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Rearrangement of fused tetracyclic heterocycles induced by alkyl halides and formation of a new type of 'proton sponge'

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ABSTRACT

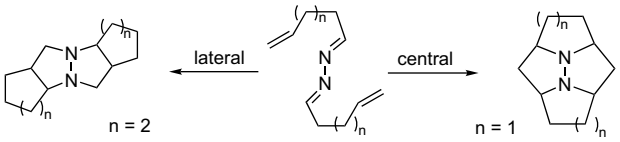
Intramolecular criss-cross cycloaddition of 3-substituted symmetrical homoallenyl azines **2** by heating in xylene lead to interesting fused heterocyclic systems consisting of four five-membered rings with two nitrogen atoms in the skeleton **3**. These compounds **3** were found to be sensitive to attack by alkyl halides. Their presence, depending on the reaction conditions, resulted in a new type of rearrangement leading to compounds **4** and **5**, respectively. With an excess of alkyl halide and in the presence of $NaBH_3CN$ a new structure **6** with signs of the molecule corresponding a 'proton sponge' moiety was created. The scope of the rearrangement and reaction products structure was investigated.

1. Introduction

In the past we have reported some of our achievements in the applications of allene derivatives, especially those starting with homoallenyl aldehyde **1** and its derivatives. Thus, we have recently published a paper on an easy and interesting transformation of substituted homoallenyl oximes to stable nitrones,[1] and their application either in further transformation with exploitation of the nitrone moiety, or other transformations on the cyclic skeleton.[2]

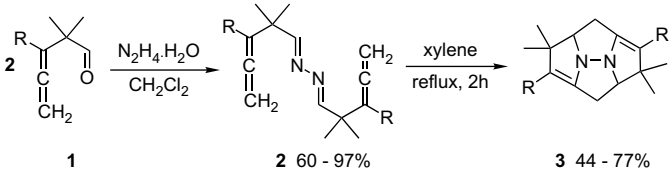
A rather rich chapter deals with application of symmetrical homoallenyl azines **2** in criss-cross cycloaddition reaction.

Criss-cross cycloadditions represent a way to the formation of fused heterocyclic compounds in a 'one pot' arrangement, but most of them described in the literature are intermolecular processes leading to two fused five-membered rings.[3,4] Only few are intramolecular reactions. Thus, Suschitzky and Marthur[5] performed intramolecular reactions on benzalazines and naphthalene azines, respectively, having in the *ortho* position to the azine, allyloxy and propargyloxy groups, respectively. In the case where the other *ortho* position to the alkenyloxy group was blocked in order to prevent Claisen rearrangement, the reaction led to formation of cycloadducts with a lateral connection of rings. Another type of intramolecular reaction we found on homoallenyl azines.[6] During this reaction a completely new type of compound was formed, having centrally fused four five-membered heterocyclic rings. Apparently, the distance between the azine group and the multiple bonds determines whether a 'lateral' or 'central' type cyclization is preferred (Scheme 1).



Scheme 1.

One of our papers deals with the central type of intramolecular criss-cross cycloadditions and the influence of substitution upon the reaction.[7] The prepared symmetrical azines **2** with a substitution in position 3 are stable compounds and were able to undergo intramolecular criss-cross cycloaddition reactions. Intramolecular criss-cross cycloadditions consist of two successive 1,3-dipolar cycloadditions in the same molecule.[8] By this reaction two new stereogenic centres are formed. These compounds exist as racemic mixtures of enantiomers with configuration (*R*,*R*) and (*S*,*S*). Generally, we can observe that an electron donating substituent in the 3-position increases the reactivity towards criss-cross cycloaddition. As soon as a bulky substitution appears, steric hindrance leads to decreasing reactivity in the shown direction. The thermally initiated criss-cross reaction is a source of interesting fused heterocyclic compounds consisting of four fused five-membered heterocycles **3** (Scheme 2).[7]



Scheme 2.

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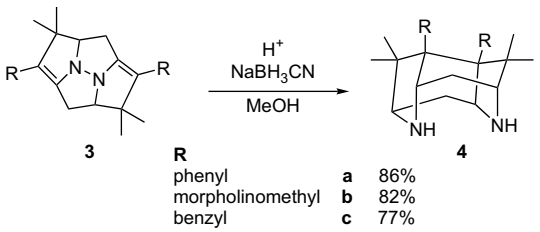
When investigating their chemical properties, we found very interesting behaviour of these structures when treated with acid in the presence of reducing agent $NaBH_3CN$ (Scheme 3).



Scheme 3. Rearrangement of cycloadduct **3** in acidic medium and in the presence of $NaBH_3CN$.

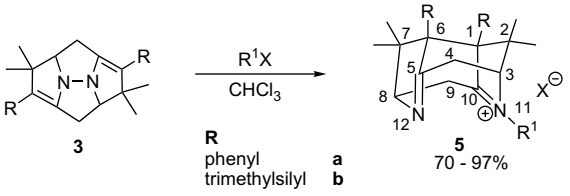
They underwent a completely new reaction, breaking the N–N bond in the molecule and rearranging to a caged compound **4**, having two five-membered and two six-membered rings.[9]

In this paper, we describe our attempts to extend our knowledge of the behaviour of these 'basket like' cyclic structures **3**. Some of the molecules that were formed during the rearrangement represent a new structure with signs of the molecule corresponding to a 'proton sponge'.

