# The Synthetic Potential of the Isocyanide-Cyanide Rearrangement

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Excellent chemical and optical yields (>96% retention) of cyanides are achieved by vapor phase thermolysis or short contact flow thermolysis of isocyanides. *trans*-2-Butenyl isocyanide rearranges without concomitant allylic isomerization to *trans*-2-butenyl cyanide. Optically active 1-(formyloxymethyl)-2-phenylethyl cyanide is obtained from optically active L-phenylalanine as a new type of chiral pool synthon.

# Introduction

$$\begin{array}{ccc} R - NC \rightarrow & R - CN \\ 1 & 2 \end{array} \tag{1}$$

The isocyanide-cyanide rearrangement (1) is known to be a noncatalytic high yielding unimolecular thermal gas phase reaction<sup>1)</sup>. The isomerizations of methyl- and ethyl isocyanides, therefore, have proved to be excellent model reactions for testing unimolecular kinetic theories<sup>1,2)</sup>. In recent work<sup>3,4)</sup>, it was shown that this reaction can be performed also in hydrocarbon solution when an inhibitor is added or when oxygen is meticulously excluded to suppress an accompanying isomerization via the radical chain composed of steps (2) and (3)<sup>3)</sup>.

$$\mathbf{R}^{\bullet} + \mathbf{C}\mathbf{N} - \mathbf{R} \rightarrow \mathbf{R} - \mathbf{C} = \mathbf{N} - \mathbf{R}$$
(2)

$$\mathbf{R} - \dot{\mathbf{C}} = \mathbf{N} - \mathbf{R} \quad \rightarrow \quad \mathbf{R} - \mathbf{CN} + \mathbf{R}^* \tag{3}$$

Under these conditions, high yields of cyanides and clean first order kinetics for reaction (1) were observed for a large variety of isocyanides<sup>3,4)</sup>. In these investigations, the rates and activation parameters of reaction (1)<sup>4)</sup> as well as the heats of isomerization<sup>5)</sup> proved to be quite independent of the group R for primary, secondary, tertiary alkyl, benzyl as well as polycyclic bridgehead groups and only slightly different for aryl groups. The half-time of the isomerization is 1 h between 194 and 246 °C and  $\Delta G^{\pm}$  (250 °C)  $\approx$  38 kcal · mol<sup>-1 4)</sup>,  $\Delta S^{\pm} \approx 0$  e. U.<sup>4)</sup>, and  $\Delta H_{isom} \approx -20$  kcal · mol<sup>-1 5)</sup>.

Earlier attempts to use reaction (1) for synthesis were frustrated not only by the high temperature required but also by the lack of stereospecificity. When secondary optically active isocyanides like 1-methylpropyl isocyanide or 1-phenylethyl isocyanide were isomerized, the acidities of the  $\alpha$ protons in 1 or 2 were assumed responsible for the observed partial racemization<sup>6,7</sup>. However, even the isomerization of optically active tertiary isocyanides was accompanied by partial racemization<sup>8</sup>. The free radical chain (2) and (3) rec-

### Das synthetische Potential der Isocyanid-Cyanid-Umlagerung

Isocyanide werden durch Gasphasen-Blitzthermolyse oder Kurzzeitthermolyse von Lösungen in ausgezeichneten chemischen und optischen Ausbeuten (>96% Retention) in die entsprechenden Cyanide übergeführt. *trans*-2-Butenylisocyanid isomerisiert zu *trans*-2-Butenylcyanid ohne begleitende Allylverschiebung. Optisch aktives 1-(Formyloxymethyl)-2-phenylethylcyanid wurde aus optisch aktivem L-Phenylalanin als neuer Typ von Synthon aus dem Chiral Pool dargestellt.

ognized later<sup>3)</sup> is apparently responsible for this racemization.

A more detailed understanding of the isocyanide-cyanide rearrangement acquired by its kinetic<sup>3,4</sup> and thermochemical<sup>5</sup> investigation pointed the way to its use in synthesis.

