SYNTHESES AND THE STRUCTURES OF POLYMETHYLPOLYCYCLIC
AND POLYCYCLIC "CAGE" MOLECULES

THESIS

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By

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The structures of Diels-Alder cycloaddition of cyclopentadiene to 2,6-dimethyl-\( \text{p} \)-benzoquinone and methylcyclopentadiene to 2,6-dimethyl-\( \text{p} \)-benzoquinone were assigned by analysis of 1-D and 2-D proton and carbon-13 NMR spectra. The structures of the cycloadduct of methylcyclopentadiene to 2,6-dimethyl-\( \text{p} \)-benzoquinone and that of the corresponding intramolecular [2+2] photocyclization product were also obtained by single crystal X-ray structural analysis.

As the second part of the study, a new polycyclic "cage" molecule, a substituted trishomocubane isomer, was synthesized. In this synthesis, reductive bond cleavage followed by Dieckmann condensation was employed. Wolff-Kishner reduction then was used to convert a \( \beta \)-keto ester "cage" molecule to the corresponding carboxylic acid. A compound that possesses twofold symmetry was isolated from reaction product mixture. The structure of this compound has been established by single crystal X-ray crystallography.
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CHAPTER I

SYNTHESIS OF NEW POLYMETHYLPOLYCYCLIC COMPOUNDS AND 2-D NMR ANALYSIS

Introduction

There is considerable current interest in Diels-Alder cycloadditions (1)(2)(3)(4). An example of the Diels-Alder reaction is that which occurs when 1,3-butadiene is heated with maleic anhydride at 100°C and the product is obtained in quantitative yield (5). The reaction is shown as follow:

\[
\text{1,3-Butadiene (diene)} + \text{Maleic anhydride (dienophile)} \xrightarrow{100^\circ C \text{Benzene}} \text{100% adduct}
\]

The Diels-Alder reaction requires a conjugated diene (4\pi-electron system) and compound containing a double or triple bond (2\pi-electron system) called a dienophile. The product of this reaction is a [4+2] cycloadduct. Since the Diels-Alder reaction is highly stereospecific, a stereochemical study can offer insight into its mechanism. It was recognized very early that the Diels-Alder reaction
is a "syn" addition and the configurations of substituents in the diene and in the dienophile are retained in the products. Two examples that illustrate this aspect of the Diels-Alder reaction are shown as follows:

In the first example, a dienophile with trans hydrogens reacts with 9,10-dimethyl anthracene to give an adduct with trans hydrogens. In the second example, the cis configuration of hydrogens in the dienophile is retained in the product (6).

The combination of cyclic dienes with cyclic dienophiles could in principle follow two courses, in general however, the Diels-Alder reaction occurs primarily in an endo rather than an exo fashion when the reaction is kinetically controlled (1). For example, the addition of maleic anhydride to cyclopentadiene leads almost exclusively to endo adduct. The thermodynamically more
A stable exo compound is formed in yields of less than 1.5% as shown follow (6):

![Chemical structures](image)

In the present study, Diels-Alder cycloaddition of cyclopentadiene and of methylcyclopentadienes to 2,6-dimethyl-p-benzoquinone were studied. The reactions of interest are shown as follows:

![Chemical structures](image)
Only one 1:1 endo Diels-Alder cycloadduct can result via [4+2] addition of cyclopentadiene to 2,6-dimethyl-p-benzoquinone. However, four endo isomers potentially can result via Diels-Alder cycloaddition of methylcyclopentadienes to 2,6-dimethyl-p-benzoquinone. That is because thermal cracking of methylcyclopentadiene dimer affords mainly two different methylcyclopentadiene monomers, i.e. 60% 1-methylcyclopentadiene and 40% 2-methylcyclopentadiene, as shown follow (7):

Methylcyclopentadiene dimer

2-methylcyclopentadiene

1-methylcyclopentadiene

The four endo isomers that can result via this Diels-Alder cycloaddition are shown as follows:
Indeed, Diels-Alder addition of methylcyclopentadiene to 2,6-dimethyl-p-benzoquinone was found to afford a mixture of all four isomers, 2a-2d. After purification (see experimental section) one isomer was separated from this mixture. The structure of this isomer and also that of the Diels-Alder adduct of cyclopentadiene to 2,6-dimethyl-p-benzoquinone (i.e. 1) was elucidated by analysis of their respective 1-D and 2-D proton and carbon-13 NMR spectra.