There is rather rich list of papers related to such structures.[10] Anyway, as mostly cited structure is 1,8-bis(dimethylamino)naphthalene and its derivatives. This compound was firstly reported by Alder and co-workers[11] with all its manifestations. Since then, many other families of proton sponges have been created and new are appearing.[12] We believe that also our structure fit among them. All are characterized with a high basicity and this property is according up to date knowledge produced by a strong crowding of unshared electron pairs on nitrogen atoms kept in close proximity by the molecular structure. Formation of intramolecular hydrogen bond between the nitrogen atoms –N···H···N– in protonated form brings relief of the steric strain upon protonation. Although most of the described structures contain an aromatic ring, our structure has got a polycyclic aliphatic skeleton where the whole structure is rigid. A close structure of a proton sponge is described and studied by Estrada and Simón-Manso[13] and another was described and studied by Alder.[14]

2. Results and discussion

Our experiments were started by preparation of homoallenyl aldehyde **1**. Compounds **1** and **2** for the proposed research were prepared accordance with the procedure in our previous paper.[7] Heating of azines **2** in xylene under inert atmosphere led to criss-cross cycloaddition and formation of compounds **3** (Scheme 2). It is generally accepted that the reaction proceeds via 1,3-dipole formed by the attack of one of the nitrogen atoms to C_{sp} atom of the allenyl skeleton present. A successive attack of the dipole on the second allenyl group then leads to formation of criss-cross adduct consisting of four five-membered rings. During the reaction two stereogenic centres are formed. A proton catalyzed rearrangement had already been observed. Now we tried to investigate whether



Scheme 4. Rearrangement of cycloadducts **3** to products **5** induced by alkyl halides.

Table 1
Reaction times and yields of compounds **5** found during the rearrangement of **3** (Scheme 4)

Educt	R^1	Reagent	Product	Yield [%]	Reaction time [h]
3a	–Ph	Methyl iodide	**5a**	82	2
3a	–Ph	Benzyl iodide	**5b**	88	2
3a	–Ph	Chlorallyl iodide	**5c**	86	4
3a	–Ph	Allyl bromide	**5d**	97	24
3b	$–SiMe_3$	Methyl iodide	**5e**	81	2
3b	$–SiMe_3$	Benzyl iodide	**5f**	70	2
3b	$–SiMe_3$	Benzyl chloride	**5g**	90	48
3b	$–SiMe_3$	Chlorallyl iodide	**5h**	90	4
3b	$–SiMe_3$	Allyl bromide	**5i**	97	24

also other electrophiles may act as catalysts in a similar reaction. Therefore several alkyl halides were tested (Scheme 4).

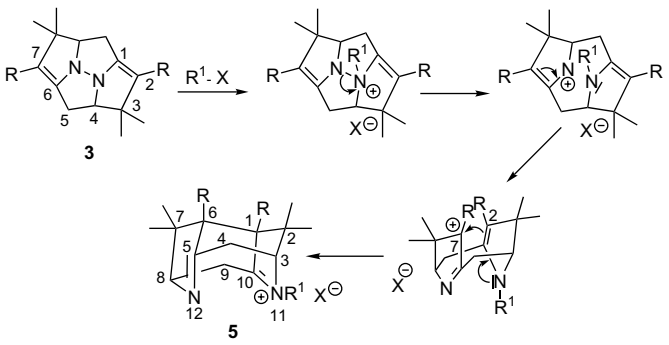
The reaction was carried out in dry chloroform. This reaction proceeds very well when methyl iodide or benzyl iodide is used as reagent because of their rather high reactivity with nucleophilic nitrogen atom. Reaction was monitored by thin layer chromatography. After the reaction, we found rearranged products **5** as a stable quaternary iminium salts (Scheme 4).

For full identification and description of the new structure, 1D and 2D NMR spectroscopy was used. Although NMR identification supported our expectations concerning the structure, the elemental analyses did not fit. Problems arose with identification of the contra anions, especially when the starting compounds were iodides. Finally, after X-ray analysis it was found that instead of pure iodides a mixture of iodides and triiodides is formed. But we have not succeeded with their separation. We have not faced such problems in the case of chlorides and bromides. On the other hand, the reaction times of reactions with alkyl chlorides and bromides had to be prolonged due to their lower reactivity.

In Table 1, the tested alkyl halides are presented with the reaction times and yields of products **5**. The influence of substitution R upon the reactivity was more pronounced in case of the reaction with less reactive benzyl chloride. Probably conjugation of phenyl group (R=Ph) with the nitrogen atom in compound **3a** diminish nucleophilicity of the nitrogen atom entering as nucleophile into reaction with benzyl chloride and causes the fact that benzyl chloride does not react with compound **3a** (R=Ph) at all. But when R is trimethylsilyl, compound **3b** afforded with the same reagent a high yield of the product **5b**, however, within longer reaction time.

Mechanism of the reaction can be explained by the following Scheme 5. Nucleophilic nitrogen atom attacks the carbon atom next to halogen in alkyl halide.

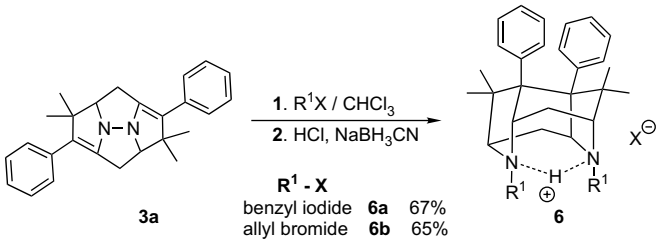
Formation of ammonium nitrogen leads to polarization of the bond N–N in the molecule **3**, which leads to its fission under



Scheme 5. Proposed mechanism of the rearrangement of compound **3** to compound **5**.

formation of enamine. After a flip of the molecule, the enamine then reacts in β-position as a nucleophile with the formed positively charged carbon atom in the second part of the molecule, which gets to a close distance and a new bond C–C is created. This way a new molecule **5** is formed.

When the reaction was carried out with compound **3a** with an excess of benzyl iodide and with reducing agent $NaBH_3CN$ (again in chloroform), compound **6a** was identified as a product. In this case, probably the primary formed iminium salt is reduced, then alkylated and product as ammonium salt isolated. In case of compound **6b** (R^1=allyl), the procedure of its preparation had to be carried out stepwise. The monoalkylated intermediate was immediately reduced under acid catalysis with $NaBH_3CN$ and after treatment of NaOH and isolation the crude product was alkylated in the excess of allyl bromide and afforded compound **6b** (Scheme 6).



