Pergamon

Tetrahedron Vol. 50, No. 22, pp. 6549-6558, 1994
Elsevier Science Ltd
Printed in Great Britain
0040-4020/94 $7.00+0.00

0040-4020(94)E0314-J

The Introduction of Nitrile-Groups into Heterocycles and Conversion of Carboxylic Groups into their Corresponding Nitriles with Chlorosulfonylisocyanate and Triethylamine

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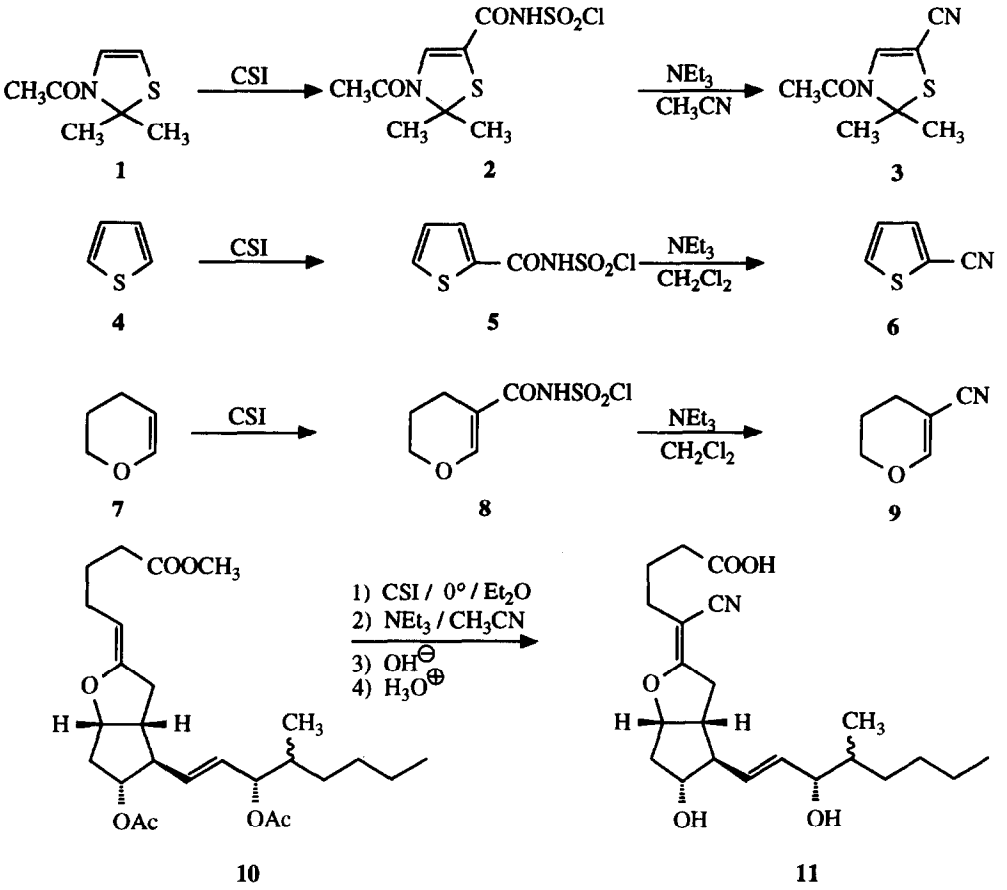
Abstract: Addition of chlorosulfonylisocyanate (CSI) to heterocycles such as thiophene (**4**) or indole (**15**) and unsaturated systems such as dihydropyran (**7**) gives N-chlorosulfonylamides $RCONHSO_2Cl$, which can be converted by equivalent amounts of triethylamine to their corresponding nitriles. Since carboxylic acids react with CSI to N-chlorosulfonylamides, subsequent treatment with triethylamine affords the corresponding nitriles, but no isocyanates as claimed by other authors. The mechanisms of the conversion of the intermediate N-chlorosulfonylamides into the corresponding nitriles are discussed.

In a detailed paper R. Graf described in 1963[1] the various applications of chlorosulfonylisocyanate (CSI) in preparative organic chemistry. Subsequently, new applications of CSI were described and reviewed.[2-5] In this paper our experiments with CSI for the synthesis of nitriles are summarized, which were as yet only communicated in a preliminary publication[6] in 1968. The delay of this detailed publication is partly due to the fact that S. M. Atkins and E. M. Burgess[7,8] reported about simultaneously to our preliminary paper[6] the conversion of N-chlorosulfonylbenzamide with excess triethylamine to phenylisocyanate instead of benzonitrile, and we tried repeatedly over the years to elucidate this discrepancy.

The Introduction of Nitrile Groups into Heterocycles and Unsaturated Systems.