Under proper conditions, it was hoped that the free radical chain reaction and the  $\alpha$ -proton exchange by base could be suppressed. Vacuum flash thermolysis (VFT)<sup>9)</sup> and short contact flow thermolysis (SCFT)<sup>9)</sup> should be suited for this purpose because radical chains are restricted in the gas phase and no basic agents are present if the experiments are performed in quartz equipment.

# **Results and Discussion**

Both methods were applied with excellent yields under standard conditions at 520-550 °C/ $10^{-2}$  Torr and 350 °C, respectively, quite independent of the isonitrile starting material. Results are recorded in Table 1.

For primary, secondary and even cyclopropyl (cf. 10) or sterically strained (6 and 9) or bridgehead isocyanides, no side reactions could be detected. Only with some tertiary isocyanides (see 18) was the elimination of HCN detected as a side reaction. In most instances, this undesired pathway could be avoided. Even an  $\alpha$ -amino cyanide was converted to a malodinitrile via isocyanide 17.

For *trans*-2-phenylcyclopropyl isocyanide (27) and 1-homocubyl isocyanide (28) ring-opened product mixtures were found under the above reaction conditions. A very complex product mixture resulted also with 1,3,4,6-tetra-O-acetyl-2deoxy-2-isocyano-D-glucose.



The stereospecificity in vacuum flash thermolysis experiments was higher than for short contact flow thermolysis as

Table 1. Synthetic use of the isocyanide-cyanide rearrangement by vacuum flash thermolysis (VFT)<sup>9)</sup> and short contact flow thermolysis (SCFT)<sup>9)</sup>

| $\frac{R - NC}{R =}$   |    | Method <sup>a)</sup> | % R-CN <sup>b)</sup> |
|--|----|----------------------|----------------------|
| 1-C <sub>8</sub> H <sub>17</sub> -                               | 3  | VFT                  | 98                   |
|  | 3  | SCFT                 | 98                   |
| C <sub>4</sub> H <sub>4</sub> CH <sub>2</sub> -                  | 4  | VFT                  | 99                   |
| p-CH1OC4H4CH2-   | 5  | VFT                  | 98                   |
| $C_{1}H_{1}C_{1}C_{1}H_{1}C_{1}H_{2}-$                           | 6  | VFT                  | 96                   |
| CH <sub>1</sub> O <sub>2</sub> CCH <sub>2</sub> -                | 7  | VFT                  | 97                   |
| $C_{\rm cH_{\rm c}CH(CH_{\rm s})} -$                             | 8  | VFT                  | 95                   |
| 000000000000000000000000000000000000000                          | Ř  | SCET                 | 94                   |
| [(CH <sub>2</sub> ) <sub>2</sub> CH <sub>2</sub> CH <sub>2</sub> | ğ  | VFT                  | 99                   |
| Cyclopropyl-   | 10 | VFT                  | 92                   |
| 1-Adamantyl-   | 11 | VFT                  | 98                   |
| 3-Homoadamantyl-   | 12 | VFT                  | 100                  |
| Bicyclo[2,2,2]oct-1-y]-  | 13 | VFT                  | 97                   |
| $C_{H_{i}}(CH_{i})C =$   | 14 | VFT                  | 92°)                 |
| endo-2MNB <sup>d</sup>   | 15 | VFT                  | 97°)                 |
| exo-2MNB <sup>d</sup>  | 16 | VFT                  | 950                  |
|  | 16 | SCET                 | 858)                 |
| NC(C.H.).C-  | 17 | VFT                  | 80-88                |
| C.H.(CH.).C-   | 18 | VFT                  | 77 <sup>h)</sup>     |
| 9-Triptycenyl-   | 19 | SCFT                 | 96                   |
| Triphenylmethyl-   | 20 | SCET                 | <b>6</b> 0           |
| PCH.C.H.   | 21 | VFT                  | 99                   |
| 246 (CH.) C.H.   | 22 | VFT                  | 00                   |
| $a t C_1 H_0 C_2 H_1 - $   | 23 | VFT                  | 98                   |
| trans-CH - CH = CH - CH - CH                                     | 24 | vFT                  | 98                   |
| $C_{H}CH_{J}CH_{J}CO_{J}C_{H}CH_{J}C_{-}$                        | 25 | VFT                  | 86 <sup>i)</sup>     |
| C,H,CH,(CH,OCHO)CH –   | 26 | VFT                  | 75 <sup>j)</sup>     |

