

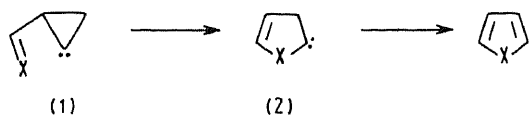
Substituted Pyrroles by Carbene-Carbene Rearrangements^{†,1}J. Chem. Research (S),
1983, 100-101†

UDO H. BRINKER* and MICHAEL BOXBERGER

Abteilung für Chemie der Ruhr-Universität Bochum, D-4630 Bochum, Federal Republic of Germany

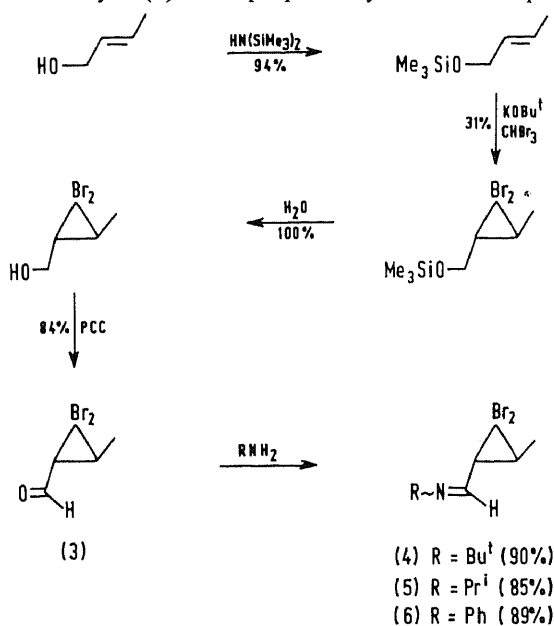
We find that reaction of six *gem*-dibromocyclopropanimines with methyl-lithium at temperatures between 0 and 25 °C leads to specifically substituted pyrroles.⁶

The report of the preparation of a pyrrole by a carbene-carbene rearrangement by Arct and Skattebøl² earlier this year prompts us to communicate the results of our efforts directed towards the application and extension of carbene-carbene rearrangements with 1,3-carbon migration of the type (1)→(2) (X = CH₂, CHR).³ While this type of rearrangement has often been utilized for the synthesis of carbocyclic five-membered rings, its application to the construction of the corresponding heterocyclic systems is unknown.

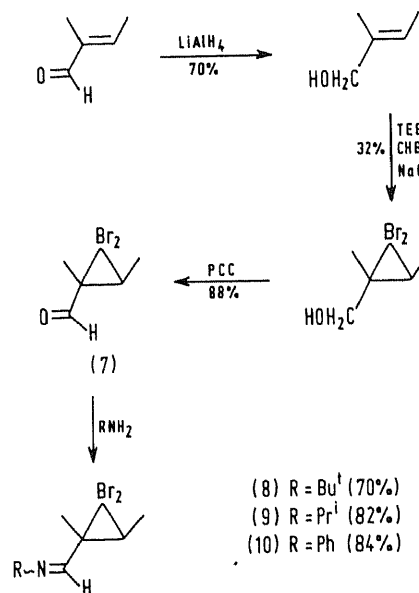


Compared with the vinylcyclopropane-cyclopentene rearrangement⁴ which requires temperatures generally above 300 °C, the vinylcyclopropylidene-cyclopent-3-en-1-ylidene rearrangement (1)→(2) (X = CH₂) proceeds below 0 °C. The conversion of cyclopropanimines into 2-pyrrolines with the addition of acid catalysts generally takes place at temperatures above 110 °C.⁵ The corresponding rearrangement involving carbenes (1)→(2) (X = NR), however, is unknown.