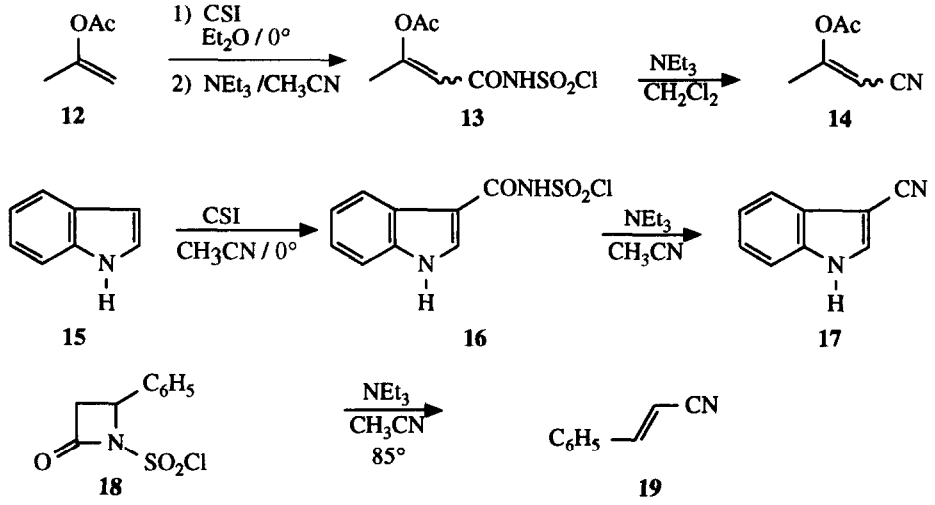
During experiments directed towards the total synthesis of cephalosporin[9] CSI was added to 2,2-dimethyl-3-N-acetyl-Δ^4-thiazoline[10] (**1**) in ether at -15°C to give a high yield of the addition-product **2**, which afforded on solvolysis in acetone the nitrile **3** in low yield. Addition of equivalent amounts of triethylamine to a solution of the CSI-adduct **2** in acetonitrile gave, however, the nitrile **3** in 67% yield.[6,10] Since R. Graf[1] and M. Seefelder[11] and later F. Effenberger and R. Gleiter[12] had described the addition of CSI to a series of heterocycles and unsaturated systems, the subsequent reaction of these CSI-adducts with equivalent amounts of tert. bases such as triethylamine permits the direct introduction of nitrile groups into these heterocycles and unsaturated systems. Thus thiophene **4** reacts with CSI in high yield to **5**[1], which gives with equivalent amounts of triethylamine the thiophen-2-nitrile **6** in 87% yield. Subsequently, the intermediate **5** was converted by S. Gronowitz et al.[13] by solvolysis in N,N-dimethylformamide (DMF) (the Lohaus-method[14]) into **6** in 72% overall yield. Dihydropyran **7** gave via the previously described[12] CSI-adduct **8** in 84% overall yield the new 5,6-dihydropyran-3-carbonitrile **9**. This enolether nitrile **9** turned out to be quite stable due to the

delocalized cation, which forms on addition of protons or Lewis acids. Consequently, we anticipated that the strained and very acid labile cyclic enolether system of the natural prostacyclin and its analogues would be stabilized by the introduction of an electron-withdrawing nitrile-group. Thus the methylester of 11,15-di-O-acetyl-16-methyl prostacyclin **10** was treated with CSI and subsequently by triethylamine to result after removal of the protecting groups in the chemically stable and biologically potent 5-cyano-16-methyl-prostacyclin (nileprost) **11**[15].



In analogy to the enolether system, the enol acetate isopropenyl acetate **12** gave via the CSI adduct **13** the cis/trans 3-acetoxy-crotonnitrile **14** in 31% overall yield, which can certainly be improved. Indole **15** reacted readily with CSI in acetonitrile to the crystalline adduct **16**, which gave with slightly less than equivalent amounts of triethylamine a nearly quantitative yield of the known[16] crystalline 3-cyanoindole **17**. Equivalent or excess triethylamine apparently generates the N-anion of **17**, which will react with the intermediate **16** to give N-substituted sideproducts and thus leads to drastically diminished yields of 3-cyano-indol **17**. The same reaction sequence **15** → **17** was subsequently described[17] with the difference that **16** was converted into **17** by solvolysis in DMF (the Lohaus method[14]). 3-Cyanoindole **17** can also be prepared by reaction of indole **15** with $(C_6H_5)_3P(SCN)_2$[18,19]. The analogous preparation of N-methyl-3-cyanoindole **42** is subsequently de-

scribed in the section on the mechanisms of nitrile formation.



