Tetrahedron Vol. 39, No. 6, pp 961 to 965, 1983
Printed in Great Britain.

0040-4020/83/060961-05$03.00/0

TRIMETHYLSILYL CYANIDE PROMOTED CYANATION OF TERTIARY ALKYL CHLORIDES AND OTHER S_N1 ACTIVE COMPOUNDS

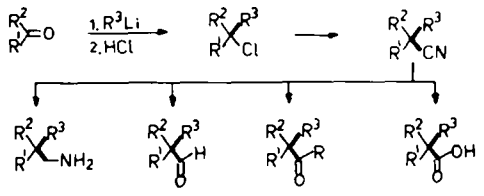
MANFRED T. REETZ*, IOANNIS CHATZIIOSIFIDIS, HERMANN KÜNZER and HANS MÜLLER-STARKE
Fachbereich Chemie der Universität, Hans-Meerwein-Strasse, D 3550 Marburg, West Germany

(*Received in U.S.A.* 14 *April* 1982)

Abstract—Tertiary chlorides are readily cyanated in a one-pot procedure using trimethylsilyl cyanide in the presence of $SnCl_4$. The mechanism of this novel and synthetically useful reaction involves initial isonitrile formation followed by rearrangement to the tertiary nitrile. Other S_N1 active compounds also undergo smooth cyanation.

Cyano groups are synthetically useful because they provide easy access to a host of other functional groups.[1] Besides dehydration of amides or aldoximes,[1] they can be prepared by such procedures as addition of HCN or Et_2AlCN to Michael acceptors,[2] alkylation of deprotonated nitriles[3] or substitution of alkyl halides and tosylates by sodium or potassium cyanide.[1,4] In the latter case, the ambident cyanide ions[5] undergo S_N2 reactions preferentially at carbon, in accord with the Kornblum rule[6] and the HSAB principle.[7] Unfortunately, the yields are acceptable only in case of primary and certain secondary alkyl halides. Tertiary derivatives fail because S_N2 reactions at a tertiary C atom are generally not possible. Switching to S_N1 conditions is of no help, since alkylation then occurs at N with formation of tertiary amines or amides (Ritter reaction).[8]

Our motivation for solving this long-pending problem[9] stemmed from the idea that a new and simple method for geminal dialkylation of ketones[10] would then be possible as shown in Scheme 1. Compounds containing quarternary atoms frequently occur in natural products and in theoretically and spectroscopically interesting compounds.[11] Furthermore, not readily accessible classes of compounds such as neopentyl amines are of industrial use.



Scheme 1. Geminal dialkylation of ketones (bond faced lines symbolize new bonds).

We reasoned that the reaction of tertiary alkyl chlorides **1** with trimethylsilyl cyanide **2** yielding the nitrile **3** and trimethylsilyl chloride **4** should be thermodynamically favorable. The real problem was to find a catalyst which (1) makes the process kinetically feasible, and (2) does not result in the sole formation of isonitriles. It appeared reasonable to test Lewis acids as catalysts, since they are known to promote the formation of tertiary carbocations, which in turn could interact with the nucleophilic but non-basic trimethylsilyl cyanide **2**. A related principle holds in Lewis acid induced α-t-alkylations of silyl enol ethers.[12]

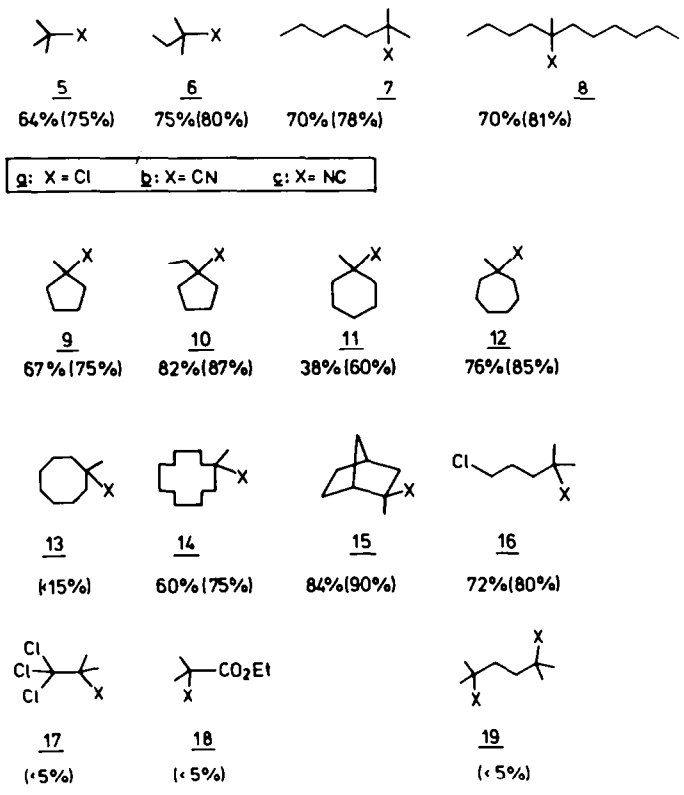
$$\underset{\mathbf{1}}{R_3C\text{–}Cl} + \underset{\mathbf{2}}{(CH_3)_3Si\text{–}CN} \xrightarrow{SnCl_4} \underset{\mathbf{3}}{R_3C\text{–}CN} + \underset{\mathbf{4}}{(CH_3)_3Si\text{–}Cl}$$

