Synthesis of 2,7-Methano-aza[10]annulene Derivatives

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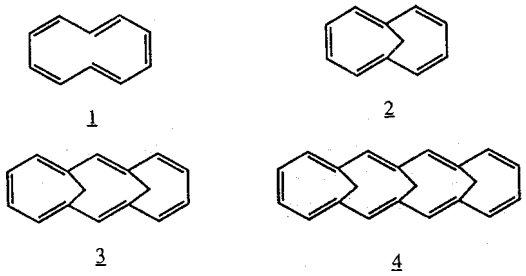
Electrocyclic ring-closure of 6-vinylcyclohepta-1,3,5-isocyanate has been carried out in the presence of triphenylphosphine to examine a catalyzing effect of the triphenylphosphine. The preparation of 10-(1-carboalkoxyalkyl)-2,7-methanoaza[10]annulenes by the electrocyclic ring-closure of ketenimine intermediates, which are formed by the reaction of triphenylalkylidenephosphorane and 6-vinylcyclo-hepta-1,3,5-isocyanate, is described. 10-Alkyl-2,7-methanoaza[10]anulenes were prepared by basic hydrolysis of the carboalkoxyaza[10]annulenes and decarboxylation of the acid intermediates. In the same manner, 10-(N-alkyl(or aryl))-2,7-methanoaza[10]annulenes were prepared from the reaction of the isocyanate and N-alkyl(or aryl)iminotriphenylphosphorane via electrocylic ring-closure of carbodiimide intermediate.

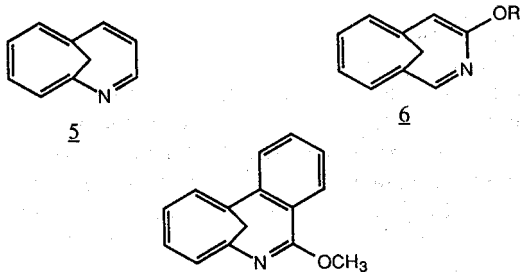
Introduction

The nonaromatic character of the [10]annulene (**1**) due to nonplanarity of the molecule can be demonstrated by study of a 10π-electron conjugated carbocyclic compound in which the steric problems associated with the [10]annulene are avoided. Vogel and his coworkers[2] have intensively investigated on bridged (4n+2)-annulenes in which bridges avoid the nonbonded steric repulsion between the two internal hydrogens in the carbocyclic structure of the [10]annulene.



1 2 3 4

In accordance with expectation, the bridged (4n+2)-annulenes (**2**, **3**, **4**) are sufficiently flattened out to allow delocalization of the π-electron system regarded as being aromatic. These pioneering studies on the bridged annulenes have also led to synthesis of novel bridged heterocycles such as 2,7-methanoaza[10]annulene (**5**),[3] 10-methoxy (or ethoxy) 3,8-methanoaza[10]annulene (**6**)[3,19,20] and 5-methoxy-7,12-methano-6-azabenz[10]annulene(**7**).[21]



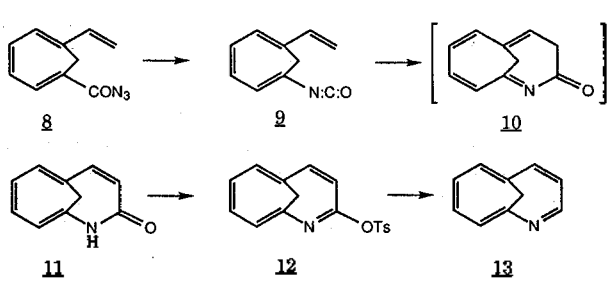
5 6

All the compounds exhibit ^{1}H NMR shifts characteristic of an aromatic-type ring current. The 2,7-methanoaza[10]annulene (**5**) has pK_a value of 3.20 (20 ℃) and thus its basicity is weaker than pyridine (pK_a=5.23) or quinoline (pK_a=4.94).

The synthesis and properties of the macrocyclic azaannulenes provided strong support for the aromaticity based on Hückel's predictions, and led to a vigorous, and continuing investigation in this area. In addition to this, the bridged aza (4n+2) annulenes and their derivatives have received special attention from the view point of aromaticity studies and modification of physiological and pharmacological activity in drugs containing such skeletons. The purpose of this study is to synthesize aza-[10]annulene derivatives and to evaluate their chemical behavior in comparison with their benzenoid analogues.

