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Ring Enlargement of Three-Membered Heterocycles by Treatment with In Situ Formed Tricyanomethane**

Klaus Banert,*^[a] Madhu Chityala,^[a] and Marcus Korb^[b]

Dedicated to Professor Akhila Kumar Sahoo, University of Hyderabad

Abstract: Although the chemistry of elusive tricyanomethane (cyanoform) has been studied during a period of more than 150 years, this compound has very rarely been utilized in the synthesis or modification of heterocycles. Three-membered heterocycles, such as epoxides, thiirane, aziridines, or 2H-azirines, are now treated with tricyanomethane, which is generated in situ by heating azidomethylidene-malonodinitrile in tetrahydrofuran at 45 °C or by adding sulfuric acid to potassium tricyanomethanide. This leads to ring expansion with formation of 2-(dicyanomethylidene)oxazolidine derivatives or creation of the corresponding thiazolidine, imidazolidine, or imidazoline compounds and opens up a new access to these push-pull substituted olefinic products. The regio- and stereochemistry of the ring-enlargement processes are discussed, and the proposed reaction mechanisms were confirmed by using ¹⁵Nlabeled substrates. It turns out that different mechanisms are operating; however, tricyanomethanide is always acting as a nitrogen-centered nucleophile, which is quite unusual if compared to other reactions of this species.

Introduction

The history of tricyanomethane (5) dates back to 1864 when the first isolation of so-called cyanoform was reported.^[1] But this and a second synthesis^[2] could not be reproduced by other chemists,^[2,3] and later it was found that 5, even if generated, would not have been able to survive the described drastic reaction conditions. In 1896, Schmidtmann treated sodium tricyanomethanide (1a) with dilute sulfuric acid and then with diethyl ether (Scheme 1).^[4] He obtained a three-phase system, which comprised a greenish yellow middle layer 2 that was claimed to include cyanoform (5), although first experiments to remove the solvents did not lead to characterizable substances. Three years later, Hantzsch and Osswald confirmed these phenomena and stated that tautomerism of 5 is likely to form

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- Supporting information, including full experimental details and compound characterization, and the ORCID identification number(s) for the author(s) of this article can be found under ...

ketenimine **3**.^[5] In 1963, Trofimenko used the salt **1b** to repeat the synthesis of **2** and called this compound "aquoethereal cyanoform".^[6] He successfully liberated **2** from the solvents by rapid evaporation and vacuum sublimation to receive unstable white crystals, to which he erroneously assigned the structure of **3**. When Dunitz et al. performed the rapid evaporation of **2** without sublimation, they were able to isolate single crystals of hydronium tricyanomethanide (**4**), and that facilitated the structure verification by X-ray diffraction studies.^[7] In 2017, it was shown that Trofimenko's experiment did not produce **3** because



Scheme 1. Previous syntheses of tricyanomethane (5).

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rapid evaporation and sublimation of **2** led to the isolation of a mixture of **4** and **5**.^[8] Under special conditions of vacuum sublimation, single crystals of tricyanomethane (**5**) were accessible, which allowed structure confirmation by X-ray diffraction. If moisture was excluded, such single crystals could be handled at ambient temperature for a short time. But cyanoform (**5**) could not be analyzed in solution by NMR spectroscopy at room temperature due to rapid decomposition. Moreover, **5** was easily converted into **4** even if only trace amounts of water were present. Especially, mixtures of **4** and **5** tended to dynamic processes, which led to extremely broad ¹H and ¹³C NMR signals at temperatures between –50 and 0 °C. Thus, even lower temperatures, for example, –70 °C, were necessary to detect sharp ¹³C NMR signals for pure **5** in [D₈]THF.^[8]

Cyanoform (5) was prepared not only from 1a or 1b via 2, but also by reacting 1c with hydrogen sulfide,^[9] or alternatively by treatment of 1d with an excess of anhydrous hydrogen fluoride,^[10] and finally by short-time thermolysis or photolysis of vinyl azide 7.^[8] The products 5 and 6 could not be separated in the case of precursor 1d; however, convincing spectroscopic identification of 5 was nevertheless possible.^[10] Whereas thermolysis of 7 produced only 5 and small amounts of 4, irradiation of 7 in solution led to 5 and the 2*H*-azirine 8.^[8] The photolysis of 7 isolated in an argon matrix did not generate 5 since ketenimine 3 and the heterocycle 8 were formed instead.