<sup>a)</sup> VFT = Vacuum Flash Thermolysis at 520-550 °C,  $10^{-2}$  Torr; for the apparatus used see Fig. 2.6. in ref.<sup>9)</sup> SCFT = Short Contact Flow Thermolysis at 350 °C; for the apparatus see Fig. 2.2 in ref.<sup>9)</sup>. – <sup>b)</sup> The reactions were performed on a 0.1-4.0-g scale and the products identified by GLC, IR and <sup>1</sup>H NMR. – <sup>c)</sup> In addition, 8% 2-methylheptane, 2-methyl-1-heptene and 2-methyl-2-heptene by GLC. – <sup>d)</sup> exo-2MNB = exo-2-methylbicyclo[2.2.1]hept-2-yl isocyanide. endo-2MNB = endo-2-methylbicyclo[2.2.1]hept-2-yl isocyanide. – <sup>e)</sup> Containing 0.3% exo-2-methylbicyclo[2.2.1]hept-2-yl cyanide. – <sup>f)</sup> Containing 0.6% endo-2-methylbicyclo [2.2.1]hept-2-yl cyanide. – <sup>f)</sup> Containing 0.6% endo-2-methylbicyclo [2.2.1]hept-2-yl cyanide. – <sup>f)</sup> In addition 20%a-methylbicyclo[2.2.1]heptane and -heptene. – <sup>h)</sup> In addition 20%a-methylbicyclo[2.2.1]heptane and -heptene. – <sup>h)</sup> In addition 20%a-methylstyrene. – <sup>1)</sup> In addition 9% 2-cyano-1-phenylpropane. – <sup>1)</sup> In addition 15% 2-cyano-1-phenyl-1-propene.

represented in the case of 16 in Table 1. Consequently, stereochemical experiments were performed by vacuum flash thermolysis.

trans-2-butenyl isocyanide (24) was isomerized by VFT in 98% yield to trans-2-butenyl cyanide without detectable allylic rearrangement

$$trans-CH_3-CH = CH - CH_2NC \rightarrow trans-CH_3 - CH = CH - CH_2CN$$

This reaction, in combination with the Overman reaction<sup>10</sup>, can be used as a one-C elongation method for allylic alcohols.

Optically active  $\alpha$ -phenylethyl cyanide was obtained from the isocyanide **8** with 95% chemical yield and 96% o.y. Ethyl S-(-)-2-benzyl-2-cyanopropionate could be isolated from thermolysis of **25** in 86% chemical yield and 96% o.y.; as a side product, 9% of 2-cyano-1-phenylpropane, the product of ester pyrolysis and decarboxylation, was chromatographically separated. Attempts to prepare the optically active isocyanide of the methyl ester of L-phenylalanine were unsuccessful because of extensive racemization<sup>11</sup>. Therefore, optically active L-2isocyano-3-phenylpropyl formate (26), obtained in four steps from L-phenylalanine, was isomerized in 75% yield and 98% optical yield to the cyanide. From ester pyrolysis, 15% of 2-cyano-1-phenyl-1-propene was formed as a side product.

By this method, a new route is provided for the synthesis of interesting optically active synthons, e.g.  $\beta$ -hydroxy cyanides,  $\gamma$ -amino alcohols, and others from secondary and tertiary amino acids. This aspect is currently under active investigation.

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# Experimental

The instrumentation for the spectroscopic and chromatographic work has been already listed <sup>12</sup>. Optical rotation: Polarimeter 141 (Perkin Elmer), 1-cm cuvettes.