In the hitherto described additions of CSI to **1**, **4**, **7**, **12** and **15** we did not detect any N-chlorosulfonyl-β-lactams, which can often be isolated as labile intermediates during the addition of CSI or other reactive sulfonyl or acylisocyanates to unsaturated systems[2] such as enolethers[12] or enol acetates[20]. We found, however, that the stable crystalline 4-phenyl-azetidin-2-one-1-N-sulfochloride **18**, readily obtained from styrene and CSI,[1] affords with equivalent amounts of triethylamine on boiling in acetonitrile cinnamonitrile **19** in 67.5% yield. Compound **19** is also obtained in 50% yield on aqueous hydrolysis of **18** at 70°C,[1,21] as well as in 73% yield by direct treatment of cinnamic acid with CSI followed by addition of triethylamine or by solvolysis in DMF[22] as subsequently discussed.

The Conversion of Carboxylic Acids into Nitriles.

Since carboxylic acids **20** are converted by CSI acc. to R. Graf[1] with evolution of carbon dioxide into their corresponding N-chlorosulfonylamides **21**, subsequent treatment with slightly less than one equivalent of triethylamine (or other tert. bases) in acetonitrile, CH_2Cl_2, CH_2Cl-CH_2Cl or $CHCl_3$ gave readily the corresponding nitriles **22**. The less nucleophilic, stronger carboxylic acid p-nitrobenzoic acid had to be heated with CSI for 2h at 70°C in 1,2-dichloroethane to afford the corresponding N-chlorosulfonylcarboxamide **21** followed by treatment with triethylamine in 1,2-dichloroethane to give 53.5% of pure p-nitrobenzonitrile. In the case of anisic acid addition of ca. 0.05 equiv. of BF_3•OEt_2 seemed to accellerate the formation of the corresponding intermediate N-chlorosulfonylcarboxamide **21**. Cinnamonitrile **19** was prepared in 73% yield from cinnamic acid as well as aforediscussed from the β-lactam-N-sulfochloride **18**. Due to σ-complex formation of CSI with the basic pyridine-nitrogen, nicotinic acid reacts only with CSI on heating in the presence of equivalent amounts of triethylamine (to generate the nucleophilic nicotinate-anion) to give a 46% yield of 3-cyanopyridine. This yield might be improved on adding solutions of the triethylammonium salt of nicotinic acid as well as CSI simultaneously and slowly to boiling acetonitrile in order to minimize the formation of

nicotinic acid anhydride, resulting from the attack of unchanged triethylammonium nicotinate on the corresponding N-chlorosulfonylamide[23]. **Thus triethylammonium carboxylates can be converted in one step to the corresponding nitriles.**

$$\underset{\mathbf{20}}{RCOOH} \xrightarrow[-CO_2,\ 10-50^\circ]{CSI} \underset{\mathbf{21}}{RCONHSO_2Cl} \xrightarrow[CH_3CN]{NEt_3} \underset{\mathbf{22}}{RC{\equiv}N}$$

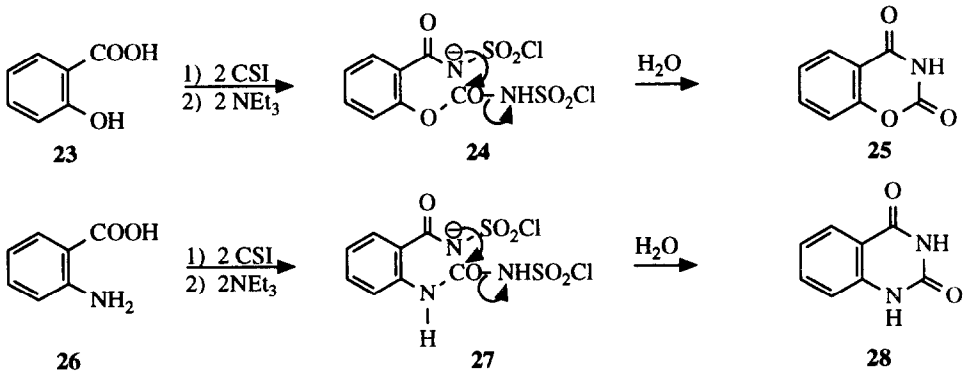
The conversions of the carboxylic acids **20** in Table I via **21** to their corresponding nitriles **22** proceeded readily with triethylamine or diisopropylethylamine (Hünig's base).