During a period of more than 150 years, the chemistry of cyanoform (5) has been studied thoroughly.^[11] Its gas-phase structure was investigated by photoelectron spectroscopy^[12] and microwave spectroscopy.^[9] The relative stabilities, spectroscopic data, and isomerization reactions of **3**, **5**, and other C₄HN₃ species were analyzed by utilizing quantum-chemical methods.^[13] In particular, the acidic properties of **5** as well as its tautomer **3** were discussed intensively.^[5,6,14] Hence, **5** is presented in textbooks of organic chemistry as one of the strongest carbon acids.

As a Brønsted acid, tricyanomethane (5) should be able to catalyze the ring opening of three-membered heterocycles, for example, epoxides. If no other reactive species such as competing nucleophiles are present, interesting novel types of open-chain or ring-expanded products may result. Herein, we report on surprising transformations which were induced by treatment of oxiranes, thiirane, aziridines, and 2H-azirines with in situ formed cyanoform (5).

Results and Discussion

At first, we utilized the commercially available cyclohexene oxide (**9a**) as a substrate that was exposed to the precursor **7** in anhydrous THF at 45 °C (Scheme 2). We expected that **5** resulting from **7** would O-protonate **9a**, and the nucleophilic attack of the central carbon atom of the tricyanomethanide counterion would lead to the ring-opened product **10a**, which can

possibly react to 12a by nucleophilic addition of the hydroxy group at a cyano unit. The former assumption was seemingly well-known^[15] supported by the C-alkylation of tricyanomethanide salts such as 1b with the help of alternative electrophiles, [16-18] for example, primary alkyl halides. But instead of 10a or 12a, we obtained the isomeric product 13a after treatment of 9a with 7. Obviously, protonated 9a was attacked by a nitrogen atom, and after ring opening, the resulting ketenimine 11a was transformed into the final product 13a, which includes a push-pull substituted C=C unit. Whereas both rings are cis-fused in the starting compound 9a, the ¹H NMR data of the ringexpanded product 13a indicated a large vicinal coupling of the two axial bridgehead protons with ${}^{3}J = 12.0$ Hz. Consequently, both rings in 13a are trans-fused.



Scheme 2. Ring enlargement of 9a by treatment with 7 and in situ generation of tricyanomethane (5).

Besides **9a**, we similarly treated also the epoxides **9b**-h with vinyl azide **7** to obtain the ring-enlargement products **13** (Table 1). While the parent oxirane (**9b**) exclusively led to the single product **13b**,^[19] the reaction of propylene oxide (**9c**) resulted in the formation of two regioisomeric oxazole derivatives, which were substituted with a methyl group in the 5- or in the 4-position. Both isomers were easily separated by chromatography, and assignment by ¹H and ¹³C NMR spectroscopy was simple since the adjacent oxygen atom always induced significantly stronger deshielding properties than the amine unit. In the case of styrene oxide (**9d**), treatment with **7** regioselectively led to **13d** as the sole product, and the analogous reaction of the unsymmetrical epoxide **9e** similarly resulted in the exclusive formation of the oxazole derivative **13e**, which was isolated in 79% yield. Thus, the well-known^[20] regiochemistry of acid-catalyzed epoxide ring

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opening was also observed for the conversion of **9** into **13** although the involved reagents did not include an acid on the first view. However, slight warming of vinyl azide **7** generated the Brønsted acid cyanoform (**5**), which initiated the desired transformation by O-protonation of **9**.