Results and discussion

1. Structural assignment for 5,7-dimethyltricyclo[6,2,1,0^2,7]undeca-4,9-dien-3,6-diones 1

The Chem Abstracts numbering system used for the endo adduct 1 is shown as follow:
In the $^1$H NMR spectrum of 1 (see Figure 1) the peaks at δ5.95, δ6.03 and δ6.44 correspond to the three vinyl protons (i.e. H$_2$, H$_3$ and H$_7$) in 1. There are two methyl singlets which resonate at δ1.40 and δ1.89. The remaining peaks are due to the other aliphatic protons. The $^{13}$C NMR spectrum of 1 (Figure 2) shows 13 carbon resonances. There are two carbonyl carbon resonances (δ202.4 and δ198.5) and four olefinic carbon resonances in the region δ130-155. The two peaks at highest field correspond to the two methyl groups. The remaining aliphatic absorptions are located in the δ40-60 region. An attached proton test (APT) reveals the presence of four quaternary carbons and one secondary carbon in 1.

The COSY spectrum (Figure 3) assignment is given below (8): The H$_7$ resonance is the furthest downfield, compared to the other two vinyl protons, H$_2$ and H$_3$. This is due to the deshielding resonance effect of the carbonyl group shown as follow:
Proton H7 is coupled allylically to (CH$_3$)$_{11}$. The next two peaks at low field, due to H$_2$ and H$_3$, will be assigned later. The two peaks between δ3.0-3.4, which are coupled to H$_9$a and H$_9$s (AB Pattern), are due to H$_1$ and H$_4$. Proton H$_1$ is coupled to H$_2$, H$_8$a, H$_9$a, H$_9$s and "W-shape" long range coupled to H$_4$ (8). Proton H$_4$ is coupled to H$_3$, H$_9$a, H$_9$s and H$_4$. Since H$_1$ is coupled with one more proton in the region δ3.0-3.4 than is H$_4$, and the downfield peak is H$_1$, so the upfield peak can be assigned to H$_4$. Tracing back, H$_1$ should be coupled to H$_2$, and H$_4$ should be coupled to H$_3$. The two vinyl peaks at δ5.9-6.1 are thus easily recognized; the downfield peak is due to H$_3$ and the upfield peak can be assigned to H$_2$.

The peak next to H$_4$ can be assigned to H$_8$a because of its coupling to H$_1$. Since methyl group (CH$_3$)$_{11}$ has been assigned already, the remaining methyl group signal (which appears at higher field), can be assigned to (CH$_3$)$_{10}$.

All protons except H$_9$a and H$_9$s have now been assigned. A nuclear magnetic double resonance (NMDR) experiment was
employed to assign these two protons (9). This double resonance spectrum is shown in Figure 4. When proton \( H_3 \) (peak at \( \delta 6.03 \)) was irradiated, some of the fine structure in the peak at \( \delta 1.58 \) disappeared, whereas the multiplicity of the peak at \( \delta 1.47 \) was unaffected. Thus, the peak at \( \delta 1.58 \) can be assigned \( H_9s \), and the peak at \( \delta 1.47 \) can be assigned to \( H_9a \). That if because \( H_9a \) has stronger "zigzag" or "W shape" lone range coupling to \( H_2 \) (or \( H_3 \)) than does \( H_9a \) as shown below (8):

![Chemical structure diagram]

When \( H_2 \) or \( H_3 \) was irradiated, decoupling between \( H_2 \) (or \( H_3 \)) and \( H_9s \) resulted in the disappearance of some of the fine structure in the peak that corresponds to \( H_9s \).

The HETCOR spectrum (Figure 5) correlates directly bonded protons and carbons. For example, \( H_7 \) is coupled to \( C_7 \), \( H_3 \) is coupled to \( C_3 \), etc. Therefore, carbons can be assigned in a straightforward fashion.

2. Structural assignment for 5,7,9,-trimethyltricyclo [6.2.1,0^2.7] undeca 4,9-dien-3,6-diones 2a

The chem Abstracts numbering system used for the endo adduct 2a-2d is shown as follow:
In the downfield region (δ5.5-6.5) of the $^1$H NMR spectrum (Figure 6), only two vinyl proton resonances are observed. From this observation, we conclude that 2c and 2d cannot be the correct structures, and only 2a and 2b remain as candidates. This point is also revealed in $^{13}$C spectrum (Figure 7). The APT spectrum shows a total of six quaternary plus secondary carbons. In the Olefinic region (δ140-160) only two quaternary peaks are observed. This confirms the earlier conclusion that either 2a or 2b (and not 2c or 2d) can be the correct structure.