As a result of an extensive search, we discovered that catalytic amounts of $SnCl_4$ mediate the desired transformation at room temperature. Herein we wish to describe the scope and mechanism of this reaction.[13]

Trimethylsilyl cyanide **2** has been employed in a number of other synthetically useful processes, including reactions with aldehydes, ketones and acid chlorides.[14] Until recently, the best procedure for its preparation involved the reaction of an excess of sodium or potassium cyanide with trimethylsilyl chloride **4** in N-methylpyrrolidinone at 90–100° (60–70% yields).[15] An improved synthesis makes use of sodium or potassium iodide, which effectively catalyze the reaction at *room temperature* (87–88% yield).[16]

Optimization. Using t-butyl and t-amyl chloride a number of reactions with **2** and various amounts of different Lewis acids in methylene chloride were carried out.[17] Approximate conversion to the desired nitrile was monitored by NMR spectroscopy, but the nature of the side products was not determined in all cases. It turned out that such Lewis acids as $ZnCl_2$, $ZnBr_2$, ZnI_2, $BiCl_3$, $AlCl_3$, $FeCl_3$, $SnCl_2$ and $TiCl_4$ were either unreactive or caused partial decomposition. The formation of tertiary nitriles or isonitriles in amounts exceeding 30% did not occur.[17] In sharp contrast, $SnCl_4$ was found to be effective. The reaction time and quantity of $SnCl_4$ were then optimized. In case of equivalent amounts, maximum conversion was about 50% (22°, 35 hr). The optimum was reached by using approximately 25 mol% of $SnCl_4$, conversion to the nitrile being >80% (22°, 35 hr). Isonitriles were not observed under these conditions.

Synthetic scope. Based on the above optimization the tertiary alkyl chlorides **5a–19a** (20–30 mmol) were reacted with trimethylsilyl cyanide **2** (25–38 mmol) in the presence of $SnCl_4$ (25 mol%) and the amount of tertiary nitrile **5b–19b** determined. The numbers refer to isolated yields, those in brackets to approximate conversion. In order to determine whether the reaction could also be carried out on a larger scale, 0.5 mol methylcyclopentyl chloride **9a** was employed. The yield of isolated product **9b** (64%) turned out to be approximately the same as in the previous case (20 mmol scale, 67%).



The above results provide a picture of the synthetic scope of the reaction. Open chain tertiary alkyl chlorides devoid of additional functional groups are readily cyanated. However, compounds containing electron withdrawing groups near the reaction center (e.g. **17–18**) remain inert, presumably because S_N1 activity is drastically reduced. For successful cyanation, the solvolytic rates of tertiary alkyl halides[18] may be used as a rough guideline.[19] The rate should be at least as high as that of methylcyclohexyl chloride **11a**. The 1,4-dichloride **16a** reacts smoothly with complete chemoselectivity. In case of the dichloride **19a** having *two* tertiary centers, the corresponding dicyano derivative **19b** was not formed to any appreciable extent.[19] It is likely that in this case substitution at one carbon atom actually occurs, but that the carbonium ion generated thereafter undergoes cyclization or other side reactions. In the cyclic series methylcyclooctyl chloride **13a** is clearly an exception. The compound is extremely reactive,[18] and even at lower temperatures (−30°) tar formation results.[19] Since we did not look at the products in detail, undesired *trans*-annular hydride shifts cannot be excluded. Finally, the exceptionally smooth reaction of the norbornyl derivative **15a** to form **15b** with complete stereoselectivity is worthy of mention. The compound has the cyano group in the *exo* position as shown by hydrolysis to the corresponding amide, which is a known compound.[20] Preferred *exo* addition of carbon nucleophiles to the corresponding classical tertiary carbocation is sterically controlled and has been observed in other cases.[21]

Mechanism. Although a number of mechanisms can be envisioned, two particular possibilities appeared most likely (mechanism I and II). In order to explain why detectable amounts of *isonitriles* are *not* formed, trimethylsilyl isocyanide **20** may be invoked. Although the equilibrium **2** ⇌ **20** is known to lie far on the left side,[22] **20** could actually be the reacting species, continuous replenishment being possible. A similar hypothesis has been invoked to explain the formation of acyl cyanides in the reaction of acid chlorides with **2**.[14b] According to mechanism I, $SnCl_4$ induces ionization of **1** to the tertiary carbocation **21**, which is attacked by the carbon atom of **20**. The intermediate nitrilium ion **22** is rapidly desilylated to produce **3** and trimethylsilyl chloride **4**, both of which are observed experimentally.[19]

Mechanism I:

$$(CH_3)_3Si\text{–}CN \leftrightarrows (CH_3)_3Si\text{—}N{=}C$$
2 **20**

$$R_3C\text{—}Cl + SnCl_4 \leftrightarrows R_3C^{\oplus}\ SnCl_5^{\ominus}$$
1 **21**

$$\mathbf{21} + \mathbf{20} \leftrightarrows (CH_3)_3Si\text{—}\overset{\oplus}{N}{\equiv}C\text{–}CR_3SnCl_5^{\ominus}$$
22

$$\mathbf{22} \leftrightarrows R_3C\text{–}CN + \mathbf{4} + SnCl_4$$
3

According to mechanism II, the intermediate tertiary carbocation **21** adds to **2** at N, forming a nitrilium ion **23** which is isomeric to **22**. Desilylation generates the isonitrile **24** which is alkylated by additional **21** to produce a new nitrilium ion **25**. In the final step dealkylation affords the product **3**. Nitrilium ions are known to be involved as intermediates or stable salts in other processes.[23] Fragmentation to nitriles has been observed in a number of cases, whereby the more stable carbocation is split off preferentially.[23]