Results and Discussion

Intense current interest in electrocyclic ring-closure reactions has generated elegant synthetic routes to noble heterocycles, particulary those accessible by thermally allowed electron bond reorganization. Recent examples for the preparation of six-membered or fused ring heterocyclic compounds are synthesis of pyridone,[4] pyrimidone,[5] 2-pyrone,[6] and 2-oxazinone[7] *via* electrocyclic ring-closure of 1,3,5-hexatrienes in which one or more carbon atoms are replaced by heteroatoms. However, only one investigation on the 10π-electrocyclic ring-closure has been reported by Vogel and his coworkers[3,8] in a synthetic sequence for the preparation of bridged aza[10]annulene outlined in Scheme 1.



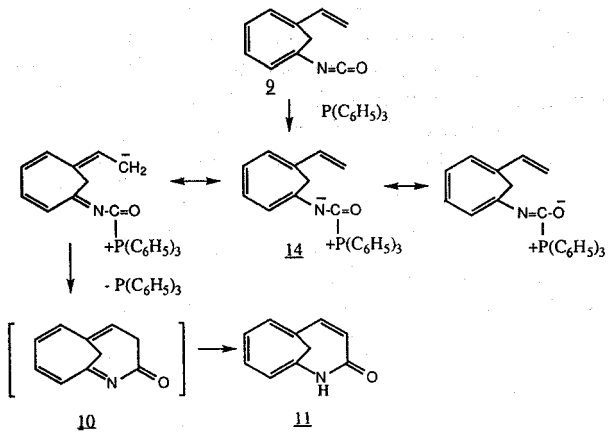
8 9 10 11 12 13

Scheme 1.

In this synthetic sequence, the high dilution approach in the formation of the lactam (**11**) would be an indispensable condition for favoring unimolecular cyclization rather than a polymerization pathway. Therefore, the cyclization reaction of the cyanate (**9**) carried out in diluted solution (0.0075 M) of the acylazide (**8**) and long reaction time (15-20 hrs) at 105 ℃ under an extremely anhydrous condition. Washburne[4c] and Overmann[4a] also employed the dilution technique for the electrocyclic ring-closure of 1,3-diene isocyanate to 2-pyridone.

This evidence clearly shows experimentally that the yield of the lactam (**11**) is drastically decreased at high concentaion of the reactant. The dilution technique, also gives many limitations for a large scale operation of this reaction sequence. The study on this concern led to the consideration of a catalyst with an expectation that the electrocyclic ring-closure of the isocyanate (**9**) would be facilitated by enhancing ionic character on π-electron system of the molecule.

The thermal ring-closure reaction of the isocyanate **9**, was conducted in the presence of triphenylphosphine (an equal mole of the acylazide) with one tenth of the solvent and much shorter reaction time employed to the previous method.[3] The desired lactam (**11**) was obtained in 70-75% yield with quantitative recovery of the triphenylphosphine. The result clearly shows that the triphenylphosphine facilitates the electrocyclic ring-closure of the isocyanate (**9**) with suppressing a polymerization and bimolecular reaction even at high concentration. The catalytic effect of the triphenylphosphine may have arisen due to enhancing the nucleophilic character of the terminal carbon atom of the vinyl group by forming the resonance stabilized ionic intermediate as outlined in Scheme 2. Apparently, this triphenylphosphine-catalyzed electrocyclic ring-closure would offer great merits for a large scale operation in the preparation of the lactam **11**.

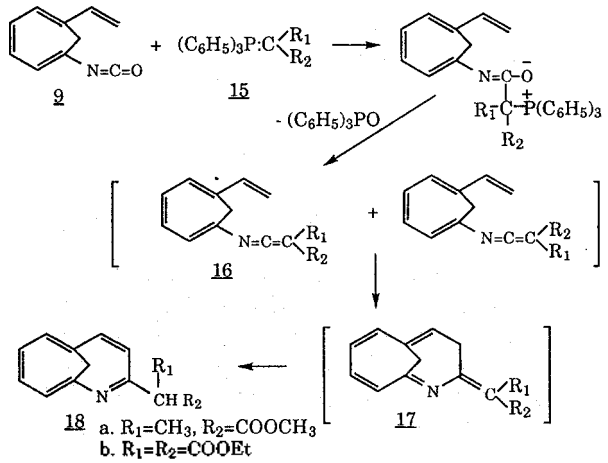


Scheme 2.