The COSY spectrum is shown in Figure 8. Proton H7 resonates farthest downfield due to the deshielding resonance effect of the carbonyl group. Proton H7 is coupled allylically to the protons in group (CH$_3$)$_{11}$. Proton H$_2$ is coupled to H$_1$, to H$_4$, and allylically coupled to the protons in methyl group (CH$_3$)$_{12}$. Thus, the most upfield methyl group resonance should be due to (CH$_3$)$_{10}$. The two AB pattern peaks close to the resonance that corresponds to (CH$_3$)$_{12}$ are due to H$_{9a}$ and H$_{9s}$, but we cannot yet assign which one is due to H$_{9a}$ and which one is due to H$_{9s}$. 
The remaining three peaks at δ2.5-3.5 are H₁, H₄ and H₈a respectively. Since H₈a is not coupled to either H₉a or H₉s, it can be readily discerned. Among these three peaks, the middle one corresponds to H₈a, which is coupled H₁. Thus, the peak at ca δ3.3 is due to H₁, and the resonance at δ2.8 can be assigned to H₄. Examination of structure 2a reveals that H₁ should be coupled to H₂, H₈a, H₄, H₉a and H₉s. Proton H₄ in this structure should be coupled to H₁, H₂, H₉a and H₉s. In structure 2b, H₁ should be coupled to H₈a, H₃, H₄, H₉a and H₉s, and H₄ should be coupled to H₃, H₁, H₉a and H₉s. Thus the resonance at ca δ 5.5 could be assigned either to H₂ in 2a or to H₃ in 2b. However, compare the magnitudes of the expected coupling constants for H₂-H₁ and H₂-H₄ in 2a, and for H₃-H₄ and H₃-H₁ in 2b. We note that J₁₂ > J₂₄ in 2a, while J₃₄ > J₃₁ in 2b. When comparing the two crosspeaks that correspond to H₂-H₁ and H₂-H₄ in the COSY spectrum, the former coupling can be seen to be much stronger than the latter. Therefore, the assignment of structure 2a is more consistent with the COSY spectrum, and we conclude that 2a is the correct structure of the Diels-Alder adduct. A nuclear magnetic double resonance (NMDR) experiment (Figure 9 and Figure 10) was employed to differentiate between H₉a and H₉s. When proton H₂ was double-irradiated, some of the fine structure in the peaks centered at δ1.62 disappeared, whereas the peaks centered at δ1.52 were unaffected. Thus the peaks at
δ1.62 can be assigned to H9γ, and the peaks at δ1.52 can be assigned to H9α.

The HETCOR spectrum is shown in Figure 11. It is very straightforward to assign couplings between directly bonded protons and carbons, (e.g., C7 is coupled to H7, C2 is coupled to H2, etc.) until all the carbon resonances are assigned.

The results of single crystal X-ray analysis confirm the conclusion based upon analysis of the NMR spectrum that 2a is indeed the correct structure of the Diels–Alder adduct (Figure 12).

3. The structure of cage compound 1,10-dimethylpentacyclo[5,4,0,0^2.6,0^3.10,0^5.9]undecane-8,11-diones 3

The photolyzation product of 1 is 3. The structure of compound 3 is shown as follow:

![Diagram of compounds 1 and 3]

The 1H NMR and 13C NMR spectrum are shown in Figure 13 and Figure 14. Both the 1H and 13C spectrum are consistent with the suggested cage structure, 3. The 1H spectrum
displays two methyl resonances between δ1.0-1.2. The 13C spectrum (with APT) indicates the presence of a total of thirteen carbon atoms. The two downfield carbon resonances (δ212.668 and δ214.668) are due to the two carbonyl carbons in 3. No olefinic carbon resonances are observed. Two peaks which are furthest upfield (δ15-17), correspond to the two methyl groups in 3.