Mechanism II:

$$2 + 21 \leftrightarrows R_3C\text{–}\overset{\oplus}{N} \equiv C\text{–}Si(CH_3)_3\overset{\ominus}{S}nCl_5$$
23

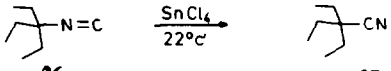
$$23 \leftrightarrows R_3C\text{–}N{=}C + 4 + SnCl_4$$
24

$$24 + 21 \leftrightarrows R_3C\text{–}\overset{\oplus}{N}{\equiv}C\text{–}CR_3\ \overset{\ominus}{S}nCl_5$$
25

$$25 \leftrightarrows R_3C\text{–}CN + 21$$
3

In order to obtain direct experimental evidence for the intermediate formation of isonitriles, the $SnCl_4$ mediated reaction of t-butyl chloride **5a** with **2** in methylene chloride was checked after about one half-life. The NMR spectrum[a] of the mixture showed no evidence for the presence of t-butyl isocyanide **5c**. The same was found for a hydrolyzed sample. This means that either mechanism II does not apply, or that rearrangement is faster than isonitrile formation. Upon carrying out the same experiment in 1,2-dichlorethane, different results were obtained. A hydrolyzed sample contained about 50% t-butyl chloride **5a**, 15% tert-butyl cyanide **5b** *and* 30% t-butylisocyanide **5c** as well as unidentified products (~5%). Longer reaction times caused the gradual disappearance of the isonitrile and the formation of t-butyl cyanide **5b** (~80% conversion).

The above observations suggest that cyanation may occur via initial isocyanide formation.[b] We therefore studied the influence of $SnCl_4$ (20 mol%) on independently synthesized t-butyl isocyanide **5c** in methylene chloride at room temperature. After 16 hr the mixture contained appreciable amounts of rearranged t-butyl cyanide **5b** (~50%). After a total reaction time of about 35 hr **5c** could no longer be detected. The mixture showed the presence of t-butyl cyanide **5b** to the extent of >90%, from which 54% was isolated by distillation.[c] Similarly, isonitriles **9c**, **10c**, **11c** and **26** were rearranged to **9b** (65%), **10b** (74%), **11b** (30%) and **27** (70%) on a preparative scale.



26 **27**

The results show that $SnCl_4$ cleanly catalyzes the isonitrile→nitrile rearrangement[24] under conditions which are similar to those employed in the cyanation of tertiary alkyl chlorides. It is known that Lewis acids such as BF_3 cause dimerization, oligomerization and partial rearrangement of isonitriles.[24] Although our observations speak for mechanism II, the fact that isonitriles are not observed during latter process (in CH_2Cl_2) does not seem to fit into the picture. However, the cyanation conditions are different, since large amounts of tertiary alkyl chlorides are present which may increase the rate of rearrangement. Indeed, the addition of 10 mol% of t-butyl chloride **5a** to a mixture of **5c** and $SnCl_4$ caused rate acceleration by a factor of about four, rearrangement being complete within 9 hr. Tert-butyl cations very likely *catalyze* the rearrangement as follows:

$$(CH_3)_3C\text{–}Cl + SnCl_4 \leftrightarrows (CH_3)_3\overset{\oplus}{C}\ \overset{\ominus}{S}nCl_5$$
5a **28**

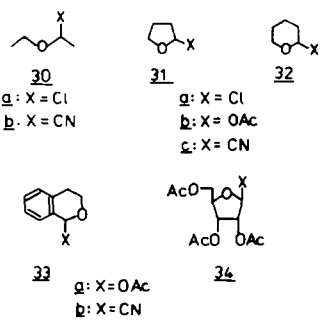
$$(CH_3)_3C\text{–}N{=}C + 28 \rightleftarrows (CH_3)_3C\text{–}\overset{\oplus}{N}{\equiv}C\text{–}C(CH_3)_3\ \overset{\ominus}{S}nCl_5$$
5c **29**

$$29 \leftrightarrows (CH_3)_3C\text{–}CN + 28$$
5b

Obviously, **29** is a special case of the general nitrilium ion **25** in mechanism II. Various attempts to prepare and isolate such nitrilium salts as **23** and **25** failed, because fragmentation is rapid.[19] Indeed, if this were not the case, the cyanation process would not be expected to occur with such high conversion. All of the present results are in line with mechanism II. However, it is not meant to represent a detailed account of the cyanation reaction, since isonitrile formation may be more complex. Although we have not been able to detect such species as Cl_3Sn–CN, they could be transient reactive intermediates.

Other cyanide donors. Besides trimethylsilyl cyanide **2** other metal cyanides such as NaCN, KCN and $Zn(CN)_2$ in combination with various Lewis acids (e.g. $ZnCl_2$, $SnCl_4$, $TiCl_4$) were tested as cyanation reagents for tert-butyl chloride **5a**. Either HCl elimination and/or decomposition of **5a** occured, or the system remained inert.[17] This underlines the central role of silicon in the cyanation reaction as delineated in mechanism II.

