# SYNTHESIS, REACTIONS, AND REARRANGEMENTS OF 2,4-DIAZABICYCLO[3.1.0]HEXAN-3-ONES

**Helmut Quast,\* Josef Walter Stawitz, and Bodo Mueller**

Institute of Organic Chemistry, University of Wuerzburg, Am Hubland, 97074 Wuerzburg, Germany; hquast@uni-osnabrueck.de

**Abstract** – Copper-mediated cyclopropanation of 1,3-dialkyl-1,3-dihydroimidazol-2-ones with diazomethane and methyl diazoacetate yields 2,4-diazabicyclo[3.1.0]hexan-3-ones and the first diaza[4.3.1]propellane. The bicyclic system survives elevated temperatures and in strongly basic and acidic solutions, but drastic conditions cleave the (C-1)–(C-6) bond affording 1,3-dihydroimidazol-2-ones. Catalytic hydrogenation removes *N*-benzyl groups and opens the (C-1)–(C-6) bond. Lithium aluminium hydride reduces 2,4-dibenzyl-2,4-diazabicyclo[3.1.0]hexan-3-one to a bicyclic aminal. Acid-induced cleavage of its imidazolidine ring is followed by unexpected transformations that probably procede via an acyclic intermediate, which comprises an azomethine ylide and an iminium moiety. 1,3-Cyclization involving both functional groups leads to *N,N'*-dibenzyl-*trans*-1,2-cyclopropanediamine, while 1,5-cyclization gives rise to the formation of *N*-benzylpyrrole along with *N*-benzylamine.

## INTRODUCTION

Since the Sixties, an increasing number of heterobicyclo[3.1.0]hexanes have been synthesized by [2+1] cycloaddition reactions of carbenes and carbenoids at CC double bonds that are part of five-membered heterocycles.[1–6] In search of a novel route to *cis*-1,2-cyclopropanediamines, we employed the [2+1] cycloaddition strategy and synthesized the first 2,4-diazabicyclo[3.1.0]hexan-3-ones by copper-mediated cyclopropanation of 1,3-dihydroimidazol-2-ones with diazo compounds.[7] Thereafter, several examples appeared in the literature: 2,4-Diazabicyclo[3.1.0]hexan-3-ones **1** were obtained as byproducts of the Curtius degradation of *cis*-1,2-cyclopropanedicarboxylic acids.[8,9] Cyclopropanation of 1,3-diacetyl-1,3-dihydroimidazol-2-ones, either copper-catalyzed with diazomethane[10] or by Simmons-Smith reaction,[11]

*Dedicated to Professor Waldemar Adam on the occasion of his 75th birthday*

furnished low yields of **2a** and **2b**, respectively. The latter was converted into **2c** and **2d**.[11] Recently, Schaumann and coworkers reported formation and X-ray diffraction analysis of the annelated 2,4-diazabicyclo[3.1.0]hexan-3-one **3**.[12] Apart from being attractive in their own right, 2,4-diazabicyclo[3.1.0]hexan-3-ones promise to show interesting pharmacological properties as they are homologues of 1,3-dihydroimidazol-2-ones, which exhibit broad biological activities.[13] Therefore, it comes as no surprise that the 2,4-diazabicyclo[3.1.0]hexane system emerged as integral part of bioactive molecules in the medicinal chemistry literature.[14]

Here we give a full account of our earlier[7] and subsequent experiments with the view of (i) exploring scope and limitations of the copper-mediated cyclopropanation of 1,3-dihydroimidazol-2-ones with diazo compounds and (ii) probing stability and some aspects of the reactivity of 2,4-diazabicyclo[3.1.0]hexanones.
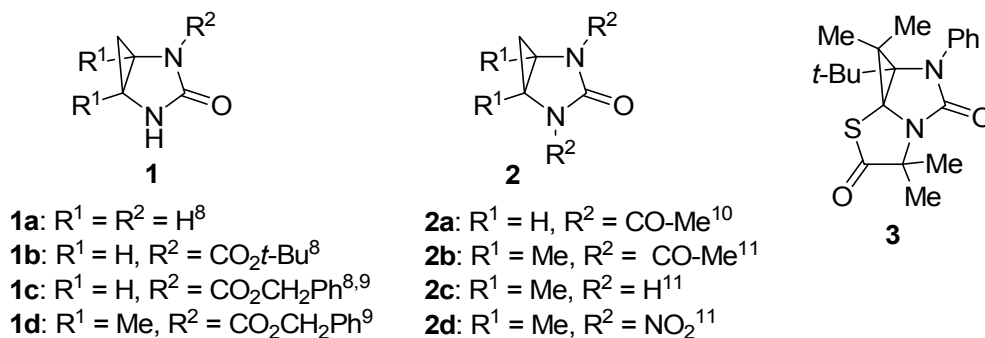


**1a**: $R^1 = R^2 = H^8$
**1b**: $R^1 = H$, $R^2 = CO_2t$-$Bu^8$
**1c**: $R^1 = H$, $R^2 = CO_2CH_2Ph^{8,9}$
**1d**: $R^1 = Me$, $R^2 = CO_2CH_2Ph^9$

**2a**: $R^1 = H$, $R^2 = CO$-$Me^{10}$
**2b**: $R^1 = Me$, $R^2 = CO$-$Me^{11}$
**2c**: $R^1 = Me$, $R^2 = H^{11}$
**2d**: $R^1 = Me$, $R^2 = NO_2^{11}$

**Chart 1**. 2,4-Diazabicyclo[3.1.0]hexan-3-ones

**RESULTS AND DISCUSSION**

Cyclopropanation of *cis*-1,2-ethenediamines whose configuration is fixed by a ring may be imagined as key step of a novel access to *cis*-1,2-cyclopropanediamines.[7] In principle, this strategy for the synthesis of *cis*-1,2-substituted cyclopropanes is not new: For example, Maier and Sayrac employed it as early as 1966 to synthesize *cis*-1,2-cyclopropanedicarboxaldehyde.[2] In pursuit of our synthetic objective, we conceived 1,3-dihydroimidazol-2-ones (**4**, **6**) as equivalents of *cis*-1,2-ethenediamines in the projected [2+1] cycloaddition reaction, which thus would lead to 2,4-diazabicylo[3.1.0]hexan-3-ones.[7] *N*-Benzyl compounds **4** were preferred over the corresponding *N*-methyl analogs, because these tend to be hygroscopic.[15] More important, *N*-benzyl substituents provide a convenient criterion for the distinction between planar starting materials and 2,4-diazabicylo[3.1.0]hexanes: *N*-Benzyl protons of the former are enantiotopic (i. e., they appear equivalent in normal $^1$H NMR spectra), whereas those of the latter are diastereotopic.

While 1,3-dihydroimidazol-2-ones undergo sensitized [2+2] and [4+2] photocycloaddition reactions,[16] they are reluctant toward thermal cycloaddition. Therefore, we tried in exploratory experiments one of the most efficient cyclopropanation procedures, viz. the Gaspar-Roth method,[17] which involves passing gaseous diazomethane carried in a stream of dry nitrogen[18] into a suspension of cuprous chloride in the liquid, olefinic substrate or concentrated solutions thereof. Even benzene is attacked by the intermediate in the copper-mediated decomposition of diazomethane.[17] Likewise, the Gaspar-Roth method cyclopropanated *N*-carbomethoxypyrrol to afford the first example of the 2-azabicyclo[3.1.0]hexane ring system.[3]

It was gratifying to observe a single product (**5a**) when the Gaspar-Roth protocol was applied to **4a**. Unfortunately, numerous attempts to achieve more than ca. 15 – 20 % conversion in this way met with failure. The conversion increased to 50 %, however, when a very large excess of diazomethane in diethyl ether[19] was allowed to distill into concentrated solutions of **4a** in the presence of cuprous chloride (under nitrogen and strict exclusion of moisture). The mixture turned dark due to formation of colloidal copper(0)[20] and was worked-up with the view to avoid the deleterious effect of further dilution and to renew the catalyst. The resulting oil was again subjected to the cyclopropanation procedure to improve the ratio **4a**:**5a** to 18:82. Chromatography on silicagel readily separated **4a** and **5a,** which could be purified further by short-path distillation under high vacuum. A yield of almost 80% was realized in this way.