4. The structure of cage compound 1,2,10-trimethylpentacyclo [5,4,0,02.6,03.10,05.9] undecane-8,11-diones 4

The product obtained by irradiation of 2a is 4. The structure of 4 is shown as follows:

![Structure of 4](image)

The 1H NMR and 13C NMR spectrum of 4 are shown Figure 15 and 16, respectively. Both the 1H and 13C spectrum are consistent with the suggested cage structure for 4. The 1H spectrum displays two large peaks between δ1.0-1.2 which correspond to the three methyl groups. The 13C spectrum shows a total of fourteen nonequivalent carbon atoms. Among these carbons, the two quaternary carbons which are most
downfield (δ212.626 and δ214.473) are due to the two carbonyl carbons in 4. No olefinic carbon resonances are observed. The three resonances at highest field (δ12-18), correspond to the three methyl group carbons.

The results of single crystal of X-ray structural analysis confirm the suggested cage structure for 4(Figure 17).

Experimental

Melting points and boiling points are uncorrected. Proton and 13C NMR spectra were recorded on a VXR-300 NMR spectrometer. In all cases, signals are reported in parts per million (δ) downfield from internal tetramethylsilane. Infrared spectra were obtained with PerKin-Elmer Model 1330 infrared spectrophotometer. Mass spectra were obtained with a Hewlett-Packard Model 5970 A GC/MS system operating at 70 eV. Elemental microanalyses were performed by Galbraith Laboratories, Inc., Knoxville, TN.

1. 5,7-Dimethyltricyclo [6,2,1,02.7] undeca-4,9-dien-3,6-diones 1

To a solution of 2,6-dimethyl-p-benzoquinone (1.36 g, 10 mmol) in benzene (25 ml) was added freshly cracked cyclopentadiene (0.79 g,
12 mmol). The reaction mixture was placed in a sealed glass tube and heated with stirring at 90°C for 7 h. The reaction mixture was cooled and concentrated in vacuo, thereby affording 1 as a yellow oil (1.56 g, 77.2% yield). The mixture was purified via flash column chromatography (Silica gel stationary phase, 2% ethyl acetate-hexanes eluent). Pure 1 was thereby obtained as a light yellow viscous oil (1.21 g, 60% yield); bp 100-102°C/0.5 mm; IR(CCl4) 3000 (s), 1750 (vs), 1660 (vs), 1625 (w), 1295 (s) cm⁻¹; ¹H NMR (CDCl3) 1.40 (s, 3H), 1.47 (d, 1H), 1.62 (d, 1H), 1.89 (s, 3H), 2.76 (d, 1H), 3.03 (s, 1H), 3.36 (s, 1H), 5.95 (m, 1H), 6.03 (m, 1H), 6.44 (s, 1H); ¹³C NMR (CDCl3) 16.050 (q), 26.066 (q), 45.811 (t), 48.354 (d), 51.910 (s), 53.196 (d), 57.199 (s), 134.418 (d), 137.202 (d), 138.539 (d), 150.593 (s), 198.515 (s), 202.428 (s); mass spectrum (70 eV), m/e (relative intensity) 202.15 (100.0), 187.15 (46.4), 159.15 (43.4), 131.20 (92.1), 91.10 (56.9), 77.10 (39.3), 66.10 (59.9), 65.10 (34.1).


2. 5,7,9,-Trimethyltricyclo [6,2,1.0².7] undeca- 4,9-dien-3,6-diones 2a

To a solution of 2,6-dimethyl-p-benzoquinone (1.36 g, 10 mmol) in benzene (25 ml) was added freshly cracked methylcyclopentadienes (0.79 g, 12 mmol). The reaction mixture was placed in a sealed glass tube and heated with
stirring at 90°C for 5 h. The reaction mixture was then concentrated in vacuo, thereby affording a yellow oil (1.66 g, 77.0% yield). The crude product was purified via flash column chromatography (silica gel stationary phase, 2% ethyl acetate-hexanes eluent). A mixture of from isomeric Diels-Alder cycloadducts, 2a-2d, was thereby obtained as a pale yellow viscous oil. A light yellow crystalline solid could be isolated from this mixture via careful fractional recrystallization from hexanes and ethyl acetate. Pure 2a (0.45 mg, 21.0% yield) was thereby obtained: mp 87-88°C; IR (KBr) 2920 (s), 2870 (w), 1645 (vs), 1450 (w), 1380 (w), 1320 (s), 1270 (2), 1260 (s), 1110 (w) cm⁻¹; ¹H NMR (CDCl₃) 1.42 (s, 3H), 1.52 (d, 1H), 1.56 (s, 3H), 1.63 (d, 1H), 2.79 (s, 1H), 2.82 (d, 1H), 3.28 (s, 1H), 5.51 (s, 1H), 6.48 (s, 1H); ¹³C NMR (CDCl₃) 16.554 (q), 16.702 (q), 26.535 (q), 47.190 (t), 50.034 (d), 52.075 (s), 58.873 (d), 59.284 (d), 127.995 (d), 139.376 (d), 147.864 (s), 150.925 (s), 199.866 (s), 202.584 (s); mass spectrum (70 eV), m/e (relative intensity) 136.00 (28.84), 108.05 (38.02), 107.05 (16.91), 80.05 (17.09), 79.05 (40.14), 68.00 (67.35), 67.00 (6.54), 65.10 (5.48), 40.00 (56.77), 39.00 (100), 38.00 (29.16).

