A New and Facile Synthesis of Ketene Imines and Their 2-Iminoazetidine Dimer from Nitriles via Their Nitrilium Salts

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Received April 10, 1987

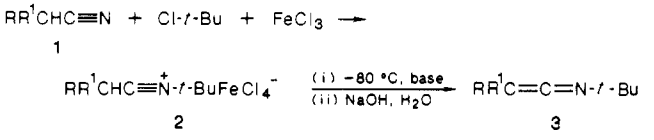
A new one-pot synthesis of *N-tert*-butylketene imines **3** was accomplished on the basis of the reaction of *N-tert*-butylacetonitrilium tetrachloroferrate **2** with an organic base such as triethylamine or N-trisubstituted amidine **4**. The α-hydrogen in **2** is particularly acidic, thus allowing very smooth experimental conditions to remove it with the organic base at −80 °C. The usefulness of this synthesis was demonstrated by the facile preparation of alkyl or functionally substituted ketene imines and especially the as yet undescribed unsubstituted **3f** on a preparative scale. The nitrilium salt **2** was easily formed "in situ" from the corresponding nitrile, *tert*-butyl chloride, and $FeCl_3$, all commercially available starting materials. When the reaction was similarly carried out at −40 °C instead of −80 °C, the major compound isolated was a 2-iminoazetidine **5** a dimer of **3**. Owing to its a priori unexpected structure, an X-ray analysis was carried out to confirm the formula **5a**. The same dimer was isolated by adding 1 mol of HCl and 1 mol of $FeCl_3$ to 2 mol of **3** and it was then left for several hours at room temperature. This easy dimerization is rationalized assuming the formation of a very reactive ketene iminium **8** by the protonation of the ketene imine **3**, which, by a two-step polar cycloaddition with **3**, leads to **5** (Scheme IV). A similar synthesis failed to give *N*-isopropylketene imines, except when two phenyl groups stabilized the ketene imine (e.g., **14**). Only a *s*-triazine **15**, a trimer of the parent ketene imine was isolated from *N*-isopropylisobutyronitrilium salt. Thus, the *N-tert*-butyl substituent appeared to be crucial to stabilize the ketene imines prepared from nitrilium tetrachloroferrates.

In a previous paper we described the addition of enamines to *N-tert*-butylnitrilium salts to give enamino ketones.[1] A ketene imine was also obtained in one case in which 1-piperidinocyclohexene reacted as a base instead of a nucleophile. We have now found that the reaction of a wide variety of *N-tert*-butylacetonitrilium salts **2** with an organic base such as triethylamine or *N-tert*-butyl-*N'*,*N'*-pentamethyleneisobutyramidine (**4**) lead to the corresponding ketene imine **3**.[2]

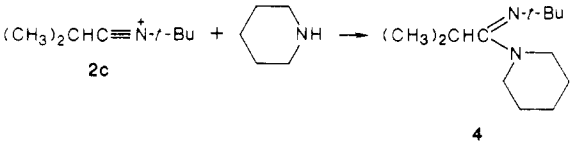
Indeed a series of *N-tert*-butylacetonitrilium tetrachloroferrates **2** was prepared in situ from an acetonitrile derivative **1**, *tert*-butyl chloride and ferric chloride in dichloromethane at −30 °C according to a method previously described.[3-6] The reaction mixture containing **2** was then cooled down to about −80 °C, and the base (triethylamine or **4**) was added at once, keeping the temperature below −40 °C. The mixture was then made basic with aqueous NaOH and extracted and the ketene imine **3** purified (Scheme I).

Tables I and II describe the 11 different ketene imines **3** prepared with their physical and spectral properties. All of them are liquid except **3d**, which has two phenyl groups. It has been reported that alkylketene imines are thermally labile liquids and that the smaller ones resinify easily.[7,8]

Scheme I



Scheme II



We in fact observed this for chloroketene imine (**3e**), which decomposed during the vacuum distillation. To some extent, the low yield for **3f** might also be due to this. Usually ketene imines **3** do not endure distillation at a temperature higher than 80–100 °C. Their purity checked by GC was not usually higher than 95–98%. The contaminants were mainly starting nitrile, and the corresponding *N-tert*-butylamide or triethylamine. With the lower members we therefore used a strong organic base with a high boiling point; this provided easier purification than with triethylamine and thermal protection during distillation. The best results were obtained with the isobutyramidine derivative **4**, easily prepared by the amino-

(1) Baudoux, D.; Fuks, R. *Bull. Soc. Chim. Belg.* **1984**, *93*, 1009.
(2) Fuks, R.; Baudoux, D. Presented at the 4th International Conference on Organic Synthesis, IUPAC, Tokyo, 1982.
(3) Meerwein, H.; Laasch, P.; Mersch, R.; Spille, J. *Chem. Ber.* **1956**, *89*, 209.
(4) Klages, F.; Grill, W. *Ann.* **1955**, *594*, 21.
(5) Fuks, R. *Tetrahedron* **1973**, *29*, 2147.
(6) Van den Bril, M.; Fuks, R. *Bull. Soc. Chim. Belg.* **1980**, *89*, 433.
(7) Krow, G. R. *Angew. Chem.* **1971**, *83*, 455; *Angew. Chem., Int. Ed. Engl.* **1971**, *7*, 435.
(8) Barker, M. W. M.; McHenry, W. E. In *Ketenes* and Allenes; Patai, S., Ed.; Wiley: New York, 1981; Vol. 21, Part 2, p 701.

