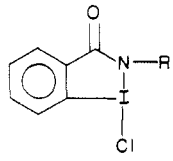
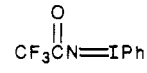
N-Phenyliodonio Carboxamide Tosylates: Synthesis and Hydrolysis to Alkylammonium Tosylates

Summary: The synthesis of *N*-phenyliodonio carboxamide tosylates from carboxamides and [methoxy(tosyloxy)-iodo]benzene and their degradative hydrolysis in acetonitrile to alkylammonium tosylates are described.

Sir: The direct conversion of primary, aliphatic carboxamides to alkylammonium tosylates with [hydroxy(tosyloxy)iodo]benzene (HTIB, **1**) in hot acetonitrile has recently been described.[1,2] A mechanism for this reaction involving the initial formation of *N*-phenyliodonio amide tosylates and their subsequent collapse to alkyl isocyanates, iodobenzene, and *p*-toluenesulfonic acid was proposed (Scheme I).[3] However, while such a mechanism bears some resemblance to that of the classical Hofmann degradation of carboxamides (i.e., amide → *N*-halo amide $\xrightarrow{(OH^-)}$ isocyanate),[4] it remained speculative since the *N*-iodonio amides were not isolated and characterized. Among organoiodine(III) compounds, *N*-iodonio carboxamides are rare. We are aware of only three azabenzoxiodoles **2**,[5] the nitrogen–iodine ylide **3**[6,7a-c] and a series of "phenyliodine(III) bisimidates".[7d] We now report a mild, efficient synthesis of the first acyclic *N*-iodonio carboxamide "salts" and a demonstration of their hydrolytic decomposition in acetonitrile to alkylammonium tosylates.



2: R = H, Me, Cl



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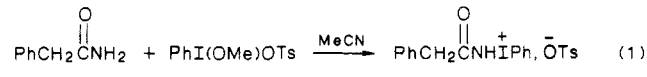
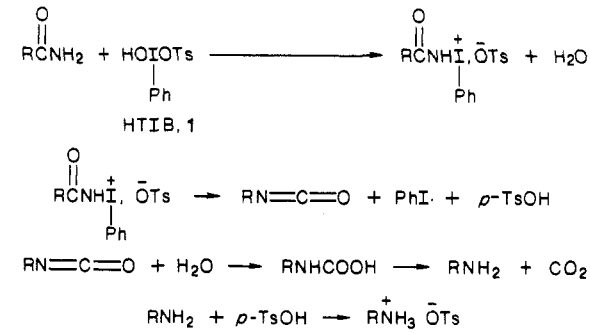
[Methoxy(tosyloxy)iodo]benzene (MTIB, **4**), prepared from HTIB and trimethyl orthoformate,[8] is much more soluble in acetonitrile at room temperature than HTIB and is the reagent of choice for the preparation of *N*-phenyliodonio amide tosylates. For example, when α-phenylacetamide (20 mmol) was added *as the solid* to a solution of MTIB (20 mmol) in MeCN (40 mL) at room temperature, the amide soon "dissolved". Shortly thereafter (ca. 1 min), *N*-phenyliodonio α-phenylacetamide tosylate (**5**) precipitated and was isolated in 76.5% yield; eq 1.[9] The

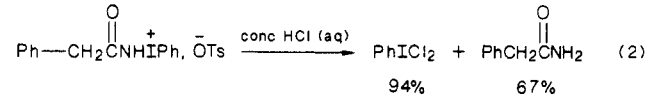


MTIB, **4** **5** (1)

Scheme I

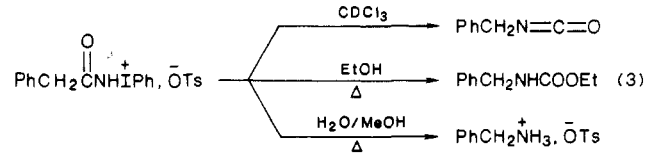


structure assigned to **5** is consistent with its elemental analysis (C, H, I), IR spectrum (Nujol, 1699 cm^{-1} (C=O)), and conversion in concentrated hydrochloric acid to (dichloroiodo)benzene and α-phenylacetamide; eq 2. Al-