3. **1,10-dimethylpentacyclo [5.4.0.2.6.03.10.05.9] undecane-8,11-diones 3**

A solution of 1 (1.01 g, 5.0 mmol) in ethyl acetate (250 ml) was irradiated for 24 h under nitrogen in a quartz and pyrex filter immersion photolysis apparatus equipped with a 450 watt Hanovia medium pressure mercury vapor lamp. The solution was concentrated in vacuo to afford 3 as a colorless oil. The crude product was purified via column chromatography (silica gel stationary phase, 2% ethyl acetate-hexanes eluent), thereby affording pure 3 (0.86 g, 85.0% yield) as a colorless microcrystalline solid: mp 27-28°C; IR (CCl4) 2960(vs), 2870 (s), 1730 (vs), 1460 (s), 1380 (w), 1290 (w), 1250 (w), 1220 (w), 1180 (w), 1120 (s), 1090 (s), 1070 (s) cm⁻¹; ¹H NMR (CDCl₃) 1.05 (s, 3H), 1.16 (s,3H), 1.82 (d,1H), 2.06 (d, 1H), 2.11 (m, 1H), 2.28 (m,1H), 2.40 (d, 1H), 2.72 (q, 1H), 2.86 (m,1H), 3.08 (n, 1H); ¹³C NMR (CDCl₃) 15.880 (q), 17.059 (q), 35.582 (d), 39.448 (t), 43.890 (d), 44.633 (d), 47.781 (s), 49.499 (d), 50.017 (d), 58.555 (s), 62.082 (d), 212.668 (s), 214.668 (s), mass spectrum (70 eV), m/e (relative intensity) 202.15 (100), 187.15 (46.1), 159.15 (47.0), 131.20(99.4), 122.10 (38.3), 91.10 (68.9), 79.10 (53.7), 66.10 (84.0), 65.10 (48.1), 53.10 (40.5), 51.10 (44.2).
Anal. Calcd for C_{13}H_{14}O_2: C, 77.20; H, 6.98.
Found: C, 77.17; H, 6.64.

4. 1,2,10,-Trimethylpentacyclo[5.4.0.0^{2.6}.0^{3.1}.0^{5.9}]undecane-8,11-diones

A solution of 2a (0.65 g, 3.0 mmol) in ethyl acetate (250 ml) was irradiated for 24 h under nitrogen in a quartz and Pyrex filter immersion photolysis apparatus equipped with a 450 Watt Hanovia medium pressure mercury vapor lamp. The solution was concentrated in vacuo to afford 4 as a colorless oil (0.62 g, 95%). The crude product was purified via column chromatography (silica gel stationary phase, 2% ethyl acetate-hexanes eluent); a colorless solid was thereby obtained. Further purification of the crude solid by recrystallization from hexane afforded a colorless microcrystalline solid (0.53 g, 83% yield): mp 103-104°C; IR (KBr) 2960 (s), 2950 (vs), 2930 (s), 2870 (w), 1730 (vs), 1460 (s), 1380 (w), 1290 (w), 1250 (w), 1230 (w), 1180 (w), 1130 (s), 1090 (w), 1070 (w), 1010 (w) cm^{-1}; 1H NMR (CDCl_{3}) 1.07 (s, 6H), 1.14 (s, 3H)
1.90 (m, 1H), 1.96 (t, 1H), 2.00 (d, 1H), 2.10 (m, 1H), 2.22 (q, 1H), 2.68 (t, 1H), 2.86 (m, 1H); 13C NMR (CDCl_{3}) 12.124 (q), 16.954 (q), 17.757 (q), 37.544 (t), 42.503 (d), 45.235 (d), 47.479 (s), 48.410 (d), 49.690 (s), 56.390 (d), 58.365 (s), 61.142 (d), 212.626 (s), 214.473 (s); mass spectrum
(70 eV), m/e (relative intensity) 216.15 (42.59), 201.15 (13.74), 188.15 (13.37), 173.20 (25.37), 145.10 (24.90), 91.05 (20.15), 80.15 (100.00), 79.05 (31.78), 77.05 (25.31), 53.05 (22.58), 39.05 (30.35).