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Table I. Synthesis and Properties of Ketene Imines 3

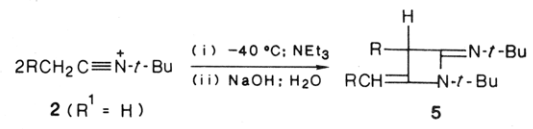
	R	R^1	bp (Torr) or mp (solv), °C	MS M^+, m/e	yield, %	organic base	IR ν(C=C=N), cm^{-1}
3a	C_6H_5	H	57 (0.05)[a]	173	60	$N(Et)_3$	2020
3b	COOEt	H	60 (0.01)	169	65	$N(Et)_3$	2070
3c	CH_3	CH_3	57 (50)[b]	125	55	4	2025
3d	C_6H_5	C_6H_5	50 (EtOH–H_2O)[c]	249	73	$N(Et)_3$	2020
3e	Cl	H		131	20	4	2035
3f	H	H	75 (760)	97	25	4	2030
3g	CH_3	H	50–52 (50)	111	40	4	2020
3h	C_2H_5	H	62–64 (50)	125	80	4	2020
3i	n-C_3H_7	H	73 (50)	139	63	$N(Et)_3$	2020
3j	n-C_6H_{13}	H	60 (0.1)	181	45	$N(Et)_3$	2020
3k	CH_2=CH	H	67 (50)[d]	123	30	4	2010

[a] Cf. ref 11; bp not reported. [b] Bp 34 °C (13 Torr).[12] [c] Cf. ref 13 and 14; mp not reported. [d] Bp 70 °C (35 Torr).[11]

Table II. ^{1}H NMR Spectral Data of Ketene Imines 3

	^{1}H NMR ($CDCl_3$), δ
3a	7.4–7.0 (5 m, Ar *H*), 4.75 (1 s, ArC*H*=), 1.35 (9 s, t-C_4H_9)
3b	4.4–3.9 (3 H, 2 q, CH_3CH_2, +1 s, C*H*=), 1.4 (9 s, t-C_4H_9), 1.25 (3 t, CH_3CH_2)
3c	1.6 (6 s, 2 × CH_3C), 1.2 (9 s, t-C_4H_9)
3d	7.3 (10 m, Ar *H*), 1.4 (9 s, t-C_4H_9)
3e	5.05 (1 s, ClC*H*=), 1.35 (9 s, t-C_4H_9)
3f	3.1 (2 s, CH_2=), 1.25 (9 s, t-C_4H_9)
3g	3.5 (1 q, CH_3CH=), 1.55 (3 d, CH_3CH), 1.2 (9 s, t-C_4H_9)
3h	3.6 (1 t, CH_2CH=), 2.0 (2 m, CH_3CH_2CH=), 1.25 (9 s, t-C_4H_9), 1.0 (3 t, CH_3CH_2)
3j	3.6 (1 t, CH_2CH=), 2.0 (2 m, CH_2CH_2CH=), 1.6–0.9 (14 CH_3CH_2, + 9 s, t-C_4H_9 (1.25))
3j	3.6 (1 t, CH_2CH=), 2.1–0.8 (22, 9 s, t-C_4H_9 (1.20), 13 m, alkyl)
3k	6.4–5.7 (1 m, CH_2=CHCH=), 5.1–4.4 (3 m, CH_2=CHCH=), 1.3 (9 s, t-C_4H_9)

Scheme III



lysis of *N-tert*-butylisobutyronitrilium tetrachloroferrate **2c** with piperidine (Scheme II), according to the general experimental conditions published earlier.[5,6] This amidine was largely recovered at the end by fractional distillation.

This synthetic method allows not only the synthesis of the smallest member ever isolated on a preparative scale but also the preparation of functionalized (e.g., **3b**) or conjugated (e.g., **3k**) ketene imines. The unsubstituted compound **3f** is characterized by a very suffocating and unpleasant smell, very different from the characteristic smell of other ketene imines. Once purified, **3f** remains stable for several weeks in a refrigerator. It is difficult to have it completely free of the starting acetonitrile without a dramatic lost of yield. The IR of **3** displays the typical very strong ν(C=C=N) band[7-10] near 2000 cm^{-1} (see Table I), and for **3f** the IR (in cm^{-1}) is particularly simple: 3020 (w), $\nu(CH_2)$; 2970 (s), $\nu_{as}(CH_3)$; 2920 (sh) and 2860 (m), $\nu_s(CH_3)$; 1470 (sh) and 1450 (m), $\delta_{as}(CH_3)$; 1360 (s), $\delta_s(CH_3)$; 1260 (m), 1235 (s), and 1210 (s), ν (skeletal $C(CH_3)_3$. Its ^{1}H NMR shows the CH_2 peak as a singlet of δ 3.1 and the $C(CH_3)_3$ as a singlet at δ 1.25 (see Table II).