Other S_N1 *active compounds.* We have discovered that α-chloro ethers such as **30a–32a** are readily cyanated at room temperature (4 hr) by trimethylsilyl cyanide **2** in the presence of 25 mol% $SnCl_4$ in CH_2Cl_2 (80–90% yields). The same applies to the acetates **31b**, **32b** and **33a**. Successful application in the synthesis of C-nucleosides requires refluxing for about 4 hr. Thus, 2,3,5-tri-O-acetyl-β-D-ribofuranosyl acetate **34a** almost quantitatively yields the nitrile **34b**. Neighboring group participation is likely to be responsible for the observed retention of configuration. These reactions are closely related to the cyanation of ketals[25a] and certain ribofuranosyl acetates[25b] induced by **2** in the presence of BF_3 or $SnCl_2$ as described by Nozaki and Utimoto, as well as aminoalkylations as reported by Anteunis.[25c]



30 a: X = Cl; b: X = CN

31 a: X = Cl; b: X = OAc; c: X = CN

32

33 a: X = OAc; b: X = CN

34

[a] Due to ^{14}N–^{1}H coupling, the tert-butyl group in **5c** appears as a triplet (I. D. Kunitz, P. V. R. Schleyer and A. Allerhand, *J. Chem. Phys.* **35**, 1533 (1961)); Complexation of **5c** with $SnCl_4$ results in an adduct which does not show this effect.[19]

[b] Note added in proof: If has been reported that adamantylchloride reacts with **2** in the presence of $TiCl_4$ to form the isonitrile; T. Sasaki, A. Nakanishi and M. Ohno, *J. Org. Chem.* **46**, 5445 (1981).

[c] No attempt was made to optimize the isolation procedure; **5c** is very volatile.

Cyanation of ether derivatives as described above has some advantages over classical methods using NaCN, $Cu_2(CN)_2$, $Hg(CN)_2$ or AgCN:[26] The yields are comparable or better, and chlorides *as well as* acetates can be cyanated.

EXPERIMENTAL

General information. All mp and bps are uncorrected. IR spectra were recorded with a Perkin-Elmer 577 or 457 instrument, ^{1}H-NMR spectra: Varian EM-360 and Bruker WH-90; ^{13}C-NMR spectra: Varian CFT-20; chemical shift values are expressed in ppm relative to TMS as the internal standard. MS (70 eV) spectra: Varian CA-711. Commercially available anhydrous $SnCl_4$ (Aldrich or Merck) was used without further purification. $SnCl_4$ and $(CH_3)_3SiCN$ were handled under nitrogen using syringes and flasks equipped with serum caps.

General procedure for cyanation of tertiary alkyl chlorides. To a stirred soln of tertiary alkyl chloride (20 mmol) and **2** (2.6 g, 26 mmol) in 60 mL anhyds CH_2Cl_2 was added 0.56 mL (25 mol%) $SnCl_4$ under N_2. After stirring at room temp for 23–38 hr, the dark soln was poured onto ice water and shaken vigorously. The organic phase was separated, the aqueous phase washed twice with CH_2Cl_2 and the combined organic phases washed with a 10% $NaHCO_3$ aq. The organic phase was dried over Na_2SO_4, concentrated and distilled (short path). Larger scale reactions were carried out in the same way using proportionally larger amounts of materials.

2-Methyl-2-propacarbonitrile[27] (**5b**). 40 mmol scale, 36 hr reaction time: 2.12 g (64%) b.p. 105–107°; ^{1}H-NMR (CCl_4): δ 1.3 (*s*, 9); IR (film): 2215 cm^{-1}.

2-Methyl-2-butacarbonitrile (**6b**). 20 mmol scale, 36 hr: 1.37 g (75%) b.p. 32° (18 mm); ^{1}H-NMR (CCl_4): δ 1.1 (t, 3), 1.3 (s, 6), 1.6 (q, 2); IR (film): 2980, 2940, 2890, 2230, 1420, 1380, 1100–1000 cm^{-1}; MS: *m/e* = 97 (M^+, 13%), 82 (M^+-CH_3, 17%) 69 ($C_4H_7H^+$, 100%); (Found: C, 73.98; H, 11.38; N, 14.27. Calc. for $C_6H_{11}N$: C, 74.17; H, 11.41; N, 14.41%).

2-Methyl-2-heptacarbonitrile (**7b**). 20 mmol scale, 30 hr: 1.94 g (70%) b.p. 72° (18 mm); ^{1}H-NMR (CCl_4): δ 0.93 (t, 3), 1.3 (s, 6), 1.4 (m, 8); IR (film): 2940, 2860, 2225, 1450, 1365, 1200 cm^{-1}; MS: *m/e* = 139 (M^+, 1%), 124 (M^+-CH_3, 8%), 111 (M^+-C_2H_4, 29%), 69 ($C_4H_7N^+$, 100%), 43 ($C_3H_7^+$, 89%); (Found: C, 77.52; H, 12.38; N, 9.92. Calc. for $C_9H_{17}N$: C, 77.64; H, 12.30; N, 10.05%).

5-Methyl-5-undecacarbonitrile (**8b**). 20 mmol scale, 30 hr: 2.76 g (70%) b.p. 54° (0.5 mm); ^{1}H-NMR (CCl_4): δ 0.93 (m, 10), 1.3 (s, 3), 1.4 (m, 12); ^{13}C-NMR ($CDCl_3$): δ 124.63, 39.37, 39.14, 36.64, 31.82, 26.89; IR (film): 2960, 2870, 2240, 1460, 1390, 1100 cm^{-1}; MS: *m/e* = 195 (M^+, 1%), 180 (M^+-CH_3, 5%), 125 (M^+-C_5H_{10}, 60%), 69 ($C_4H_6N^+$, 100%); (Found: C, 80.40; H, 13.06. Calc. for $C_{13}H_{25}N$: C, 79.93; H, 12.89%).