Table 1. Treatment of epoxides ${\bf 9}$ with azide ${\bf 7}$ to prepare the ring-enlargement products ${\bf 13}.$



	Substitute 5						
	R ¹	R ²	R ³	R ¹	R ²	R ³	Yield [%] ^{]a]}
а	н	(CH ₂) ₄		н	(CH ₂) ₄		56
b	н	н	н	н	н	н	72
с	н	н	Me	H Me	H H	Me H	25 22
d	Ph	н	н	Ph	н	н	58
е	Ph	Ph	Н	Ph	Ph	н	79
f	Ph	н	Bz	Ph H	H Ph	Bz Bz	27 26
g	н	Ph	Ph	н	Ph	Ph	46 ^{]b]}
h	Ph	н	Ph	Н	Ph	Ph	47 ^{]b]}

[a] Isolated yields; after separation of two products in the case of 13c and 13f.
 [b] 1,2-Diphenylethanone and diphenylacetaldehyde were additionally formed and isolated with a total yield of 13–14%.

When the epoxide 9f, which includes a phenyl group and an electron-withdrawing benzoyl substituent, was subjected to 7, the product 13f was formed with perfect regioselectivity. However, 13f was composed of two stereoisomers isolated with nearly equal yields; the structural assignment of cis-13f and trans-13f was based on ¹H NMR spectroscopy utilizing vicinal coupling constants and NOE experiments. In the case of trans-4,5diphenyloxazole derivative 13g/h, the synthesis was successful starting with oxirane 9g or alternatively with the stereoisomer 9h. Thus, both reactions with 7 are stereoselective, but not stereospecific since the same product (13g = 13h) was formed. The transformations of 9g and 9h were accompanied by the generation of 1,2-diphenylethanone and diphenylacetaldehyde (total isolated yield: 13-14%). These side products obviously resulted from ring opening of the O-protonated epoxides followed by hydride shift or phenyl migration of the substituted benzyl cation. Similar carbocations were involved in the reactions of 9d or 9e with 7 which explains the regioselectivity in the formation of 13d and 13e, respectively. The structure of 13g was confirmed not only by the usual spectroscopic characterization, but also by single crystal X-ray diffraction analysis (Figure 1).



Figure 1. ORTEP (30% ellipsoid probability) of the molecular structure of 13g. A second molecule in the asymmetric unit has been omitted for clarity. Selected bond properties (Å^o): C1–O1 1.45(3), C1–N1 1.31(3), C1–C4 1.37(3), O1–C2 1.45(3), C2–C3 1.60(3), C3–N1 1.43(2), C4–C5 1.40(3), C5–N3 1.15(3), C4–C6 1.43(3), C6–N2 1.21(3), N1–C1–O1 111(2), C1–N1–C3 114(2), C5–C4–C6 120(2), C7–C2–C3–C13 128(2).

The ring-enlargement reaction with the help of vinyl azide 7 was also transferred from oxiranes 9 to thiirane (14) and aziridines 16 and 18 to obtain the five-membered heterocycles 15,[21] 17, and 19, respectively (Scheme 3). The ¹³C NMR spectrum of imidazole derivative 17, measured in [D₆]DMSO at room temperature, showed only a broad signal for both cyano groups, whereas the corresponding spectrum of a solution in [D₆]acetone exhibited two signals at ambient temperature. When the temperature was raised to 45 °C in the latter case, coalescence of the two signals was observed. Rapid exchange of both cyano groups was obviously initiated by rotation about the push-pull substituted C=C bond. The π system of this bond is weakened owing to a dipolar resonance structure, which includes a positive charge, stabilized by the ring nitrogen atoms, and a negative charge delocalized by the cyano groups. The molecular structures of the heterocyclic products 15, 17, and 19 were confirmed by the usual spectroscopic characterization and also by single crystal X-ray diffraction analysis of 17 (Figure 2).



Scheme 3. Ring enlargement of 14, 16, and 18.

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Figure 2. ORTEP (50% ellipsoid probability) of the molecular structure of 17. A second molecule in the asymmetric unit has been omitted for clarity. Selected bond properties (Å^o): S1–N1 1.6929(13), N1–C8 1.4979(18), C8–C9 1.525(2), C9–N2 1.463(2), N2–C10 1.3239(18), C10–N1 1.4121(18), C10–C11 1.388(2), C11–C12 1.418(2), C12–N3 1.147(2), C11–C13 1.421(2), C13–N4 1.1508(19), C8–N1–C10 105.08(11), C9–N2–C10 112.78(13), N1–C10–N2 110.05(13), C12–C11–C13 117.06(13), N1–C8–C9–N2 26.89(14).