When nitrilium salt **2** was reacted with triethylamine at −40 °C instead of −80 °C, the major compound isolated was a cyclic dimer **5** of the corresponding ketene imine **3**, the latter also being present in minor quantities (Scheme III). Ketene imines are known to dimerize[15,16] and trimerize[17] during thermolysis to yield heterocycles whose structures depend on the ketene imine substitution pattern. It has been reported that *N*-alkyldiarylketene imines lead to an asymetrical dimer similar to **5**,[8,15] whereas other ketene imines substituted in any manner either dimerize or trimerize to other adducts or do not react at all.[8,16] In

Table III. Properties and Spectral Data of the 2-Iminoazetidines 5

	R	bp (Torr) or mp (solv), °C	MS M^+, m/e	IR, cm^{-1} ν(C=C)	IR, cm^{-1} ν(C=N)
5a	C_6H_5	88 ($EtOH/H_2O$)	346	1640	1735
5g	CH_3	50 (0.1)	222	1660	1735
5h	C_2H_5	62 (0.1)	250	1655	1735
5i	C_3H_7	74 (0.1)	278	1660	1735
5j	C_6H_{13}	110 (0.1)	362	1655	1735

Table IV. ^{1}H NMR Spectra of the 2-Iminoazetidines 5

	^{1}H NMR ($CDCl_3$), δ
5a	7.4–6.9 (10 m, Ar *H*), 5.7 (1 s, CHC_6H_5), 4.7 (1 s, CHC_6H_5), 1.65 (9 s, t-C_4H_9), 0.95 (9 s, t-C_4H_9)
5g	4.4 (1 q, =$CHCH_3$), 3.35 (1 q, $CHCH_3$), 1.6–1.0 (24, 6 d, CH_3CH), 1.45 and 1.2 (9 s, t-C_4H_9)
5h	4.5 (1 t, =$CHCH_2$), 3.5 (1 t, $CHCH_2$), 2.1–1.0 (28, 10 m, alkyl), 1.4 and 1.2 (9 s, t-C_4H_9)
5i	4.5 (1 t, =$CHCH_2$), 3.5 (1 t, $CHCH_2$), 2.3–0.7 (32, 14 m, H alkyl), 1.4 and 1.15 (9 s, t-C_4H_9)
5j	4.5 (1 t, C=$CHCH_2$), 3.5 (1 t, $CHCH_2$), 2.1–0.8 (44, 26 m, H alkyl), 1.4 and 1.2 (9s, t-C_4H_9)

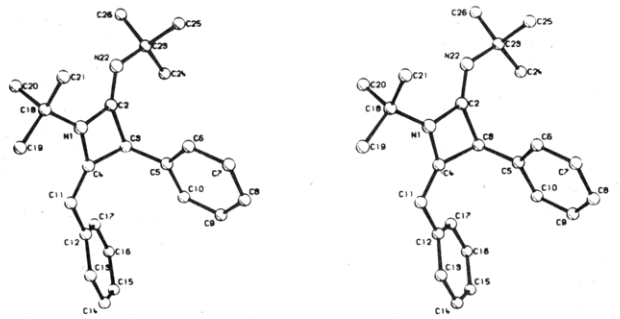


Figure 1. Stereoscopic view of the molecule **5a** and atom numbering (program, PLUTO[26]).

(9) Ripoll, J. L.; Lebrun, H.; Thuillier, A. *Tetrahedron Lett.* **1978**, 463.
(10) Gambargan, N. P. *Russ. Chem. Rev.* **1976**, *45*, 630.
(11) Ito, Y.; Hiras, T.; Okta, N.; Saegusa, T. *Tetrahedron Lett.* **1978**, 1009; *Synth. Commun.* **1980**, *10*, 233.
(12) De Kimpe, N.; Verhe, R.; De Buyck, L.; Chys, J.; Schamp, N. *J. Org. Chem.* **1978**, *43*, 2670. De Kimpe, N.; Verhe, R.; De Buyck, L.; Schamp, N. *Org. Prep. Proced. Int.* **1982**, *14*, 213.
(13) Kyu-Wang Lee; Singer, L. A. *J. Org. Chem.* **1974**, *39*, 3780.
(14) Green, J. A.; Singer, L. A. *Tetrahedron Lett.* **1969**, 5093.
(15) Barker, M. W.; Rosamond, J. D. *J. Heterocycl. Chem.* **1972**, *9*, 1147.
(16) Barker, M. W.; Rosamond, J. D. *J. Heterocycl. Chem.* **1974**, *11*, 241.
(17) Barker, M. W.; Rosamond, J. D. *J. Heterocyl. Chem.* **1973**, *9*, 1419.