Initial efforts were made to synthesize the necessary 2,2-dibromocyclopropanimines by dibromocarbene addition to the corresponding substituted 1-azabuta-1,3-dienes.⁷ However, while 6,6-dimethyl-5-azahepta-2,4-diene could be prepared from crotonaldehyde and *t*-butylamine in 76% yield, the subsequent dibromocarbene addition (CHBr₃, NaOH, TEBA) gave only minimal amounts of (4).¹⁰ An alternative strategy was therefore adopted in which dibromocarbene adducts would be made by the condensation of substituted 2,2-dibromocyclopropanecarbaldehydes with primary amines. In this way 2,2-dibromo-3-methylcyclopropanecarbaldehyde (3)¹⁰ was prepared by a reaction sequence



starting from crotyl alcohol. The reaction of (3) with *t*-butyl-, isopropyl-, and phenyl-amine gave the corresponding imines (4), (5), and (6).¹⁰ Likewise, beginning with 2-methylbut-2-enal¹¹ the synthesis of dimethyl-substituted cyclopropanimines (8), (9), and (10)¹⁰ was accomplished *via* cyclopropanecarbaldehyde (7).^{10,12}



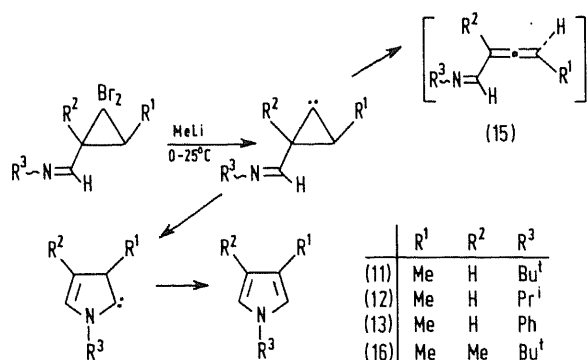
If an ethereal solution of the *t*-butyl 2,2-dibromo-3-methylcyclopropanimine (4) was added to an ethereal solution of methyl-lithium¹⁴ (*inverse* addition)^{10,15} 3-methyl-1-*t*-butylpyrrole (11)^{2,10} was formed in 17% yield.^{17,19-22} At lower temperatures (-20 °C), in addition to the pyrrole (11), two isomeric 2-bromo-3-methylcyclopropanimines (14)¹⁰ were found; (14) were the only compounds formed at -78 °C [ratio 1:1, (v.p.c. analysis)]. The iminoallene (15; R¹ = Me, R² = H, R³ = Bu^t), the product expected from the cyclopropylidene-allene rearrangement²³ of the intermediate cyclopropylidene (or corresponding carbenoid), has so far not been detected in the reaction mixture by i.r. spectroscopy. Pyrroles (12) and (13)¹⁰ were formed from the imines (5) and (6) in 7 and 1% yields^{19b} respectively.

Compared with the reaction conditions used for (4), (5), and (6), longer reaction times (4-16 h) and somewhat higher temperatures had to be used in order to decompose the imines (8), (9), and (10). This might be attributed to the steric influence of the additional methyl group at C-1. The yields of the pyrroles (16), (17), and (18)¹⁰ from the imines (8), (9), and (10) were 4, 6, and 3% respectively.^{17,19b,21} Additional products were formed which remained unidentified.

The generation of the iminocyclopropylidenes from the corresponding dibromocyclopropanimines (4)-(6) and (8)-(10) with methyl-lithium requires markedly higher temperatures compared to those at which *gem*-dibromovinylcyclopropanes decompose to vinylcyclopropylidenes (-78 °C). An intramolecular stabilization of the intermediate organolithium compounds with the nitrogen of the C-N π-bond might be responsible for this. The substitution patterns found in the six pyrroles are in accord with a mechanism by which the corresponding iminocyclopropylidenes undergo a carbene-carbene rearrangement to 2-azacyclopent-3-en-1-ylidenes which give pyrroles by subsequent 1,2-hydrogen migration.

*To receive any correspondence.

†This is a Short Paper as defined in the Instructions for Authors [J. Chem. Research (S), 1983, Issue 1, p. iv]; there is therefore no corresponding material in J. Chem. Research (M).



Our results extend the range of known carbene-carbene rearrangements with 1,3-carbon migration which were previously restricted to carbocyclic systems and suggest a further application for the synthesis of heterocyclic compounds.