Finally, we treated the 2H-azirines 21 with the azide 7 to induce the reaction of in situ generated cyanoform (5) with these highly strained three-membered heterocycles (Scheme 4). Since the addition of 5 at the C=N bond of azirine 8, which was performed by irradiating of 7 at low temperatures and warming the resulting mixture of the photoproducts **5** and **8** to ≥ -30 °C, was reported to lead to the unstable aziridine 20.[8] we expected analogous final products from substrates 7 and 21. But the latter starting compounds afforded novel ring-extended imidazole derivatives 22 instead of aziridines. The products 22a-d were formed with 56-62% yield; and in the case of the very unstable^[22] 2H-azirine 21b, which does not possess a substituent in the 3position, the yield was even slightly higher than that for the transformation of the robust^[23] substrate **21a**, although the corresponding products 22a and 22b are identical (Table 2). It turned out that acetonitrile was a better solvent for this ringenlargement reaction than tetrahydrofuran since more convenient workup was possible and pure products were obtained easily. The new heterocycles 22 were characterized not only by the usual spectroscopic methods, but also by ¹⁵N NMR spectra of 22a and 22c. After assignment of the two NH proton signals of 22a by homonuclear NOE experiments, 2D-15N,1H shift correlation (HSQC) also facilitated the allocation of the ¹⁵N NMR signals. In the ¹³C and ¹⁵N NMR spectra of the unsymmetrical heterocyclic compound 22a, both cyano groups led to a single signal because of a rapid rotation about the exocyclic C=C bond. Even at low temperature (-60 °C, 100 MHz, [D₇]DMF), the ¹³C NMR signal of the two cyano groups was not split into two lines. Apparently, the dipolar resonance structure of 22a,[24] in which the positive charge is delocalized in an aromatic imidazolium ring, is more pronounced than in the case of non-aromatic heterocycle 19. This assumption might be supported by the fact that ¹³C NMR chemical shifts of the exocyclic C=C moiety in 22a (δ = 24.5 and 149.3, $\Delta \delta$ = 124.8) show a greater difference than those of **19** $(\Delta \delta = 109.6).$



Scheme 4. Reaction of different 2*H*-azirines with cyanoform (5); for the key of R¹ and R², see Table 2.

Table 2. Treatment of 21a-d with 7 to produce 22a-d.

21/22	R ¹	R ²	Yield of 22 [%] ^[a]
а	Ph	н	58
b	Н	Ph	61
С	Ph	Ph	56
d	Ph	Me	62

[a] Isolated yields.

Whereas the formation of 20 is connected with an addition at the C=N bond of N-protonated 8 and obviously induced by tricyanomethanide, acting as a carbon nucleophile, the genesis of 22 can only be explained by interaction of the protonated 2Hazirines 21 with tricyanomethanide, which reacts as a nitrogen nucleophile. Since at least two mechanisms may rationalize the $21 \rightarrow 22$ ring enlargement, we utilized the ¹⁵N-labeled substrate ¹⁵N-21a,^[25] which was prepared by thermolysis of the corresponding $\alpha\mbox{-azidostyrene},$ and included 49% of the nitrogen label (Scheme 5). After treatment of ¹⁵N-21a with 7, we obtained, besides unlabeled 22a, the products ¹⁵N-22a and ¹⁵N-22a' in a ratio of 11:1. The quantitative analysis of ¹⁵N-22a was facilitated by the ¹H NMR signal of ¹⁵NH-1 at δ = 12.50, which indicated ${}^{1}J({}^{15}N,{}^{1}H) = 97.6$ Hz with ${}^{1}H,{}^{1}H$ triplet splitting (J = 2.2 Hz), whereas ¹⁵N-**22a'** showed a ¹H NMR signal of ¹⁵NH-3 at δ = 12.68 with ${}^{1}J({}^{15}N,{}^{1}H) = 96.0$ Hz and additional ${}^{1}H,{}^{1}H$ triplet splitting (J = 2.2 Hz). These results were supported by the ¹⁵N NMR spectrum, which included the ¹⁵NH-1 signal of ¹⁵N-22a at δ = -233.6 with ${}^{1}J({}^{15}N,{}^{1}H) = 97.4$ Hz and additional long-range coupling (dd, J =4.6 and 3.7 Hz) as well as the ¹⁵NH-3 signal of ¹⁵N-**22a'** at $\delta = -$ 238.9 with ${}^{1}J({}^{15}N,{}^{1}H) = 96.4$ Hz and triplet splitting with ${}^{3}J = 3.4$ Hz. The assignment of all ¹H and ¹⁵N NMR signals were based not only on the previous allocation of the corresponding NMR signals of 22a (see above), but also on additional NOE experiments with ¹⁵N-22a/¹⁵N-22a'.