Anal. Calcd for C\textsubscript{14}H\textsubscript{16}O\textsubscript{2} : C, 77.78; H, 7.41.

Found : C, 77.56; H, 7.75.
CHAPTER BIBLIOGRAPHY


CHAPTER II

SYNTHESIS OF NEW POLYCYCLIC COMPOUNDS

Introduction

Interest in the synthesis and chemistry of strained molecules has accelerated greatly in recent years (1). An ongoing program in this area (2), the synthesis of a new substituted trishomocubane isomer was undertaken. The scheme is shown as follow:

\[ \text{Na} \xrightarrow{\text{THF}} \text{Naphthalene} \xrightarrow{1. \text{CO}_2, 2. \text{H}_2\text{O}} \text{Major Product} \xrightarrow{\text{MeOH, H}_2\text{SO}_4} \text{Product II} \]

\[ \text{CH}_3\text{O}_2\text{C} \xrightarrow{\text{hv, Acetone}} \text{Ch}_{3}\text{O} \xrightarrow{1. \text{Na/K, pH}, 2. \text{TMSCl, } \Delta} \text{Product II} \xrightarrow{3. \text{T-BuOH}} \text{Product} \]

\[ \text{CH}_3\text{O}_2\text{C} \xrightarrow{1. \text{K, pH}, 55^\circ\text{C}, 2. \text{H}_2\text{O}^+, 0^\circ\text{C}} \text{Product 5} \xrightarrow{\text{CH}_3\text{O} \xrightarrow{\text{KOH, H}_2\text{NNH}_2}} \text{Product 6a} + \text{Product 6b} \]

\[ \text{HOOC} \xrightarrow{7\text{a}} \text{Product 7a} + \text{Product 7b} \]

20
Cyclopentadien was reacted with sodium as the starting material (3). A dicyclopentadienedicarboxylic acid (Thiele's acid) (4) was obtained by carbonation of dicyclopentadienylsodium (3). Acid-catalyzed esterification of this acid gave a crystalline dimethyl ester (Thiele's ester) (5). It has previously been shown that, of the four isomeric alternative structures can be written for Thiele's ester (Ia–Id) only structure Ia is correct (6). The structures of Ia–Id are shown as follows:

A solution of Ia in acetone irradiated for 24 h in a quartz immersion photolysis apparatus equipped with a 450 Watt Hanovia medium pressure mercury vapor lamp and Pyrex filter gave the corresponding "cage" diester II in 85% yield (6). Reaction of diester II with Na-K alloy followed by addition of chlorotrimethylsilane resulted in cleavage of the succinyl c-c bond in "cage" diester II. After the reaction mixture had been quenched by addition of t-BuoH, a
new diester, 5, was obtained (7). A mixture of Dickmann condensation products, β-keto esters 6a and 6b was obtained via reaction of 5 and potassium metal (after quenching the reaction mixture with dilute hydrochloric acid) (8) (9). Wolff-Kishner reduction (10) of this mixture of "cage" β-keto ester afforded the corresponding carboxylic acid 7a and 7b. A substituted trishomocubane isomer, 7a, was isolated by careful chromatographic purification of the reaction product.

Results and Discussion

1. Structural analysis for dimethyltetracyclo [5,3,0,03.9,04.8]decane-2,5-dicarboxylate 5

In the 1H NMR spectrum of 5 (see Figure 20), eighteen protons are observed, i.e., two protons more than are present its precursor, "cage" diester II (cf. Figure 18). A single peak at ca δ 3.6 (area 6H) corresponds to the two methoxy groups in 5.