Table 1. Conversion of Carboxylic Acids 20 into the Corresponding Nitriles 22

20	Addition of 1 equiv. of CSI	Addition of NEt_3[a] time / temp.	Workup[b]	Product **22** Yield [%]
hydrocinnamic acid	CH_3CN / 1h / 35°C	CH_3CN / 30 min / 0°C 5 d / 23°C	distillation at 99-101°C / 0.1 mm	hydrocinnamonitrile 70
adipic acid	CH_2Cl_2 / 6h / 41°C	CH_2Cl_2 / 20 min / -9°C 1h / 41°C	distillation at 105-110°C / 1 mm	adiponitrile 87
sorbic acid	CH_2Cl_2 / 25 min / 0°C 22h / 22°C	CH_2Cl_2 / 25 min / 0°C 2.5h / 22°C	distillation at 11 mm	cis / trans sorbonitrile 78
β,β-dimethylacrylic acid	$CHCl_3$ / 15 min / 0°C 2 h / 41°C / 16h / 24 °C	$CHCl_3$ / 30 min / 0°C 3h / 25°C	distillation at 141-142°C (Vigreux column)	β,β-dimethylacrylonitrile 83.5
cinnamic acid	CH_3CN / 60 min 22-39°C	CH_3CN / 16h / 22°C	distillation at 81-83°C / 1 mm	cinnamonitrile 73
benzoic acid	$CHCl_3$ / 1.5h / 51°C	$CHCl_3$ / 2h / 0°-24°C	distillation at 64-66°C / 11 mm	benzonitrile 70
anisic acid	CH_3CN / 20 min / 0°C 3h / 10°C + 0.05 mmol $BF_3{\cdot}OEt_2$	CH_3CN / 15 min / 0°C 30 min / 20°C	filtration in CH_2Cl_2 over SiO_2 mp 59-60°C Pentane	anisic acidnitrile 93.5
p-nitrobenzoic acid	CH_2Cl-CH_2Cl 2h / 90°C	CH_2Cl-CH_2Cl 5h / 90°C	crystallization from AcOH-H_2O (1:1) mp 149°C	p-nitrobenzonitrile 70
nicotinic acid	CH_2Cl-CH_2Cl + NEt_3 7h / 90°C to solution of CSI in CH_2Cl-CH_2Cl		workup with 2 N NaOH / 0°C mp 145-146°C	3-cyanopyridine 46

[a] reaction with 1 equiv. NEt_3 [b] Workup with $NaHCO_3$, crystallization or distillation

Salicylic acid **23** and anthranilic acid **26** afforded with 2 equivalents of CSI and subsequent treatment with 2 equivalents of triethylamine via **24** and **27** 1,3-2H-benzoxacin-2,4-dione (**25**) in 70% and 2,4(1H,3H)-quinazolinedione **28** in 62% yield. The former reaction was rediscovered subsequently[4,5]. For a related cyclization of a derivative of aspartic acid compare[24].



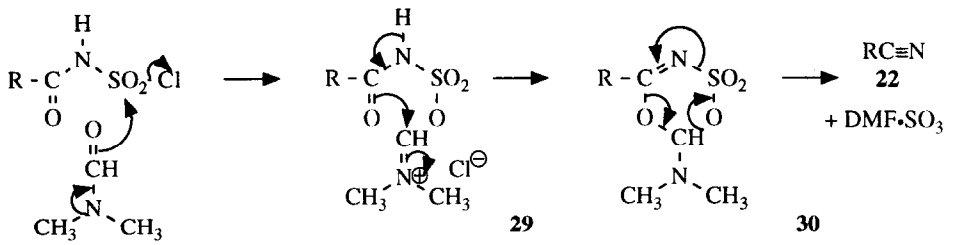
Our CSI/NEt_3-method has found some applications e. g. for the introduction of nitrile groups into protected glycals,[25] olefins[26-29] and N-acetoxy-indole,[29] the conversion of phtalide carboxylic acid[30] and isocamphelinalic acid[31] into their corresponding nitriles. Furthermore, CSI has been added to allyltrimethylsilanes followed by treatment with pyridine to give the corresponding nitriles[32-34].

The aforementioned Lohaus method,[14,22] the solvolysis of N-chlorosulfonyl-amides with N,N-dimethylformamide (DMF), was used for the introduction of nitrile groups into phenolethers[35,36] into thiophens,[13,37] pyrroles,[38-41] indoles,[17] enamides,[42] ketones,[43-45] olefines[46-48] and for the conversion of carboxylic acids into their corresponding nitriles.[49-52] But the Lohaus method[14] as well as our procedure[6] failed to convert 6-tritylaminopennicillanic acid with CSI into the corresponding 3-nitrile resulting instead in the formation of anhydro-6-tritylaminopennicillanic acid.[53]

The application of either method should depend on the lability of the starting material and intermediates as well as on the volatility of the final product.