The isocyanides  $3^{13}$ ,  $4^{14}$ , 5,  $6^{15}$ ,  $8^{7}$ ,  $9^4$ ,  $10^{16}$ ,  $11^{17}$ ,  $12-14^4$ , 15, 16<sup>18</sup>, 18<sup>15</sup>, 19<sup>1</sup>, 20<sup>19</sup>, 21<sup>20</sup>, 22<sup>5</sup>, 23<sup>4</sup>, 24<sup>21</sup>, 25<sup>8</sup>, 27<sup>21</sup>, 1,3,4,6-tetra-O-acetyl-2-deoxy-2-isocyano-D-glucose<sup>22</sup> were prepared from the corresponding formamides with POCl<sub>3</sub>/pyridine<sup>23</sup> or POCl<sub>3</sub>/ diisopropylamine<sup>24</sup>. 7 was commercially available (Janssen) and purified by distillation.

Most of the cyanides obtained from the rearrangements are known compounds and had the expected spectroscopic properties.

1-Ethyl-1-isocyanopropyl Cyanide (17): 15.0 g (0.13 mol) of 1-amino-1-ethylpropyl cyanide<sup>25)</sup> was transformed with 13.3 g of 98% formic acid and 29.8 g of acetic anhydride<sup>7)</sup> into 12.4 g (68%) of 1-ethyl-1-(formylamino)propyl cyanide. B.p. 132-135 °C/ 0.6 Torr. – IR (film): 3320 cm<sup>-1</sup> (NH), 2240 (CN), 1740 (CO).

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C<sub>7</sub>H<sub>12</sub>N<sub>2</sub>O (140.2) Calcd. C 59.98 H 8.63 N 19.98
Found C 59.63 H 8.60 N 20.18
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To 10.6 g (75.7 mmol) of 1-ethyl-1-(formylamino)propyl cyanide in 45 ml of dry pyridine and 25 ml of petroleum ether  $(30-50^{\circ}C)$ was added dropwise at 0°C 7.5 g (48.9 mmol) of POCl<sub>3</sub><sup>3)</sup>. After heating at reflux for 2 h, the reaction mixture was poured onto ice and extracted several times with CH<sub>2</sub>Cl<sub>2</sub>. The combined layers were washed with water and dried over MgSO<sub>4</sub>. Yield 3.4 g (37%). B.p. 68 °C/12 Torr, m.p. 37-38 °C. – IR (CCl<sub>4</sub>): 2250 cm<sup>-1</sup> (CN), 2140 (NC). – GLC (SE 30, 15%, 2m): >99% pure.

$$C_7H_{10}N_2$$
 (122.2) Calcd. C 68.82 H 8.25 N 22.93  
Found C 68.89 H 8.60 N 23.26

L-(-)-2-Isocyano-3-phenylpropyl Formate (26): 4.3 g (29 mmol) of L-phenylalaninol ( $[\alpha]_{L^2}^{22} = -24.98$ , c = 3.05 in ethanol, i.e. 100% o.p.)<sup>26)</sup> was treated with the mixed anhydride obtained from 5.3 g of 98% formic acid and 11.7 g of acetic anhydride (2 h, 60 °C). After hydrolysis L-(-)-2-formamido-3-phenylpropyl formate was extracted with dichloromethane and purified by chromatography on 120 g of silica gel with 1.3 1 of ethyl acetate. Yield 1.4 g (25%), m.p. 93 °C (benzene);  $[\alpha]_{L^2}^{L^2} = -23.30$  (c = 0.854 in chloroform). – IR (KBr): 3290 cm<sup>-1</sup> (NH), 1705 (CO), 1655 (CO).