In the 13C NMR spectrum of 5 (Figure 21) fourteen peaks are observed, two of which appear at δ 73.17 and δ 73.82. These can be assigned readily to the two nonequivalent ester carbonyl carbons in 5. In the upfield spectral region, an attached proton test (APT) reveals the presence of two methylene groups (CH2). The corresponding APT for "cage" diester II reveals two methylene groups and two quaternary carbon atoms (Figure 19). This evidence confirm
the fact that the succinyl bond in II indeed has been
cleaved via reaction of II with Na-K alloy.

2. Structural analysis for methylpentacyclo
\[ [5,4,0,0^2.5,03.10,04.8] \text{undecane-9-one-10-carboxylate 6a} \text{ and Methylpentacyclo} \\
\[ [5,4,0,0^2.5,03.10,04.8] \text{undecane-9-one-8-carboxylate 6b} \]

In the \textsuperscript{1}H NMR spectrum of mixture of 6a and 6b, peaks to
that correspond a total of fourteen protons are observed
(Figure 22). The resonance peak at 83.5 (area 3H)
corresponds to the methoxy groups in 6a + 6b.

The \textsuperscript{13}C NMR spectrum of 6a + 6b (Figure 23) displays
twenty four of the expected twenty six resonances. In the
dowfield spectral region two pairs of peaks are observed.
One pair is at ca 8211-225 which corresponds to ketone
carbonyl carbons in 6a and 6b, the other pair is at ca 8
165-171 which corresponds to ester carbonyl carbons in 6a
and 6b, respectively. In the aliphatic region three pairs
of methylene and quaternary carbon peaks appear as revealed
by APT. One pair, comparing to other two pairs, resonates
at relatively downfield (860-70). This pair of peaks
corresponds to the aliphatic quaternary carbons in 6a and
6b. The fact that the two aliphatic quaternary carbon peaks
are at 860-70 (whereas the other two pairs of peaks are at 8
40-44) is because the electron-withdrawing of adjacent
ketone carbonyl and ester carbonyl carbons. These evidences
confirm the structure of the mixture of two isomers, "cage" β-keto esters 6a and 6b.

One isomer 6a or 6b was separated via flash chromatographic separation. The area of fourteen protons is also observed in the 1H NMR spectrum (Figure 24). In the 13C NMR spectrum (Figure 25), there are thirteen carbon peaks, in which the peak at δ211.86 corresponds to ketone carbonyl carbon and the peak at δ171.13 corresponds to ester carbonyl carbon.

The possible reaction mechanism for this Dieckmann condensation with one α-proton in each ester group is shown as follow. The mixture of two "cage" β-keto esters 6a and 6b is thereby formed.
3. Structural analysis for pentacyclo
\[5,4,0,0^{2.5},0^{3.10},0^{4.8}\] carboxylic acid 7a

Wolff-Kishner reduction was employed to convert "cage"
\(\beta\)-keto ester 6a and 6b to the corresponding carboxylic
acid.

In the \(^1\)H NMR spectrum (Figure 26) an extremely broad
peak at ca \(\delta\) 6.11 corresponds to the carboxylic acid proton. A
total of fourteen protons can be accounted for by
integration of the proton NMR spectrum of 7a. The \(^{13}\)C NMR
spectrum (Figure 27) shows only nine carbon resonances.
This result requires that compound 7a possess twofold
symmetry which is shown as follow:
One quaternary peak at δ184.12 corresponds to the carboxyl carbon atom. In the aliphatic region, APT shows one quaternary peak and two methylene peaks. In 7a, carbon 9 and 11 are identical because of symmetry. The results of single crystal X-ray analysis confirm the structure of compound 7a (see Figure 28).

Experimental

Melting point and boiling points are uncorrected. Proton NMR spectra and 13C NMR spectra were recorded on a VXR-300 NMR spectrometer. In all cases, signals are reported in parts per million (δ) downfield from internal tetramethylsilane. Infrared spectra were obtained with a Perkin-Elmer Model 1330 infrared spectrophotometer. Mass spectra were obtained with a Hewlett-Packard Model 5970 A GC/MS system operating at 70 eV. Elemental microanalyses were performed by Galbraith Laboratories, Inc., Knoxville, TN.