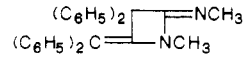
Table V. Selected Interatomic Distances (Å) in 5a

N(1)–C(2)	1.418(2)	C(3)–C(4)	1.532(2)
N(1)–C(4)	1.413(2)	C(3)–C(5)	1.513(2)
N(1)–C(18)	1.476(2)	C(4)–C(11)	1.327(2)
C(2)–C(3)	1.545(2)	C(11)–C(12)	1.473(2)
C(2)–N(22)	1.249(2)	N(22)–C(23)	1.478(2)

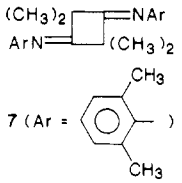
Table VI. Selected Bond Angles (deg) in 5a

C(2)–N(1)–C(4)	93.8(1)	C(3)–C(5)–C(6)	121.1(1)
C(2)–N(1)–C(18)	128.3(1)	C(3)–C(5)–C(10)	120.0(1)
C(4)–N(1)–C(18)	135.0(1)	C(4)–C(11)–C(12)	122.9(2)
N(1)–C(2)–C(3)	89.8(1)	C(11)–C(12)–C(13)	120.2(2)
N(1)–C(2)–N(22)	127.1(1)	C(11)–C(12)–C(17)	122.4(2)
C(3)–C(2)–N(22)	143.1(2)	N(1)–C(18)–C(19)	109.9(1)
C(2)–C(3)–C(4)	84.4(1)	N(1)–C(18)–C(20)	108.4(1)
C(2)–C(3)–C(5)	116.0(1)	N(1)–C(18)–C(21)	108.0(1)
C(4)–C(3)–C(5)	113.3(1)	C(2)–N(22)–C(23)	125.0(1)
N(1)–C(4)–C(3)	90.5(1)	N(22)–C(23)–C(24)	116.1(1)
N(1)–C(4)–C(11)	135.5(2)	N(22)–C(23)–C(25)	106.9(1)
C(3)–C(4)–C(11)	133.9(1)	N(22)–C(23)–C(26)	105.5(1)

particular, iminoazetidine **6** is formed in a 56% yield when *N*-methyldiphenylketene imine is heated for 2–6 weeks at 125 °C, whereas cyclobutane derivative **7** is isolated when *N*-(2,6-dimethylphenyl)dimethylketene imine is heated at 125 °C for 2–6 weeks (20–68% yield).[16]



6



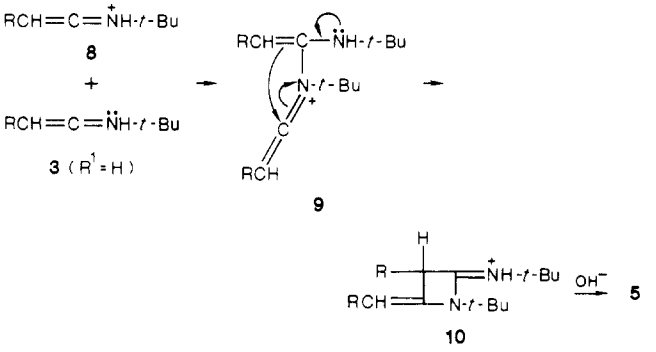
7 (Ar =)

The spectral data of our isolated dimers (Tables III and IV) agree with proposed structure **5**, which is similar to **6** and not to **7**, although most of the dimers derive from aliphatic aldoketene imines (see Tables III and IV). To confirm this, an X-ray diffraction analysis was performed on 4-benzylidene-1-*tert*-butyl-2-(*tert*-butylimino)-3-phenylazetidine (**5a**, R = C_6H_5), the dimer of *N*-*tert*-butylphenylketene imine (**3a**).

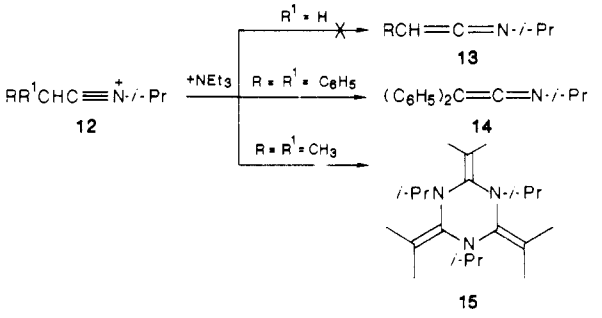
The stereoscopic view of molecule **5a** and the atom numbering are shown in Figure 1. The principal bond lengths and bond angles are listed in Tables V and VI. The azetidine ring appears slightly distorted: the endocyclic torsion angles have the values 9°, −9°, 9°, and −9° around the C(2)–C(3), C(3)–C(4), C(4)–N(1), and N(1)–C(2) bonds, respectively. In methylenebis(3,3-diethylazetidine-2,4-dione)[18] and in 3,3-di-*tert*-butyl-1-(phenylsulfonyl)-4-thioxo-2-azetidinone[19] the four-membered rings are planar, but the other molecular dimensions are very similar to those found in the present study.