 $\begin{array}{ccc} C_{11}H_{13}NO_3 \ (207.2) & Calcd. \ C \ 63.76 \ H \ 6.32 \ N \ 6.76 \\ Found \ C \ 63.95 \ H \ 6.32 \ N \ 6.96 \end{array}$ 

The isocyanide 26 was prepared by reaction of 1.40 g (6.76 mmol) of L-(-)-2-formamido-3-phenylpropyl formate with 1.15 g of POCl<sub>3</sub> and 2.10 g of diisopropylamine in 7 ml of dry  $CH_2Cl_2^{24}$ . Purification by chromatography on 200 g of silica gel with 1.1 l of  $CH_2Cl_2$  yielded 0.9 g (70%) of a colourless oil.  $- {}^{1}H$  NMR (CDCl<sub>3</sub>):  $\delta = 2.95$  (d, J = 7.5 Hz, 2H, ArCH<sub>2</sub>), 3.99 - 4.07 (m, 1H, CHN), 4.07-4.32 (m, 2H, CH<sub>2</sub>O), 7.14-7.38 (m, 5H, Ph), 8.06 (s, 1H, CHO). – IR (film): 2140 cm<sup>-1</sup> (NC), 1718 (CO). –  $[\alpha]_D^{22} = -2.26$  $(c = 1.370 \text{ in CHCl}_3)$ . - GLC (SE 30, 15%, 2 m): >99% pure. C<sub>11</sub>H<sub>11</sub>NO<sub>2</sub> (189.2) Calcd. C 69.83 H 5.86 N 7.40 Found C 69.91 H 5.72 N 7.49

1-Homocubyl Isocyanide (28): 4.9 g (29.0 mmol) of homocubylamine hydrochloride<sup>27)</sup> was treated with 2.5 g of 98% formic acid and 5.5 g of acetic anhydride. After the usual work up, 3.6 g (77%) of N-formylhomocubylamine was isolated. M.p. 78°C [ether/petroleum ether  $(30-50^{\circ}C)$ ]. – IR (KBr): 3430 cm<sup>-1</sup> (NH), 3250 (NH), 1642 (CO).

28 was prepared by reaction of 2.0 g (12.5 mmol) of N-formylhomocubylamine with 1.6 g of POCl<sub>3</sub> in 8 ml of dry pyridine and 5 ml of dry petroleum ether  $(30 - 50 \degree C)$  (2 h refluxing)<sup>23)</sup>. Yield 0.9 g (51%), b.p.  $97^{\circ}C/15$  Torr. - IR (film): 2115 cm<sup>-1</sup> (NC). - GLC (SE 30, 15%, 2 m): >99% pure.

> C10H9N (143.2) Calcd. C 83.88 H 6.34 N 9.78 Found C 83.55 H 6.16 N 9.73

Flash-Thermolysis Experiments: A standard apparatus for flash pyrolysis<sup>28)</sup> with a 50-cm quartz tube ( $\emptyset$  2.4 cm) was utilized at 520-550 °C and  $10^{-2}$  Torr pressure. The sample sizes were between 0.1 g and 4.0 g, the reaction times between 15 and 120 min. The products, in general, required no further purification (>98% pure; GLC and NMR control).

L-(+)-2-Cyano-3-phenylpropyl Formate: 0.70 g (3.70 mmol) of L- $(-)-26([\alpha]_{D}^{22} = -2.26, c = 1.370 \text{ in CHCl}_{3})$  was flash-thermolyzed at 540°C and 10<sup>-2</sup> Torr pressure over a period of 90 min. 0.08 g (15%) of cyano-1-phenyl-1-propene was removed by chromatography in 1.8 l of petroleum ether  $(30-50^{\circ}C)$  over 150 g of silica gel and 0.52 g (74%) of L-(+)-2-cyano-3-phenylpropyl formate was then isolated by elution with 2.21 of  $CH_2Cl_2$  – IR (film): 2240 cm<sup>-1</sup> (CN), 1722 (CO). - GCL (25-m-capillary, SE 30): >98% pure.  $[\alpha]_{D}^{22} = +9.10 \ (c = 1.033 \ in \ CHCl_3).$ 

> C<sub>11</sub>H<sub>11</sub>NO<sub>2</sub> (189.2) Calcd. C 69.83 H 5.86 N 7.46 Found C 69.56 H 5.72 N 7.54

The formyl proton signal appeared as a singlet, when tris-([D<sub>2</sub>]dicamphorylmethanato)europium(III) shift reagent was added to a CCl<sub>4</sub> solution of the isolated (+)-2-cyano-3-phenylpropyl formate.