Already a single treatment of 4,5-dimethylimidazolone **4b** with diazomethane/CuCl furnished a reasonable conversion to **5b**, whereas this procedure had to be repeated several times to achieve an acceptable conversion of the annelated imidazolone **6** to diaza[4.3.1]propellane **7** (Scheme 1).[21]



**4a**, **5a** (79 %): R = H
**4b**, **5b** (36 %): R = Me
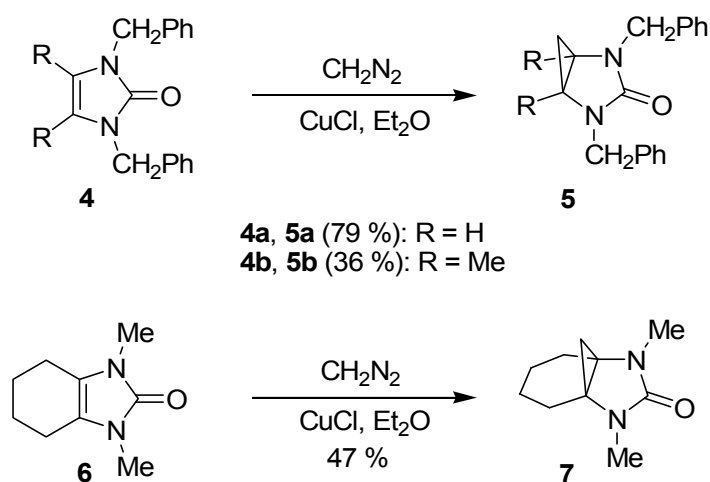
**Scheme 1**. Copper-mediated cyclopropanation of 1,3-dihydro-2*H*-imidazol-2-ones **4** and **6** with diazomethane

A number of unsaturated five-membered rings have been cyclopropanated by methyl and ethyl diazoacetate in the presence of copper bronze, copper salts, and copper complexes. The 6-alkoxycarbonyl groups of the resulting (hetero)bicyclo[3.1.0]hexane derivatives adopted preferentially the *exo* position, corresponding to a *trans*-selective [2+1] cycloaddition.[1,3–5,22]

Mixtures of **4a** and methyl diazoacetate were heated in boiling diethyl ether in the presence of copper bronze, the oldest copper catalyst[23] (Scheme 2). Two isomeric products arose in almost quantitative combined yield, along with some dimethyl fumarate and maleate. An excess of copper bronze (1.4 mol/mol **4a**) was required for a smooth reaction since smaller amounts (0.9 mol/mol **4a**) resulted in recovery of substantial fractions of starting material, even after extended periods of time. The crystalline major product **8** was isolated conveniently in good yield, while the minor, oily product had to be separated from small amounts of the former by chromatography. Analytical and spectroscopic evidence suggested structure **9** for the minor product, which corresponds to an insertion of methoxycarbonylcarbene into a ring C–H bond of the starting material **4a**. Copper-mediated insertion of methoxycarbonylcarbene into $sp^2$ C–H bonds has been observed.[6] However, **9** is also formed by rearrangement of the major product **8** at elevated temperatures (see below). Consequently, speculation as to the way of formation of **9** is not warranted in the absence of experimental evidence.

Ring-methylated imidazolone **4b** reacted slower than **4a**. Therefore, a higher excess of both methyl diazoacetate and copper bronze and THF instead of diethyl ether were employed. The product consisted of at least five components. Chromatography allowed to isolate a mixture of the isomers **10** and **11**. High-vacuum distillation of this fraction gave a mixture of **10** and **11** (2:3) and left **11** as pure oil. Apparently, **10** is thermally labile and rearranges in a homo-[1.5]H shift to **11**. This rearrangement is well-kown for alkyl *cis*-2-methylcyclopropanecarboxylates.[24] Structure **11** of the major product is suggested by NMR spectroscopic comparison with the similar compound **12**, which arises besides **4b** by benzylation of 4,5-dimethyl-1,3-dihydroimidazol-2-one (see Supporting Information). The ${}^1$H NMR spectra of both compounds exhibit the expected doublet pattern for the diastereotopic protons of methylene groups at C-4 and C-5. Other 1,3,5,5-tetraalkyl-4-methyleneimidazolidin-2-ones of type **12** are known for long.[25]

A number of attempts to employ dimethyl diazomalonate in the copper-catalyzed cyclopropanation of **4a** met with failure. Heating of solutions of **4a** and dimethyl diazomalonate in the presence of copper bronze gave complex mixtures. None of the fractions separated by chromatography showed the typical AB pattern of diastereotopic *N*-benzyl protons in the NMR spectrum.
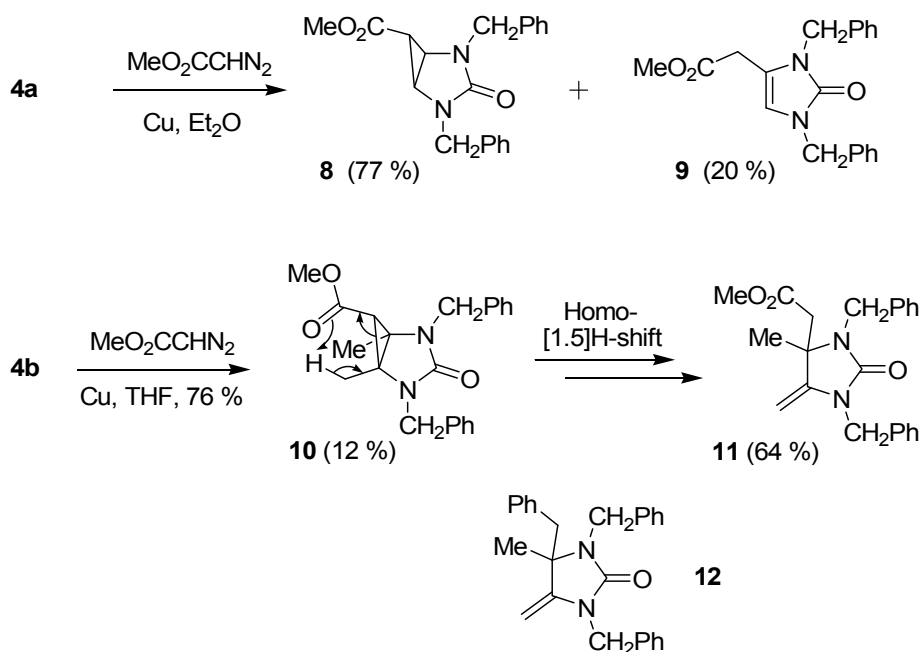
**Scheme 2**. Copper bronze-mediated cyclopropanation of 1,3-dihydro-2*H*-imidazol-2-ones **4** with methyl diazoacetate
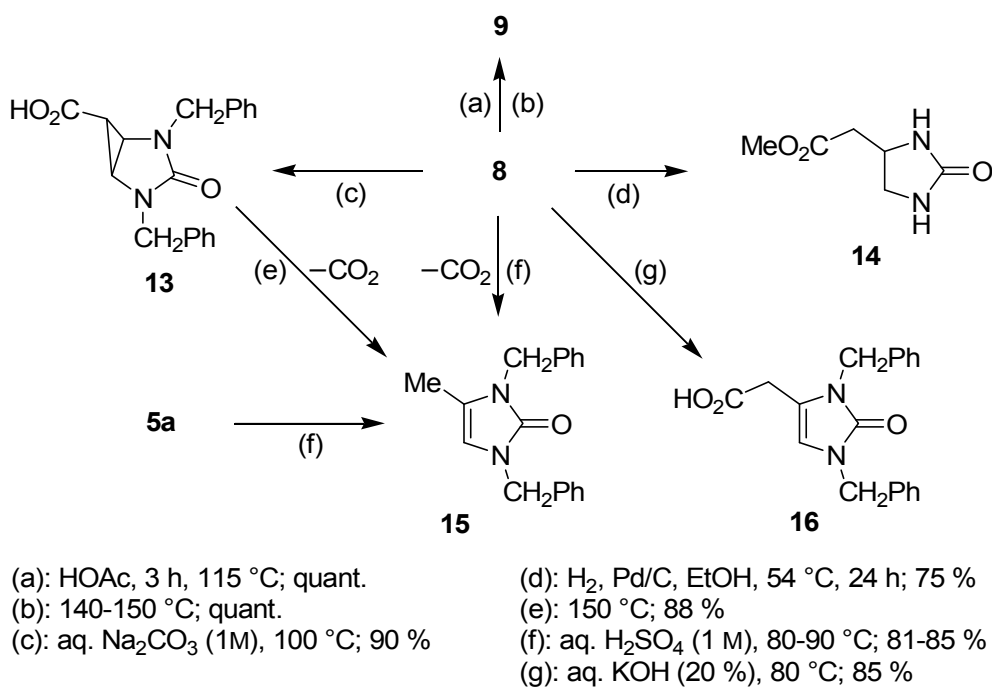
The 2,4-diazabicyclo[3.1.0]hexan-3-one structures **5**, **7**, **8**, and **10** of the cyclopropanation products were immediately evident from NMR spectra: These indicate the presence of a symmetry plane passing through C-3 and C-6 and bisecting the bond between the bridgehead carbon atoms; protons of *N*-benzyl groups are diastereotopic due to the presence of centres of chirality (C-1 and C-5); and signals of cyclopropane protons appear at high field. They were assigned for **5a** to 6-H$_{exo}$ and 6-H$_{endo}$ on the basis of the well-established rule for vicinal coupling between cyclopropane protons, viz., $^3J_{trans} < {}^3J_{cis}$.[26,27] The 6-methoxycarbonyl group of **8** was attributed the *exo* configuration as suggested by the small size of the vicinal coupling constant $^3J_{\text{1-H,6-H}} = 1.8$ Hz $= {}^3J_{trans}$.