With the establishment of formula **5a**, the azetidine structure of the other dimers **5g–j** is supported by the analogy of their IR spectra (see Table III) and ^{1}H NMR spectra (see Table IV). It is obvious, from our very smooth experimental conditions (a few minutes at −40 to 0 °C) that **5** cannot be formed by a simple thermal dimerization of ketene imine as reported earlier (2–6 weeks at 125 °C), and this means that we have to consider the formation of a very reactive species. In order to gain more information, we attempted other experimental conditions. We successfully obtained a 60% yield of **5h** from 2 mol of *N*-*tert*-butylethylketene imine (**3h**) in the presence of 1 mol of $FeCl_3$ and 1 mol of HCl at room temperature over a period of several hours. The use of other stoichiometric ratios of $FeCl_3$ and/or HCl did not lead to **5h**. This easy dimerization is best explained by assuming the formation of ketene iminium tetrachloroferrate **8**, a very reactive intermediate, by the kinetically controlled N-protonation[22] of ketene imine **3** with HCl in the presence of $FeCl_3$. As a strong electrophile,[20,21] **8** then reacts with another molecule **3** in a stepwise polar cycloaddition to form **10** via the open-chain intermediate **9**. According to Baldwin rules,[23] this ring closure **9** → **10** is a 4-endo-dig favored process (see Scheme IV).

Scheme IV



Scheme V



The reaction carried out with *N*-isopropylacetonitrilium tetrachloroferrates **12** and triethylamine does not generally lead to the isolation of *N*-isopropylketene imines (see Scheme V). Indeed, the attempted formation of *N*-isopropylaldoketene imines **13** only gave resinified and dark residues. A 55% yield *N*-isopropyldiphenylketene imine **14** was isolated from diphenylacetonitrile via its *N*-isopropylnitrilium salt **12** (R = R^1 = C_6H_5) and triethylamine. When **12** (R = R^1 = CH_3) was reacted with triethylamine, only trimer **15** was isolated, as a white solid, in a 40% yield. The elementary analysis, the mass spectrum (*m*/*e* 333), and IR spectrum (weak ν(C=C) at 1650 cm^{-1}) were in agreement with the proposed structure **15**. A similar perhydro-*s*-triazine is described in the literature[17] as being formed during the attempted preparation of *N*-cyclohexyldimethylketene imine. Trimer **15** might be formed by a 1,4-polar cycloaddition of an open chain intermediate similar to **9** with another molecule of ketene imine.

In conclusion, the presence of a *N*-*tert*-butyl substituent appears to be crucial to stabilize the variously substituted ketene imines prepared from nitrilium tetrachloroferrates. However, when other stabilization factors are present (e.g.,

(18) Buchanan, G. L.; Sim, G. A. *J. Chem. Soc., Perkin Trans. 1* **1983**, 801.
(19) Schauman, E.; Röhr, A.; Adiwidjaja, G. *Tetrahedron Lett.* **1980**, 4247.
(20) Saimoto, H.; Houge, C.; Hesbain-Frisque, A. M.; Mockel, A.; Ghosez, L. *Tetrahedron Lett.* **1983**, 2251.
(21) Review: Ghosez, L.; O'Donnell, M. J. In *Pericyclic Reactions*; Marchand, A. P., Lehr, R. E., Eds.; Academic: New York, 1977; Vol. 2, p 79.
(22) See a study on the protonation of ketene imines: McCarthy, D. G.; Hegarty, A. E. *J. Chem. Soc., Perkin Trans. 1* **1980**, 579.
(23) Baldwin, J. E. *J. Chem. Soc., Chem. Commun.* **1976**, 734.

two phenyl groups as in **14**) then other N-substituted ketene imines can be isolated. The α-hydrogen in **2** is particularly acidic, thus allowing very smooth experimental conditions to remove it with an organic base. The usefulness of this synthesis is demonstrated by the facile preparation of alkyl or functionally substituted ketene imines and even the unsubstituted one, on a preparative scale. Moreover, this new and facile synthesis takes place from commercially available starting material and in a "one pot" synthesis.

Experimental Section

Melting points were determined on a Kofler hot-stage apparatus. Boiling points were determined by distillation with a Vigreux column but not corrected. IR spectra were measured on a Perkin-Elmer 177 spectrophotometer as KBr pellets or, when liquid, on films over NaCl plates. ^{1}H NMR spectra were recorded in $CDCl_3$ with TMS as an internal reference on a Hitachi-Perkin-Elmer R 24 B instrument. Mass spectra were recorded on a Hitachi-Perkin-Elmer RMU-60 instrument. Anhydrous CH_2Cl_2, the technical solvent, was washed with 5% Na_2CO_3 and water, dried over $CaCl_2$, for 24 h, and distilled, it was kept over molecular sieves (4 Å).