Racemic cyanide obtained by racemization of (+)-2-cyano-3phenylpropyl formate with the strong base BEMP<sup>29)</sup> in acetonitrile had a formyl-hydrogen doublet NMR signal under identical conditions.

Short-Contact-Flow Thermolysis<sup>9</sup>: The experiments were performed in an apparatus described previously<sup>30</sup>. 0.01 M solutions of the isonitriles (40-200 mg) in benzene were passed at a rate of 15 drops per min under a constant stream of nitrogen through a hot tube which was kept at 350 °C. The contact time was approximately 15 s. The yields are recorded in Table 1.

9-Triptycenecarbonitrile: By thermolysis of 48.7 mg (0.17 mmol) of 19 at 420°C a 46.8-mg (96%) yield of 9-triptycenecarbonitrile

was isolated by evaporation of the benzene solvent. M. p. 284 °C. -IR (KBr): 2220  $\text{cm}^{-1}$  (CN).

> C21H31N (279.3) Calcd. C 90.30 H 4.69 N 5.01 Found C 90.49 H 4.42 N 5.21

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3: 70159-85-2 / 4: 10340-91-7 / 5: 1197-58-6 / 6: 3126-46-3 / 7: 39687-95-1 / 8: 17329-20-3 / 9: 104876-24-6 / 10: 58644-53-4 / 11: 22110-53-8 / 12: 104876-25-7 / 13: 104876-26-8 / 14: 88523-50-6 / 15: 104876-27-9 / 16: 104876-28-0 / 17: 104876-29-1 / 18: 1195-15: 104876-27-9 / 16: 104876-28-0 / 17: 104876-29-1 / 18: 1195-99-9 / 19: 104876-30-4 / 20: 1600-49-3 / 21: 7175-47-5 / 22: 57116-96-8 / 23: 104876-31-5 / 24: 62398-13-4 / 25: 32755-48-9 / 26: 104876-33-6 / 27: 62398-17-8 / 28: 104876-39-3 / endo-2 MNBCN: 104876-33-7 / exo-2 MNBCN:  $104876-34-8 / 1-C_8H_{17}CN$ :  $2243-27-8 / PhCH_2CN$ :  $140-29-4 / p-CH_3OC_6H_4CH_2CN$ :  $104-47-2 / C_4H_3(CH_3)_2CH_2CN$ :  $17684-33-2 / H_3CO_2CCH_2CN$ :  $105-34-0 / PhCH(CH_3)_2CH$ :  $17684-33-2 / [C(CH_3)_2CH_2CN$ :  $105-34-0 / PhCH(CH_3)_2CH$ :  $104876-36-0 / C_5H_{11}(CH_{32}-2CN)$ :  $20923-70-0 / NC(C-H_2)-CCN$ :  $20923-4 / C_4H_3(CH_2)-CCN$ :  $104576-36-0 / C_5H_{11}(CH_3)-2CN$ :  $20923-70-0 / NC(C-H_2)-CCN$ :  $20923-4 / C_4H_3(CH_2)-CCN$ :  $105-34 / 20923-4 / C_5H_{11}(CH_{12})-CCN$ :  $105-34 / 20923-4 / C_{20}(CH_2)-CCN$ : 105-34 / 20023-4 / 20020923-70-0 / NC(C<sub>2</sub>H<sub>3</sub>)<sub>2</sub>CCN: 28118-33-4 / C<sub>6</sub>H<sub>5</sub>(CH<sub>3</sub>)<sub>2</sub>CCN: 1195-98-8 / p-CH<sub>3</sub>C<sub>6</sub>H<sub>4</sub>CN: 104-85-8 / 2,4,6-(CH<sub>3</sub>)<sub>3</sub>C<sub>6</sub>H<sub>2</sub>CN: 2571-52-0 /  $o-tC_4H_9C_6H_4CN$ : 68527-72-0 / trans-CH<sub>3</sub>CH = CHCH<sub>2</sub>CN: 16529-66-1 / C<sub>6</sub>H<sub>5</sub>CH<sub>2</sub>(CH<sub>3</sub>)(CO<sub>2</sub>C<sub>2</sub>H<sub>5</sub>)CCN: 104876-35-9 / cyclopropanecarbonitrile: 5500-21-0 / 1-adamantanecarbonitrile: 23074-42-2 / 3-homoadamantanecarbonitrile: 57293-34-2 / 1-bicyclo[2.2.2 octanecarbonitrile: 25938-93-6 / 9-triptycenecarbonitrile: 1092 1092-87-1 / triphenylmethanecarbonitrile: 6639-43-6 /  $\alpha$ -methylstyrene: 98-83-9 / 2-cyano-1-phenylpropane: 33802-51-6 / 2-cyano-1-phenyl-1-propene: 1197-33-7 / 1-amino-1-ethylpropyl cyanide: 22374-51-2 / 1-ethyl-1-(formylamino)propyl cyanide: 104876-37-1 / L-phenylalaninol: 3182-95-4 / L-(-)-2-formamido-3-phenylpropyl for-mate: 69231-11-4 / homocubylamine hydrochloride: 15844-09-4 / N-formylhomocubylamine: 104876-38-2 1,3,4,6-tetra-O-acetyl-2-deoxy-2-isocyano-D-glucose: 104876-40-6