General chemical properties and stability of 2,4-diazabicyclo[3.1.0]hexan-3-ones have not been reported so far. An exploratory study of these aspects employed those of the present work. Reaction conditions and results are summarized in Scheme 3.

The 2,4-diazabicyclo[3.1.0]hexan-3-ones **5a** and **5b** can be recovered unchanged after dry heating at 150 °C or heating for several hours in boiling acetic acid. Under these conditions, **8** opens the (C-1)–(C-6) bond to afford 1,3-dihydroimidazol-2-one **9**. In strongly basic media, **5a** and **8** differ in the same way: While **5a** survives unchanged in an ethanolic solution of 10% potassium hydroxide at elevated temperatures, **8** undergoes (C-1)–(C-6) ring opening with concomitant hydrolysis of the ester group under similar conditions (→**16**). However, the bicyclic system remains intact and only hydrolysis is observed when **8** is heated in aqueous sodium carbonate (→**13**). Decarboxylation and (C-1)–(C-6) ring cleavage

occur on heating of the acid **13** at 150 °C to yield **15**. The same compound is obtained on brief heating of both **5a** and **8** in dilute aqueous sulfuric acid. Catalysis by both strong acid and strong base of these rearrangements indicate operation of polar mechanisms.

As expected, catalytic hydrogenation removes the *N*-benzyl groups of **8** and selectively cleaves one of the cyclopropane bonds adjacent to the methoxycarbonyl group to furnish **14**.



(a): HOAc, 3 h, 115 °C; quant.
(b): 140-150 °C; quant.
(c): aq. $Na_2CO_3$ (1M), 100 °C; 90 %
(d): $H_2$, Pd/C, EtOH, 54 °C, 24 h; 75 %
(e): 150 °C; 88 %
(f): aq. $H_2SO_4$ (1 M), 80-90 °C; 81-85 %
(g): aq. KOH (20 %), 80 °C; 85 %

**Scheme 3.** Reactions and rearrangements of 2,4-diazabicyclo[3.1.0]hexan-3-ones **5a** and **8**

The results of the preceding section suggest that selective cleavage of the five-membered ring of 2,4-diazabicyclo[3.1.0]hexan-*3-ones* is not feasible. In pursuit of our original objective of developing a novel route to *cis*-1,2-cyclopropanediamines, we reduced of **5a** using lithium aluminium hydride.[28] An almost quantitative yield of the corresponding bicyclic aminal **17** was realized in this way. Aminal **17** can be distilled under high vacuum and is stable in methanol in the presence of sodium hydroxide but decomposes slowly, even under nitrogen, yielding red-brown polymeric products.

While *N,N'*-dibenzyltetrahydroimidazol was rapidly hydrolyzed by dilute hydrochloric acid to afford a quantitative yield of *N,N'*-dibenzyl-1,2-ethanediamine dihydrochloride,[7] **17** reacted in acidic media in puzzling ways. It dissolved in acetic acid with dark red color. An intense red color was also observed on addition of strong acids to solutions of **17** in ethanol. Work-up yielded resin-like products that lacked cyclopropane rings. Introduction of dry hydrogen chloride into a solution of **17** in dry diethyl ether gave a colorless precipitate, which decomposed above 68 °C and deliquesced on exposure to air. The ^{1}H NMR spectrum recorded for a solution in trifluoracetic acid showed an $ABX_2$ spectrum attributable to protons of a *cis*-1,2-disubstituted cyclopropane, which disappeared overnight, however.
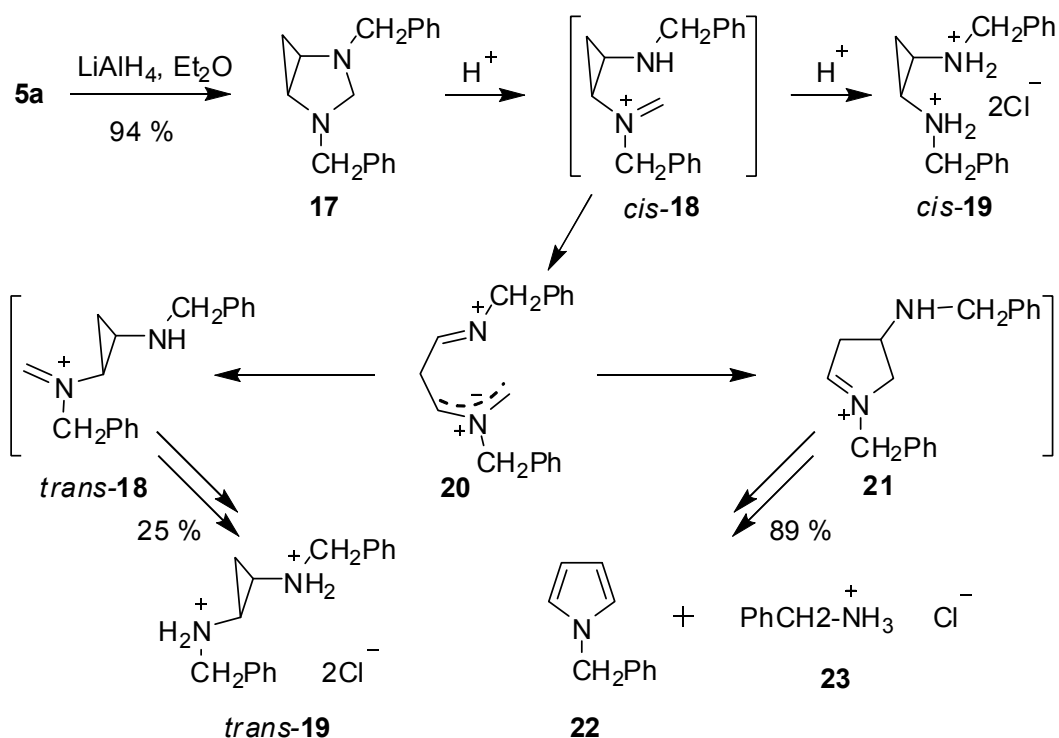
**Scheme 4**. Synthesis and acid-induced cleavage of 2,4-dibenzyl-2,4-diazabicyclo[3.1.0]hexane (**17**)