10-Methyl-2,7-methanoaza[10]annulene and 10-amino-2,7-methanoaza[10]-annulene were also prepared by a multi-step synthetic sequence.[8,9] These synthetic routes would appear limited mainly by the availability of the starting compounds and the low yield of the intermediates and products in each steps.

There have been several examples that isocyanates react with disubstituted phosphonium ylids or iminophosphoranes to form corresponding ketenimines and carbodiimides in a manner of a Wittig reaction.[10] These findings led to the consideration of the carbodiimide and ketenimine as an intermediate to introduce a substituent at C-10 of the aza[10]annulene ring skeleton since the heterocumulenes, which would be prepared from the noble isocyanate (**9**) in this manner, would expect to undergo an electrocyclic ring-closure as in the thermolysis of the isocyanate (**9**).

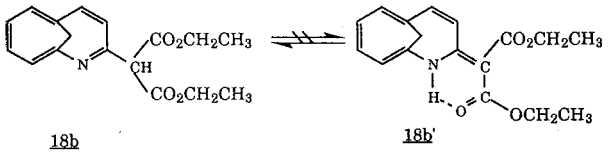
As shown in Scheme 3, 10-alkylsubstituted aza[10]annulenes were conveniently synthesized in good yield.



Scheme 3.

The intermediate ketenimine (**16**) could not be isolated because the electrocyclic ring-closure presumably occurs very rapidly under the reaction condition employed for the Wittig type reaction of the isocyanate (**9**) and the phosphorane (**15**). Apparently, the rapid electrocyclic ring-closure of the resulting ketenimine (**16**) may have arisen due to the fact that the central carbon atom of the ketenimine is a very reactive electrophile. The ^{1}H NMR spectrum shows that the product (**18**) is a mixture of two isomers because the resonances of the one of two bridged methylene protons, methyl protons, methine proton, and the proton attached to C-9 of the ring are clearly duplicated. This duplication would be represented by two diastereomers of four possible isomers (two diastereomers and two enantiomers) because of the presence of two chiral centers in the molecule. Ratio of the two isomers was about 3 : 2 based on integration of the duplicated peaks. Seperation of these two diastereomers by a column chromatography was successful only with seperation of the major diastereomer while the other diastereomer was always contaminated by the major isomer.

In the same manner, when dicarboethoxymethylenetriphenylphosphorane (**15b**) was reacted with the isocyanate for 5 hours, 10-dicarboethoxymethyl-2,7-methano-aza[10]-annulene (**18b**) was obtained in 61% yield. By analogy to 2-substituted quinolines[11] when the substitutent bears electron withdrawing groups, tautomeric possibilities such as **18b-18b'** must be considered in assigning structure to the resulting product.

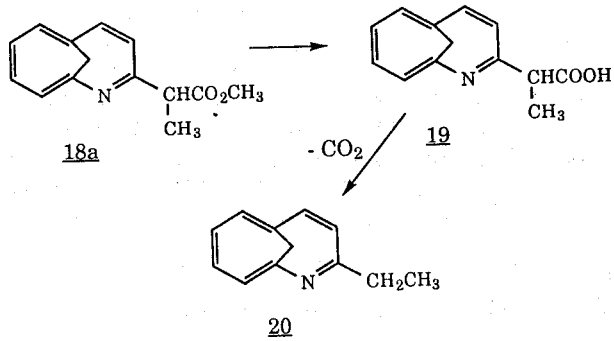


18b 18b'

Infrared and ^{1}H NMR spectra indicate that the compound (**18b**) exists as the structure **18b**. The infrared spectra of the compound (**18b**) in neat film does not show absorption in the 3500-3200 cm^{-1} region which covers N-H stretching vibrations.

The ^{1}H NMR spectrum of the compound (**18b**) in dueterio acetonitrile shows a sharp singlet signal attributable to the methine proton of the substituent at 5.10 ppm, two doublets at −0.20 and 0.78 ppm due to two bridged-methylene protons, and a complex set of signals from 6.75-7.75 ppm. These data clearly indicate that the malonic ester group was not tautomerized into the exocyclic double-bonded structure **18 b'**.

It has been known that 2-pyridylacetic and 2-quinoylacetic acid are easily decarboxylated to corresponding 2-alkyl substituted pyridine and quinoline.[11a,12] These findings have offered a noble way to transform the compound 18 into 10-alkyl-2,7-methanoaza[10]annulenes (**20**).