- <sup>(1) 1a)</sup> K. M. Maloney, B. S. Rabinovitch, in *Isonitrile Chemistry* (I. Ugi, Ed.), Chapter 3, Academic Press, New York, 1971. <sup>(16)</sup> H. M. Walborsky, M. P. Periasamy, in *The Chemistry of Triple Bonded Functional Groups*, Part 2, Suppl. C. (S. Partei, Z. Rappoport, Ed.), p. 835, Wiley-Interscience, New York, 1983.
   <sup>(2)</sup> See also <sup>(2)</sup> P. Q. E. Clothier, M. T. J. Glionna, H. O. Pritchard, J. Phys. Chem. 89 (1985) 2992. <sup>(2b)</sup> D. C. Tardy, B. S. Rabinovich, J. Phys. Chem. 89 (1985) 2442
- novitch, J. Phys. Chem. 89 (1985) 2442.
- <sup>3)</sup> M. Meier, C. Rüchardt, *Tetrahedron Lett.* **24** (1983) 4671. <sup>4)</sup> M. Meier, B. Müller, C. Rüchardt, submitted for publication.
- <sup>5)</sup> M. Meier, B. Dogan, H.-D. Beckhaus, C. Rüchardt, Nouv. J. Chim., in print
- <sup>6)</sup> J. Casanova, N. D. Werner, R. F. Schuster, J. Org. Chem. 31 (1966) 3473.
- <sup>7)</sup> S. Terashima, K. Takashima, T. Sato, S. Yamada, Chem. Pharm. Bull. 21 (1973) 1135
- <sup>8)</sup> M. Shibasaki, T. Sato, N. Ohashi, S. Terashima, S. Yamada, Chem. Pharm. Bull. 21 (1973) 1868, and ref. cited therein. 9 R. F. C. Brown, Pyrolytic Methods in Organic Chemistry, Or-
- ganic Chemistry, a Series of Monographs (H. H. Wasserman, Ed.), Academic Press, New York, 1980.
- <sup>10)</sup> L. E. Overman, Acc. Chem. Res. 13 (1980) 218. <sup>11)</sup> See also <sup>11a)</sup> C. Failli, V. Nelson, H. Immer, M. Götz, Can. J. Chem. **51** (1973) 2769. <sup>11b)</sup> G. Giesemann, E. v. Hinrichs, I. Ugi, J. Chem. Res. (S) 1982, 79
- <sup>12)</sup> M. A. Flamm-ter Meer, H.-D. Beckhaus, K. Peters, H. G. von Schnering, C. Rüchardt, Chem. Ber. 118 (1985) 4665.
- <sup>13)</sup> H. Feuer, H. Rubinstein, A. T. Nielsen, J. Org. Chem. 23 (1958) 1107.
- <sup>14)</sup> I. Ugi, R. Meyr, Chem. Ber. 93 (1960) 239.
- <sup>15</sup> I. Ugi, U. Fetzer, K. Eholzer, H. Knupfer, K. Offermann, Angew. Chem. 77 (1965) 492; Angew. Chem., Int. Ed. Engl. 4 (1965) 472.
   <sup>16</sup> H. Schröder, F. Gerhardt, Horne P. Horney Y. Horney.
- <sup>16)</sup> U. Schöllkopf, F. Gerhardt, I. Hoppe, R. Harms, K. Hantke, K.-H. Scheunemann, E. Elers, E. Blume, *Liebigs Ann. Chem.* 1976, 183.
- <sup>17)</sup> T. Sasaki, S. Eguchi, T. Katada, J. Org. Chem. **39** (1974), 1239. <sup>18)</sup> H. Langhals, G. Range, E. Wistuba, C. Rüchardt, Chem. Ber.
- 114 (1981) 3813. T. Austad, J. Songstad, Acta Chem. Scand. 1972, 3141. -<sup>19b)</sup> N. E. Alexandrou, J. Org. Chem. 30 (1965) 133:
- <sup>20)</sup> G. Kohlmaier, B. S. Rabinovitch, J. Phys. Chem. 63 (1959), 1793.