Treatment of **17** with 0.1–1 M hydrochloric acid and separation of neutral, unknown products furnished, surprisingly, *trans*-**19** rather than expected *cis*-**19.** The *trans* configuration of this product was evident from an AA'XX' spin system, present according to the $^1$H NMR spectrum, and established by comparison with the authentic dihydrobromide.[9] Experiments using higher concentrations of hydrochloric acid (10–35 %) afforded substantial amounts of colored decomposition products and, after basic work-up and distillation at $10^{-3}$ Torr, oily mixtures that exhibited $ABX_2$ systems at high field, corresponding to *cis*-1,2-substituted cyclopropanes. Weakly acidic media such as 2 M aqueous acetic acid or a two-phase system consisting of chloroform and a saturated aqueous solution of copper(II) sulfate converted **17** into *N*-benzylpyrrole (**22**)[29] and *N*-benzylammonium chloride (**23**). Signals of cyclopropane protons were not observed in these experiments. The appearance of acid-sensitive **22** would explain the deep red-brown colors developed by **17** in acidic media.

The results may be rationalized in terms of Scheme 4, which is based on extensive studies of the reactions of 1,2-cyclopropanediamines with aldehydes and ketones.[30] Opening of the five-membered ring of protonated **17** leads to the iminium ion *cis*-**18**. In strongly acidic solution, this can be hydrolyzed in part to yield *cis*-**19**, because ring cleavage to azomethine ylide **20** is disfavored due to protonation of the amino group of *cis*-**18.** Lower concentrations of hydrochloric acid give rise to *cis/trans* isomerization *cis*-**18**→**20**→*trans*-**18** followed by hydrolysis of the latter (→*trans*-**19**). Weakly acidic media favor

ring-expansion *cis*-**18**→**20**→**21**, which finally leads to **22**. Azomethine ylide **20** is invoked as common intermediate that may explain the *cis/trans* rearrangement to *trans*-1,2-cyclopropanediamine *trans*-**19** as well as the cyclization to *N*-benzylpyrrol (**22**). Clearly, these unexpected transformations prevented realization of our original objective. However, they provided the impetus for productive studies of 1,2-cyclopropanediamines.[30]

The present work delineates a straightforward route to and some reactions of 2,4-diazabicyclo[3.1.0]hexan-3-ones, as yet a somewhat neglected heterobicyclic system. It is quite robust under a variety of conditions due to the inherent urea partial structure. Owing to the stability, 2,4-diazabicyclo[3.1.0]hexan-3-ones may replace cyclic urea moieties in many instances and thus lead to novel systems and properties. Reduction yields an aminal (2,4-diazabicyclo[3.1.0]hexane). This undergoes surprising reactions, probably involving an acyclic intermediate, which comprises an azomethine ylide and an iminium moiety. The results of this study may be expected to foster investigations of heterobicyclo[3.1.0]hexanes with the view of advanced applications. Extensions could include cyclopropanation of differently substituted 1,3-dihydroimidazol-2-ones and heteroanalogs thereof using modern transition metal catalysts.

## EXPERIMENTAL

**General Experimental** and preparation of the 1,3-dialkyl-1,3-dihydroimidazol-2-ones **4a**, **4b**, and **6** used as starting materials are detailed in the Supporting Information. $^1H^1H$ coupling constants given are absolute values.

**Copper-mediated cyclopropanation of 1,3-dihydroimidazol-2-ones with diazomethane, General Procedure.** Diazomethane was generated from *N*-nitroso-*N*-methylurea according to the method of Arndt.[19] ***Caution!*** *N-nitroso-N-methylurea is suspected of being a carcinogen and diazomethane is highly toxic and explosive. It must be handled in an efficient fume hood behind a protection shield.* In a brand-new 1L-Erlenmeyer flask (not etched or scratched), a solution of diazomethane was prepared from *N*-nitroso-*N*-methylurea (51.5 g, 0.50 mol), aq. KOH (40%, 175 mL) and $Et_2O$ (0.3–0.5 L), cooled at 5 °C. The ethereal solution was decanted, carefully dried with KOH pellets, and distilled under $N_2$. To avoid ground-glass joints, we used a distillation apparatus made in a single piece from a 1L-flask, attached to a $N_2$ supply, and a Liebig condensor, which was cooled at −30 °C. The adapter at the lower end of the condensor carried a fire-polished glass tube. The tube passed through a two-holed rubber stopper and reached almost the surface of a stirred, cooled (−15 to −10 °C) suspension in a 0.5-L-Erlenmeyer flask protected by a drying tube. The suspension consisted of CuCl (dried over $P_2O_5$), the 1,3-dihydroimidazol-2-one and dry $Et_2O$ (**4a**, **7**) or dry $CH_2Cl_2$ (**4b**). Distillation was interrupted as soon

as the distillate became colorless. The dark suspension was filtered (Celite) and the solvent distilled i. vac. to afford a pale yellow oily residue. The ratio 2,4-diazabicyclo[3.1.0]hexan-3-one vs. 1,3-dihydroimidazol-2-one was determined by $^1$H NMR. Treatment with diazomethane/CuCl was repeated with the residue until a satisfactory ratio was obtained. Starting material and product were separated by preparative layer or flash chromatography on silicagel with Et$_2$O/hexane. The cyclopropanation products were collected in the first fractions. Further purification by recrystallization (**5b**) or short-path distillation in a sublimation apparatus (cold finger kept at –30 °C) under high vacuum (**5a**, **7**) afforded the pure cyclopropanation products (TLC, $^1$H NMR).

**2,4-Dibenzyl-2,4-diazabicyclo[3.1.0]hexan-3-one (5a)**: The first treatment of **4a** (7.92 g, 30 mmol, solution in Et$_2$O, 50 mL) with diazomethane in the presence of CuCl (5.0 g, 50 mmol) resulted in a pale yellow oil (8.67 g) with a ratio **4a**:**5a** = 52:48, the second gave a pale yellow oil (9.41 g) with a ratio **4a**:**5a** = 18:82. Chromatography followed by distillation at 70–90 °C bath temp./10$^{-5}$ Torr afforded a pale yellow oil (6.80 g, 79%). IR (neat oil) $v$ [cm$^{-1}$] = 1690 (s). MS (EI, 70 eV) $m/z$ = 278 (M$^+$). $^1$H NMR (600.1 MHz, CDCl$_3$): $\delta$ [ppm] = –0.130 (dt, $^2J$ = 6.3 Hz, $^3J_{trans}$ = 2.7 Hz, 1 H, 6-H$_{endo}$), 0.296 (dt, $^2J$ = 6.3 Hz, $^3J_{cis}$ = 5.6 Hz, 1 H, 6-H$_{exo}$), 2.837 (dd, $^3J_{cis}$ = 5.6 H, $^3J_{trans}$ = 2.7 Hz, 2 H, 1-H, 5-H), 4.265 (d, $^2J$ = 14.8 Hz, 1 H, ½ CH$_2$), 4.517 (d, $^2J$ = 14.8 Hz, 1 H, ½ CH$_2$), 7.17–7.27 (m, 10 H, 2 Ph). IR (neat oil) $v$ [cm$^{-1}$] = 1705 (s). MS (EI, 70 eV) $m/z$ = 180 (M$^+$). $^{13}$C NMR (150.9 MHz, CDCl$_3$): $\delta$ [ppm] = 9.74 (CH$_2$), 29.29 (CH), 47.82 (CH$_2$), 127.21 (*p*-CH), 128.04, 128.33 (*o*, *m*-CH), 137.15 (*ipso*-C), 158.92 (C=O). Anal. Calcd for C$_{18}$H$_{18}$N$_2$O: C, 77.67; H, 6.52. Found: C, 77.49; H, 6.86.