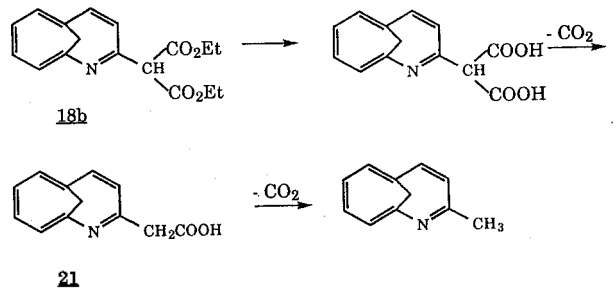


18a 19 20

When 10-(1-carbomethoxyethyl)-2,7-methanoaza[10]annulene (**18a**) was treated with methanolic potassium hydroxide, the expected acid (**19**) could not be isolated even under a low temperature operation. The product isolated was a mixture of the acid and decarboxylated product, 10-ethyl-2,7-methanoaza[10]annulene (**20**). On standing the mixture at room or low temperature, the acid was completely decarboxylated to 10-ethyl-2,7-methanoaza[10]annulene (**20**). The pure ethyl compound (**20**) was also obtained by distilling the work-up mixture.

In the ^{1}H NMR spectrum of the ethyl compound (**20**), ring protons are very much similar to that of the methyl compound[8,9] except for resonances of the substitutents. Instead of the expected quartet and triplet, the ethyl protons in the compound 20 shows a complex splitting pattern at 3.03 and 1.45 ppm that must be classified as an ABX3 spectrum. The non-equivalence of the methylene protons would be explained by its conformations represented as Newman projection. The two methylene protons are always located in different chemical environment because of the presence of the chiral aza[10]annulene group.[13]

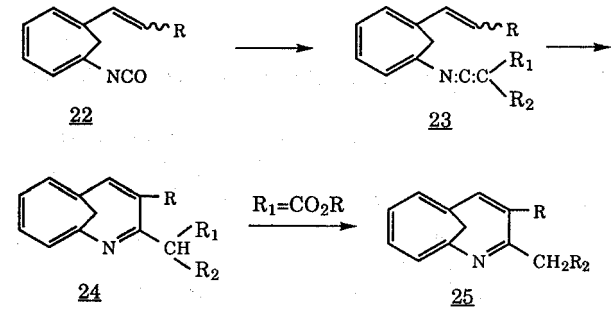
In the same manner, when 10-dicarbethoxymethyl-2,7-methanoaza[10]-annulene (**18b**) was conducted to hydrolysis, only the mono acid derivative (**21**) was isolated by a careful work-up of the reaction mixture. However, attempts to purify the 2,7-methanoaza[10]annulen-10-yl acetic acid (**21**) were fruitless because of easy decarboxylation. Only an acceptable ^{1}H NMR spectrum could obtain in DMSO-d_6 solution before the acid (**21**) would undergo spontaneous decomposition (decarboxylation).



18b 21

It is noteworthy that this synthetic route is also applicable to synthesize 9,10-dialkyl substituted-2,7-methanoaza[10]annulene (**24** and **25**) from the isocyanate **22** as outlined in Scheme 4.

The electrocyclic ring-closure of the substituted ketenimine (**23**), which could be formed by the reaction of the substituted vinyl isocyanate (**22**) and disubstituted methylenetriphenylphosphorane, has been proved to be operable while the isocyanate (**22**) itself does not undergo this cyclization to form a substituted lactam.[14]



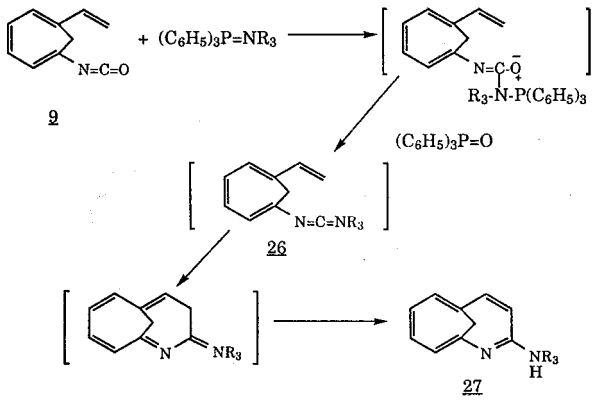
22 23 24 25

Scheme 4.