(2)

though **5** is moderately stable in the solid state, it is quite labile in those solvents capable of effecting its dissolution, and an ^1H NMR spectrum of the *intact* compound was not obtained. Even so, the ^1H NMR spectrum of "**5**" in $CDCl_3$ was informative since benzyl isocyanate was among the decomposition products (ca. 34–48% yield)[10] and was identified by peak enhancement with authentic material and IR analysis (2270 cm^{-1} (C=O)) of a concentrated sample. When a solution of **5** (1.96 mmol) in EtOH (15 mL) was heated under reflux, the isocyanate was captured by the solvent, and ethyl benzylcarbamate was isolated in 63% yield. Judging from the results of hydrolysis experiments, the collapse of **5** to benzyl isocyanate also proceeds efficiently in hot acetonitrile. When a mixture of **5** (4.0 mmol) in reagent-grade MeCN (25 mL, 0.1% H_2O lot analysis) was heated for 30 min under reflux and cooled at ca. −15 to −20 °C, benzylammonium tosylate was isolated in only 24% yield. However, treatment of the filtrate with H_2O (72 μL) delivered an additional 62.6% yield of the ammonium salt. In a similar experiment, in which **5** (6.0 mmol) was heated in MeCN (30 mL) to which H_2O (10 mmol) had been deliberately added, benzylammonium tosylate was obtained in 81% yield; the results are summarized in eq 3.



(3)

The isolation of **5**, its degradative rearrangement to benzyl isocyanate in the absence of water, and its hydrolysis to benzylammonium tosylate establish the viability of the proposed mechanism for the conversion of amides to ammonium tosylates with HTIB.

The synthesis of *N*-phenyliodonio amides with MTIB has been extended to other carboxamides and appears to be general (Table I). So too does the hydrolysis of aliphatic *N*-phenyliodonio amide tosylates to alkylammonium tosylates in acetonitrile (Table II).

The successful phenyliodination of acetamide with MTIB was employed to address one final structural

(1) Lazbin, I. M.; Koser, G. F. *J. Org. Chem.* **1986**, *51*, 2669.
(2) This study was prompted by the investigations of Loudon and his co-workers on the use of [bis(trifluoroacetoxy)iodo]benzene, $PhI(OOCCF_3)_2$, as a mildly acidic Hofmann reagent: see (a) Loudon, G. M.; Radhakrishna, A. S.; Almond, M. R.; Blodgett, J. K.; Boutin, R. H. *J. Org. chem.* **1984**, *49*, 4272. (b) Boutin, R. H.; Loudon, G. M. *J. Org. Chem.* **1984**, *49*, 4277 and references therein.
(3) Loudon has reported kinetic evidence consistent with the intermediacy of similar *N*-iodine(III) species in the [bis(trifluoroacetoxy)-iodo]benzene-induced rearrangement of hexanamide; see ref 2b.
(4) Wallis, E. S.; Lane, J. F. In *Organic Reactions*; Wiley: New York, 1946; Vol. 3, Chapter 7, pp 267–306.
(5) Naae, D. G.; Gougoutas, J. Z. *J. Org. Chem.* **1975**, *40*, 2129.
(6) Mansuy, D.; Mahy, J.-P.; Dureault, A.; Bedi, G.; Battioni, P. *J. Chem. Soc., Chem. Commun.* **1984**, 1161.
(7) Iodine–nitrogen ylides (i.e., iminoiodinanes) of general structure $ArI{=}NSO_2R$ (R = Me, Ar) have also been prepared from sulfonamides: see ref 6 and (a) Abramovitch, R. A.; Bailey, T. D.; Takaya, T.; Uma, V. *J. Org. Chem.* **1974**, *39*, 340. (b) Yamada, Y.; Yamamoto, T.; Okawara, M. *Chem. Lett.* **1975**, 361. (c) Svastits, E. W.; Dawson, J. H.; Breslow, R.; Gellman, S. H. *J. Am. Chem. Soc.* **1985**, *107*, 6427. (d) For the synthesis of the iodine(III) bisimidates, see: Papadopoulou, M.; Varvoglis, A. *J. Chem. Res., Synop.* **1983**, 66.
(8) Koser, G. F.; Wettach, R. H. *J. Org. Chem.* **1980**, *45*, 4988.
(9) **5** has also been prepared by the addition of solutions of MTIB in acetonitrile to solid α-phenylacetamide.
(10) Estimated in several NMR samples from relative areas of benzylic singlet of $PhCH_2NCO$ and methyl singlet of tosylate species.