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Scheme 5. Ring enlargement of ¹⁵N-21a.

We assume that formation of tricyanomethane (5) from 7 and subsequent N-protonation of ¹⁵N-21a with generation of the ion pair 23 are always the first steps in the ring enlargement reaction of ¹⁵N-21a (Scheme 6). Thereafter, attack of the nitrogen nucleophile tricyanomethanide at the highly activated C=N unit of 23 leads to the addition product 24, which undergoes a ring expansion by a 1,3-migration process. The resulting imidazole derivative 25 tautomerizes to yield the main product ¹⁵N-22a. However, a minor pathway with nitrogen-centered nucleophilic attack of tricyanomethanide at the sp³-hybridized carbon atom achieves ring opening of 23 with formation of 26; and successional cyclization of this ketenimine intermediate, followed by tautomerism of 25', generates ¹⁵N-22a'. The sequence ¹⁵N- $21a \rightarrow 23 \rightarrow 26 \rightarrow 25'$ is similar to the mechanisms, which we suggest for the corresponding ring-enlargement reactions of epoxides 9, thiirane 14, and aziridines 16 and 18.

In order to confirm the proposed reaction mechanisms of the transformation 7 + 21a \rightarrow 22a, we utilized also the ¹⁵N-labeled azide ¹⁵N-7, which prepared was from (chloromethylidene)malonodinitrile and sodium azide that included 98% of the isotope label at one of the terminal positions (Scheme 7). Since we used a smaller amount of ¹⁵N-7 and because of the label distribution on the three cyano positions of the resulting cyanoform, the experiment with ¹⁵N-7 was significantly less sensitive than that with ¹⁵N-21a. As expected, we detected just a small NH signal of ¹⁵N-22a besides strong signals of ¹⁵N-22a' and NH-unlabeled 22a and ¹⁵N-22a'' in the ¹H NMR spectrum, which was measured after treating ¹⁵N-7 with 21a. The corresponding ¹⁵N NMR spectrum indicated only ¹⁵NH-3 (δ = -238.6, dt, ¹J = 96.4 Hz, ³J = 3.4 Hz) of ¹⁵N-**22a'** and C=¹⁵N (δ = -113.3, s) of ¹⁵N-22a". Thus, the transformation of ¹⁵N-7 proved to be a complementary confirmation of the experiment with ¹⁵N-21a.







Scheme 7. Ring enlargement of 21a with the help of ¹⁵N-7.

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Ring-expansion reactions of 9, 14, 16, 18, and 21 were performed with the aid of cyanoform precursor 7, which was used under aprotic starting conditions and without competing nucleophiles. Hence, the question arose whether the corresponding ring-enlargement products can also be prepared if aquoethereal cyanoform (2) or similar reagents are utilized. In order to find an answer to this question, we treated epoxide 9a with compound 2 and obtained the desired product 13a in 75% yield (Scheme 8). However, 13a was accompanied by a small amount of trans-cyclohexane-1,2-diol, which was simultaneously generated from 9a owing to the presence of water. Thus, the separation and purification of 13a was quite tedious if compared to the workup after the transformation $7 + 9a \rightarrow 13a$ and similar reactions. Consequently, we tried anhydrous acidification of 1b and added concentrated sulfuric acid to a solution of 1b and 9a in 1,2-dimethoxyethane (DME). After optimization of the reactions conditions, we isolated 13a by simple washing of the crude product with a limited amount of dichloromethane in 79% vield. When we exposed the azirine 21a to the reagent 2, we obtained the wanted product 22a, but the yield was disappointing low (10%). By using the procedure with 1b and concentrated sulfuric acid in DME, we did not get the desired compound 22a from 21a at all. Hence, ring enlargement of three-membered heterocycles with the help of the alternative cyanoform precursor 1b is possible, but there are limitations in some cases.