- <sup>21)</sup> U. Schöllkopf, K.-W. Henneke, K. Madawinata, R. Harms, Lie-bigs Ann. Chem. 1977, 40.
- <sup>22)</sup> D. H. R. Barton, G. Bringmann, D. Lamotte, W. B. Motherwell, R. S. H. Motherwell, J. Chem. Soc., Perkin Trans 1 1980, 2657.
- <sup>23)</sup> I. Ugi, R. Meyr, M. Lipinski, F. Bodesheim, R. Rosendahl, Org. Synth., Coll. Vol V (1973) 300.
   <sup>24)</sup> R. Obrecht, R. Hermann, I. Ugi, Synthesis 1985, 400.
   <sup>25)</sup> W. Collevit E. T. Warmur, Par. Disch. Cham. Gas. 39 (1906).
- <sup>25)</sup> W. Gulewitsch, T. Wasmus, Ber. Dtsch. Chem. Ges. 39 (1906) 1184.
- <sup>26)</sup> I. Frič, V. Špirko, K. Bláha, Collect. Czech. Chem. Commun. 33 (1968) 4008.

- <sup>27)</sup> G. L. Dunn, V. J. Di Pasquo, J. R. E. Hoover, J. Org. Chem. 33 (1968) 1454; L. E. Paquette, J. S. Ward, *ibid.* 37 (1972) 3569.
  <sup>28)</sup> See Fig. 2.6. in ref.<sup>9)</sup> on p. 28.
  <sup>29)</sup> R. Schwesinger, Chimia 39 (1985) 269. We thank Dr. Schwesinger for providing a sample of BEMP [2-tert-butylimino)-2-(dieth-ylamino)-perhydro-1,3-dimethyl-1,3,2-diazaphosphorine].
  <sup>30)</sup> W. Eberbach, B. Burchardt, Chem. Ber. 111 (1978) 3665. We thank Prof. Eberbach and T. Hübner for the opportunity to use this apparenties and for technical assistance.
- this apparatus and for technical assistance.

[180/86]