1-Methylcyclopentacarbonitrile[28] (**9b**). 20 mmol scale, 32 hr: 1.5 g (67%); 500 mmol scale, 32 hr: 34.9 g (64%) b.p. 52° (18 mm); ^{1}H-NMR (CCl_4): δ 1.4 (s, 3), 1.6–2.3 (m, 8); ^{13}C-NMR ($CDCl_3$): δ 126.08, 39.51, 37.59, 30.83, 24.84; IR (film): 2960, 2870, 2225 cm^{-1}; MS: *m/e* = 109 (M^+, 2%), 94 (M^+-CH_3, 4%), 81 (M^+-C_2H_4, 12%), 68 ($C_4H_6N^+$, 100%).

1-Ethylcyclopentacarbonitrile[29] (**10b**). 30 mmol scale, 32 hr: 3.0 g (82%) b.p. 67° (18 mm); ^{1}H-NMR (CCl_4): δ 1.1 (t, 3), 1.5 (q, 2), 1.5–2.2 (m, 8); ^{13}C-NMR ($CDCl_3$): δ 125.19, 41.87, 37.64, 31.49, 23.27, 17.22; IR (film): 2975, 2880, 2230, 1450, 1380, 1100 cm^{-1}; MS: *m/e* = 123 (M^+, 3%), 108 (M^+-CH_3, 8%), 95 (M^+-C_2H_4, 22%), 82 ($C_6H_8^+$, 100%).

1-Methylcyclohexacarbonitrile[30] (**11b**). 20 mmol scale, 36 hr: 0.9 g (38%) b.p. 62° (18 mm); H-NMR (CCl_4): δ 1.3 (s, 3), 1.4–2.1 (m, 10); ^{13}C-NMR ($CDCl_3$): δ 124.41, 34.30, 27.22, 24.22, 23.06, 22.50; IR (film); 2985, 2940, 2880, 2235, 1460, 1370, 1100 cm^{-1}; MS: *m/e* = 123 (M^+, 6%), 108 (M^+-CH_3, 30%), 95 ($M^+ - C_2H_4$, 18%), 68 ($C_4H_6N^+$, 100%).

1-Methylcycloheptacarbonitrile (**12b**). 20 mmol scale, 32 hr: 2.1 g (76%) b.p. 82° (18 mm); ^{1}H-NMR (CCl_4): δ 1.4 (s, 3), 1.5–2.0 (m, 12); ^{13}C-NMR ($CDCl_3$): δ 125.46, 38.14, 36.90, 30.29, 29.78, 25.70; MS: *m/e* = 137 (M^+, 9%), 122 (M^+-CH_3, 19%), 108 ($C_8H_{12}^+$, 74%), 68 ($C_4H_4N^+$, 90%), 55 ($C_3H_5N^+$, 100%); (Found: C, 78.41; H, 11.19; N, 9.98. Calc. for $C_9H_{15}N$: C, 78.70; H, 11.01; N, 10.20%).

1-Methylcyclododecacarbonitrile (**14b**). 20 mmol scale, 32 hr: 2.4 g (60%) obtained by sublimation; m.p. 65°; ^{1}H-NMR (CCl_4): δ 1.3 (s, 3), 1.3–1.5 (m, 22); IR (KBr): 2990, 2930, 2870, 2230, 1480, 1380, 1389, 1200 cm^{-1}; MS: *m/e* = 207 (M^+, 4%), 192 (M^+-CH_3, 12%), 179 (M^+-C_2H_4, 32%), 68 ($C_4H_6N^+$, 100%) (Found: C, 80.91; H, 11.28; N, 6.52. Calc. for $C_{14}H_{25}N$: C, 81.09; H, 12.14; N, 6.75%).

exo - 2 - *Methyl* - 2 - *norbornacarbonitrile*[31] (**15b**). 30 mmol scale, 24 hr: 3.6 g (84%) b.p. 85° (18 mm); ^{1}H-NMR (CCl_4): δ 1.0–2.0 (m, 10), 1.4 (s, 3); ^{13}C-NMR ($CDCl_3$): δ 126.77, 46.52, 44.46, 39.35, 37.07, 28.24, 22.48, 22.07; IR (film): 2960, 2940, 2860, 2235, 1460, 1380, 1200, 1100 cm^{-1}: MS: *m/e* = 135 (M^+, 16%), 120 (M^+-CH_3, 31%), 108 (M^+-HCN, 14%), 68 ($C_4H_6N^+$, 100%).

5 - *Chloro* - 2 - *methylpentacarbonitrile* (**16b**). 20 mmol scale, 20 hr: 2.1 g (72%) b.p. 90° (18 mm); ^{1}H-NMR (CCl_4): δ 1.3 (s, 6), 1.5–2.2 (m, 4), 3.5 (t, 2); ^{13}C-NMR ($CDCl_3$): δ 124.51, 43.10, 38.25, 33.20, 32.37, 26.51; IR (film): 2990, 2940, 2860, 2225, 1450, 1370, 1220, 1100 cm^{-1}; MS: *m/e* = 146 (M^-, 0.8%), 145 (M^+, 0.6%), 130 (M^+-CH_3, 23%), 69 ($C_7H_7N^+$, 100%) (Found: C, 57.64; H, 8.56; N, 9.95. Calc. for $C_7H_{12}ClN$: C, 57.73; H, 8.30; N, 9.61%).