As described above, 10-[N-alkyl(or aryl)-amino]methanoaza[10]annulene (**27**) was also prepared by the electrocyclic ring-closure of carbodiimide intermediate (**26**) which can be generated by a reaction of the isocyanate (**9**) and N-substituted iminotriphenylphosphorane outlined in Scheme 5.

When the isocyanate (**9**) was reacted with N-phenyliminotriphenyl-phosphorane at 100 ℃ for 3hrs, 10-(N-phenylamino)-2,7-methanoaza[10]annulene (**27a**) was obtained in 66 % yield as a yellow crystal.

In the above manner, 10-(N-benzylamino)-2,7-methanoaza [10]-annulene (**27b**) was also obtained in 89% yield. The ^{1}H NMR spectrum of the compound (**27b**), indicates that the two protons are not equivalent as shown in the ethyl group of the compund **20**.



a. $R_3=C_6H_5$; b. $R_3=CH_2C_6H_5$; c. $R_3=SiMe_3$

Scheme 5.

Experimental

General. Unless otherwise indicated, all the reactions except for aqueous reactions were run in anhydrous conditions. Solvents were freshly dried and distilled; toluene from lithium aluminum hydride, tetrahydrofuran (THF) from potassium in the presence of benzophenone, methylene chloride and acetonitrile from phosphorous pentoxide.

All melting points were uncorrected and obtained on a capillary melting point apparatus. The ^{1}H NMR spectra were recorded on a Varian EM 390. Infrared spectra were obtained with a Perkin-Elmer 283 Grating spectrophotometer, ultraviolet spectra from a Beckmann Model 24 spectrophotometer and mass spectra on one or more of the following instruments: Finnigan 3200-GC/MS, Datensystem 6110, or Varian Mat 731.

6-Vinylcyclohepta-1,3,5-trien-1-carboxylic acid-azide (8)[3,9]

Method A. The 6-vinylcyclohepta-1,3,5-trien-1-carboxylic acid (**8g**) was dissolved in 300 mL of acetone and added 15 mL of water. To the clear solution was slowly added 6.6 g of triethylamine at −5 ℃. To the resultant was added 6.6 g of ethyl chloroformate at −5 ℃, and stirred for 30 minutes at the above temperature. An aqueous solution of NaN_3 (5.8 g) dissolved in 15 mL of H_2O was added dropwise over a period of 20 minutes with keeping the temperature at −5 ℃. The mixture was stirred for an additional 30 minutes at −5 ℃, and at 5-10 ℃ for 1 hour. The reaction mixture was poured into water and extracted with ether. The ether layer was washed with water, dried over $MgSO_4$, and evaporated to obtain a brown oil. The residual oil was chromatagraphed on Alumina (activity IV) by eluting with hexane. The eluted solution was evaporated to give 6.5 g (71%) of a yellow liquid. The product could be stored at −5~−10 ℃ for few days without a considerable decomposition.

Method B. In a 100 mL flask was dissolved 1.62 g of the vinyl acid in 30 mL of dried acetonitrile, and added 3.6 g of diphenylphosphorylazide (DPPA). After cooling the reaction mixtrue to 0 ℃, 1.4 g of triethylamine was added dropwise. The reaction mixture was allowed to stirr for 1 hour with removing the cooling bath. Most of CH_3CN was removed under vacuum. The residue was chromatographed by the same procedure as the method A. The yield was 1.2 g (64%).

2-Azabicyclo[4,4,1]undeca-4,6,8,10-tetraen-3-one (11)

Method A. Thermolysis of the acylazide (**8**) in the absence of triphenylphosphine.[3,9]

In a 4 L round bottom flask was placed 3 L of dried toluene and added 3.8 g of the acylazide (**17**). The mixture was allowed to heat at 105 ℃ for 18 hours under argon gas atmosphere. After cooling to room temperature, the reaction mixture was filtered through a column (20 cm long, ϕ4-5 cm) loaded with silica gel. The product lactam (**11**) was eluted with ethyl acetate-hexane (3 : 1) mixture after removing fore-fractions eluted with ethyl acetate-hexane (1 : 3) mixture. After evaporating the eluted solvent, the lactam was obtained in 64% yield (2.1 g) as a yellow solid.

Method B. Thermolysis of the acylazide (**8**) in the presence of triphenylphosphine.