Scheme 8. Ring enlargement of 9a and 21a with cyanoform generated from tricyanomethanide salts.

Conclusions

In summary, we have demonstrated that tricyanomethane (5), in situ generated by thermal decay of vinyl azide 7 or by acidification of tricyanomethanide salt 1b, can successfully be used to perform ring expansion reactions with three-membered heterocycles. The resulting products are formed via varying reactions mechanisms; however, tricyanomethanide always acts as nitrogen nucleophile. This is quite different to the known simple alkylation of this nucleophilic species in the presence of alkyl halides, which leads to 1,1,1-tricyanoalkanes by attack of a carbon nucleophile.^[15] It can be argued that different reaction conditions of ring enlargement and alkylation are the reason for distinct nucleophilic properties of tricyanomethanide. But we will

show in near future that tricyanomethane (5), also generated in situ by warming of 7 or by acidification of 1b, operates as a carbon nucleophile in Michael addition reactions.

Products of ring expansion, such as 13, 15, 17, 19, and 22, include an exocyclic push-pull substituted C=C unit, and similar compounds were previously investigated intensively because of their structures, electronic properties, and rotational barriers.^[24,26] Moreover, such substances were utilized for organic synthesis, in particular, as precursors of (other) heterocyclic skeletal structures,^[27] and in some cases, the biological properties were tested, for example, as plant growth regulators^[28] or for histamine H₃ receptor-binding affinities.^[29] Several methods are known to prepare these push-pull substituted olefinic compounds. In most cases. however, the access required a multi-step synthesis.^[19,21,30] Thus, the simple cyanoform-induced transformation of three-membered heterocycles into ringenlargement products, such as 13, 15, 17, 19, and 22, offers a new synthetic approach for the desired push-pull substituted alkenes.

Experimental Section

Experimental details, ¹H, ¹³C, ¹⁵N NMR spectra, crystal structure data and refinement details are given in the Supporting Information.

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Keywords: cyanoform • nitrogen heterocycles • reaction mechanisms • reactive intermediates • ring expansion

- [1] T. Fairly, Ann. Chem. Pharm. 1864/1865, Supl. 3, 371-374.
- a) F. Pfankuch, J. Prakt. Chem. 1871, 4, 35–39; b) F. Pfankuch, J. Prakt. [2] Chem. 1873, 6, 97-116.
- a) A. Claus, Ber. Dtsch. Chem. Ges. 1876, 9, 223-228; b) A. Claus, [3] Justus Liebigs Ann. Chem. 1878, 191, 33-93.
- H. Schmidtmann, Ber. Dtsch. Chem. Ges. 1896, 29, 1168-1175. [4]
- A. Hantzsch, G. Osswald, Ber. Dtsch. Chem. Ges. 1899, 32, 641-650. [5]
- S. Trofimenko, J. Org. Chem. 1963, 28, 217-218. [6]
- D. Šišak, L. B. McCusker, A. Buckl, G. Wuitschik, Y.-L. Wu, W. B. [7] Schweizer, J. D. Dunitz, Chem. Eur. J. 2010, 16, 7224-7230.
- K. Banert, M. Chityala, M. Hagedorn, H. Beckers, T. Stüker, S. Riedel, [8] T. Rüffer, H. Lang, Angew. Chem. 2017, 129, 9710-9714; Angew. Chem. Int. Ed. 2017, 56, 9582-9586.
- B. Bak, H. Svanholt, J. Mol. Struct. 1977, 37, 153-156. [9]

