The oxidation of 1.02 g (3.50×10^{-3} mol) of 1-benzyloxy-3-α-naphthylurea with 1.60 g (3.61×10^{-3} mol) of lead tetraacetate in 60 ml of chloroform, using the same procedure as given above for 1-benzyloxy-3-phenylurea, afforded 0.96 g (97% yield) of a solid product. The nmr spectrum (DMSO-d_6) of this product indicated the presence of a benzyloxynaphthimidazolone compound as the only reaction product. A pure sample with a mp of 156–157° was obtained upon recrystallization of this product from a chloroform–benzene solution: ir (Nujol) 1706, 796, 720, 690 cm^{-1}; nmr (DMSO-d_6) δ 5.32 (s, 2), 7.03–8.32 (m, 11), 12.01 ppm (s, 1). *Anal.* Calcd for $C_{18}H_{16}N_2O_2$: C, 73.96, H, 5.52, N, 9.58. Found: C, 74.02, H, 5.59, N, 9.61.

Table V

Time, min	Ml of N_2 at STP	Time, min	Ml of N_2 at STP
0.0	0.0	945.0	18.0
120.0	0.5	1140.0	20.0
280.0	3.4	1345.0	22.0
370.0	6.0	1535.0	23.2
475.0	9.0	1920.0	23.5
585.0	12.0	∞	23.5 (1.05 mmol)
760.0	15.7		

Table VI
Summary of Physical Data and Analyses for Products of Oxidation of 1-Benzyloxy-3-Ortho-Substitued Arylureas

Aryl substituent on urea reactant	Registry no.	Product	Registry no.	% yield of isolated material	Mp, °C	Analysis, % Calcd	Found
o-Fluoro		Benzyl *o*-fluorophenylcarbamate	53820-98-7	43	61–62	C 68.56	68.77
						H 4.93	4.96
						N 5.71	5.71
		1-Benzyloxy-4-fluorobenzimidazolone	53820-99-8	34[a]	202–203	C 65.11	65.26
						H 4.29	4.40
						N 10.85	10.87
o-Chloro		Benzyl *o*-chlorophenylcarbamate	53821-00-4	98[a] 74[b]	53–54	C 64.25	64.40
						H 4.62	4.58
						N 5.35	5.26
		1-Benzyloxy-4-chlorobenzimidazolone	53821-01-5	16[b] 97[c]	211–212	C 61.21	61.01
						H 4.04	4.10
						N 10.20	10.36
2,5-Dichloro	538-20-97-6	Benzyl 2,5-dichlorophenylcarbamate	53821-02-6	97[a,b]	115.5–116.5	C 56.78	56.98
						H 3.74	3.79
						N 4.73	4.86
o-Methoxy		1-Benzyloxy-4-methoxybenzimidazolone	53821-03-7	98	167–168	C 66.65	66.67
						H 5.22	5.27
						N 10.37	10.33
o-Methyl		1-Benzyloxy-4-methylbenzimidazolone	53821-04-8	96[a]	180–181	C 70.85	70.88
						H 5.55	5.58
						N 11.02	10.80

[a] Using method I. [b] Using method II. [c] Using method II with acetic acid instead of chloroform as solvent.

Table VII
***N*-Acyl-*O*-alkylhydroxylamines**

Compd	Registry no.	% yield	Mp/bp, °C	Analysis, %	C	H	N
N-Acetyl-*o*-*p*-methoxybenzylhydroxylamine	23993-49-9	36	140 (0.15 mm)	Calcd	61.33	6.71	7.17
				Found	61.60	6.75	7.10
N-Phenoxyacetyl-*O*-benzylhydroxylamine	53821-05-9	39	89–90	Calcd	70.02	5.88	5.44
				Found	70.03	5.93	5.39
N-*p*-Methoxyphenylacetyl-*O*-benzylhydroxylamine	53821-06-0	59	93–95	Calcd	70.83	6.32	5.16
				Found	70.91	6.31	5.08

Table VIII
***N,N'*-Diacetyl-*N,N'*-dialkoxyhydrazines**

Compd	Registry no.	Mol wt	Nmr[a]
N,N'-Diacetyl-*N,N'*-di-*p*-methoxybenzyloxyhydrazine	53821-07-1	Calcd 388	2.08 (s, 6) 3.78 (s, 6)
		Found 371	5.08 (s, 4) 6.72–7.53 (m, 8)
N,N'-Diphenoxyacetyl-*N,N'*-dibenzyloxyhydrazine	53821-09-3	Calcd 510	4.64 (s, 4) 5.09 (s, 4)
		Found 488	6.62–7.65 (m, 20)
N,N'-Di-*p*-methoxyphenylacetyl-*N,N'*-dibenzyloxyhydrazine	53821-09-3	Calcd 340	3.63 (s, 4) 3.76 (s, 6)
		Found 325	5.0 (s, 4) 6.73–7.48 (m, 18)

[a] Nmr samples were run in $CDCl_3$ solution. Chemical shifts are expressed in ppm relative to TMS.