This work was financially supported by the Deutsche Forschungsgemeinschaft and the Zentrale Forschungsfond der Ruhr-Universität Bochum (Titel 61).

Paper: E/169/82

Received: 7th October 1982

References and notes:

¹Part XIII in the series 'Carbene Rearrangements.' Part XII, M. Fukushima, M. Jones, Jr., and U. H. Brinker, *Tetrahedron Lett.*, 1982, 3211.

²J. Arct and L. Skattebøl, *Tetrahedron Lett.*, 1982, 113.

³(a) L. Skattebøl, *Tetrahedron*, 1967, **23**, 1107. For reviews, see (b) W. M. Jones and U. H. Brinker, in 'Pericyclic Reactions' eds. A. P. Marchand and R. E. Lehr, Academic Press, New York, 1977, vol. 1, pp. 159 ff; (c) R. A. Moss and M. Jones, Jr., in 'Reactive Intermediates', eds. M. Jones, Jr. and R. A. Moss, Wiley, New York, 1981, vol. 2, pp. 113 ff; for a recent application see (d) U. H. Brinker and I. Fleischhauer, *Tetrahedron*, 1981, **37**, 4495.

⁴(a) E. Vogel, *Angew. Chem.*, 1960, **72**, 4; (b) G. C. Overberger and A. E. Borchert, *J. Am. Chem. Soc.*, 1960, **82**, 1007; (c) E. M. Mil'vitskaya, A. V. Tarakanova, and A. F. Platé, *Russ. Chem. Rev.*, 1976, **45**, 469.

⁵(a) J. B. Cloke, *J. Am. Chem. Soc.*, 1929, **51**, 1147; (b) R. V. Stevens, *Acc. Chem. Res.*, 1977, **10**, 393.

⁶(a) R. A. Jones and G. P. Bean, 'The Chemistry of Pyrroles', Academic Press, New York, 1977; (b) J. M. Patterson, *Synthesis*, 1976, 281; (c) A. Gossauer, 'Die Chemie der Pyrrole', Springer Verlag, Berlin, 1974.

⁷To our knowledge, dichloro- or dibromo-carbene additions to 1- or 2-azabuta-1,3-dienes have not yet been reported. While dichlorocarbene generated by the phase-transfer method attacks the C—C π -bond of 2,6-dimethyl-4-azahepta-2,4-diene⁸ to give ca. 80% of the adduct, the corresponding dibromo-carbene adduct could not be purified.⁹

⁸R. H. Hasek, E. U. Elam, and J. C. Martin, *J. Org. Chem.*, 1961, **26**, 1822.

⁹W. Steinert, Diplomarbeit, Bochum, May 1981; U. H. Brinker and W. Steinert, unpublished results.

¹⁰(a) Experimental details are as follows. 2,2-Dibromo-3-methylcyclopropanecarbaldehyde (3) (1 g, 4.0 mmol) [2,2-dibromo-1,3-dimethylcyclopropanecarbaldehyde (7) (3.9 mmol)] and t-butylamine (0.3 g, 4 mmol) were covered with NaOH pellets. After 16 h at -20°C [5 h at 0°C , followed by 16 h at -20°C] cyclopropanimine (4) [(8)] was extracted with ether and distilled (b.p. $58-60^\circ\text{C}$ at 0.05 Torr [$58-62^\circ\text{C}$ at 0.05 Torr]). Cyclopropanimines (5) and (6) [(9) and (10)] were prepared similarly. Reaction with methyl-lithium. Cyclopropanimine (4) (1 g, 3.4 mmol) [(3.2 mmol) (8)] was added dropwise at 0°C [25°C] to an ethereal solution (1.45 M) of methyl-lithium.¹⁴ The reaction mixture was stirred at 0°C [25°C] for 1 h [4–16 h]. After hydrolysis with water and extraction with ether, the pyrrole (11) [(16)] was isolated by preparative t.l.c. [CCl_4 ; Kieselgel 60 F (Merck)]. Pyrroles (12) and (13) [(17) and (18)] were prepared similarly. In addition (18) had to be purified by v.p.c. [20% Carbowax (50 cm \times 6 mm O.D.), 160°C , 60 ml N_2 per min]. (b) ¹H N.m.r. data of key compounds [(A) (80 MHz, CDCl_3);