In a 500 mL round bottom flask was placed 2.9 g (0.016 M) of the acylazide (**8**) with 300 mL of dried toluene. The yellow resulting colorled solution was refluxed for 30 minutes under argon gas atmosphere. Disappearance of the color indicated that the acylazide was transformed to the isocyanate (**9**) *via* a Curtius rearrangement. The reaction mixture was cooled to 50-60 ℃ and added 4.7 g (0.018 M) of triphenylphosphine. The mixture was heated to 100-110 ℃ for 3 hours and cooled to room temperature. The resultant was chromatographed by the same procedure as the above. The product isolated was 1.8 g (72.6%). A pure sample could be obtained by recrystallization from water-methanol (9 : 1) mixed solvent; mp 143-145 ℃. ^{1}H NMR ($CDCl_3$/TMS) δ : 0.17 (d, 1, H-11a, J=9.6 Hz), 1.85 (d, 1, H-11b), 6.17 (d, 1, H4, J=11.4), 6.5-7.4 (m, 4, H-7, 8, 9, 10), 7.54 (d, 1, H-5, J=11.4), 11.7 (br. s. 1. N-H) ; IR (KBr) cm^{-1}, 3100-2600 (C-H and N-H stretching vibration), 1621 (C=O), 803 (N-H wagging).

10-(1-carbomethoxyethyl)-1,7-methanoaza[10]annulene (18a)

In a 250 mL flask was placed 2.35 g (0.0126 M) of freshly prepared 6-vinyl-cyclohepta-1,3,5-trienyl-1-carboxylic acidazide (**8**) with 100 mL of dried toluene. The yellow solution was refluxed for 20-30 minutes under argon gas atmosphere. The reaction mixtrue was cooled to ~60 ℃, and added 4.46 g (0.0128 M) of 1-carbomethoxy-ethylidenetriphenylphosphorane.[15] The reaction mixture was heated at ~100 ℃ for 3 hours, and evaporated to give a viscous oily residue. Ether (30 mL) was added to the residue, and stirred for few minutes. Solid (mostly triphenylphosphine oxide) formed was removed by filtration. The filtrate was chromatographed on alumina to obtain 2.03 g (70.5%) of a viscous yellow liquid (eluting solvent : ether-hexane = 1 : 4). A pure sample was obtained by a short path distillation at 140 ℃ (oil bath temp.) under 0.5 mmHg. The ^{1}H NMR spectrum shows that the distilled product is a mixture of two isomers. One of two isomers was seperated by a column chromatography on silica gel with a long column (100 cm long, ϕ 2 cm). ^{1}H NMR; major isomer (CCl_4/CD_2Cl_2) δ ; −0.18 (d, 1, H-11b, J=9.0 Hz), 1.72 (d, 3, -CH_3, J=7.5 Hz), 3.70 (s, 3, -OCH_3), 4.05 (q,

1, methine proton), 6.50 (d, 1, H-9, J=9.0 Hz), 6.75-720 (m, 3, H-4, 5, 6), 7.50 (d, 2, H-3, 8, J=9.0 Hz), 6.75-7.20 (m, 3, H-4, 5, 6), 7.50 (d, 2, H-3, 8, J=9.0 Hz); minor isomer (CCl_4 /CD_2Cl_2) δ ; −0.21 (d, 1, H-11b, J=9.0 Hz), 0.76 (d, 1, H-11a), 1.62 (d, 3, -CH_3, J=7.5 Hz), 3.70 (s, 3, -OCH_3), 3.96 (q, 1, methine proton), 6.55 (d, 1, H-9, J=9.0 Hz), 6.70-7.15 (m, 3, H-4, 5, 6), 7.50 (d, 2, H-3, J=9.0 Hz); IR (neat) cm^{-1}, 2980 and 2950 (C-H streching vibration), 1735 (C=O), 1170 (C-O-); Mass spectra (relative intensity) m/e, 229 (10), 150 (100), 149 (30), 115 (32), 57 (28).

10-Dicarboethoxymethyl-2,7-methanoaza[10]annulene (18b)