Scheme 6. Product of compound **3a** rearrangement in the presence of benzyl iodide excess and $NaBH_3CN$.

This way we have succeeded to prepare compounds with a structure characteristic for proton sponges. The first indications of such behaviour we have already observed at compounds **4** with similar skeleton after rearrangement by acid. When we tried to transfer the prepared ammonium salts to a free base we were faced problems with not easy procedure. We succeeded only with concentrated NaOH (c=1 mol/L) under heating. The structure of **6** is rigid and contains tertiary amines in a suitable neighbourhood (distance N–N over space according with X-ray analysis is 2.607 Å) and the bound proton is situated between both nucleophilic nitrogen atoms. We tried to estimate the basicity of compound **6** by NMR experiment. In the case of D_2O addition, full exchange of the ammonium proton in compound **6a** was observed and after addition of a strong base tetramethylquanidine (pK_{BH+}=23.3) the protonation of our compound **6a** completely disappeared. The transprotonation experiment on **6a** and the known proton sponge 1,8-bis(dimethylamino)naphthalene (pK_{BH+}=18.2–18.7 in CH_3CN)[15,16] was carried out by ^{1}H NMR spectroscopy. The NMR experiments using different ratio mixtures of **6a** and proton sponge showed that our compound **6a** pK_{BH+} ranges between 20 and 21.

The described method in this paper, when compared with rearrangement of compound **3** carried out under acid catalysis, enables preparation of proton sponges with different substitution on both nitrogen atoms.

3. Conclusions

In continuation of chemical properties' investigation of the criss-cross cycloaddition products **3** we found that products consisting of four five-membered rings undergo rearrangement not only in the presence of proton and $NaBH_3CN$ to cyclic secondary amines **4** with skeleton formed by two six and two five-membered rings. But similar transformation of compounds **3** is initiated by various reactive alkyl halides. The reaction proceeds smoothly at room temperature, leads to a new structure **5** and proceeds in high yield and purity. The products are *N*-substituted iminium salts **5**. In an excess of alkyl halide and a presence of reducing agent $NaBH_3CN$, new type of tertiary amines **6** with a rigid skeleton, which is supposed to work as proton sponge, were created.

4. Experimental section

4.1. General remarks

Melting points were measured on a Boetius Rapido PHMK 73/2106 (Wägetechnik) instrument with TM-1300K thermometer. TLC was carried out on Silica gel 60 F_{254} (Merck), detection was made by Fluotest Universal (Quazlampen, Hanau) or in I_2 vapors. NMR spectra were recorded on Bruker Avance DRX 300 in chloroform. $CHCl_3$ was used as an internal standard for ^{1}H NMR spectra (7.27 ppm) and $CDCl_3$ was used as an internal standard for ^{13}C NMR spectra (triplet 77.23 ppm). The measured ^{13}C and ^{1}H NMR spectra were correlated with those obtained by simulation (Advanced Chemistry Development, Inc., Toronto, Canada). FTIR spectra were measured at GENESIS ATI (Unicam) in KBr pallets (wave numbers in cm^{-1}), mass spectra (EI, 30 eV) were determined on FISONS TRIO 1000. Elemental analyses were performed with a FlashEA 1112, MS at Thermo Finnigan and HRMS at Waters-Micromas, Q-Tof Micro (ESSI positive). The yields of the products are calculated to the described compounds, but they can be only informative in respect to the changeable composition of the anion in some cases. For basicity of compound **6a** estimation, commercially available (Aldrich) 'proton sponge' was used.

4.2. X-ray crystallographic study

A perspective view of the molecular structures of **5b** and **6a** is shown in Figures 1 and 2, respectively. Organic cations and triiodide anions in both structures are situated on coplanar planes.

The asymmetric unit of **5b** consists of one organic cation (containing two six-membered rings and two five-membered rings in the central molecular skeleton and four methyl, two phenyl and one benzyl exoskeleton groups) and one (triiodide) anion each with

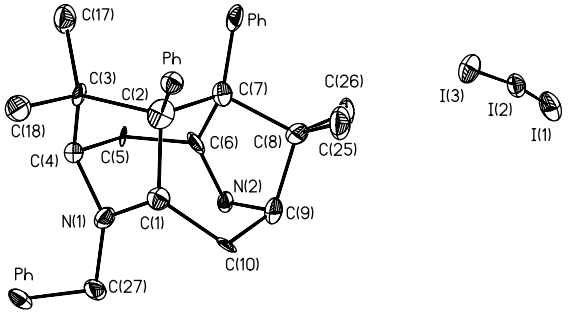


Figure 1. Molecular structure of **5b**. The thermal ellipsoids were drawn at the 50% probability level and hydrogen atoms and phenyl groups were omitted for clarity.

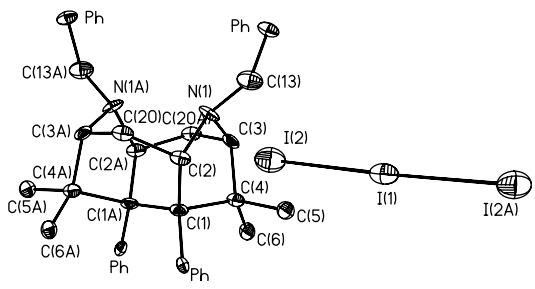


Figure 2. Molecular structure of **6a**. The thermal ellipsoids were drawn at the 50% probability level and hydrogen atoms and phenyl groups were omitted for clarity.