**2,4-Dibenzyl-1,5-dimethyl-2,4-diazabicyclo[3.1.0]hexan-3-one (5b)**: According to the General Procedure, diazomethane was distilled into a mixture of **4b** (8.77 g, 30 mmol), CuCl (5.0 g, 50 mmol) and dry CH$_2$Cl$_2$ (35 mL). Filtration, distillation of the solvent i. vac., and treatment of the residue with cold pentane yielded colorless crystals (9.17 g), which consisted of **4b** and **5b** with a ratio 38:62 (TLC, $^1$H NMR). Chromatography and recrystallization from pentane yielded colorless crystals (3.35 g, 36 %), mp 88–90 °C. IR (KBr) $v$ [cm$^{-1}$] = 1695 (s), 1680 (m). MS (EI, 70 eV) $m/z$ = 306 (M$^+$). $^1$H NMR (60 MHz, CDCl$_3$): $\delta$ [ppm] = –0.13, 0.01 (AB spectrum, $^2J$ = 6.4 Hz, 2 H, 6-H$_{endo}$, 6-H$_{exo}$), 1.24 (s, 6 H, 2 CH$_3$), 4.35, 4.69 (AB spectrum, $^2J$ = 15.4 Hz, 4 H, 2 CH$_2$), 7.34 (mc, 10 H, 2 Ph). Anal. Calcd for C$_{20}$H$_{22}$N$_2$O: C, 78.40; H, 7.24; N, 9.14. Found: C, 78.34; H, 7.21; N, 9.16.

**7,9-Dimethyl-7,9-diazatricyclo[4.3.1.0$^{1,6}$]decan-8-one (7):** According to the General Procedure, diazomethane was distilled into a mixture of **6** (15.0 g, 90 mmol), CuCl (5.0 g, 50 mmol) and Et$_2$O (30 mL). The resulting pale yellow oil was treated once again with diazomethane/CuCl. Short-path distillation of the oil at 50–75 °C bath temp./3×10$^{-5}$ Torr yielded a colorless oil (14.0 g) consisting of polymethylene ($\delta_H$ = 1.26 ppm), **6** and **7** (45:55, $^1$H NMR). Two further treatments of the oil with diazomethane/CuCl and short-path distillation of the product at 50–75 °C bath temp./3×10$^{-5}$ Torr gave a

colorless oil (12.9 g, **6**:**7** = 27:73, $^1$H NMR). Flash chromatography on silicagel with CHCl$_3$ and short-path distillation at $3 \times 10^{-5}$ Torr yielded a colorless, hygroscopic oil (7.61 g, 47%). IR (neat oil) $v$ [cm$^{-1}$] = 1705 (s). MS (EI, 70 eV) $m/z$ = 180 (M$^+$). $^1$H NMR (600.1 MHz, CDCl$_3$): $\delta$ [ppm] = –0.020 (d, $^2J$ = 5.9 Hz, 1 H), 0.195 (dd, $^2J$ = 5.9 Hz, $J$ = 0.8 Hz, 1 H), 0.97–1.05 (m, 2 H), 1.22–1.30 (m, 2 H), 1.65–1.77 (m, 4 H), 2.587 (dd, $J$ = 1.7 Hz, $J$ = 0.6 Hz, 6 H, 2 CH$_3$). $^{13}$C NMR (150.9 MHz, CDCl$_3$): $\delta$ [ppm] = 16.11 (CH$_2$), 20.38 (2 CH$_2$), 25.09 (2 CH$_2$), 27.56 (2 CH$_3$), 160.21 (C=O).

*exo*-**2,4-Dibenzyl-6-carbomethoxy-2,4-diazabicyclo[3.1.0]hexan-3-one (8):** A solution of methyl diazoacetate (2.20 g, 22 mmol) in dry Et$_2$O (25 mL) was added dropwise during 30 min to a stirred, boiling mixture of **4a** (2.64 g, 10 mmol), copper bronze (0.89 g, 14 mmol) and dry Et$_2$O (25 mL). Heating under reflux was continued for 5 h followed by filtration and distillation of the solvent i. vac. Short-path distillation at rt/10$^{-3}$ Torr removed decomposition products of methyl diazoacetate (dimethyl fumarate and maleate, $^1$H NMR). The solid, pale yellow residue was treated with cold Et$_2$O (0 °C, 2 × 10 mL) and the insoluble material recrystallized from cyclohexane to afford colorless crystals (2.06 g, 62%) mp 105–106 °C. The solvent from the combined washings and mother liquor was distilled i. vac. and the residue separated by chromatography to yield a second crop of **8** (1$^{st}$ fraction, 0.52 g, 15%) mp 103–105 °C, and **9** as pale yellow oil (2$^{nd}$ fraction, 0.71 g, 20%), which was identical with the isomerization product of **8** (IR, $^1$H NMR, see below). **8**: IR (KBr) $v$ [cm$^{-1}$] = 1723 (s), 1688 (s). MS (EI, 70 eV) $m/z$ = 336 (M$^+$). $^1$H NMR (600.1 MHz, CDCl$_3$): $\delta$ [ppm] = 1.010 (t, $^3J_{trans}$ = 1.8 Hz, 1 H, 6-H$_{endo}$), 3.477 (d, $^3J_{trans}$ = 1.8 Hz, 2 H, 1-H, 5-H), 3.574 (s, 3 H, OCH$_3$), 4.324 (d, $^2J$ = 14.8 Hz, 1 H, ½ CH$_2$), 4.666 (d, $^2J$ = 14.9 Hz, 1 H, ½ CH$_2$), 7.28–7.32 (m, 6 H, Ph), 7.33–7.38 (m, 4 H, Ph). $^{13}$C NMR (150.9 MHz, CDCl$_3$): $\delta$ [ppm] = 23.88 (CH-6), 39.08 (CH-1, CH-5), 47.77 (CH$_2$), 51.81 (OCH$_3$), 127.81 (*p*-CH), 128.16, 128.77 (*o*-, *m*-CH), 136.30 (*ipso*-C), 158.57 (C=O), 170.68 (CO$_2$Me). Anal. Calcd for C$_{20}$H$_{20}$N$_2$O$_3$: C, 71.41; H, 5.99; N, 8.32. Found: C, 71.80; H, 6.02; N, 8.36.

**1,3-Dibenzyl-4-carbomethoxymethyl-1,3-dihydroimidazol-2-one (9):** (a) **8** (1.35 g, 4.0 mmol) was heated at 140–150 °C for 1 h to afford a pale yellow, very viscous oil (1.35 g, quant.). Attempts at crystallization met with failure. IR (neat oil) $v$ [cm$^{-1}$] = 1735 (CO$_2$Me), 1678 (C=O). MS (EI, 70 eV) $m/z$ = 336 (M$^+$). $^1$H NMR (60 MHz, CDCl$_3$): $\delta$ [ppm] = 3.08 (s, 2 H, CH$_2$), 3.47 (s, 3 H, OCH$_3$), 4.69 (s, 2 H, CH$_2$), 4.80 (s, 2 H, CH$_2$), 6.00 (s, 1 H, 5-H), 7.13, 7.19 (mc, 10 H, 2 Ph). Anal. Calcd for C$_{20}$H$_{20}$N$_2$O$_3$: N, 8.32. Found: N, 8.42.