To 6-vinylcyclohepta-1,3,5-trienyl-1-isocyanate solution, prepared in situ with 3.0 g (0.016 M) of the acylazide (**8**) and 100 mL of dried toluene as the above was addded 7.56 g (0.018 M) of dicarboethoxylphosphorane (**15b**)[16] at 50 ℃. The reaction mixture was refluxed for 5 hours under argon gas atmosphere, and evaporated to give a dark brown viscous oil. The oily residue was chromatographed on silica gel. The product was obtained by evaporating the eluted solvent (ether-hexane=3 : 1) in 61% yield (3.0 g). An analytical sample was achieved by a short path distillation at 160 ℃ (oil bath temp.)/0.6 mmHg. ^1H NMR (CD_3CN) δ ; −0.20 (d, 1, H-11b, J=9.0 Hz), 0.78 (d, 1, H-11a), 1.25 (t, 6, -CH_3, J=7.5 Hz), 4.32 (q, 4, -CH_2-), 5.19 (s, 1, methine proton), 6.75 (d, 1, H-9, J=9 Hz), 6.83-7.75 (m, 3, H-4, 5, 6), 7.45-7.72 (m, 2, H-3.8); IR; Ir (neat) cm^{-1}, 2980 (C-H stretching vibration), 1730 (C=O), 1145 (C-O); Mass spectra (relative intensity) m/e, 301 (20), 183 (100), 182 (53), 172 (48), 157 (55), 156 (50), 155 (60), 154 (75), 128 (35), 127 (43), 115 (40), 77 (22).

10-Ethyl-2,7-methanoaza[10]annulene (20)

To a solution of 0.8 g of potassium hydroxide dissolved in 30 mL of methanol and 3 mL of water was added 0.75 g (3.3 mM) of 10-(1-carbomethoxyethyl)-2,7-methanoaza-[10]-annulene (**18a**), and refluxed for 2 hours. Solvent of the reaction mixture was evaporated, and the residue was dissolved in 20 mL of water. The aqueous solution was acidified with d-HCl (10%) to pH=~5 in the presence of ether (50 mL). The organic phase was seperated, and the water phase was extracted with ether (50 mL) one more time. The combined ether extract was dried over $MgSO_4$, and evaporated to remove the ether. The visous residue was distilled by a short path distilling apparatus. The product was obtained in quantitative yield (0.56 g) as a yellow liquid at 130 ℃ (oil bath temp.)/0.5 mmHg. Decarboxylation of the acid was also carried out by refluxing the viscous residue in THF for 2 hours. ^1H NMR (CCl_4/CD_2Cl_2) δ ; −0.13 (d, 1, H-11b, J=9.0 Hz), 0.72 (d, 1, H-11a), 1.47 (t, 3, -CH_3, J=7.5 Hz), 3.03 (d, q, 2, -CH_2-, J_{gem}=4.5), 6.46 (d, 1, H-8, J=9.3 Hz), 6.75-7.30 (m, 3, H-4, 5, 6), 7.45 (d, 2, H-3, 8); IR (neat) cm^{-1}, 2960, 2940, 1580, 1545, 1490, 1440, 810, 785, 710; Mass spectrum (relative intensity) m/e; 171 (52), 170 (100), 156 (21), 142 (32), 143 (32), 115 (47).

2,7-Methanoaza[10]annulen-10-ylacetic Acid (21)

10-Dicaboethoxymethyl-2,7-methanoaza[10]annulene (**18b** ; 1.5 g ; 5.0 mM) was added to a solution of 0.5 g of potassium hydroxide dissolved in 30 mL of methanol and 3 mL of water, and the mixture was refluxed for 90 minutes. Solvent was removed, and the residue was dissolved in 30 mL of water. The aqueous solution was acidified with d-HCl (10%) to pH=~5 in the presence of ether (100 mL) under cooling in an ice bath. The ether phase was seperated, and water phase was extracted with ether (30 mL) one more time. The combined ether extract was dried over $MgSO_4$ with cooling, and concentrated to yield crude acid. The crude acid was suspended with ether-hexane (1 : 3) mixture for few minutes, and filtered to obtain 0.95 g (100%) of a pale brown solid; mp 10-102 ℃ (dec.). The acid was considerably stable in solid state but slowly decarboxylated in solution. ^1H NMR (DMSO-d_6) δ ; −0.28 (d, 1, H-11b, J=9 Hz), 0.62 (d, 1, H-11a), 3.95 (s, 2, -CH_2-), 3.70 (br, s, 1, OH), 6.65 (d, 1, H-8, J=9.0 Hz), 6.83-7.30 (m, 3, H-4, 5, 6), 7.66 (d, 2, H-3, 8); IR (KBr) cm^{-1}, 1720 (C=O), 1335, 1320, 1235, 1205, 1170, 1135, 755, 725; Mass spectrum (relative intensity) m/e, 201 (11), 157 (100), 156 (70), 154 (32), 127 (32), 115 (53), 77 (22).