Table 2
Selected bond lengths and angles of **5b** and **6a**

Bond length [Å]	5b	6a	Ref. 1
N(1)–N(1)$^{\#1}$	2.702	2.607	1.497
N(1)–C(2)*	1.287	1.508	1.430
N(1)–C(3)*	1.475	1.518	1.502
I(1)–I(2)*,$^{\#2}$	2.885	2.919	—
C(1)–C(2)*	1.515	1.557	1.329
C(3)–C(4)*	1.515	1.520	1.563
Angle [°]	**5b**	**6a**	**Ref. 1**
C(2)–N(1)–C(3)*	106.79	106.44	103.76
C(1)–C(2)–N(1)*	115.41	107.19	113.71
C(4)–C(3)–N(1)*	103.89	104.33	102.83
C(2)–C(1)–C(4)*	98.04	97.87	108.53
C(3)–C(4)–C(1)*	99.45	100.52	100.59
I(2)–I(1)–I(2)$^{\#2}$	175.67	178.17	—

*Average symmetry: #1 $-x+1, y, -z+1/2$; #2 $-x, y, -z+1/2$.

a point symmetry C_s. The point-group symmetry of molecule **6a** consists of one organic cation (containing two six-membered rings and two five-membered rings in the central molecular skeleton and four methyl, two phenyl and two benzyl exoskeleton groups) and one (triiodide) anion is C_2.

Related structures for bond lengths and angle data comparison are presented in papers.[6,7] Tables 2 and 3 then show their comparison with **5b** and **6a**. As concerns of the five-membered rings' geometry in **5b** and **6a** they have shown only small variation in the bond lengths and angles, which can be easily explained by changes in exoskeleton groups. However, the comparison of **5b** and **6a** with the two referred structures can be approximate only, because the bonding system in the central cage is a quite different.

The highest difference can be found in the N–N distance, which is in our present structures 2.607 Å and 2.702 Å (non-bonding distance), but in referred structures 1.477 Å and 1.497 Å as a typical single bond. This difference is slightly shown also around nitrogen atoms (N–C bonds and all angles around). The rest of the central molecular cage is quite similar and small difference can be explained by measurement errors. The geometry of triiodide anion is in good accordance with related structures in papers[17,18] and ranges in length near 2.911 Å and in angle near 177.7°. The crystal structures of **5b** and **6a** have not shown any H-bridges or other shorter interactions.

Diffraction data were collected on a KUMA KM-4 four-circle single crystal diffractometer (λ=0.71069 Å) equipped with CCD camera using ω-scan mode and corrected for Lorentz and polarization effects. The temperature during data collection was 120(2) K. The intensity data were corrected for Lorentz and polarization effects. All structures were solved by direct methods and refined by full-matrix least-squares methods using anisotropic thermal parameters for the non-hydrogen atoms. The hydrogen atoms were inserted from geometry and refined as riding. The software packages used were Xcalibur CCD system for the data collection/reduction,[19] and Shelxtl for the structure solution, refinement and drawing preparation.[20] In figures the thermal ellipsoids were drawn at the 50% probability level and hydrogen atoms were omitted for clarity. Selected bond lengths and angles are listed in Table 2. Details of the data collection and structure refinement are listed in Table 3.

CCDC 671034 and 671035 contain the supplementary crystallographic data for this paper.

These data can be obtained free of charge at www.ccdc.cam.ac.uk/conts/retrieving.html [or from the Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, UK; fax: +44 1223 336 033; e-mail: deposit@ccdc.cam.ac.uk].

Table 3
Crystal data and structure refinement

Structure	5b	6a
Empirical formula	$C_{33}H_{35}I_3N_2$	$C_{40}H_{44}I_3N_2$
Formula weight	840.33	933.47
Temperature (K)	120	120
Wavelength (Å)	0.71069	0.71069
Crystal system	Triclinic	Monoclinic
Space group	*P*-1	*C*2/*c*
Unit cell dimensions	a=10.792(2) Å b=10.848(2) Å c=13.548(3) Å α=83.28(3)° β=82.34(3)° γ=74.60(3)°	a=16.915(3) Å b=18.231(4) Å c=11.471(2) Å α=90° β=96.03(3)° γ=90°
Volume (Å^3)	1509.9(5)	3517.7(12)
Z	2	4
Calculated density (Mg m^{-3})	1.848	1.763
Absorption coefficient (mm^{-1})	3.130	2.697
F(000)	812	1828
Crystal size (mm)	0.10×0.07×0.05	0.30×0.07×0.05
θ range for data collection	3.03°–28.71°	3.30°–28.74°
Limiting indices	$-14\le h\le 14$, $-14\le k\le 14$, $-14\le l\le 18$	$-22\le h\le 22$, $-18\le k\le 24$, $-15\le l\le 13$
Reflections collected/unique	18,117/7022 [R_{int}=0.1453]	16,429/4201 [R_{int}=0.0807]
Completeness to 2θ=25.00 (%)	99.6	99.8
Absorption correction	Psi-scan	Psi-scan
Max. and min. transmission	1.000 and 0.8669	1.000 and 0.5680
Refinement method	Full-matrix least-squares on F^2	Full-matrix least-squares on F^2
Data/restrains/parameters	7022/0/332	4201/0/206
Goodness-of-fit on F^2	0.807	0.867
Final *R* indices [$I>2\sigma(I)$]	*R*1=0.0607, *wR*2=0.1120	*R*1=0.0394, *wR*2=0.0687
R indices (all data)	*R*1=0.1725, *wR*2=0.1560	*R*1=0.1135, *wR*2=0.0854
Largest diff. peak and hole (e Å^{-3})	2.603 and −2.572	1.559 and −0.713

4.3. General procedure for the rearrangement of criss-cross cycloadducts 3

Cycloadduct **3** was dissolved in dry chloroform under argon atmosphere and then an alkyl halide was added. The reaction mixture was stirred at ambient temperature till the reaction completed. Then, solvent was removed under vacuum and the solid residue was washed with diethyl ether. Compounds were purified by column chromatography (diethylether, methanol).