0022-3263/87/1952-0476$01.50/0

Table I. *N*-Phenyliodonio Amide Tosylates from Amides and MTIB in Acetonitrile[a]

$RCONH\overset{+}{I}Ph$, $\bar{O}Ts$,[b] R =	yield,[c] %
CH_3	66
$(CH_3)_2CH$	68
$(CH_3)_3C$	80
$CH_3(CH_2)_4$	89
Ph	90

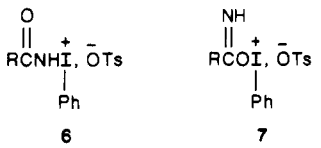
[a] Reactions were conducted on ca. a 5-mmol scale in MeCN (13 mL) by the procedure described for the reaction of α-phenylacetamide with MTIB. [b] Satisfactory analytical data (±0.40%) for C, H, I were finally obtained for all compounds, sometimes only after a second analysis of the same sample. [c] Rounded off to the nearest percent and based on the limiting reagent.

Table II. Hydrolysis of *N*-Phenyliodonio Amide Tosylates to Alkylammonium Tosylates in Acetonitrile

$RCONH\overset{+}{I}Ph$, $\bar{O}Ts$					$R\overset{+}{N}H_3$, $\bar{O}Ts$[c]
R	mmol	H_2O,[a] mmol	MeCN vol, mL	time,[b] h	yield, %[d]
CH_3	2.31	2.3	15	1	83
$(CH_3)_2CH$	2.17	2.2	13	0.5	64[e]
$(CH_3)_3C$	2.10	2.2	15	0.5	81
$CH_3(CH_2)_4$	2.04	2.2	10	0.5	75[f]

[a] Based on volume of H_2O in μL. [b] Reaction mixtures were heated to reflux and maintained under reflux for the specified periods of time. [c] The products separated from the solvent when the reaction mixtures were kept at room temperatues (R = *t*-Bu, *n*-C_5H_{11}) or in a refrigerator freezer (R = Me, *i*-Pr). [d] Based on unrecrystallized products and rounded off to nearest percent: R (mp, uncorrected); Me (145.5–147 °C), *i*-Pr (121.5–127 °C), *t*-Bu (220.5–222 °C), *n*-C_5H_{11} (88–104 °C). [e] A second fraction (mp 120–125 °C, uncorrected) was obtained from the concentrated filtrate by treatment of the residual material with Et_2O; combined yield, 90%. [f] Recrystallization of 0.20 g of the crude product from MeCN returned 0.16 g, mp 118–119.5 °C (uncorrected).

question. Although the foregoing results are consistent with the *N*-phenyliodonio amide structure **6** for the products derived from carboxamides and MTIB, they are not sufficient to rule out the isomeric *O*-phenyliodonio imidate structure **7**. In addition to sharing the same



6 **7**

elemental composition, the *O*-iodonio imidates should exhibit C=N stretching absorption in the same infrared region as the C=O band of **6**[11] and might be expected to rearrange to *N*-iodonio amides and hence to isocyanates in solution.[12] This structural ambiguity was resolved by the preparation and FT-IR analysis (Nujol)[13] of the phenyliodonio derivatives of ^{15}N- and ^{18}O-labeled acetamides.[14] If structure **6** (R = Me) is correct, the absorption band at 1681 cm^{-1} in the IR spectrum of the unlabeled iodonio amide should appear at about the same frequency in the spectrum of **6**-^{15}N but at a substantially lower frequency in the spectrum of **6**-^{18}O. If structure **7** is correct, the opposite would be true. The experimental data confirm the *N*-phenyliodonio amide tosylate assignment. Thus, the absorption band in question appears at 1681 cm^{-1} in the spectrum of the ^{15}N-isotopomer and at 1654 cm^{-1} (and a bit broadened) in the spectrum of the ^{18}O-isotopomer.