Synthesis of Ketene Imines 3. General Procedure. In a typical experiment, nitrilium salt **2** was prepared[6] from 0.11 mol of ferric chloride (17.8 g) suspended in 100 mL of anhydrous dichloromethane at −30 °C and magnetically stirred. *n*-Butyronitrile **1h** (0.1 mol, 8.5 mL) was added and the ferric chloride dissolved, and the mixture becomes dark red at a temperature of −10 °C (formation of complex RCN–$FeCl_3$). The reaction mixture was then cooled down to −30 °C, and *tert*-butyl chloride (0.1 mol, 11 mL) was added. The color changed rapidly to yellow-brown within 2–3 min, with the formation of a precipitate (the nitrilium salt **2h**). The mixture was then cooled again to −80 °C (with liquid nitrogen as external cooling), and *N*-*tert*-butyl-*N*′,*N*′-pentamethylene isobutyramidine (**4**, 0.15 mol, 31.5 g) was immediately added with an ampule and the mixture kept below −40 °C after the addition process. When the temperature went up again to between −20 and 0 °C, a 7 M aqueous sodium hydroxide solution (75 mL) was added and the mixture extracted three times with dichloromethane. The combined extracts were dried over $MgSO_4$ and concentrated with a rotary evaporator, the water bath being kept at 20 °C. The residue was fractionated with a small Vigreux column, producing *N*-*tert*-butylethylketene imine (**3h**) at 62–64 °C (50 Torr), 10 g (80% yield). All fractions were analyzed by GC, and the first crops contained some unreacted nitrile, while the following fractions were pure **3h**. Amidine **4** was largely recovered by further distilling at 65 °C (0.1 Torr). All the ketene imines **3c**, **e**–**g**,**k** were prepared similarly and purity checked by GC. The ketene imine **3e** is too thermolabile to determine its boiling point, but all spectral data are recorded. Triethylamine was used instead of amidine **4** as the strong organic base for the synthesis of ketene imines **3a**,**b**,**d**,**i**,**j**, which have higher boiling points. The triethylamine was easily distilled off with the rotary evaporator, and the last traces were eliminated by distillation.

N-*tert*-Butylketene imine (**3f**)—the smallest representative—was similarly prepared from acetonitrile, but the crude dried dichloromethane solution of **3f** was fractioned at normal pressure; dichloromethane, bp 42 °C, was, first collected; the temperature then slowly increased, and fraction **3f** was collected at 75 °C, containing 80% of **3f** (by GC). What remained consisted of the initial acetonitrile and dichloromethane. This fraction was further purified by distillation.

Nitrilium salt **2b** from ethyl cyanoacetate must be kept 15 min at −10 °C with vigorous stirring before being reacted with triethylamine at −80 °C.

2-Iminoazetidines 5 from Nitrile 1 via Nitrilium Salt 2. General Procedure. Nitrilium salt **2** was prepared as described above, typically from octanenitrile (12.5 g, 0.1 mol), *tert*-butyl chloride (0.11 mol, 12 mL), and ferric chloride (0.11 mol, 17.8 g). When the reaction mixture was cooled to −40 °C, triethylamine (0.15 mol, 22 mL) in 25 mL of dichloromethane was added at once with an ampule. When the temperature increased to +10 °C, a 7 M aqueous sodium hydroxide solution (75 mL) was added to the mixture, now cooled down to 0 °C. After three extractions with dichloromethane, the combined dried ($MgSO_4$) and concentrated extracts furnished crude oily residue, whose GC mainly displayed two peaks, the major one corresponding to **5j** and the minor one to **3j**, in a ratio of 4:1. The iminoazetidine **5j** was purified by vacuum distillation at 110 °C (0.1 Torr).

2-Iminoazetidine 5h from Ketene Imine 3h. General Procedure. To a suspension of ferric chloride (1.62 g, 0.01 mol) in dichloromethane (25 mL) was added *N*-*tert*-butylethylketene imine (**3h**, 2.5 g, 0.02 mol). To the mixture, cooled to 0 °C, was added HCl (0.365 g, 0.01 mol) in an anhydrous ether solution; a slight exothermal reaction took place. After 6 h at room temperature, 80 mL of 7 M aqueous sodium hydroxide was added and the mixture extracted 3 times with dichloromethane. The combined organic phases were dried ($MgSO_4$), and concentrated. The residue distilled at 62 °C (0.1 Torr) gives a 60% yield of **5h**, 1.5 g, its IR was identical with the one prepared using the preceding method.

***N*-*tert*-Butyl-*N*′,*N*′-pentamethyleneisobutyramidine (4).** The nitrilium salt was prepared as above from isobutyronitrile (9.5 ml, 0.1 mol), $FeCl_3$ (16.1 g, 0.1 mol), 11 mL of *tert*-butyl chloride in 150 mL of anhydrous dichloromethane. The suspension was cooled down to −80 °C, and 8.5 g (0.1 mol) of piperidine in 50 mL of dichloromethane was then added; an exothermal reaction took place, and at the end of the addition, the inside temperature was between −20 and 0 °C. The mixture was then poured onto 75 mL of ice-cooled NaOH (30%) and energetically stirred. It was decanted and extracted three times with $CHCl_3$. The organic phase, dried over $MgSO_4$, was then concentrated. The residue was fractionated and **4** collected at 82 °C, (0.5 Torr) in a 75% yield. On a 1-mol scale, $FeCl_3$ (162.5 g, 1 mol), isobutyronitrile (91 mL), *tert*-butyl chloride (92.5 g), piperidine (104 mL), and 125.5 g of **4** were collected at 75 °C (0.2 Torr) (58% yield). Anal. (perchlorate) found: C, 51.74; H, 8.63; N, 8.63. $C_{14}H_{29}N_2O_4Cl$ requires: C, 51.93; H, 8.71; N, 8.65.

