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# SYNTHESIS OF [4.5.5.5]FENESTRANE AND A [4.4.5.5]FENESTRANE DERIVATIVE

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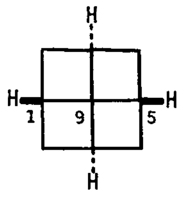
Abstract: The synthesis of tetracyclo[5.4.1.0$^{4,12}$.0$^{9,12}$]dodecan-6-one 12 via an intramolecular photocycloaddition, its reduction to the hydrocarbon 13 and its ring-contraction to tetracyclo-[4.4.1.0$^{3,11}$.0$^{9,11}$]undecane derivative 16 is described.

The hydrocarbon tetracyclo[3.3.1.0$^{3,9}$.0$^{7,9}$]nonane 1, known as [4.4.4.4]fenestrane, or simply windowpane, has been the subject of several recent discussions[1] and synthetic studies.[2] The synthetic work has resulted in the synthesis of [5.5.5.5]fenestrane derivatives 2[2b] and 3[2c] and the [4.4.4]fenestranes 4[2e] and 5[2f]. In addition to the overall aesthetic appeal of windowpane, the central quaternary carbon is of particular interest. This carbon, although not constrained to planarity, is expected to be severely distorted from the normal tetrahedral geometry. It has been estimated that the $C_1$-$C_9$-$C_5$ angle in 1 should be 140° and the strain at the central carbon would be roughly 40 kcal/mol.[1b] This degree of distortion and strain is unprecedented and thus the stability and reactivity of 1 is difficult to predict. We have therefore embarked on a stepwise program designed to synthesize the homologous series of [4.5.5.5], [4.4.5.5], [4.4.4.5] and [4.4.4.4]fenestranes and to study the effects of increasing distortion at the central carbon on the properties of these compounds.



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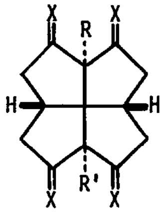
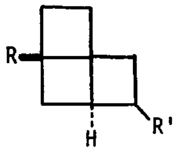


2 R = R' = H; X = O

3 $X = H_2$; $R,R' = -\overset{\overset{O}{\|}}{C}O-$



4 R = R' = H

5 R = Me; R' = $CO_2Me$

Our basic synthetic approach (Scheme I) is to use an intramolecular photocycloaddition of a bicyclic enone with an olefin to generate simultaneously the central quaternary carbon and the final two rings of the fenestrane.[3] Subsequent ring contractions of the initial photoadduct could then be used to generate lower and more strained homologues. We would herein