(b) A solution of **8** (1.35 g, 4.0 mmol) in acetic acid (15 mL) was heated at 80 °C for 3 h followed by evaporation of the solvent at rt/10$^{-2}$ Torr to afford **9** (1.36 g, quant.) as a pale yellow viscous oil (TLC, IR, $^1$H NMR).

*exo*-**2,4-Dibenzyl-6-carbomethoxy-2,4-diazabicyclo[3.1.0.]hexan-3-one (10) and 1,3-Dibenzyl-5-carbomethoxymethyl-5-methyl-4-methylene-1,3-dihydroimidazol-2-one (11):** A solution of methyl

diazoacetate (4.30 g, 43 mmol) in dry THF (30 mL) was added dropwise during 30 min to a stirred, boiling mixture of **4b** (1.82 g, 6.2 mmol), copper bronze (2.0 g, 31 mmol) and dry THF (20 mL). Heating under reflux was continued for 6 h followed by filtration of the brown suspension and distillation of the solvent at 15 Torr and finally at 70 °C bath temp./$10^{-2}$ Torr to afford a brown resin (2.96 g), which consisted of at least 5 components (TLC). Chromatography and drying of the main fraction for 1 h at 40–50 °C/$10^{-5}$ Torr yielded a yellow oil (1.79 g). Short-path distillation at 100–120 °C bath temp./$10^{-5}$ Torr furnished a colorless oil (0.69 g, 30%) consisting of **10** and **11** (2:3, TLC, $^1$H NMR). The residue was pure **11** as yellow oil (1.04 g, 46%), (TLC, $^1$H NMR).

**10**: $^1$H NMR (60 MHz, CDCl$_3$): $\delta$ [ppm] = 0.80 (s, 1 H, 6-H$_{endo}$), 1.44 (s, 6 H, 2 CH$_3$), 3.46 (s, 3 H, OCH$_3$), 4.37, 4.61 (AB spectrum, $^2J$ = 15.4 Hz, 4 H, 2 CH$_2$), 7.29 (m, Ph).

**10, 11** (2:3): Anal. Calc. for C$_{22}$H$_{24}$N$_2$O: C, 72.51; H, 6.64; N, 7.69. Found: C, 72.38; H, 6.59; N, 7.65

**11**: $^1$H NMR (60 MHz, CDCl$_3$): $\delta$ [ppm] = 1.25 (s, 3 H, CH$_3$), 2.47, 2.66 (AB spectrum, $^2J$ = 16 Hz, 2 H, CH$_2$), 3.39 (s, 3 H, OCH$_3$), 3.85, 3.95 (AB spectrum, $^2J$ = 2.8 Hz, 2 H, = CH$_2$), 4.45, 4.62 (AB spectrum, $^2J$ = 16 Hz, 2 H, CH$_2$), 4.69 (s, 2 H, CH$_2$), 7.29 (mc, 10 H, 2 Ph).

***exo*-2,4-Dibenzyl-6-carboxy-2,4-diazabicyclo[3.1.0]hexan-3-one (13):** A suspension of **8** (1.35 g, 4.00 mmol) in aq. Na$_2$CO$_3$ (1 M, 25 mL) was heated under reflux for 4 h. Filtration and acidification of the filtrate with aq. HCl (2 M) yielded a preciptate, which was isolated by filtration and washed with water to yield colorless crystals (1.16 g, 90 %) mp 119–120 °C (dec.). IR (KBr) $v$ [cm$^{-1}$] = 1710 (s, br.), 1670 (s, br.). $^1$H NMR (60 MHz, CDCl$_3$): $\delta$ [ppm] = 0.88 (br., 1 H, 6-H$_{endo}$), 3.45 (d, $^3J_{trans}$ = 1.6 Hz, 1-H, 5-H), 4.37, 4.62 (AB spectrum, $^2J$ = 15 Hz, 4 H, 2 CH$_2$), 7.30 (mc, 10 H, 2 Ph), 9.74 (br., 1 H, CO$_2$H). Anal. Calcd for C$_{19}$H$_{18}$N$_2$O$_3$: N, 8.69. Found: N, 8.62.

**4-Carbomethoxymethyl-1,3-dihydroimidazol-2-one (14):** A quantitative micro hydrogenation apparatus by NORMAG, O. Fritz, Hofheim am Taunus, Germany, was used. A vigorously stirred suspension of Pd/C (10%, 200 mg) in a solution of **8** (342 mg, 1.02 mmol) in EtOH (15 mL) was kept at 735 Torr H$_2$ pressure and 54 °C. Consumption of H$_2$ ceased after 24 h, when 85.3 mL of H$_2$ (3.08 mmol) had been consumed. Filtration, washing of the catalyst with EtOH (50 mL), distillation of the solvent i. vac., and recrystallization of the residue from benzene yielded colorless crystals (121 mg, 75%), mp 108–109 °C. IR (KBr) $v$ [cm$^{-1}$] = 1730 (s), 1695 (s). MS (EI, 70 eV) $m/z$ = 158 (M$^+$). $^1$H NMR (90 MHz, D$_2$O, LAOCOON III simulation of the ABMX$_2$ spectrum): $\delta$ [ppm] = 2.71 (d, X part of an ABMX$_2$ spectrum, $^3J_{MX}$ = 6.4 Hz, 2 H$_X$, 4-CH$_2$), 3.25 (m, $^2J_{AB}$ = –9.3 Hz, $^3J_{AM}$ = 6.2 Hz, H$_A$, 5-H), 3.72 (m, $^2J_{AB}$ = –9.3 Hz, $^3J_{BM}$ = 9.1 Hz, H$_B$, 5-H), 4.21 (m, $^3J_{AM}$ = 6.2 Hz, $^3J_{BM}$ = 9.1 Hz, $^3J_{MX}$ = 6.4 Hz, H$_M$, 4.H), 3.76 (s, 3 H, OCH$_3$); $^1$H NMR in CDCl$_3$: Ref.[31] Anal. Calcd for C$_6$H$_{10}$N$_2$O$_3$: C, 45.56; H, 6.37. Found: C, 45.02; H, 6.36.

**1,3-Dibenzyl-4-methyl-1,3-dihydroimidazol-2-one (15):** (a) The acid **13** (645 mg, 2.00 mmol) was heated at 120–140 °C for 2 h. The product was dissolved in a small amount of $Et_2O$. Filtration followed by cooling to –25 °C yielded pale yellow crystals (490 mg, 88 %), mp 68–70 °C.[32] IR (KBr) $v$ [cm$^{-1}$] = 1682 (s), 1673 (s). ^{1}H NMR (60 MHz, CDCl$_3$): $\delta$ [ppm] = 1.85 (d, $^4J$ = 1.4 Hz, 3 H, CH$_3$), 4.80 (s, 2 H, CH$_2$), 4.87 (s, 2 H, CH$_2$), 5.83 (q, $^4J$ = 1.4 Hz, 1 H, 5-H), 7.25, 7.28 (mc, 10 H, 2 Ph). Anal. Calcd for C$_{18}$H$_{18}$N$_2$O: N, 10.06. Found: N, 10.02

(b) A stirred mixture of **8** (673 mg, 2.00 mmol), and aq. H$_2$SO$_4$ (1 M, 10 mL) was heated at 80 °C for 30 min followed by extraction with Et$_2$O. The org. layer was dried with K$_2$CO$_3$, the solvent distilled i. vac., and the residue recrystallized from Et$_2$O at –25 °C to yield pale yellow crystals (451 mg, 81%), mp 69–70 °C.