*4.3.1. 11-N-Methyl-1,6-diphenyl-2,2,7,7-tetramethyl-11,12-diazatetracyclo[4.4.0.1^{3,10}.1^{5,8}]dodeca-5(12),10-diene-11-ium (**5a**)*[†]

Reaction mixture: cycloadduct **3a** (100 mg, 0.27 mmol) in dry chloroform (5 mL), methyl iodide (38.5 mg, 0.27 mmol). Yield 170 mg (82%). Yellow solid, mp 182–183 °C. ^{1}H NMR ($CDCl_3$): δ=0.22 (s, 3H, CH_3), 0.55 (s, 3H, CH_3), 1.06 (s, 3H, CH_3), 1.13 (s, 3H, CH_3), 3.61 (dd, J=12.9, 4.5 Hz, 1H, CH_2), 3.64 (d, J=12.9 Hz, 1H, CH_2), 3.88 (d, J=13.2 Hz, 1H, CH_2), 4.08 (dd, J=13.2, 5.2 Hz, 1H, CH_2), 4.17

[†] The procedure indicates that the described ammonium cation may be accompanied by a mixture of anions in dependence on the used halogenides.

(s, 3H, CH_3), 4.47 (d, J=5.2 Hz, 1H, CH), 4.91 (d, J=4.5 Hz, 1H, CH), 7.4–7.8 (m, 10H, Har.) ppm. ^{13}C NMR ($CDCl_3$): δ=18.9, 19.5, 25.9, 27.2, 36.4, 38.6, 42.4, 46.7, 49.1, 83.7, 83.8, 128.9, 129.2, 129.9, 135.6, 137.9, 179.7, 199.4 ppm. IR (KBr): ν_{max} 704, 748, 1182, 1396, 1468, 1576, 1624, 2937, 2972, 3498 cm^{-1}. For $C_{27}H_{31}N_2^+$: calcd M^+ 383.2487. HRMS: found M^+ 383.2488.

4.3.2. 11-N-Benzyl-1,6-diphenyl-2,2,7,7-tetramethyl-11,12-diazatetracyclo[4.4.0.1^{3,10}.1^{5,8}]dodeca-5(12),10-diene-11-ium (**5b**)†

Reaction mixture: cycloadduct **3a** (100 mg, 0.27 mmol) in dry chloroform (5 mL), benzyl iodide (59.2 mg, 0.27 mmol). Yield 200 mg (88%). Yellow solid, mp 112–118 °C. ^{1}H NMR ($CDCl_3$): δ=0.27 (s, 3H, CH_3), 0.40 (s, 3H, CH_3), 1.01 (s, 3H, CH_3), 1.12 (s, 3H, CH_3), 3.51 (d, J=2.6 Hz, 2H, CH_2), 3.87 (d, J=2.6 Hz, 1H, CH), 4.10 (d, J=13.2 Hz, 1H, CH_2), 4.42 (dd, J=13.2, 5.1 Hz, 1H, CH_2), 4.55 (d, J=5.1 Hz, 1H, CH), 4.90 (d, J=15.2 Hz, 1H, CH_2), 6.74 (d, J=15.2 Hz, 1H, CH_2), 7.4–7.7 (m, 15H, Har.) ppm. ^{13}C NMR ($CDCl_3$): δ=18.6, 19.3, 25.7, 26.7, 35.9, 39.8, 45.9, 49.0, 56.9, 79.2, 83.9, 128.8, 129.0, 129.7, 129.8, 130.1, 130.1, 130.9, 135.1, 137.8, 179.8, 200.1 ppm. IR (KBr): ν_{max} 705, 752, 1182, 1454, 1600, 2925, 3426 cm^{-1}. For $C_{33}H_{35}N_2^+$: calcd M^+ 459.2800. HRMS: found M^+ 459.2798.

4.3.3. 11-N-(3-Chloroallyl)-1,6-diphenyl-2,2,7,7-tetramethyl-11,12-diazatetracyclo[4.4.0.1^{3,10}.1^{5,8}]dodeca-5(12),10-diene-11-ium (**5c**)†

Reaction mixture: cycloadduct **3a** (100 mg, 0.27 mmol) in dry chloroform (5 mL), 3-chloroallyl iodide (54.9 mg, 0.27 mmol). Yield 190 mg (86%). Light yellow solid, mp 158–162 °C. ^{1}H NMR ($CDCl_3$): δ=0.23 (s, 3H, CH_3), 0.49 (s, 3H, CH_3), 1.06 (s, 3H, CH_3), 1.12 (s, 3H, CH_3), 3.62 (d, J=12.9 Hz, H, CH_2), 3.70 (dd, J=12.9, 4.6 Hz, 1H, CH_2), 3.96 (d, J=13.2 Hz, 1H, CH_2), 4.27 (dd, J=13.2, 5.3 Hz, 1H, CH_2), 4.52 (d, J=5.0 Hz, 1H, CH), 4.6–4.7 (m, 2H, CH_2), 5.91 (dd, J=14.9, 6.9 Hz, 1H, CH), 6.3–6.4 (m, 1H, CH), 7.18 (d, J=13.2 Hz, 1H, CH), 7.3–7.7 (m, 10H, Har.) ppm. ^{13}C NMR ($CDCl_3$): δ=18.7, 19.3, 25.7, 26.8, 36.3, 39.0, 46.3, 48.9, 52.8, 79.7, 83.0, 122.2, 128.8, 129.1, 130.0, 135.1, 137.6, 178.8 ppm. IR (KBr): ν_{max} 707, 750, 1182, 1450, 1490, 1606, 2919, 2970, 3027, 3420 cm^{-1}. For $C_{29}H_{32}N_2Cl^+$: calcd M^+ 443.2254. HRMS: found M^+ 443.2255.