***N*-Isopropyldiphenylketene Imine (14).** Nitrilium salt **12** (R = R^1 = C_6H_5) was prepared from 8.1 g of $FeCl_3$ (0.05 mol) suspended in 25 mL of isopropyl chloride and cooled to −20 °C. To the stirred mixture was added 10.6 g of diphenylacetonitrile (0.055 mol), and the reaction was kept at room temperature for 3 h. The mixture was then poured into a −80 °C cooled solution of 9.9 mL of triethylamine (0.11 mol) in 50 mL of anhydrous CH_2Cl_2. When the temperature had gone up to about 0 °C, an ice-cooled 7 M aqueous NaOH (75 mL) was poured into the reaction mixture with vigorous stirring. Then, 100 mL of water and 100 mL of dichloromethane were added and the two phases of the mixture separated. The aqueous phase was further extracted with three portions of 50 mL of dichloromethane. The organic phases collected were dried over $MgSO_4$ and filtered over Celite. A little hydroquinone was added to the solution, which was then evaporated to dryness with a rotary evaporation. The residue was distilled with a Kugelrohr apparatus at 130–145 °C (0.05 Torr). The oily distillate solidified and was recrystallized from hexane; yield, 6.5 g (55%); mp 47 °C (capillary tube); IR (KBr) ν(C=C=N) 2005 cm^{-1}; ^{1}H NMR (CCl_4) δ 1.3 (6 H, d), 3.85 (1 H, m), 7.2 (10 H, m); mass spectrum, M^+ m/e 235. Anal. found: C, 87.03; H, 7.53; N, 6.05. $C_{17}H_{17}N$ requires: C, 86.76; H, 7.18; N, 5.95.

***s*-Triazine 15 from *N*-Isopropylisobutyronitrilium Tetrachloroferrate 12 (R = R^1 = CH_3).** A three-necked 100-mL flask contained ferric chloride (16.2 g, 0.1 mol), and this was immediately covered with isopropyl chloride (50 mL, 0.55 mol). The mixture was ice cooled, and isobutyronitrile (6.9 g, 0.1 mol) was added dropwise under magnetic stirring. The reaction mixture was then kept 1.5 h at room temperature, while stirring was continued. During that period the color changed from deep red to green-yellow. The excess of isopropyl chloride was evaporated off (rotary evaporator), and the residue was immediately covered with 150 mL of anhydrous dichloromethane. The reaction mixture was then cooled to −80 °C under magnetic stirring, and triethylamine (11.1 g, 0.11 mol) in 50 mL of dichloromethane was immediately added with an ampule. The reaction was strongly exothermal, and at the end of the addition phase the internal temperature was about 0 °C. A 7 M aqueous sodium hydroxide (75 mL) was then added to the mixture and the organic phase extracted three times with dichloromethane. The extracts col-

lected were dried ($MgSO_4$) and concentrated. The solid residue **15** was recrystallized from ether: mp 230 °C dec; yield, 40%; mass spectrum, M^+ m/e 333; IR (KBr) ν(C=C) 1650 cm^{-1} (weak); Anal. found: C, 74.37; H, 12.45; N, 12.45; H_2O, 1.7. $C_{21}H_{39}N_3$ + 1.7% H_2O requires: C, 74.3; H, 12.0; N, 12.4.

X-ray Structure Determination of 5a ($C_{24}H_{30}N_2$). The crystallographic data are as follows: triclinic, $P\bar{1}$, a = 5.893 (1) Å, b = 12.825 (3) Å, c = 14.199 (3) Å, α = 96.15 (2)°, β = 100.28 (2)°, γ = 99.16 (2)°, V = 1032.2 (4) Å^3, D_x = 1.12 g cm^{-3} for Z = 2. A total of 2796 independent reflections were measured (Syntex $P2_1$ diffractometer, graphite monochromatized Cu Kα radiation, $2\theta_{max}$ = 114°) of which 2457 with $I \geq 2.5\sigma(I)$ were considered as having been observed. The structure was solved by direct methods using MULTAN80.[24] The H atoms were located in computed positions. Anisotropic least-squares refinement was carried out with the SHELX76 program.[25] The H atoms were refined with an overall isotropic temperature factor (B = 6.7 Å^2). The final conventional R index was 0.051. The lists of final atomic coordinates, atomic thermal parameters, and molecular dimensions have been deposited as supplementary material.

Registry No. 3a, 50743-11-8; **3b**, 111583-31-4; **3c**, 63742-29-0; **3d**, 26149-14-4; **3e**, 111583-32-5; **3f**, 71804-62-1; **3g**, 111583-33-6; **3h**, 111583-34-7; **3i**, 63742-28-9; **3j**, 111583-35-8; **3k**, 63742-38-1; **4**, 111583-40-5; **5a**, 111583-36-9; **5g**, 111583-37-0; **5h**, 111583-38-1; **5i**, 111583-39-2; **5j**, 111615-34-0; **14**, 4185-21-1; **15**, 111583-41-6; $PhCH_2CN$, 140-29-4; $EtOC(O)CH_2CN$, 105-56-6; $(CH_3)_2CHCN$, 78-82-0; Ph_2CHCN, 86-29-3; $ClCH_2CN$, 107-14-2; CH_3CN, 75-05-8; CH_3CH_2CN, 107-12-0; $CH_3(CH_2)_2CN$, 109-74-0; $CH_3(CH_2)_3CN$, 110-59-8; $CH_3(CH_2)_7CN$, 2243-27-8; CH_2=$CHCH_2CN$, 109-75-1; t-BuCl, 507-20-0; i-PrCl, 75-29-6; isobutyronitrile, 78-82-0; piperidine, 110-89-4.