2-Methyl-exo-2-norbornyl carbonic acid amide. The soln of 1.0 g (7 mmol) of **15b** and 1.6 g (28 mmol) KOH in 20 mL 90% EtOH was refluxed for 9 hr. The mixture was diluted with 30 mL H_2O and poured onto 20 mL ether. The organic phase was separated and the aqueous phase extracted with 100 mL ether. The combined organic phases were concentrated and the residue crystallized from EtOH: 0.82 g (72%) white crystals; m.p. 160° (lit.[20] 159°); ^{13}C-NMR ($CDCl_3$): δ 181.74, 49.16, 45.18, 41.84, 38.80, 37.44, 28.71, 23.86, 23.47.

Preparation of tertiary isonitriles. Using the general method of Ugi,[32] the following isonitriles were synthesized on a 100 mmol scale.

1-Methylcyclopentyl isocyanide (**9c**). 91% yield; b.p. 49° (18 mm); ^{1}H-NMR (CCl_4): δ 1.3 (t, 3), 1.5–2.3 (m, 8); ^{13}C-NMR ($CDCl_3$): δ 153.25 (t, J_{C-N} = 4.3 Hz), 63.36 (t, J_{C-N} = 5.1 Hz), 40.66, 26.22, 22.73; IR (film): 2970, 2880, 2130, 1450 cm^{-1}. MS: *m/e* = 109 (M^+, 5%), 108 (M^+-H, 63%), 94 (M^+-CH_3, 34%), 83 (M^+-CN, 83%), 68 ($C_5H_8^+$, 74%), 41 (CH_3CN^+, 100%); (Found: C, 76.86; H, 10.17; N, 12.36. Calc. for $C_7H_{11}N$: C, 77.01; H, 10.16; N, 12.83%).

1-Ethylcyclopentyl isocyanide (**10c**). 97% yield; b.p. 68° (18 mm); ^{1}H-NMR (CCl_4): δ 0.96 (t, 3), 1.2–2.2 (m, 10); ^{13}C-NMR ($CDCl_3$): δ 153.65 (t, J_{C-N} = 4.7 Hz), 68.58 (t, J_{C-N} = 4.6 Hz), 39.16, 32.30, 22.87, 8.9; IR (film): 2960, 2870, 2125, 1460 cm^{-1}; MS: *m/e* = 123 (M^+, 2%), 122 (M^+ - H, 21%), 108 (M^+-CH_3, 33%), 97 (M^+-CN, 20%), 95 (M^+-C_2H_4, 51%), 67 ($C_5H_7^+$, 100%), 41 (CH_3CN^+, 40%); (Found: C, 77.86; H, 10.65; N, 11.03. Calc. for $C_8H_{13}N$: C, 77.99; H, 10.64; N, 11.37%).

1-Methylcyclohexyl isocyanide (**11c**). 89% yield; b.p. 69° (18 mm); ^{1}H-NMR (CCl_4): δ 1.3 (t, 3), 1.4–2.1 (m, 10); ^{13}C-NMR ($CDCl_3$): δ 153.67 (t, J_{C-N} = 4.7 Hz), 57.05 (t, J_{C-N} = 4.8 Hz), 37.46, 29.09, 23.92, 20.98; IR (film): 2940, 2870, 2130, 1470 cm^{-1}; MS *m/e* = 123 (M^+, 2.8%), 122 (M^+-H, 12%), 108 (M^+-CH_3, 21%), 97 (M^+-CN, 28%), 81 ($C_6H_9^+$, 100%), 41 (CH_3CN^+, 89%); (Found: C, 77.96; H, 10.70; N, 11.10. Calc. for $C_8H_{13}N$: C, 77.99; H, 10.64; N, 11.37%).

1-Methylcyclooctyl isocyanide (**13c**). 92% yield; b.p. 118° (18 mm); ^{1}H-NMR (CCl_4): δ 1.3 (t, 3), 1.4–2.1 (m, 14); ^{13}C-NMR ($CDCl_3$): δ 152.15 (t, J_{C-N} = 4.4 Hz), 60.48 (t, J_{C-N} = 4.6 Hz), 36.65, 29.22, 27.29, 23.79, 21.67; IR (film): 2910, 2850, 2125, 1475, 1445 cm^{-1}; MS: *m/e* = 151 (M^+, 2%), 150 (M^+-H, 17%), 136 (M^+-CH_3, 33%), 123 (M^+-CN, 37%), 81 ($C_6H_9^+$, 85%), 67 ($C_5H_7^+$, 77%), 41 (CH_3CN^+, 100%); (Found: C, 79.88; H, 11.35; N, 9.09. Calc. for $C_{10}H_{17}N$: C, 79.41; H, 11.33; N, 9.26%).

3-Ethylpentyl isocyanide (**26**). 88% yield; b.p. 57° (18 mm); ^{1}H-NMR (CCl_4): δ 0.9 (t, 9), 1.3–1.9 (m, 6); ^{13}C-NMR ($CDCl_3$): δ 153.54 (t, J_{C-N} = 4.7 Hz), 64.21 (t, J_{C-N} = 4.7 Hz), 29.21, 7.19; IR (film); 2970, 2930, 2870, 2130, 1460 cm^{-1}; MS: *m/e* = 110 (M^+-CH_3, 8%), 97 (M^+-CN, 33%), 69 ($C_5H_9^+$, 100%), 41 (CH_3CN^+, 65%); (Found: C, 76.63; H, 12.64; N, 10.38. Calc. for $C_8H_{15}N$: C, 76.74; H, 12.08; N, 11.19%).