(B) (60 MHz, CCl_4); δ (p.p.m. from Me_4Si , J in Hz)]; (3) (B), 1.4 (3 H, d, J 5, CH_3), 1.85–2.5 (2 H, m, cyclopropyl), 9.2 (1 H, d, J 5, CHO); (7) (B), 1.2 (3 H, d, J 5, CH_3), 1.25 (3 H, s, CH_3), 2.2 (1 H, q, J 6.5, cyclopropyl), 9.1 (1 H, s, CHO); (4) (A) 1.05 (9 H, s, Bu^t), 1.25 (3 H, d, J 5.5, CH_3), 1.55–2.1 (2 H, m, cyclopropyl), 7.1 (1 H, d, J 6, $\text{CH}=\text{N}$); (5) (A) 1.05 (3 H, d, J 6, Pr^t), 1.1 (3 H, d, J 6, Pr^t), 1.2 (3 H, d, J 6, CH_3), 1.55–2.0 (2 H, m, cyclopropyl), 3.25 (1 H, sept., J 6, Pr^t), 7.2 (1 H, d, J 6, $\text{CH}=\text{N}$); (6) (B) 1.35 (3 H, d, CH_3), 1.65–2.4 (2 H, m, cyclopropyl), 6.65–7.5 (6 H, m, Ph + $\text{CH}=\text{N}$); (8) (B) 1.1–1.5 (15 H, m, CH_3), 2.2 (1 H, q, J 6.5, cyclopropyl), 7.45 (1 H, s, $\text{CH}=\text{N}$); (9) (B) 0.9–1.45 (12 H, m, CH_3), 2.0 (1 H, q, J 6.5, cyclopropyl), 3.35 (1 H, sept., J 6, Pr^t), 7.4 (1 H, s, $\text{CH}=\text{N}$); (10) (A) 1.25 (3 H, d, J 6, CH_3), 1.45 (3 H, s, CH_3), 2.2 (1 H, q, J 6, cyclopropyl), 6.9–7.45 (5 H, m, Ph), 7.65 (1 H, s, $\text{CH}=\text{N}$); (11) (A) 1.55 (9 H, s, Bu^t), 2.15 (3 H, s, CH_3), 6.0 (t, J 2.5, H-4), 6.65 (br s, H-2), 6.75 (t, J 2.5, H-5); (12) (A) 1.45 (6 H, d, J 6.5, Pr^t), 2.15 (3 H, s, CH_3), 4.15 (1 H, sept., J 6.5, Pr^t), 5.95 (t, J 2.5, H-4), 6.5 (br s, H-2), 6.65 (t, J 2.5, H-5); (13) (A) 2.2 (3 H, s, CH_3), 6.2 (t, J 2.5, H-4), 6.9 (br s, H-2), 7.05 (t, J 2.5, H-5), 7.35–7.45 (5 H, m, Ph); (16) (A) 1.5 (9 H, s, Bu^t), 2.05 (6 H, s, CH_3), 6.55 (s, H-2, H-5); (17) (A) 1.4 (6 H, d, J 6.5, Pr^t), 2.05 (6 H, s, CH_3), 4.15 (1 H, sept., J 6.5, Pr^t), 6.45 (s, H-2, H-5); (18) (A) 2.1 (6 H, s, CH_3), 6.85 (s, H-2, H-5), 7.35 (5 H, s, Ph); (14) (ratio, 1 : 1) (A) 0.85–1.3 (24 H, m, Bu^t , CH_3), 1.3–1.7 (4 H, cyclopropyl), 2.75–2.95 (1 H, m, CHBr), 3.05–3.25 (1 H, m, CHBr), 7.15 (1 H, d, J 6, $\text{CH}=\text{N}$), 7.2 (1 H, d, J 6, $\text{CH}=\text{N}$). $\nu_{\text{C}=\text{N}}$ (cm^{-1}) ($\text{CCl}_4/\text{CDCl}_3$): (4), 1660; (5), 1650; (6), 1640; (8), 1645; (9), 1650; (10), 1635; (14), 1655*; $\nu_{\text{C}=\text{O}}/\nu_{\text{C}=\text{N}}$ (cm^{-1}): (3), 1705*; (7), 1705*; (11), 1370; (12), 1325; (13), 1350; (16), 1350; (17), 1360; (18), 1380. m/e (70 eV; %): (3), 244, 242, 240 (11, 9, 4, M^+); (4), 299, 297, 295 (0.2, 0.5, 0.3, M^+); (5), 281, 283 (0.2, 0.3, M^+); (6), 319, 317, 315 (2, 6, 2, M^+); (7), 256 (0.2, M^+); (8), 313, 311, 309 (0.5, 0.8, 0.4, M^+); (9), 284, 282, 280 (0.4, 0.9, 0.4, M^+); (10), 252, 250 (15, 17, M^+ – Br); (11), 137 (42, M^+); (12), 123 (45, M^+); (13), 157 (81, M^+); (14), 219, 217 (3, 3, M^+); (16), 151 (10, M^+); (17), 137 (55, M^+); (18), 171 (80, M^+).