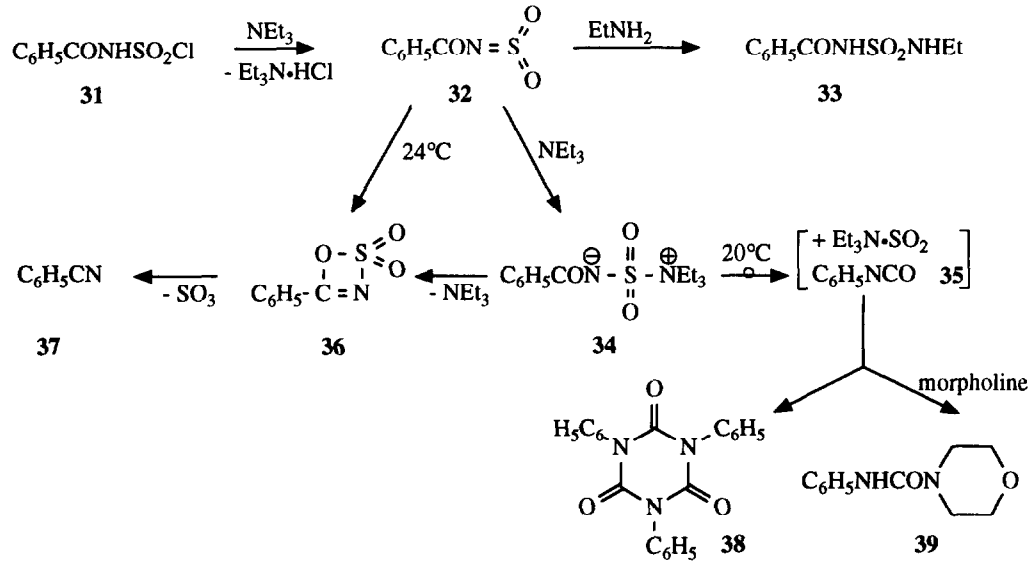
Mechanisms of Nitrile Formation

Whereas the solvolysis of N-chlorosulfonylamides **21** in N,N-dimethylformamide (DMF) acc. to G. Lohaus[14] proceeds probably via the cyclic transition-states **29** and **30** to give the nitriles **22** and DMF•SO_3, the reaction of N-chlorosulfonylamides with triethylamine or other tert. bases is much more complex.



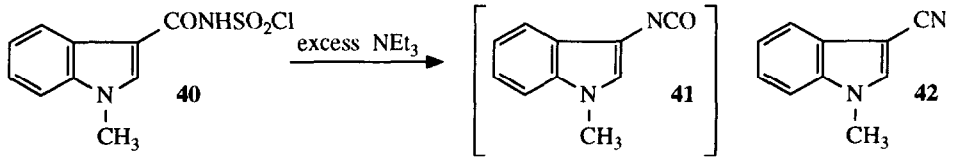
At about the same time as our preliminary publication[6] S. M. Adkins and E. M. Burgess[7,8] described the conversion of N-chlorosulfonylbenzamide **31** with triethylamine at -78°C to the reactive intermediate N-sulfonylbenzamide **32**, which gave **in situ** with ethylamine the N-benzoyl-N'-ethyl-sulfamide **33** in ca.

50% yield and underwent furthermore cycloadditions e. g. with ethyl-vinylether.[8]



Most importantly, according to E. M. Burgess[8] et al., reaction of **31** with a large excess of triethylamine at -78°C in THF afforded the inner salt **34**, which was assumed to rearrange on warming up to room temperature to phenylisocyanate **35** and triethylamine•SO_2. On repeating and varying the experimental conditions of E. M. Burgess et al[8] at various times we were, however, never able to isolate or identify any phenylisocyanate **35** or the corresponding trimer of **35** the N,N,N-triphenylcyanuric acid **38**[54] but identified and isolated instead **only** benzonitrile **37**. Apparently, the authors have accidentally mistaken benzonitrile **37** (-C≡N bond at 2228.5 cm^{-1}) with phenylisocyanate **35** (-N=C=O bond at 2258 + 2275 cm^{-1}). Furthermore, addition of morpholine at +24°C to the supposed intermediate **34** or the isocyanate **35** did not give any of the urea **39**, which was synthesized independently by reacting phenylisocyanate **35** with morpholine[55]. Thus the conversion of the N-sulfonylbenzamide **32** (or the inner salt **34**) to benzonitrile **37** and SO_3 via the potential intermediate **36** is apparently thermodynamically favored over the formation of phenylisocyanate **35** and SO_2.

We furthermore added CSI to N-methylindole to **40**, which cannot form an anion at the indole-nitrogen as the indole-derivatives **16** and **17**, and tried in vain to convert **40** with excess triethylamine into the interesting N-methyl-3-isocyanatoindole **41** but obtained instead only the known N-methyl-3-cyanoindole **42**[18] in 80% yield. Thus N-chlorosulfonylamides give with tert. amines or on solvolysis in DMF[14] **only** the corresponding nitriles!