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- [10] T. Soltner, J. Häusler, A. J. Kornath, Angew. Chem. 2015, 127, 13979– 13980; Angew. Chem. Int. Ed. 2015, 54, 13775–13776.
- [11] For a more detailed description of the cyanoform story, see references [7,8,18].
- [12] H. Bock, R. Dammel, Z. Naturforsch. 1987, 42b, 315-322.
- [13] a) M. Szczepaniak, J. Moc, J. Phys. Chem. A 2017, 121, 1319–1327; b)
 H. Brand, J. F. Liebman, A. Schulz, Eur. J. Org. Chem. 2008, 4665–4675; c) B. Bak, C. Bjorkman, J. Mol. Struct. 1975, 25, 131–140;
 d) S. S. Stoyanov, J. A. Tsenov, I. G. Binev, Asian Chem. Lett. 2009, 13, 155–162; e) S. A. Elroby, Chem. Cent. J. 2016, 10, 20.
- [14] a) R. H. Boyd, J. Phys. Chem. 1963, 67, 737–744; b) E. Raamat, K. Kaupmees, G. Ovsjannikov, A. Trummal, A. Kütt, J. Saame, I. Koppel, I. Kaljurand, L. Lipping, T. Rodima, V. Pihl, I. A. Koppel, I. Leito, J. Phys. Org. Chem. 2013, 26, 162–170; c) A. Kütt, T. Rodima, J. Saame, E. Raamat, V. Mäemets, I. Kaljurand, I. A. Koppel, R. Y. Garlyauskayte, Y. L. Yagupolskii, L. M. Yagupolskii, E. Bernhardt, H. Willner, I. Leito, J. Org. Chem. 2011, 76, 391–395.
- [15] a) K. Rakus, S. P. Verevkin, H.-D. Beckhaus, C. Rüchardt, *Chem. Ber.* **1994**, *127*, 2225–2234; b) S. Lotz, G. Gattow, *Z. Anorg. Allg. Chem.* **1992**, *611*, 134–136; c) M. B. Frankel, A. B. Amster, E. R. Wilson, M. McCormick, M. McEachern, *Adv. Chem. Ser.* **1965**, *54*, 108–117.
- [16] For the analogous reaction of 1c with the electrophile bromine and for the transformations of 5 with amine bases, see the references [17] and [18], respectively.
- [17] L. Birckenbach, K. Huttner, Ber. Dtsch. Chem. Ges. 1929, 62, 153–163.
- [18] K. Banert, M. Hagedorn, Synlett 2019, 30, 1427–1430.
- For an alternative synthesis of 13b, see: M. Bakavoli, H. Beyzaie, M. Rahimizadeh, H. Eshgi, R. Takjoo, *Molecules* 2009, *14*, 4849–4857.
- [20] R. E. Parker, N. S. Isaacs, Chem. Rev. 1959, 59, 737–799.
- For an alternative synthesis of 15, see reference [19] and L. G. Chanu,
 O. M. Singh, S. H. Jang, S.-G. Lee, *Bull. Korean Chem. Soc.* 2010, *31*, 859–862.
- [22] K. Isomura, M. Okada, H. Taniguchi, Tetrahedron Lett. 1969, 4073– 4076.
- [23] a) G. Smolinsky, J. Am. Chem. Soc. 1961, 83, 4483–4484; b) A.
 Hassner, F. W. Fowler, J. Am. Chem. Soc. 1968, 90, 2869–2875.
- [24] For quantum chemical calculations of the structure, the electronic properties and the rotation barrier in the case of 2-(dicyanomethylidene)2,3-dihydro-1*H*-imidazole, and similar compounds, see: a) R. Benassi, C. Bertarini, L. Hilfert, G. Kempter, E. Kleinpeter, J. Spindler, F. Taddei, S. Thomas, *J. Mol. Struct.* **2000**, *520*,

273–294; b) R. Benassi, C. Bertarini, E. Kleinpeter, F. Taddei, S. Thomas, J. Mol. Struct. (Theochem) 2000, 498, 201–215; c) R. Benassi,
C. Bertarini, E. Kleinpeter, F. Taddei, J. Mol. Struct. (Theochem) 2000, 498, 217–225; d) R. Benassi, C. Bertarini, F. Taddei, E. Kleinpeter, J. Mol. Struct. (Theochem) 2001, 541, 101–110; e) F. Taddei, J. Mol. Struct. (Theochem) 2001, 544, 141–150; f) R. Benassi, F. Taddei, J. Mol. Struct. (Theochem) 2001, 572, 169–183; g) E. Kleinpeter, S. Klod,
W.-D. Rudorf, J. Org. Chem. 2004, 69, 4317–4329; h) E. Kleinpeter. A. Schulenburg, Tetrahedron Lett. 2005, 46, 5995–5997.