4.3.4. 11-N-Allyl-1,6-diphenyl-2,2,7,7-tetramethyl-11,12-diazatetracyclo[4.4.0.1^{3,10}.1^{5,8}]dodeca-5(12),10-diene-11-ium bromide (**5d**)

Reaction mixture: cycloadduct **3a** (50 mg, 0.14 mmol) in dry chloroform (3 mL), allyl bromide (16.4 mg, 0.14 mmol). Yield 64 mg (97%). Light yellow solid, mp 210–215 °C. ^{1}H NMR ($CDCl_3$): δ=0.23 (s, 3H, CH_3), 0.51 (s, 3H, CH_3), 1.07 (s, 3H, CH_3), 1.12 (s, 3H, CH_3), 3.59 (d, J=3.8 Hz, 2H, CH_2), 3.97 (d, J=13.3 Hz, 1H, CH_2), 4.28 (dd, J=13.3, 5.3 Hz, 1H, CH_2), 4.49 (d, J=5.3 Hz, 1H, CH), 4.55 (dd, J=14.8, 9.0 Hz, 1H, CH_2), 4.59 (d, J=4.3 Hz, 1H, CH), 4.60 (d, J=9.9 Hz, 1H, CH), 5.78 (d, J=17.0 Hz, 1H, CH), 5.90 (dd, J=14.8, 5.3 Hz, 1H, CH_2), 7.2–7.4 (m, 10H, Har.) ppm. ^{13}C NMR ($CDCl_3$): δ=18.7, 19.3, 25.8, 26.9, 36.0, 38.7, 46.1, 48.9, 55.9, 79.7, 83.1, 125.5, 127.8, 128.8, 129.7, 135.4, 137.8, 179.2 ppm. IR (KBr): ν_{max} 705, 750, 1180, 1450, 1496, 1604, 1639, 2917, 2969, 3421 cm^{-1}. MS (EI, 30 eV): m/z (%) 409 (M^+, 8), 226 (77), 225 (100), 210 (74), 184 (93), 170 (25), 128 (28), 83 (38). $C_{29}H_{33}BrN_2$ (484.49): calcd C 71.16, H 6.80, N 5.72. Found: C 71.23, H 6.76, N 5.70.

4.3.5. 11-N-Methyl-1,6-di(trimethylsilyl)-2,2,7,7-tetramethyl-11,12-diazatetracyclo[4.4.0.1^{3,10}.1^{5,8}]dodeca-5(12),10-diene-11-ium (**5e**)†

Reaction mixture: cycloadduct **3b** (100 mg, 0.28 mmol) in dry chloroform (5 mL), methyl iodide (39.4 mg, 0.28 mmol). Yield 170 mg (81%). Yellow solid, mp 198–200 °C. ^{1}H NMR ($CDCl_3$): δ=0.04 (s, 9H, CH_3), 0.15 (s, 9H, CH_3), 1.12 (s, 3H, CH_3), 1.15 (s, 3H, CH_3), 1.18 (s, 3H, CH_3), 1.43 (s, 3H, CH_3), 2.5–2.6 (m, 2H, CH_2), 3.1–3.2 (m, 2H, CH_2), 3.71 (s, 3H, CH_3), 4.21 (dd, J=10.4, 2.6 Hz, 1H, CH), 5.12 (dd, J=10.4, 2.0 Hz, 1H, CH) ppm (signals overlapped). ^{13}C NMR ($CDCl_3$): δ=0.1, 0.5, 24.9, 25.2, 25.6, 27.2, 29.6, 29.9, 51.0, 55.5, 55.8, 75.7, 84.6, 124.9, 141.0, 149.9, 151.4 ppm. IR (KBr): ν_{max} 763, 849, 1026, 1095, 1252, 1444, 1639, 2960, 3415, 3491 cm^{-1}. MS (EI, 30 eV): m/z (%) 360 (30), 345 (10), 180 (50), 142 (22), 108 (8), 73 (100), 59 (5). For $C_{21}H_{39}N_2Si_2^+$: calcd M^+ 375.2652. HRMS: found M^+ 375.2653.

4.3.6. 11-N-Benzyl-1,6-di(trimethylsilyl)-2,2,7,7-tetramethyl-11,12-diazatetracyclo[4.4.0.1^{3,10}.1^{5,8}]dodeca-5(12),10-diene-11-ium (**5f**)†

Reaction mixture: cycloadduct **3b** (100 mg, 0.28 mmol) in dry chloroform (5 mL), benzyl iodide (60 mg, 0.28 mmol). Yield 160 mg (70%). Yellow solid, mp 169–171 °C. ^{1}H NMR ($CDCl_3$): δ=0.16 (s, 9H, CH_3), 0.29 (s, 9H, CH_3), 1.21 (s, 3H, CH_3), 1.22 (s, 3H, CH_3), 1.29 (s, 3H, CH_3), 1.32 (s, 3H, CH_3), 2.61 (dd, J=15.5, 1.6 Hz, 1H, CH_2), 2.69 (dd, J=16.8, 2.8 Hz, 1H, CH_2), 2.94 (dd, J=15.5, 10.6 Hz, 1H, CH_2), 3.20 (dd, J=16.8, 10.2 Hz, 1H, CH_2), 4.22 (dd, J=10.2, 2.8 Hz, 1H, CH), 4.86 (dd, J=10.6, 1.6 Hz, 1H, CH), 5.00 (d, J=13.5 Hz, 1H, CH_2), 5.59 (d, J=13.5 Hz, 1H, CH_2), 7.4–7.5 (m, 3H, Har.), 7.6–7.7 (m, 2H, Har.) ppm. ^{13}C NMR ($CDCl_3$): δ=0.3, 0.8, 25.5, 25.7, 26.2, 27.3, 29.2, 30.5, 56.1, 56.2, 66.0, 76.6, 81.7, 126.3, 127.6, 129.5, 131.3, 132.5, 144.0, 148.8, 150.5 ppm. IR (KBr): ν_{max} 760, 843, 1034, 1249, 1367, 1456, 1641, 2897, 2967, 3433 cm^{-1}. MS (EI, 30 eV): m/z (%) 360 (33), 345 (14), 180 (58), 166 (15), 108 (13), 91 (100), 73 (95), 65 (18). For $C_{27}H_{43}N_2Si_2^+$: calcd M^+ 451.2965. HRMS found M^+ 451.2965.