EXPERIMENTAL

Melting points were determined with a Kofler hot-stage melting point apparatus. Acetonitrile was distilled from P_2O_5 and subsequently from CaH_2, triethylamine from KOH. The preparation of 2,2-dimethyl-3-N-acetyl-5-cyano-Δ^4-thiazoline **3** was described elsewhere[10].

2-Cyanothiophene (6):
11.285 g (50 mmmol) N-chlorosulfonyl-thiophene-2-carboxamide **5**[1] were suspended in 150 ml abs. CH_2Cl_2 and at 0°C a solution of 7.7 ml (55 mmol) triethylamine in 50 ml abs. CH_2Cl_2 added under stirring within 25 min. After 16 h stirring at 22°C, the reaction mixture was filtered over a layer of celite, the celite washed with CH_2Cl_2 and the filtrate extracted with sat. $NaHCO_3$-solution. After drying ($MgSO_4$) and evaporation of the CH_2Cl_2-solution the residue was distilled at 11 mm to give 4.834 g (87%) pure **6**, which was identified by its IR- and ^{1}H-NMR-spectra.

5,6-Dihydropyran-3-carbonitrile (9):
To a stirred solution of 4.42 ml (50 mmol) 5,6-dihydropyran **7** in 78 ml abs. diethylether a solution of 4.35 ml (50 mmol) CSI in 25 ml abs. diethylether was given dropwise within 15 min at 0°C. Subsequently a solution of 7 ml (50 mmol) triethylamine in 100 ml abs. CH_2Cl_2 was added at +3 → +7°C within 35 min, whereupon a colorless substance precipitated. The reaction mixture was warmed up to 21°C within 45 min, treated with ice cold sat. $NaHCO_3$-solution and the combined CH_2Cl_2-extracts dried ($MgSO_4$) and evaporated. The yellowish residue was distilled at 88-89°C/11 min with cooling of the distillate to -70°C to give 4.598g (84,3%) of pure **9**. n_D = 1.4884 IR (film) 2222, 1706 cm^{-1}; ^{1}H-NMR (60 MHz, $CDCl_3$) δ = 1.7-2.7 (m) 7.15 (s,1H); Anal. Calcd. for C_6H_7NO (109.12): C, 66.03; H.6.47; N 12.84; Found: C, 66.28; H 6.52; N, 12.88

3-Acetoxy-crotonnitrile (14):
To a stirred solution of 5 g (50 mmol) freshly distilled isopropenylacetate **12** in 75 ml abs. diethylether a solution of 4.35 ml (50 mmol) CSI was added within 20 min at +0°C and the reaction mixture kept for further 10 min at +3°C. A solution of 7 ml (50 mmol) triethylamine in 100 abs. CH_2Cl_2 was then added dropwise, whereupon the reaction mixture turned dark and a redbrown oil separated. After subsequent warming up to 21°C within 45 min the reaction mixture was worked up with excess ice-cold sat. $NaHCO_3$-solution and the combined CH_2Cl_2-extracts dried ($MgSO_4$) and evaporated. The brown liquid residue gave on distillation at 125°C/11 min 1.948 g (31,1%) of pure **14**, which consisted acc. to its ^{1}H-NMR-spectrum of a E/Z = 1/2 mixture. IR (film) 2237, 1763, 1706 cm^{-1}; ^{1}H-NMR (60 MHz, $CDCl_3$) δ: 2.13 (s,1H) 2.27 (s,3H) 4.68-4.75 (m, 1H area = 1) 5.03-5.18 (m, 1H, area = 2) Anal. calcd for $C_6H_7NO_2$ (125.12): C, 57.59; H, 5.64; N, 11.20; Found: C, 57.70; H, 6.35; N, 10.92

3-Cyanoindole (17):
To a stirred solution of 5.857 g (50 mmol) indole **15** in 150 ml abs. acetonitrile a solution of 4.35 ml (50 mmol) CSI in 50 ml abs. acetonitrile was added within 45 min at 0°C, whereupon yellowish N-chlorosulfonyl-indole-3-carboxamide **16** precipitated. After 1 h stirring at 0°C, a solution of 6.82 ml (49 mmol) triethylamine in 50 ml abs. acetonitrile was given dropwise within 45 min at 0°C → +2°C, whereupon the precipitate of **16** dissolved. After warming up within 1 h to +24°C and keeping the mixture for 2 h at +24°C, the reaction mixture was evaporated and the residue taken up with $CHCl_3$ and ice-cold sat. $NaHCO_3$ solution. The combined $CHCl_3$-phase was dried (Na_2SO_4) and evaporated to give 9.985 g crude product, which was extracted with 3x200 ml boiling ethyl acetate. The extracts were decolorized with a small amount of charcoal and evaporated to give 6.803 g (95.7%) of crystalline **17**, mp. 178-180°C. Recristallization from toluene afforded in several crops analytically pure **17**, mp. 180-181.5°C (lit.[22] 179.5-182.50°C)