Acknowledgment. We thank the Dow Chemical Company for financial support.

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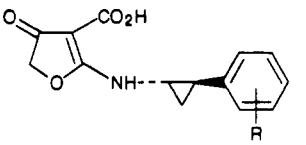
Received September 18, 1986

(11) Colthup, N. B.; Daley, L. H.; Wiberly, S. E. *Introduction to Infrared and Raman Spectroscopy*, 2nd ed.; Academic Press: New York, 1975; Chapter 11, p 325.
(12) By analogy to the Chapman rearrangement; see: Schulenberg, J. W.; Archer, S. In *Organic Reactions*; Wiley: New York, 1965; Vol. 14, Chapter 1.
(13) The FT-IR spectra (Nujol mulls) were recorded on a Beckman FT-2100 infrared spectrophotometer by Mr. Ketan Shah. The IR experiment with labeled compounds was suggested by Dr. G. Edwin Wilson, Jr.
(14) These compounds were prepared from [^{15}N]acetamide (99 atom %, Cambridge Isotope Laboratories) and [^{18}O]acetic acid (88.2 atom %, MSD Isotopes).

A Novel 3(2*H*)-Furanone-2(5*H*)-Furanone Rearrangement

Summary: A novel 3(2*H*)-furanone-2(5*H*)-furanone rearrangement that led to the facile preparation of a new class of γ-lactone amides **6** and **8** is reported herein.

Sir: Recently,[1,2] the synthesis of a number of 2-[*N*-(*trans*-2-phenylcyclopropyl)amino]-4,5-dihydro-4-oxo-3-furancarboxylic acids (**1**) was reported. In the present



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communication we wish to report a further extension of this work, namely, a novel 3(2*H*)-furanone-2(5*H*)-furanone rearrangement which was accomplished by treating 2-[*N*-(*trans*-2-phenylcyclopropyl)amino]-4,5-dihydro-4-oxo-3-furancarboxylic acid (**2**) with 1 equiv of *N*,*N*-bis(2-oxo-3-oxazolidinyl)phosphorodiamidic chloride (BOP-Cl) (**3**)[3] and an appropriately substituted aromatic amine **5** (1 equiv), in the presence of triethylamine.[4] The rearrangement resulted in the facile synthesis of a new class of 2(5*H*)-furanone amides **6** (Scheme I). The mechanism of the rearrangement appears to be complex. It is assumed[3] to involve an activation of the carboxyl group of acid **2** by BOP-Cl via an initial nucleophilic attack on the phosphorus atom by the carboxylate anion to give the intermediate adduct **4**. The latter then rearranges to form, in the presence of aromatic amine **5**, the 2(5*H*)-furanone amide derivative **6**.

In addition to the γ-lactone amides **6**, a number of 4-(*N*-phenylamino)-2,5-dihydro-2-oxo-3-furancarboxamide derivatives **8** were obtained by a similar 3(2*H*)-furanone-2(5*H*)-furanone rearrangement of 2-(*N*-phenylamino)-4,5-dihydro-4-oxo-3-furancarboxylic acids **7** (Scheme II).

(1) Georgiev, V. St.; Mack, R. A.; Kinsolving, C. R. U.S. Patent 4614810, 1986.
(2) Georgiev, V. St.; Mack, R. A.; Kinsolving, C. R. *Heterocycles* **1986**, *24*, 3195.
(3) Diago-Meseguer, J.; Palomo-Coll, A. L.; Fernández-Lizarbe, J. R.; Zugaza-Bilbao, A. *Synthesis* **1980**, 547.
(4) The rearrangement was carried out in methylene dichloride solution at 0–10 °C (stirring for 15–45 min) then at ambient temperature (stirring for 2–2.5 h). Following its completion, the reaction mixture was poured into ice–water, acidified with 2 N hydrochloric acid, and worked up.

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