Supplementary Material Available: Tables of atomic coordinates, thermal parameters, and bond lengths and angles for **5a** (3 pages). Ordering information is given on any current masthead page.

(24) Main, P.; Fiske, S. J.; Hull, S. E.; Lessinger, L.; Germain, G.; Declercq, J. P.; Woolfson, M. M. "MULTAN80: A System of Computer Programs for the Automatic Solution of Crystal Structures from X-ray Diffraction Data"; Universities of York, England, and Louvain-la-Neuve, Belgium, 1980.

(25) Sheldrick, G. M. SHELX76: Program for Crystal Structure Determination; University of Cambridge, England, 1976.

(26) Motherwell, S.; Clegg, W. "PLUTO"; University of Cambridge, England, 1978.

$TiCl_4$-Catalyzed Addition of HN_3 to Aldehydes and Ketones. Thermolysis and Photolysis of α-Azido Ethers[1]

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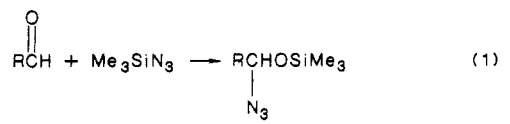
Received May 18, 1987

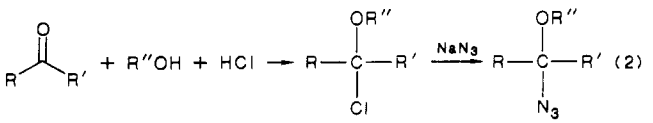
Aldehydes react with hydrazoic acid and alcohols in the presence of catalytic amounts of $TiCl_4$ to produce α-azido ethers. The conversion of simple ketones to methyl α-azido alkyl ethers can be accomplished by means of hydrazoic acid and methyl orthoformate. Both gas-phase thermolysis and photolysis of representative α-azido ethers were studied and shown to produce mainly imino ethers. In the thermolysis, migratory preference decreases in the series H ≫ CH_3 > Ph ≫ OR.

Introduction

Compared to other organic azides, azido ethers represent a little studied class of compounds.[2] The two known methods of synthesis of azido ethers are addition of trimethylsilyl azide to aldehydes (eq 1) and azide substitution on α-halo ethers (eq 2). However, these methods are not



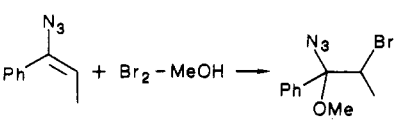
(1)



(2)

free of shortcomings. Trimethylsilyl azide reacts well with aldehydes but does not add to ketones;[3-5] furthermore, one is limited to formation of the trimethylsilyl ether. The reaction of α-halo ethers with azide ions is applicable to both aldehydes and ketones but the method necessitates first the synthesis of α-halo ethers.[6]

Another entry into such compounds, specifically into β-halogenated α-azido ethers, involves addition of bromine in methanol to vinyl azides (eq 3).[7]



(3)

Recently, we found that HN_3 addition proceeds readily to enol ethers (eq 4) as well as to silyl enol ethers, although in the latter case the products were sometimes a mixture of azide and carbonyl compound (eq 5).[8] To other alkenes, HN_3 adds only in the presence of Lewis acids, preferably $TiCl_4$.[8]

Synthesis of Azido Ethers from Aldehydes. Though HN_3 does not react with aldehydes readily, we now report that this can be facilitated by addition of catalytic amounts of $TiCl_4$. For instance, when 0.05 equiv of $TiCl_4$ was added

(1) Synthetic Methods. 25. For paper 24, see: Hassner, A.; Murthy, K. K. S. *Tetrahedron Lett.* **1987**, *28*, 683.

(2) Biffrin, M. F. C.; Miller, J.; Paul, D. B. *The Chemistry of The Azido Group*; Patai, S., Ed.; Wiley: London, 1971; Chapter 2.

(3) Birkofer, L.; Kaiser, W. *Justus Liebigs Ann. Chem.* **1975**, 266.

(4) Birkofer, L.; Muller, F.; Kaiser, W. *Tetrahedron Lett.* **1967**, 2781.

(5) Evans, D.; Truesdale, L. *Tetrahedron Lett.* **1973**, 4929.

(6) Bohme, H.; Morf, D.; Mundlos, E. *Chem. Ber.* **1959**, *89*, 2869.

(7) Hassner, A.; Levy, A. B. *J. Am. Chem. Soc.* **1971**, *93*, 5469.

(8) Hassner, A.; Fibiger, R. F.; Andisik, D. *J. Org. Chem.* **1984**, *49*, 4237.

0022-3263/88/1953-0022$01.50/0