10-Methyl-2,7-methanoaza[10]annulene[8,9]

The residue of the ether extract obtained in the preparation of the acid (**21**) or the solid acid (**21**) was placed in a short path distilling flask and heated to 130 ℃ (oil bath temp.) under vacuum (0.5 mmHg). The product was distilled immediately in quantitative yield. ^1H NMR (CCl_4) δ ; −0.24 (d, 1, H-11b, J=9 Hz), 0.59 (d, 1, H-11a), 2.70 (s, 2, -CH_2-), 6.35 (d, 1, H-9, J=9.3 Hz), 6.68-7.10 (m, 3, H-4, 5, 6), 7.33 (d, 2, H-3, 8).

10-(N-Phenylamino)-2,7-methanoaza[10]annulene (27a)

6-Vinylcyclohepta-1,3,5-trien-1-carboxylic acidazide (**8**, 4.2 g, 2.0 mM) was refluxed with 300 mL of dried toluene for 30 minutes under argon gas atmosphere. To the resulting isocyanate solution was added 10.6 g (3.0 mM) of N-phenyliminotriphenyl-phosphorane,[18] and heated the mixture at 100 ℃ for 3 hours under argon gas atmoshpere. Reaction mixsture was concentrated to yield a brown viscous oil. The oily residue was suspended in 20 mL of ether, and filtered off a solid (triphenylphosphine oxide) formed. The filtrate was chromatographed on silica gel. The product was eluted with ether-hexane (2 : 5) to yield 3.4 g (66%) of a yellow solid. An analytical sample was obtained by recrystallization from ether-hexane (1 : 5) as needle crystal : mp 93 ℃. ^1H NMR (Acetone-d_6) δ ; 0.25 (d, 1, H-11b, J=9.0 Hz), 0.56 (d, 1, H-11a), 6.10 (d, 1, H-9, J=10.5 Hz), 6.65-7.65 (m, 8, H-4, 5, 6 and 5 phenyl protons), 7.90 (d, 2, H-3, 8) 8.60 (br. s, 1, NH); IR (KBr) cm^{-1}, 3230, 3180 (NH), 1600, 1590, 1495, 1440, 1320, 715; UV (methanol) λ_{max}, 237 (log ε=4.4), 297 (log ε= 4.50, 410 (log ε=4.0)mu : Mass spectrum, m/e (relative intensity), 234 (918), 233 (45), 130 (28), 116 (37), 77 (43), 71 (50), 57 (73), 33 (100). Anal : Calcd. for $C_{16}H_{14}N_2$: C, 82.05; H, 5.98; N, 11.97, Found: C, 81.96; H, 6.00; N, 11.77.

10-(N-Benzylamino-2,7-methanoaza[10]annulene (27b)

To the isocyanate solution, prepared from 1.2 g (6.4 mM) of the acidazide (**8**) and 70 mL of dried toluene in the above manner, was added 2.4 g (6.4 mM) of N-benzyl-iminotriphenylphosphorane at room temperature, and heated at ~ 100 ℃ for 3 hours under argon gas atmosphere. The reaction mixture was concentrated to yield a viscous oil. The viscous

oil was suspended in ether (20 mL). Triphenylphosphine oxide solidified out was filtered off. The filtrate was chromatographed on silica gel. The product was obtained by eluting with ether-hexane (1 : 5) in 88.6% yield (1.4 g) as a viscous oil which was solidified on standing. Recrystallized from ether-hexane (1 : 7) for an analytical sample : mp 70-71 ℃. ^{1}H NMR (CCl_4/CD_3CN) δ ; 0.67 (d, 1, H-11b, J=9.0 Hz), 0.98 (d, 1, H-11a), 5.05 (d, 2, -CH_2-, J_{gem}=6.0 Hz), 5.45 (m, 1, NH), 5.90 (d, 1, H-8, J=9.5 Hz), 7.10-7.95 (m, 10, H-3, 4, 5, 6, 8 and 5 phenyl protons), IR (neat film) cm^{-1}, 3410 (NH), 3020, 2930, 1580, 1510, 1450, 1230, 1170, 770; Mass spectrum, m/e (relative intensity), 248 (17), 247 (12), 143 (50), 106 (100), 91 (93), 57 (33), 33 (43). Anal: Calcd. for $C_{17}H_{16}N_2$: C, 82.26; H, 6.45; N, 11.29, Found: C, 81.18; H, 6.47; N, 11.35.

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