Cinnamonitrile (19) from 4-phenyl-azetidinone-2-N-sulfochloride (18):
To a stirred solution of 12.285 g (50 mmol) 4-phenyl-azetidinone-2-N-sulfochloride **18** in 150 ml abs. acetonitrile 7 ml (50 mmol) of triethylamine were added within 45 min at 0°C, whereupon the reaction-mixture turned yellow as a precipitate formed. After 8 h boiling under reflux and exclusion of moisture, a second 7 ml (50 mmol) portion of triethylamine was added at +24°C and the reaction mixture boiled for another 3 h at reflux. After 16 h at +24°C, the mixture was evaporated in vacuo, the residue worked up with $CHCl_3$ and ice cold sat. $NaHCO_3$-solution. The combined $CHCl_3$-extracts gave after drying ($MgSO_4$), evaporation and distillation at 81-83°C/1 mm 4.358 g (67.5%) of pure cinnamonitrile **19**, which was identical with an authentic sample.

Anisic acid nitrile from anisic acid:
To a stirred solution of 4.564 g (30 mmol) of anisic acid and 0,1 ml BF_3•OEt_2 in 75 ml abs. acetonitrile 2.9 ml (33.3 mmol) of CSI were added at 0°C and the reaction mixture kept for 3 h at 20°C. Then a

solution of 4.2 ml (30 mmol) of triethylamine in 30 ml abs. acetonitrile was given within 30 min, and the reaction mixture warmed up to 22°C within 2 h. After evaporation in vacuo, the residue was taken up with CH_2Cl_2 - 100 ml ice cold sat. $NaHCO_3$-solution, the combined CH_2Cl_2-phase dried ($MgSO_4$) and evaporated. The oily residue (5.574 g) was filtered in CH_2Cl_2 over a column of 50 g SiO_2, whereupon the first 200 ml eluate afforded 3.725 g (93.5%) of pure anisic acid nitrile, which crystallized spontaneously (mp 56-58°C). Recrystallization from pentane gave crystalls, mp. 59-60°C identical with an authentic sample.

3-Cyanopyridine from nicotinic acid:

To a stirred and boiling solution of 6.155 g (50 mmol) nicotinic acid and 7ml (50 mmol) triethylamine in 600 ml abs. 1,2-dichloroethane, a solution of 4.35 ml (50 mmol) of CSI in 500 ml abs. 1,2-dichloroethane was given dropwise within 7 h and the reaction mixture heated subsequently for further 52 h at 90-95°C bath temperature. The precipitate formed, which increased on concentrating to 200 ml, was filtered (nicotinic acid anhydride?). The filtrate was extracted with 100 ml ice cold 2 N NaOH and the combined $CHCl_3$-phase washed with H_2O, and dried (Na_2SO_4) to give on evaporation 2.4 g (46%) of solidifying 3-cyanopyridine, mp. 50 -51°C, identical with an authentic sample.

The other examples from Table 1 can be readily reproduced by following the previous two examples and the details given in Table 1.

2H-1,3-Benzoxazine-2,4(3H)-dione (25):

To a stirred solution of 4.113 g (30 mmol) salicylic acid in 50 ml abs. $CHCl_3$ 5,8ml (66mmol) CSI were given at 0°C and the mixture gradually warmed up to 24°C and kept there for 15 min. Subsequently a solution of 4,2 ml (30 mmol) triethylamine in 30 ml abs. $CHCl_3$ was added at 0°C within 30 min and the reaction mixture warmed up to 23°C and kept at 23°C for 6 h, whereupon further 1.4 ml (10 mmol) triethylamine were added and the reaction mixture kept for 72 h at 23°C. The colorless precipitate was filtered and washed with $CHCl_3$ to afford 2.756 g **25**. The filtrate was worked up with 50 ml H_2O and 150 ml sat. $NaHCO_3$, the collected $CHCl_3$ extracts dried ($MgSO_4$) and evaporated to give crude **25**, which afforded on recrystallization from ethanol in two crops 0,672 g additional **25**. Combined yield of **25** = 3.428 g (70.0%), mp. 211-214°C (lit.[56] 227°C), identical with an authentic sample.