- [25] a) E. Orton, S. T. Collins, G. C. Pimentel, J. Phys. Chem. 1986, 90, 6139–6143; b) A. G. Hortmann, D. A. Robertson, B. K. Gillard, J. Org. Chem. 1972, 37, 322–324.
- N. Kuhn, A. Abu-Rayyan, A. Al-Sheikh, K. Eichele, C. Maichle-Mößmer, M. Steimann, K. Sweidan, Z. Naturforsch. B 2005, 60, 294–299.
- [27] a) S. Chakrabarti, K. Panda, N. C. Misra, H. Ila, H. Junjappa, Synlett, **2005**, 1437–1441; b) E. I. Al-Afaleq, Synth. Commun. **2001**, *31*, 3557–3567; c) M. A. Zaharan, A. M. Sh. El-Sharief, M. S. A. El-Gaby, Y. A. Ammar, U. H. El-Said, Farmaco **2001**, *56*, 277–283; d) A. M. El-Sayed, H. Abdel-Ghany, A. M. M. El-Saghier, Synth. Commun. **1999**, *29*, 3561–3572; e) Y. Tominaga, T. Michioka, K. Moriyama, A. Hosomi, J. Heterocycl. Chem. **1990**, *27*, 1217–1225; f) R. C. F. Jones, S. C. Hirst, Tetrahedron Lett. **1989**, *30*, 5361–5364; g) Z.-t. Huang, H. Wamhoff, Chem. Ber. **1984**, *117*, 1926–1934; h) Z.-t. Huang, H. Wamhoff, Chem. Ber. **1984**, *117*, 1856–1867; i) N. I. Viswanathan, V. Balakrishnan, J. Chem. Soc., Perkin Trans. *1* **1979**, 2361-2362; j) H. Schäfer, K. Gewald, Z. Chem. **1978**, *18*, 335–336.
- [28] P. Bocion, W. de Silva, P. Winternitz, (Hoffmann-La Roche), DE 2512564, 1975.
- [29] S. Sasho, T. Seishi, M. Kawamura, R. Hirose, S. Toki. J.-i. Shimada, Bioorg. Med. Chem. Lett. 2008, 18, 2288–2291.
- [30] a) H. Boulebd, S. Zama, A. Bouraiou, S. Bouacida, H. Merazig, A. Belfaitah, *Tetrahedron Lett.* 2014, *55*, 4701–4704; b) G. Mlostoń, M. Jasiński, A. Linden, H. Heimgartner, *Helv. Chim. Acta* 2006, *89*, 1304–1316; c) R. P. Subrayan, P. G. Rasmussen, *Main Group Chem.* 1997, *2*, 51–60; d) Y. Okamoto, K. Takagi, A. Takada, T. Ueda, *J. Org. Chem.* 1984, *49*, 908–912; e) S. Rajappa, M. D. Nair, R. Sreenivasan, B. G. Advani, *Tetrahedron* 1982, *38*, 1673–1676; f) S. Rajappa, B. G. Advani, R. Sreenivasan, *Tetrahedron* 1977, *33*, 1057–1060; g) Z.-t. Huang, L.-h. Tzai, *Chem. Ber.* 1986, *119*, 2208–2219; h) R. Gompper, H. Schaefer, *Chem. Ber.* 1967, *100*, 591–604.

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Hidden acid: Cyanoform, which is generated in situ from azidomethylidene-malonodinitrile or other precursors, induces ringexpansion reactions of epoxides, thiirane, aziridines, or 2*H*azirines. The transformations are always initiated through protonation of the heteroatom X by cyanoform, but lead to the five-membered heterocycles via different mechanisms (see scheme).

 $R^{3} + NC N_{3}$ $R^{2} R^{1} + NC N_{3}$ $X = 0, S, NR | HC(CN)_{3} | R^{3} + CN CN CN$

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