¹¹M. B. Green and W. J. Hickinbottom, *J. Chem. Soc.*, 1957, 3262.

¹²It has been found that in the reaction of (*E*)-2-methylbut-2-en-1-ol with dibromocarbene (from CHBr_3 , NaOH, TEBA) the *E*- and *Z*-isomers of the corresponding dibromocyclopropanes are formed in the ratio 1 : 1.¹³

¹³K. Kleveland, L. Skattebøl, and L. K. Sydnes, *Acta Chem. Scand., Ser. B.*, 1977, **31**, 463.

¹⁴Methyl-lithium was made from lithium and bromomethane.

¹⁵Compared with the normal addition of methyl-lithium to the substrate the yield of (11) almost doubled when the inverse addition method¹⁶ was applied.

¹⁶L. K. Sydnes and L. Skattebøl, *Acta Chem. Scand., Ser. B.*, 1978, **32**, 547.

¹⁷The orientation of the methyl group at C-3 (*cis* or *trans*) in the imines (4)–(6) and (8)–(10) could not be determined.¹² For a vinylcyclopropylidene the decisive influence of a *cis*-orientated methyl group at C-3 has been shown.¹⁸ Thus, from the reaction of *cis*-2,2-dibromo-3-methyl-1-vinylcyclopropane with methyl-lithium at 0°C , no methyl-cyclopentadienes result. Owing to steric hindrance in the transition state of the vinyl-cyclopropylidene, the cyclopentenylidene cannot be formed and the competing cyclopropylidene–allene rearrangement takes place. Therefore, only those iminocyclopropylidenes are expected to undergo a carbene-carbene rearrangement in which the imino group at C-1 and the methyl group at C-3 are held in a *trans*-position.

¹⁸U. H. Brinker and K. Gomann, unpublished results.

¹⁹(a) (11) proved to be unstable under the reaction conditions: only 60% of it could be recovered; (b) the yields of all pyrroles were determined by v.p.c. with (11) as external standard.

²⁰For (11), formed from the reaction of 2,2-dibromo-1-methylcyclopropane-*t*-butylimine and methyl-lithium, no absolute yield has been reported.²

²¹The organolithium intermediates are probably stabilized by intramolecular co-ordination of the lithium atom with the nitrogen of the imino group. Intermolecular condensation reactions¹⁶ of these species and/or their reactions with the imines (4)–(6) and (8)–(10) might be responsible for the considerable amounts of viscous residues found.

²²The presence of molar amounts of 12-crown-4 or *NNN'*-tetramethylethylenediamine did not increase the yield of (11).
²³W. Kirmse, 'Carbene Chemistry', Academic Press, New York, 2nd edn., 1971, pp. 462 ff.