2,4(1H,3H)-Quinazolinedione (28):

To a stirred suspension of 4.114 g (30 mmol) anthranilic acid **26** in 50 ml abs. $CHCl_3$ 5.8 ml (66 mmol) CSI were added. After 15 min at 0°C and 16 h at 24°C, a solution of 9.8 ml (70 mmol) triethylamine in 30 ml abs. $CHCl_3$ was given dropwise within 20 min at 0°C, whereupon the colorless precipitate passed into solution. The yellow solution was gradually warmed up and kept for 6 h at 23°C. After evaporation, the yellow, partially crystalline oil was stirred for 16 h at +2°C with 200 ml sat. $NaHCO_3$-solution, filtered to give 1.345 g **28** mp. 322-323°C. The filtrate was stirred for additional 3 days at 24°C and filtered to afford further 1.670 g **28**, mp. 323-328°C. Combined yield = 3.015 g (62%) of **28** identical with an authentical product obtained from the reaction of anthranilic acid with KCNO.[57]

Reaction of N-chlorosulfonylbenzamide (31) with excess triethylamine in THF to benzonitrile (37):

Following the literature procedure[8] a solution of 10g (45.5mmol) N-chlorosulfonylbenzamide **31**[1] in 100ml abs. THF was added dropwise with stirring within 35 min. to a solution of 50ml (358mmol) abs. triethylamine in 200ml abs. THF cooled to -74°C → -78°C, whereupon crystalline triethylamine hydrochloride was precipitated. After further 7 h stirring at -78°C, the reaction mixture was filtered under exclusion of humidity. The precipitated crystalls were washed with additional 50ml of abs. THF and dried to give 5.83g (92.9%) of pure triethylamine hydrochloride. The combined filtrate was gradually warmed up to 24°C.

50ml of the THF-filtrate was admixed at 24°C with excess abs. morpholine, kept for 72h at 24°C and evaporated at 0.1mm. The residue on tlc (SiO_2, EtOAc) did not show any trace of 4-morpholine-4-carboxylic acid phenylamide **39** (R_f = 0.56), which was prepared by reaction of neat phenylisocyanate **35** with neat morpholine and subsequently recrystallized from methanol mp. 157.8°C (lit.[55] 161.5-162°C).

Further 150 ml THF solution were kept for 24 h at 24°C, whereupon the IR-spectrum of an evaporated sample only showed a benzonitrile band at 2228.5cm^{-1} but **no** phenylisocyanate band of 2258 + 2275cm^{-1}! After further 72 hours the IR-spectra did **not** change. Evaporation, extraction with methyl-*tert.*-butylether and finally distillation gave 0.896g (50.9%) of pure benzonitrile **37**. The extraction and distillation residues did not show any trace of the phenylisocyanate trimer the N,N,N-triphenylcyanuric acid **38** prepared by treatment of neat phenylisocyanate **35** with catalytical amounts of tetrabutylammonium fluoride-trihydrate in THF mp. 282-284°C (lit.[54] mp. 282-284°C).

Reaction of N-methylindole with chlorosulfonylisocyanate (CSI) and excess triethylamine to N-methyl-3-cyanoindole (42):

A solution of 2.62g (20mmol) of N-methyl-indole in 50ml abs. THF was cooled to -5°C and 2.83g

(20mmol) CSI added dropwise with stirring within 15 min and stirring continued for further 60 min at -4°C. On cooling to -72°C , part of the CSI adduct **40** precipitated. A solution of 27.9ml (200mmol) abs. triethylamine in 60ml abs. THF was added within 80 min at -70° → -74°C, whereupon a viscous suspension resulted. After warming up overnight to +15°C, tlc (SiO_2, EtOAc) as well as the IR-spectrum of a crude sample indicated the exclusive formation of N-methyl-3-cyano indole **42** (R_f = 0.69) and no trace of the corresponding isocyanate **41**. The suspension was filtered, the precipitated triethylamine hydrochloride washed with additional 75ml abs. THF and the combined filtrate evaporated and distilled in a Kugelrohr apparatus at $bp_{10^{-2}mbar}$ = 145 -150°C to give 2.49 g (79.8%) of crystalline N-methyl-3-cyanoindole **42**. Recrystallization from methyl-t-butylether-cyclohexane gave colorless crystals of pure **42**, mp. 62-63°C (lit.[19] mp. 65°C).

Acknowledgments: We are obliged to Drs. D. Rosenberg and G. Michl for the measurements and interpretation of the NMR- and MS-spectra and especially to Ms. N. Schidniogrotzki for competently and patiently writing and rewriting the English text.

Dedicated to Björn Åkermark on the occasion of his 60th birthday.

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(*Received in Germany* 18 *February* 1994; *accepted* 30 *March* 1994)