(c) A solution of **5a** (279 mg, 1.00 mmol) in aq. H$_2$SO$_4$ (1 M, 5 mL) was heated at 90 °C for 1 h. The mixture was neutralized with aq. NaOH (2 M) and extracted with CH$_2$Cl$_2$. The org. layer was dried with K$_2$CO$_3$. Distillation of the solvent i. vac. gave a yellow-brown oil (237 mg, 85 %), which was a single compound (TLC) and identical with **15** (^{1}H NMR).

**1,3-Dibenzyl-4-carboxymethyl-1,3-dihydroimidazol-2-one (16):** A stirred mixture of **8** (1.35 g, 4.00 mmol) and aq. KOH (20%, 20 mL) was heated at 70–80 °C for 30 min. The mixture was filtered and the filtrate neutralized with aq. conc. HCl to afford colorless crystals (1.10 g, 85 %), mp 147–149 °C (dec). ^{1}H NMR (60 MHz, CDCl$_3$): $\delta$ [ppm] = 3.17 (s, 2 H, CH$_2$), 4.83 (s, 2 H, CH$_2$), 4.92 (s, 2 H, CH$_2$), 7.23, 7.27 (mc, 10 H, 2 Ph), 9.2 (br., 1 H, CO$_2$H).

**2,4-Dibenzyl-2,4-diazabicyclo[3.1.0]hexane (17):** A solution of **5a** (2.79 g, 10 mmol) in Et$_2$O (10 mL) was added to a stirred solution of LiAlH$_4$ (1.36 g, 35 mmol) in Et$_2$O (100 mL). Stirring was continued for 2 d followed by decomposition of the excess of LiAlH$_4$ with the calculated amount of ice-water, filtration, and distillation of the solvent i. vac. to afford a pale yellow liquid (2.64 g). Short-path distillation in a sublimation apparatus (cold finger at –30 °C) at 50–70 °C bath temp./10$^{-5}$ Torr gave a colorless oil (2.49 g, 94 %). IR (neat oil) $v$ [cm$^{-1}$] = 1600 (m), 1580 (w), 1490 (s). – MS (EI, 70 eV) $m/z$ = 264 (M$^+$). ^{1}H NMR (60 MHz, CDCl$_3$, LAOCOON III simulation of the ABX$_2$ spectrum): $\delta$ [ppm] = –0.02 (dt, $^2J_{AB}$ = –6.8 Hz, $^3J_{cis}$ = 6.2 Hz, 1 H, 6-H$_{exo}$), 1.25 (dt, $^2J_{AB}$ = –6.8 Hz, $^3J_{trans}$ = 3.0 Hz, 1 H, 6-H$_{endo}$), 2.67 (d, $^2J$ = 5.6 Hz, 1 H, 3-H), 2.85 (dd, $^3J_{cis}$ = 6.2 Hz, $^3J_{trans}$ = 3.0 Hz, 2 H, 1-H, 5-H), 3.72 (s, 4 H, 2 CH$_2$), 3.87 (d, $^2J$ = 5.6 Hz, 1 H, 3-H), 7.2–7.6 (m, 10 H, 2 Ph). Anal. Calcd for C$_{18}$H$_{20}$N$_2$: C, 81.77; H, 7.62; N, 10.59. Found: C, 81.32; H, 7.63; N, 10.60.

**N,N'-Dibenzyl-*trans*-1,2-cyclopropanediamine Dihydrochloride (*trans*-19):** Under N$_2$, a solution of **17** (2.64 g, 10 mmol) in Et$_2$O (6 mL) was added to stirred aq. HCl (1 M, 50 mL). Stirring was continued for 2 h followed by extraction with CHCl$_3$. Water was distilled i. vac. at 30–40 °C bath temp. from the colorless aq. layer. The solid residue was dried at 70 °C/0.001 Torr and triturated with a small amount of

cold ethanol. The insoluble material was isolated by filtration and recrystallized from EtOH to afford pale pink crystals (0.80 g, 25%), mp 225–230 °C (dec.). The ^{1}H NMR spectrum ($D_2O$) was superimposable with the one recorded for the dihydrobromide.[9] Anal. Calcd for $C_{17}H_{22}Cl_2N_2$: C, 62.77; H, 6.82; Cl, 21.80; N, 8.61. Found: C, 62.78; H, 7.01; Cl, 21.91; N, 8.77.

***N*-Benzylpyrrole (22):** (a) A solution of **17** (132 mg, 0.50 mmol) in $CHCl_3$ (10 mL) was vigorously stirred for 1 h in the presence of sat. aq. $CuSO_4$ (5 mL). The org. layer was dried with $K_2CO_3$ followed by distillation of the solvent i. vac. to afford a pale brown oil (69 mg, 89%), which was pure and identical with an authentic sample (IR, ^{1}H NMR) prepared by phase transfer catalysed *N*-benzylation of pyrrole.[29]

(b) A solution of **17** (132 mg, 0.50 mmol) in $Et_2O$ (10 mL) was stirred for 0.5 h in the presence of aq. acetic acid (2 M, 10 mL) followed by separation of the layers and extraction of the aq. layer with $Et_2O$. Drying of the combined org. layers with $K_2CO_3$ and distillation of the solvent i. vac. yielded almost pure **22** as yellow oil (^{1}H NMR). Aq. HCl (2 M, 20 mL) was added to the aq. layer followed by distillation of the solvent i. vac. and trituration of the residue with a small amount of EtOH to furnish *N*-benzylammonium chloride (**23**) as colorless powder (IR, ^{1}H NMR); picrate (from ethanol): mp 193–195 °C; authentic sample: mp 194 °C.

## ACKNOWLEDGEMENTS

## SUPPORTING INFORMATION AVAILABLE

General experimental, preparation of 1,3-dialkyl-1,3-dihydroimidazol-2-ones (**4a**, **4b**, **6**) (6 pages), and NMR spectra recorded for **5a**, **7**, **8**, **14**, and **17** (8 pages). This material is available free of charge via the Internet at http://www.heterocycles.com or from the author.

## REFERENCES

1. F. W. Breitbeil, III, J. J. McDonnell, T. A. Marolewski, and D. T. Dennerlein, *Tetrahedron Lett.,* 1965, **6**, 4627.

2. G. Maier and T. Sayrac, *Angew. Chem., Int. Ed. Engl.,* 1966, **5**, 959.

3. S. R. Tanny, J. Grossman, and F. W. Fowler, *J. Am. Chem. Soc.*, 1972, **94**, 6495.

4. D. Seebach and G. Stucky, *Angew. Chem., Int. Ed. Engl.*, 1988, **27**, 1351; D. Seebach, G. Stucky, and E. Pfammatter, *Chem. Ber.*, 1989, **122**, 2377; M. L. Rosenberg, K. Vlašaná, N. S. Gupta, D.

Wragg, and M. Tilset, *J. Org. Chem.*, 2011, **76**, 2465.

5.   Further examples may be found in reviews: H. E. Simmons, T. L. Cairns, S. A. Vladuchick, and C. M. Hoiness, *Org. React.*, 1973, **20**, 1; T. Ye and M. A. McKervey, 'The Chemistry of the Cyclopropyl Group, Vol. 2: Metal Catalysed Cyclopropanations', ed. by Z. Rappoport, Wiley, New York, 1995, pp. 657–706; G. R. Krow and K. C. Cannon, *Org. Prep. Proced. Int.*, 2000, **32**, 103; A. Charette and A. Beauchemin, *Org. React.*, 2001, **58**, 1; H. M. L. Davies and E. G. Antoulinakis, *Org. React.*, 2001, **57**, 1; H. Lebel, J. F. Marcoux, C. Molinaro, and A.B. Charette, *Chem. Rev.*, 2003, **103**, 977; M Fedoryński, *Chem. Rev.*, 2003, **103**, 1099; H.-U. Reissig and R. Zimmer, *Chem. Rev.*, 2003, **103**, 1151; F. Gnad and O. Reiser, *Chem. Rev.*, 2003, **103**, 1603; and Ref. 6.