General procedure for the $SnCl_4$ mediated rearrangement of tertiary isonitriles. To a soln of 30 mmol isonitrile in 60 mL dry CH_2Cl_2 was slowly added 0.70 mL (20 mol-%) anhyd $SnCl_4$. The mixture slowly turned from yellow to dark red, and was allowed to stir for about 35 hr. It was then poured on 10 mL ice water,

the organic phase separated and washed three times with 10 mL H_2O. The aqueous phases were combined and extracted with 50 mL CH_2Cl_2. The combined organic phases were dried over Na_2SO_4 and Na_2CO_3 and carefully concentrated. Short path vac distillation afforded the rearranged nitriles (**5b**, 54%; **9b**, 65%; **10b**, 74%; **11b**, 30%; **27**, 70%). In the presence of 10 mol% of added t-alkyl chloride, rearrangement was complete within 10–12 hr, yields being about the same.

General procedure for the cyanation of α-chloro and α-acetoxy ethers. To a soln of 10 mmol α-chloro or α-acetoxy ether and 1.2 g (12 mmol) **2** in 30 mL anhyd CH_2Cl_2 was added 0.28 mL (25 mol-%) $SnCl_4$ under N_2. The soln was stirred at room temp for 4 hr and then poured onto 30 mL ice water. The phases were separated and the aqueous phase washed twice with 20 mL CH_2Cl_2. The combined organic phases were washed with 5% $NaHCO_3$ aq and dried over Na_2SO_4. The solvent was carefully evaporated and the residue vac. distilled (bulb-to-bulb with efficient cooling of the collector bulb).

1-Cyanoethyl ethyl ether[33] (**30b**). 0.9 g (88%); ^{1}H-NMR (CCl_4): δ 1.2 (t, 3, J = 6 Hz), 1.4 (d, 3), 3.3–3.8 (m, 2), 4.1 (q, 1).

1-Cyano-tetrahydrofuran[34] (**31c**). From **31a**: 0.81 g (84%); from **31b**: 0.84 g (87%); ^{1}H-NMR (CCl_4): δ 1.6–2.3 (m, 4), 3.8 (t, 2, J = 6 Hz), 4.5 (t, 1.5, J = 5 Hz).

1-Cyano-tetrahydropyran[35] (**32c**). From **32a**: 1.0 g (90%); from **32b**: 1.0 g (90%); ^{1}H-NMR (CCl_4): δ 1.4–1.9 (m, 6), 3.8 (m, 2), 4.7 (m, 1).

1-Cyano-3, 4-dihydro-1H-2-benzopyran[36] (**33b**). 1.2 g (76%); H-NMR ($CDCl_3$): identical with lit. values.[36]

1 - Cyano - 2,3,5 - tri - O - acetyl - β - D ribofuranose (**34b**).[a] 1.4 g (98%) syrup isolated by short path column chromatography (silica gel, CH_2Cl_2); ^{1}H-NMR ($CDCl_3$, Bruker 400 MHz spectrometer): δ 2.09 (s, 3), 2.12 (s, 3), 2.15 (s, 3), 4.10 (dd, 1, $J_{C^4H-C^5H}$ = 3 Hz, $J_{C^5H-C^5H}$ = 12 Hz), 4.41 (dd, 1, $J_{C^4H-C^5H}$ = 3 Hz), 4.35 (m, 1), 4.67 (d, 1, $J_{C^1H-C^2H}$ = 4.5 Hz), 5.38 (t, 1, $J_{C^2H-C^3H}$ = 5 Hz), 5.56 (T, 1, $J_{C^2H-C^3H} = J_{C^3H-C^4H}$ = 5 Hz); (Found: C, 50.55; H, 5.28; N, 4.96. Calc. for $C_{12}H_{15}NO_7$: C, 50.33; H, 5.26; N, 4.91%).

Acknowledgement—This work was supported by the Deutsche Forschungsgemeinschaft and the Fonds der Chemischen Industrie.

REFERENCES

[1]Z. Rappoport (edited), *The Chemistry of the Cyano Group.* Interscience, New York (1970).

[2]W. Nagata and M. Yohsioka, *Org. React.* **25**, 255 (1977).

[3]A. C. Cope, H. L. Holmes and H. O. House, *Ibid.* **9**, 107 (1957).

[4]Phase transfer and crown ether catalyzed reactions of alkyl halides with alkali cyanides: [a]C. R. Stark, *J. Am. Chem. Soc.* **95**, 3613 (1973); [b]J. W. Zubrick, B. I. Dunbar and H. D. Durst, *Tetrahedron Letters* 71 (1975) and lit. cited.

[5]R. Gompper, *Angew. Chem.* Int. Ed. Engl. **3**, 560 (1964).

[6]N. Kornblum, R. A. Smiley, R. K. Blackwood and D. C. Iffland, *J. Am. Chem. Soc.* **77**, 6269 (1955).

[7]T. L. Ho, *Hard and Soft Acids and Bases Principle in Organic Chemistry.* Academic Press, New York (1977).

[8]L. I. Krimen and D. J. Cota, *Org. React.* **17**, 213 (1969).