Hydrogenolysis of a 0.100-g sample of this product, at room temperature and atmospheric pressure using a (W-2) Raney nickel catalyst in 50 ml of absolute ethanol, required 2 mol of hydrogen per mole of sample and yielded a compound with a melting point of 349–350°. This compound was found to have an infrared spectrum identical with that of a sample of 1,2-naphthodimidazolone, mp 347–348°, prepared by the literature method of Bednyagina:[18] ir (Nujol) 1732, 795, 732, cm^{-1}. This reduction of the benzyloxynaphthimidazolone compound to 1,2-imidazolone established that in the lead tetraacetate oxidation of 1-benzyloxy-3-α-nathylurea oxidative ring closure occurred at the β position of the naphthalene ring.

***N*-Acyl-*O*-alkylhydroxylamines.** The method previously described was used for these preparations.[19] Data for these compounds are compiled in Table VII.

Lead Tetraacetate Oxidation of *N*-Acyl-*O*-alkylhydroxylamines. The high dilution procedure described for the oxidation of 1-benzyloxy-3-*m*-nitrophenylurea was used. Data for the hydrazine products are compiled in Table VIII.

1-Benzyloxy-3,3-diphenylurea. A solution of 5.00 g (40.6 mmol) of benzyloxyamine in 50 ml of benzene was added to 4.70 g (20.3 mmol) of diphenylcarbamyl chloride. The reaction mixture was stirred at room temperature for 1 day, and the precipitated benzyloxyamine hydrochloride was removed by filtration. The solvent was removed, and that part (4.6 g) of the residue which was soluble in ether was crystallized from a ether–hexane mixture. Pure product weighing 3.5 g, was obtained: 54%; mp 80–82°; ir (Nujol) 3385, 1696 cm^{-1}. *Anal.* Calcd for $C_{20}H_{18}N_2O_2$: C, 75.45; H, 5.70; N, 8.80. Found: C, 75.51; H, 5.73; N, 8.76.

Lead Tetraacetate Oxidation of 1-Benzyloxy-3,3-diphenylurea. Using the same procedure as given above for 1-benzyloxy-3-phenylurea 0.50 g (1.57 mmol) of 1-benzyloxy-3,3-diphenylurea was converted to 0.49 g (100%) of product. An analytically pure sample was obtained by recrystallization from hexane, mp 82–84°; ir (Nujol) 1725, 745, 695 cm^{-1}; nmr (DMSO-d_6) 5.32 (s, 4), 7.10 (s, 5), 7.10–7.80 (m, 9); spectrum at 70 eV, *m/e* (relatve intensities) 316 (55), 210 (24), 181 (21), 167 (11), 149 (12), 106 (7), 105 (9), 91 (100), 77 (60). *Anal.* Calcd for $C_{20}H_{16}N_2O_2$: C, 75.93; H, 5.10; N, 8.85. Found: C, 75.98; H, 5.15; N, 8.81.

Registry No.—1, 33026-77-6; **2a,** 53821-10-6; **2b,** 53821-11-7; **2c,** 615-16-7; lead tetraacetate, 546-67-8; benzyl *p*-nitrophenylcarbamate, 53821-12-8; 1-benzyloxy-6-nitrobenzimidazolone, 53821-13-9; *p*-nitrophenyl isocyanate, 100-28-7; 5-nitro-1-benzyloxybenzimidazolone, 53821-14-0; 7-nitro-1-benzyloxybenzimidazolone, 53821-15-1; benzyl *m*-nitrophenylcarbamate, 53821-16-2; benzyl *o*-nitrophenylcarbamate, 23091-35-2; 1-benzyloxy-3-α-naphthylurea, 51453-02-7; benzyloxynaphthimidazolone, 53821-17-3; 1-benzyloxy-3,3-diphenylurea, 53821-18-4; benzyloxyamine, 622-33-3; diphenylcarbamyl chloride, 83-01-2; 1-benzyloxy-3-phenylbenzimidazolone, 53821-19-5.

References and Notes

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(2) Taken in part from the Ph.D. Thesis of Paul T. Jacobs, University of Idaho, June 1971. We gratefully acknowledge a NASA Fellowship held by Dr. Jacobs from Sept 1967 to Aug 1970.
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