4.3.7. 11-N-Benzyl-1,6-di(trimethylsilyl)-2,2,7,7-tetramethyl-11,12-diazatetracyclo[4.4.0.1^{3,10}.1^{5,8}]dodeca-5(12),10-diene-11-ium chloride (**5g**)

Reaction mixture: cycloadduct **3b** (100 mg, 0.28 mmol) in dry chloroform (5 mL), benzyl chloride (35 mg, 0.28 mmol). Yield 128 mg (90%). White solid, mp 113–115 °C. ^{1}H NMR ($CDCl_3$): δ=0.11 (s, 9H, CH_3), 0.23 (s, 9H, CH_3), 1.18 (s, 6H, CH_3), 1.22 (s, 3H, CH_3), 1.23 (s, 3H, CH_3), 2.55 (dd, J=15.5, 1.6 Hz, 1H, CH_2), 2.62 (dd, J=16.5, 2.6 Hz, 1H, CH_2), 2.88 (dd, J=15.5, 10.6 Hz, 1H, CH_2), 3.15 (dd, J=16.5, 10.2 Hz, 1H, CH_2), 4.15 (dd, J=10.2, 2.6 Hz, 1H, CH), 4.81 (dd, J=10.6, 1.6 Hz, 1H, CH), 4.92 (d, J=13.5 Hz, 1H, CH_2), 5.64 (d, J=13.5 Hz, 1H, CH_2), 7.3–7.4 (m, 3H, Har.), 7.6–7.7 (m, 2H, Har.) ppm. ^{13}C NMR ($CDCl_3$): δ=0.4, 0.9, 25.6, 25.8, 26.6, 27.5, 29.0, 30.5, 55.9, 56.0, 66.3, 76.7, 81.8, 125.1, 128.9, 129.0, 130.7, 132.9, 143.1, 149.5, 151.4 ppm. IR (KBr): ν_{max} 702, 756, 840, 1033, 1251, 1367, 1456, 1639, 2898, 2962, 3423 cm^{-1}. MS (EI, 30 eV): m/z (%) 451 (M^+, 1), 360 (15), 180 (45), 166 (7), 126 (42), 108 (5), 91 (100), 83 (26), 73 (24), 65 (16). For $C_{27}H_{43}ClN_2Si_2$ (487.27): calcd C 66.55, H 8.89, N 5.75, Found C 66.45, H 8.37, N 5.50.

4.3.8. 11-N-(3-Chloroallyl)-1,6-di(trimethylsilyl)-2,2,7,7-tetramethyl-11,12-diazatetracyclo[4.4.0.1^{3,10}.1^{5,8}]dodeca-5(12),10-diene-11-ium (**5h**)†

Reaction mixture: cycloadduct **3b** (100 mg, 0.28 mmol) in dry chloroform (5 mL), 3-chloroallyl iodide (56.1 mg, 0.28 mmol). Yield 200 mg (90%). Light yellow solid, mp 172–174 °C. ^{1}H NMR ($CDCl_3$): δ=0.17 (s, 9H, CH_3), 0.28 (s, 9H, CH_3), 1.24 (s, 3H, CH_3), 1.27 (s, 3H, CH_3), 1.29 (s, 3H, CH_3), 1.52 (s, 3H, CH_3), 2.6–2.7 (m, 2H, CH_2), 3.04 (dd, J=15.7, 10.7 Hz, 1H, CH_2), 3.46 (dd, J=16.8, 10.2 Hz, 1H, CH_2), 4.34 (dd, J=10.1, 2.5 Hz, 1H, CH), 4.41 (dd, J=14.0, 8.1 Hz, 1H, CH), 4.81 (dd, J=8.9, 2.0 Hz, 1H, CH), 5.29 (dd, J=13.9, 7.6 Hz, 1H, CH), 6.2–6.3 (m, 1H, CH), 7.14 (d, J=13.2 Hz, 1H, CH) ppm. ^{13}C NMR ($CDCl_3$): δ=0.2, 1.0, 25.8, 26.0, 26.3, 27.8, 30.0, 30.6, 56.2, 56.3, 61.4, 76.4, 81.7, 114.6, 116.5, 121.3, 131.8, 149.3, 151.0 ppm. IR (KBr): ν_{max} 761, 841, 1253, 1640, 2159, 2952, 3461 cm^{-1}. For $C_{23}H_{40}N_2Si_2Cl^+$ calcd M^+ 435.2419. HRMS found M^+ 435.2420.

4.3.9. 11-N-Allyl-1,6-di(trimethylsilyl)-2,2,7,7-tetramethyl-11,12-diazatetracyclo[4.4.0.1^{3,10}.1^{5,8}]dodeca-5(12),10-diene-11-ium bromide (**5i**)

Reaction mixture: cycloadduct **2b** (100 mg, 0.28 mmol) in dry chloroform (5 mL), allyl bromide (33.5 mg, 0.28 mmol). Yield