[9]Recently, certain tertiary alcohols have been converted into nitriles, but the generality of the process is unknown; R. Davis and K. G. Untch, *J. Org. Chem.* **46**, 2985 (1981).

[10a]B. M. Trost, *Acc. Chem. Res.* 7, 85 (1974); [b]M. T. Reetz, W. F. Maier, I. Chatziiosifidis, A. Giannis, H. Heimbach and U. Löwe, *Chem. Ber.* **113**, 3741 (1980).

[11a]S. F. Martin, *Tetrahedron* **36**, 419 (1980); [b]T. T. Tidwell, *ibid.* **34**, 1855 (1978); [c]C. Rüchardt and H. D. Beckhaus, *Angew. Chem. Int. Ed. Engl.* **19**, 429 (1980).

[12a]T. H. Chan, I. Paterson and J. Pinsonnault, *Tetrahedron Letters* 4183 (1977); [b]M. T. Reetz and W. F. Maier, *Angew. Chem.* Int. Ed. Engl. **17**, 48 (1978); [c]review: M. T. Reetz, *Ibid.* Int. Ed. Engl. **21**, 96 (1982).

[13]Preliminary account: M. T. Reetz and I. Chatziiosifidis, *Ibid.* Int. Ed. Engl. **20**, 1017 (1981).

[14a]Review: W. C. Groutas and D. Felker, *Synthesis* 861 (1980); [b]K. Hermann and G. Simchen, *Ibid* 204 (1979).

[15a]S. Hünig and G. Wehner, *ibid.* 522 (1979); [b]J. K. Rasmussen and S. M. Heilman, *Ibid.* 523 (1979).

[16]M. T. Reetz and I. Chatziiosifidis, *Ibid.* 330 (1982).

[17]I. Chatziiosifidis, Dissertation, Univ. Marburg (1981).

[18]H. C. Brown and M. Borkowski, *J. Am. Chem. Soc.* **74**, 1894 (1952).

[19]H. Künzer, Diplomarbeit, Univ. Marburg (1982).

[20]W. R. Boehme, E. Schipper, W. G. Scharpe and J. Nichols, *J. Am. Chem. Soc.* **80**, 5488 (1958).

[21]M. T. Reetz, M. Sauerwald and P. Walz, *Tetrahedron Letters* 1101, (1981).

[22]M. R. Booth and S. G. Frankiss, *J. Chem. Soc. Chem. Comm.* 1347, (1968) and lit cited.

[23a]H. Meerwein, P. Saasch, R. Mersch and J. Spille, *Chem. Ber.* **89**, 209 (1956); [b]C. A. Grob, H. P. Fisher, Z. Randenbusch and J. Zerengi, *Helv. Chim. Acta* **47**, 1003 (1964); [c]I. Ugi, W. Betz and K. Offermann, *Chem. Ber.* **97**, 3008 (1964); [d]W. R. Vaughan and P. D. Carlson, *J. Am. Chem. Soc.* **84**, 769 (1962).

[24a]Thermal rearrangement of tertiary isonitriles: H. Langhals, G. Range, E. Wistube and C. Rüchardt, *Chem. Ber.* **114**, 3813 (1981); [b]Lewis acid induced rearrangement, dimerization and oligomerization of isonitriles: T. Saegusa, N. Takaishi and Y. Ito, *J. Org. Chem.* **34**, 4040 (1969); H. J. Kabbe, *Chem. Ber.* **102**, 1447 (1969); W. Drenth and R. J. M. Nolte, *Acc. Chem. Res.* **12**, 30 (1979).

[25a]K. Utimoto, Y. Wakabayashi, Y. Shishiyama, M. Inoue and H. Nozaki, *Tetrahedron Letters* 4279 (1981); [b]K. Utimoto and T. Horiie, *Ibid.* 237 (1982); [c]V. Asher, C. Becu, M. J. O. Anteunis and R. Callens, *ibid.* 141 (1981).

[26]J. Mathieu and J. Weill-Raynal, *Introduction of One Functional Carbon Atom.* Vol. I, p. 44. Georg Thieme Verlag, Stuttgart (1973).

[27a]N. G. Gaylord and L. D. Gaul, *J. Am. Chem. Soc.* **77**, 3132 (1955); [b]G. Höfle, *Z. Naturforsch.* **28b**, 831 (1973).

[28]E. Campaigne and R. A. Forsch, *J. Org. Chem.* **43**, 1044 (1978).

[29]M. Lazcheveque, P. Mulot and T. Cuvigny, *J. Organomet. Chem.* **57**, C 33 (1973).

[30]R. H. Hasek, E. U. Elam and J. Martin, *J. Org. Chem.* **26**, 1822 (1961).

[31]N. C. Deno and H. Chafetz, *Ibid.* **25**, 449 (1960).

[32]I. Ugi and R. Meyr, *Chem. Ber.* **93**, 239 (1960).

[33]W. Reppe, *Liebigs Ann.* **601**, 81, 109 (1956).

[34]N. Williams, *Ber. Ditsch. Chem. Ges.* **60**, 2509 (1927).

[35]B. A. Nelson, E. J. Hodges and J. I. Simon, *J. Org. Chem.* **21**, 798 (1956).

[36]A. T. Neyyarappally, J. S. Bindra, N. Anand and R. C. Srimal, *Ind. J. Chem.* **9**, 89 (1971).

[a]This compound has been prepared by Utimoto,[25b] but analytical and spectroscopic data is lacking.