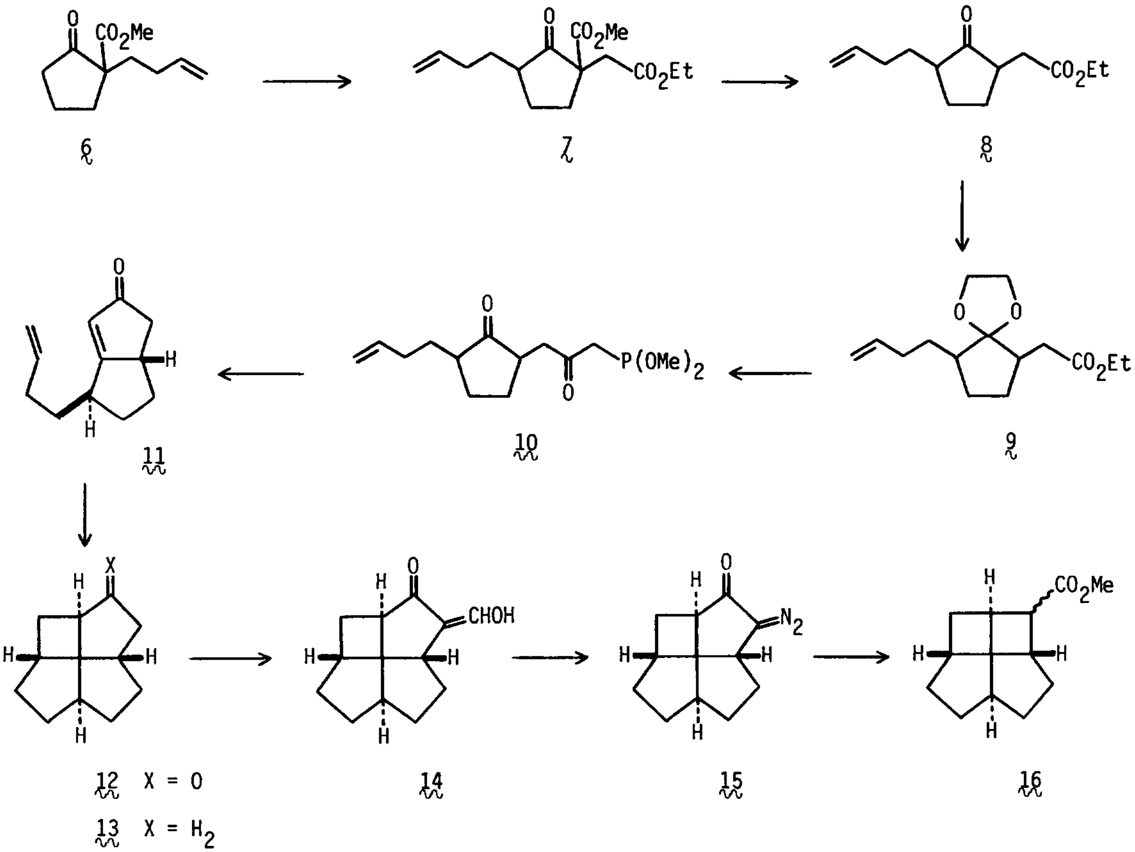
Scheme I

like to describe the successful application of this strategy to the first synthesis of [4.5 5.5]fenestrane and a [4.4.5.5]fenestrane derivative.

The synthesis of the requisite 8-substituted bicyclo[3.3.0]oct-1-en-3-one was achieved as follows (see Scheme II). The potassium salt of 2-carbomethoxycyclopentanone was alkylated with 4-bromo-1-butene (1.1 eq, $\phi CH_3$, cat. 18-crown-6, KI, reflux, 24 h) to yield β-keto ester **6**[4] in 95% yield. Reaction of **6** with methanolic sodium methoxide (1 eq, reflux, 13 h) followed by azeotropic removal of methanol with toluene effected a retro-Dieckmann reaction and subsequent recyclization to the stable β-keto ester enolate. This enolate was alkylated with ethyl bromoacetate (1.3 eq, $\phi CH_3$, reflux, 21 h) to afford a 79% yield of dialkylated cyclopentanone **7**.[4,5] The alkylation-directing carbomethoxy group was efficiently removed by $S_N2$ ester cleavage and decarboxylation[6] (4 eq anhyd. LiCl, 1.1 eq HOAc, HMPT, 110°C, 17.5 h) to give a cis-trans mixture of 2,5-disubstituted cyclopentanone **8**[4] (82%). Protection of the carbonyl was effected in quantitative yield to give **9**[4] (cis/trans = 33:67) by treatment of **8** with ethylene glycol (5 eq), triethylorthoformate (2 eq) and *p*-toluenesulfonic acid (0 06 eq, 25°C, 25 h). The ester **9** was added to lithium dimethyl methylphosphonate (2.5 eq, THF, -78°C → 25°C, 5 h) and the reaction was quenched with 2N HCl (25°C, 2.5 h) to afford the β,ε-diketophosphonate **10**[4] in 89% yield from **7**.[7] The critical intramolecular Wadsworth-Emmons cyclization was effected by a modification of the procedure of Aristoff[8] which afforded an excellent yield of enone **11** and epimerized the butenyl side chain to the more stable exo configuration without migration of the cyclopentanone double bond. Thus, treatment of **10** with anhydrous $K_2CO_3$ (2 eq) and 18-crown-6 (0.3 eq) in THF (40°C, 21 h) afforded enone **11**[4,9] in 92% yield as a 95:5 mixture of exo-endo isomers. The intramolecular photocycloaddition was smoothly accomplished by irradiation of **11** with a 450 W Hanovia (hexanes, $10^{-2}$ M, 25°C, 68 h) through a uranium glass filter (λ >330 nm) to give the [4.5.5.5]fenestrone **12**[4,10] in 95% yield  Wolff-Kishner reduction of ketone **12** ($NH_2NH_2 \cdot H_2O$, $N(CH_2CH_2OH)_3$, KOH, 210°C, 5 h) afforded the volatile [4.5.5.5]fenestrane **13**,[4,11] which was isolated in 71% yield via preparative GLC  The $^{13}C$ spectrum of **12** displayed seven lines, in full accord with the $C_2$ symmetry possessed by this molecule.