170 mg (97%). Light yellow solid, mp 201–202 °C. ^{1}H NMR ($CDCl_3$): δ=0.01 (s, 9H, CH_3), 0.02 (s, 9H, CH_3), 0.99 (s, 3H, CH_3), 1.02 (s, 3H, CH_3), 1.05 (s, 3H, CH_3), 1.27 (s, 3H, CH_3), 3.59 (d, J=14.2 Hz, 2H, CH_2), 2.75 (dd, J=15.8, 10.9 Hz, 1H, CH_2), 3.29 (dd, J=16.8, 10.2 Hz, 1H, CH_2), 3.90 (dd, J=13.7, 8.1 Hz, 1H, CH), 4.09 (dd, J=10.2, 2.6 Hz, 1H, CH), 4.66 (d, J=10.2 Hz, 1H, CH_2), 4.91 (dd, J=13.7, 6.1 Hz, 1H, CH), 5.43 (d, J=10.2 Hz, 1H, CH_2), 5.55 (d, J=16.8 Hz, 1H, CH) ppm. ^{13}C NMR ($CDCl_3$): δ=0.1, 0.3, 25.1, 25.3, 25.4, 27.0, 29.2, 29.8, 55.4, 55.5, 63.6, 75.8, 80.7, 124.9, 125.4, 127.3, 141.4, 149.5, 150.9 ppm. IR (KBr): ν_{max} 759, 841, 1009, 1252, 1639, 2951, 3382, 3463 cm^{-1}. MS (EI, 30 eV): m/z (%) 401 (M^+, 1), 360 (32), 345 (12), 180 (50), 166 (10), 108 (12), 73 (100), 41 (28). For $C_{23}H_{41}BrN_2Si_2$ (481.66): calcd C 57.35, H 8.58, N 5.82. Found C 57.30, H 8.56, N 5.63.

*4.3.10. 11,12-N,N′-Dibenzyl-1,6-diphenyl-2,2,7,7-tetramethyl-11,12-diazatetracyclo [4.4.0.1^{3,10}.1^{5,8}] dodecane-11-ium (**6a**)*[†]

Compound **3a** (0.15 g, 0.41 mmol) was dissolved in dry chloroform (10 mL) under argon and then benzyl iodide (0.18 g, 0.81 mmol) was added. The reaction mixture was stirred at ambient temperature till the reaction completed. Then, to the reaction mixture $NaBH_3CN$ (0.10 g, 1.63 mmol) and finally few drops of hydrochloric acid were added. After 2 h of stirring, the solvent was removed under vacuum and the solid residue was washed with water and extracted with dichloromethane. The solvent was evaporated and product was washed with diethyl ether.

Yield 253 mg (67%). White solid, mp 278–281 °C. ^{1}H NMR ($CDCl_3$): δ=0.60 (s, 6H, CH_3), 1.08 (s, 6H, CH_3), 2.29 (dd, J=15.7, 3.5 Hz, 2H, CH_2), 2.46 (dd, J=15.7, 3.8 Hz, 2H, CH_2), 3.47 (d, J=3.6 Hz, 2H, CH_2), 4.37 (dd, J=12.7, 3.1 Hz, 2H, CH), 4.50 (dd, J=12.7, 1.8 Hz, 2H, CH), 4.72 (br s, 2H, CH_2), 6.87 (d, J=7.8 Hz, 2H, Har), 7.13 (t, J=7.8 Hz, 2H, Har.), 7.3–7.5 (m, 16H, Har.), 12.53 (br s, 1H, NH) ppm. ^{13}C NMR ($CDCl_3$): δ=22.9, 28.0, 29.5, 50.0, 58.6, 58.2, 60.4, 70.0, 126.1, 127.9, 128.5, 129.1, 129.3, 129.6, 130.1, 132.4, 134.1, 139.0 ppm. IR (KBr): ν_{max} 700, 754, 1026, 1250, 1466, 1670, 2860, 2933, 2966, 3059, 3421 cm^{-1}. For $C_{40}H_{45}N_2^+$: calcd M^+ 553.3580. HRMS$^+$ found M^+ 553.3580.

*4.3.11. 11,12-N,N′-Diallyl-1,6-diphenyl-2,2,7,7-tetramethyl-11,12-diazatetracyclo [4.4.0.1^{3,10}.1^{5,8}] dodecane-11-ium bromide (**6b**)*

Compound **3a** (0.2 g, 0.54 mmol) was dissolved in dry chloroform (10 mL) and under argon allyl bromide (0.13 g, 1.09 mmol) was added. The reaction mixture was stirred at ambient temperature till the starting compound disappeared. Then to the reaction mixture $NaBH_3CN$ (0.14 g, 2.17 mmol) and finally few drops of hydrochloric acid were added. After stirring overnight, the solvent was under vacuum removed and the solid residue dissolved in diethyl ether and washed with 1 M NaOH. Organic layer was concentrated in vacuo and solid phase was dissolved in chloroform and stirred with another 2 equiv of allyl bromide. After overnight stirring, the solvent was evaporated and product was purified by column chromatography (CH_2Cl_2 with 1% of MeOH).

Yield 188 mg (65%). Light yellow solid, mp 254–256 °C. ^{1}H NMR ($CDCl_3$): δ=0.51 (s, 6H, CH_3), 1.09 (s, 6H, CH_3), 2.58 (dd, J=15.5, 3.6 Hz, 2H, CH_2), 2.79 (dd, J=15.5, 2.6 Hz, 2H, CH_2), 3.45 (br s, 2H, CH), 3.84 (dd, J=13.0, 7.6 Hz, 2H, CH_2), 4.11 (dd, J=13.0, 6.1 Hz, 2H, CH_2), 4.63 (br s, 2H, CH), 5.3–5.4 (m, 4H, CH_2), 6.1–6.2 (m, 2H, CH), 6.8–7.4 (m, 10H, Har.), 13.26 (br s, 1H, NH) ppm. ^{13}C NMR ($CDCl_3$): δ=22.9, 27.6, 29.0, 49.8, 58.6, 58.7, 67.7, 69.7, 122.2, 126.0, 127.7, 128.4, 129.1, 132.4, 139.2 ppm. IR (KBr): ν_{max} 714, 750, 1018, 1087, 1444, 1639, 2877, 2926, 2979, 3440 cm^{-1}. For $C_{32}H_{41}N_2^+$: calcd M^+ 453.3270. HRMS$^+$ found M^+ 453.3271.

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