6.   H. M. L. Davies and S. J. Hedley, *Chem. Soc. Rev.*, 2007, **36**, 1109.

7.   Portions of this work have been published in preliminary form: H. Quast and J. W. Stawitz, *Tetrahedron Lett.*, 1976, **17**, 3803.

8.   D. T. Witiak, H. J. Lee, H. D. Goldman, and B. S. Zwilling, *J. Med. Chem.*, 1978, **21**, 1194.

9.   W. von der Saal, R. Reinhardt, H.-M. Seidenspinner, J. Stawitz, and H. Quast, *Liebigs Ann. Chem.*, 1994, 569.

10.  K.-H. Scholz, W. Hartmann, and H.-G. Heine, *Ger. Offen.* (1978), DE 2713431 (A1) 1978-09-28.

11.  J. L. Gagnon and W. W. Zajac, Jr., *Synth. Commun.*, 1996, **26**, 837.

12.  H. Nimmesgern, E. Schaumann, and G. Adiwidjaja, *Heterocycles*, 2012, **84**, 945.

13.  See, for example: W. B. Wright, Jr., H. J. Brabander, and R. A. Hardy, Jr., *J. Med. Chem.*, 1966, **9**, 858; R. A. Schnettler, R. C. Dage, and J. M. Grisar, *J. Med. Chem.*, 1982, **25**, 1477; S. Cortes, Z. K. Liao, D. Watson, and H. Kohn, *J. Med. Chem.*, 1985, **28**, 601; M. W. Moon, C. G. Chidester, R. F. Heier, J. K. Morris, R. J. Collins, R. R. Russell, J. W. Francis, G. P. Sage, V. H. Sethy, *J. Med. Chem.* 1991, **34**, 2314; E. M. Naylor, E. R. Parmee, V. J. Colandrea, L. Perkins, L. Brockunier, M. R. Candelore, M. A. Cascieri, L. F. Colwell, Jr., L. Deng, W. P. Feeney, M. J. Forrest, G. J. Hom, D. E. MacIntyre, C. D. Strader, L. Tota, P.-R. Wang, M. J. Wyvratt, M. H. Fisher, and A. E. Weber, *Bioorg. Med. Chem. Lett.*, 1999, **9**, 755; H. S. Lozanova and G. N. Vassilev, *Bulgar. Chem. Ind.*, 2004, **75**, 24.

14.  F. H. Jung, *Eur. Pat. Appl.* (1981), EP 0031708 (A2) 1981-07-08; F. Jung, C. Delvare, D. Boucherot, A. Hamon, N. Ackerley, and M. J. Betts, *J. Med. Chem.*, 1991, **34**, 1110; X. Zhou, *PCT Int. Appl.* (2007), WO 2007085357 (A1) 2007-08-02; S. Chowdhury, N. Dales, J. Fonarev, J. Fu, D. Hou, Q. Jia, V. Kodumuru, N. Pokrovskaia, S. Sun, and Z. Zhang, *PCT Int. Appl.* (2009), WO 2009103739 (A1) 2009-08-27; C. J. Woolf and B. P. Bean, *PCT Int. Appl.* (2011), WO 2011006073 (A1) 2011-01-13.

15.  G. E. Hilbert, *J. Am. Chem. Soc.*, 1932, **54**, 3413.

16. G. Steffan and G. O. Schenck, *Chem. Ber.*, 1967, **100**, 3961; G. Steffan, *Chem. Ber.*, 1968, **101**, 3688; K.-H. Scholz, J. Hinz, H.-G. Heine, and W. Hartmann, *Liebigs Ann. Chem.*, 1981, 248.

17. W. von E. Doering and W. R. Roth, *Tetrahedron*, 1963, **19**, 715; and references cited therein.

18. B. Eistert, M. Regitz, G. Heck, and H. Schwall, in *Methoden der Organischen Chemie (Houben-Weyl-Mueller), 4th ed.*, vol. 10/4, Thieme, Stuttgart, Germany, 1968, p. 552 and 538.

19. F. Arndt, *Org. Synth., Coll. Vol.,* 1943, **2**, 165. See also J. A. Moore and D. E. Reed, *Org. Synth., Coll. Vol.*, 1973, **5**, 351.

20. R. G. Salomon and J. K. Kochi, *J. Am. Chem. Soc.*, 1973, **95**, 3300.

21. For reviews on propellanes, see: D. Ginsburg, *Acc. Chem. Res.*, 1969, **2**, 121; D. Ginsburg, *Top. Curr. Chem.*, 1987, **137**, 1.

22. J. Meinwald, S. S. Labana, and M. S. Chadha, *J. Am. Chem. Soc.*, 1963, **85**, 582; M. Hagen and U. Luening, *Chem. Ber./Recueil*, 1997, **130**, 231; F. Loeffler, M. Hagen, and U. Luening, *Synlett*, 1999, 1826; R. K. Das, M. Sarkar, S. M. Wahidur Rahaman, H. Doucet, and J. K. Bera, *Eur. J. Inorg. Chem.*, 2012, 1680.

23. W. Kirmse, *Angew. Chem. Int. Ed.*, 2003, **42**, 1088.

24. D. E. McGreer and N. W. K. Chiu, *Can. J. Chem.*, 1968, **46**, 2217; P. H. Mazzocchi and H. J. Tamburin, *J. Org. Chem.*, 1973, **38**, 2221; J. J. Gajewski, R. J. Weber, R. Braun, M. L. Manion, and B. Hymen, *J. Am. Chem. Soc.*, 1977, **99**, 816.

25. N. R. Easton, D. R. Cassady, and R. D. Dillard, *J. Org. Chem.*, 1964, **29**, 1851; S. K. Chiu, M. Dube, L. Keifer, S. Szilagyi, and J. W. Timberlake, *J. Org. Chem.*, 1978, **43**, 61.

26. For vicinal cyclopropane coupling constants in bicyclo[3.1.0]hexanes, see: W. G. Dauben and W. T. Wipke, *J. Org. Chem.*, 1967, **32**, 2976.

27. For vicinal coupling constants in *cis*-1,2-cyclopropanediamines, see Ref. 9.

28. H. A. Bates, N. Condulis, and N. L. Stein, *J. Org. Chem.*, 1986, **51**, 2228.

29. A. Jonczyk and M. Mąkosza, *Rocz. Chem.*, 1975, **49**, 1203; N.-C. Wang, K.-E. Teo, and H. J. Anderson, *Can. J. Chem.*, 1977, **55**, 4112; E. Santaniello, C. Farachi, and F. Ponti, *Synthesis*, **1979**, 617.

30. H. Quast and W. von der Saal, *Chem. Ber.*, 1984, **117**, 1591; W. von der Saal and H. Quast, *J. Org. Chem.*, 1995, **60**, 4024; W. von der Saal and H. Quast, *J. Org. Chem.*, 1996, **61**, 4920; W. von der Saal, R. Reinhardt, J. Stawitz, and H. Quast, *Eur. J. Org. Chem.*, **1998**, 1645.

31. D. Misiti, M. Santaniello, and G. Zappia, *Synth. Commun.*, 1992, **22**, 883.

32. I. Isaka, K. Kubo, M. Takashima, and M. Murakami, *Yakugaku Zasshi*, 1968, **88**, 1062.