It has been shown that the photochemical Wolff-rearrangement of α-diazo ketones derived from bicyclo[3 2.0]heptan-2-ones is an efficient ring contraction route to bicyclo[2.2.0]-hexane-2-carboxylates.[12] Therefore, ketone **12** was treated with sodium hydride (1.2 eq) and ethyl formate (2.6 eq, $Et_2O$, 0°C → 25°C) to afford the crude α-formyl ketone **14**  Reaction of **14** with tosyl azide (1 eq) and triethylamine (2 eq, $CH_2Cl_2$, 25°C, 4 h) gave α-diazo ketone **15**.[13] The crude α-diazo ketone **15** was irradiated with a 450 W Hanovia through Pyrex (MeOH, $10^{-2}$ M, 0°C, 2 h) to afford a 61·39 mixture of epimeric methyl esters **16**[4,14] in 61% yield from ketone

Scheme II



**12**. Epimerization of the mixture in refluxing methanolic sodium methoxide gave a thermodynamic ratio of 53:47 with the same epimer predominating. The fenestrane **16** does not appear to have any unusual instability and has been fully characterized as the inseparable epimeric mixture.

Thus, the synthesis of a derivative of tetracyclo[4.4.1.$0^{3,11}$.$0^{9,11}$]undecane, **16**, the smallest and most strained [m.n.p.q] fenestrane known to date, has been achieved in 11 steps in a 29% overall yield from dimethyl adipate.

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## References and Notes

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3. This approach has been successfully employed in the synthesis of [4.5.5.6] and [4.5.6.6]-fenestrane derivatives. See ref. 2a.

4. This compound has been fully characterized by spectral means and gave a satisfactory C and H combustion analysis.

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9. UV (cyclohexane) $\lambda_{max}$ 225 nm ($\epsilon$ 13100), 302 (31), 311 (35), 321 (35), 334 (26), 352 (10).

10. $^1$H-NMR (250 MHz, CDCl$_3$) $\delta$ 1.10-1.38 (m,2), 1.38-1.55 (m,1), 1 55-1.73 (m,1), 1.75-1 95 (m,2), 2.03-2.45 (m,8), 2.51 (dd, 1, J = 4.7, 10.0), 2.73 (dd, 1, J = 7.7, 17 2)

11. $^{13}$C-NMR (CDCl$_3$) $\delta$ 27.8 (t, J = 133), 33.8 (t, 2C, J = 128), 34.5 (t, 2C, J = 127), 35.3 (t, 2C, J = 127), 42.2 (d, 2C, J = 135), 51.2 (d, 2C, J = 130), 70.6 (s).

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14. $^1$H-NMR (250 MHz, CDCl$_3$) $\delta$ 0.88-1.12 (m,2), 1.53-1.74 (m,2), 1.83-2.45 (m,8), 2 66-2.80 (m,2), 3.06 (dd, 0.6H, J = 4.3, 8.5), 3.23 (dd, 0.4H, J = 3.6, 7.9), 3.65, 3.70 (2s, 3 (40:60)), $^{13}$C-NMR (CDCl$_3$, minor isomer in parentheses) $\delta$ 27.3, (31.6), (34.4), (34.9), 35.36, (35.40), 35.6, (36.37), 36.44, (39.45), 39.53, 40.4, 40.6, (40.7), 42.0, (43.7), (45.2), 45.6, 49.0, (49.2), (51.08), 51.13, (63.5), 64.6, (174.2), 174.4.

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