1. Dimethyltetracyclo [5,3,0,0^3.9,0^4.8]decane-2,5-dicarboxylate 5
To a flame-dried 500 ml three-necked round-bottom flask, equipped with a condenser, was added under nitrogen freshly cut sodium (0.8 g, 22.6 mmol) and dry toluene (100 ml). This mixture was heated with vigorous stirring under nitrogen until a fine dispersion was formed. The mixture was allowed to cool to ambient temperature, and the toluene then was decanted, dry benzene (250 ml) was then transferred into the flask, and freshly cut potassium (4 g, 103 mmol) was added. The resulting mixture was heated with vigorous stirring under nitrogen until the two metals became finely dispersed. The mixture was allowed to cool to ambient temperature. A solution of dimethyl pentacyclo [5,3,0,0².5,0³.9,0⁴.8] decane-2.5-dicarboxylate II (6.94 g, 28 mmol) in dry benzene (50 ml) and trimethylchlorosilane (25 ml) were then injected sequentially under nitrogen. The reaction mixture was refluxed under nitrogen with stirring for 16 h and then cooled to room temperature. The reaction mixture was filtered under nitrogen and tert-butyl alcohol (30 ml) was added to the filtrate. The resulting solution was concentrated in vacuo, thereby affording a yellow viscous oil (6.66 g, 95% yield). The oily residue was purified by column chromatography (silica gel stationary phase; gradient elution with 1%-4% ethyl acetate-hexane was
A colorless oil was thereby obtained which solidified when triturated with hexane after standing overnight in a refrigerator. Recrystallization of the solid from ethyl acetate-hexane afforded pure 5 as a colorless microcrystalline solid (1.54 g, 22% yield): mp 71-72°C; IR (KBr) 2950 (s), 1720 (vs), 1440 (m), 1320 (w), 1290 (m), 1250 (s), 1230 (s), 1060 (w); 1H NMR (CDCl3) 1.46 (g, 2H), 2.04 (m, 1H), 2.30 (g, 1H), 2.52 (m, 3H), 2.85 (m, 5H); 13C NMR (CDCl3) 28.014 (t), 37.139 (d), 39.254 (d), 41.600 (t), 42.966 (d), 44.123 (d), 46.252 (d), 46.463 (d), 48.730 (d), 50.984 (d), 51.365 (d), 51.625 (d), 173.169 (s), 173.824 (s); mass spectrum (70 eV), m/e (relative intensity) 218.20 (13.1), 190.20 (20.5), 131.10 (37.8), 130.20 (23.7), 125.10 (100.0), 124.20 (20.1), 66.10 (96.4), 65.10 (34.9).

Found: C, 67.55; H, 7.266.

2. Methyl pentacyclo [5,4,0,0^2.5,0^3.10,0^4.8]undecane-9-one-10-carboxylate 6a and methyl pentacyclo [5,4,0,0^2.5,0^3.10,0^4.8]undecane-9-one-8-carboxylate 6b

To a flame-dried 50 ml three-necked round-bottom flask, equipped with a condenser, was added under nitrogen freshly cut potassium (0.039 g, 1 mmol) and
dry benzene (20 ml). This mixture was heated under nitrogen with vigorous stirring until a fine dispersion had formed. The mixture was allowed to cool to ambient temperature. A solution of diester 5 (0.500 g, 2 mmol) in dry benzene (5 ml) was added under nitrogen blanket. The reaction mixture was then slowly heated to 70°C. The reaction mixture was maintained at this temperature and stirred under nitrogen for 3 h. After all of the potassium metal had reacted, the solution then was cooled to 0°C by application of an external ice bath. The reaction mixture was then quenched by dropwise addition of cold, 3% aqueous hydrochloric acid solution (15 ml) with stirring. The resulting solution was transferred into a separatory funnel. Water (30 ml) was added and the mixture was extracted with ether (2 x 30 ml). The organic layer was washed sequentially with 20% aqueous sodium bicarbonate solution (50 ml), brine (50 ml) and water (50 ml). The organic layer was then dried (anhydrous magnesium sulfate) and filtered, and the filtrate was concentrated in vacuo. A mixture of Dieckmann condensation products 6a and 6b was thereby obtained as a yellow viscous oil (0.48 g, 96%). This crude product was purified by column chromatography (silica gel stationary phase; gradient elution with 1%-4% ethyl acetate-hexane was employed). A pure mixture of 6a and 6b was afforded as a colorless oil (0.29 g, 66% yield). The 1H and 13C NMR spectra of this mixture are shown in
Figure 36 and 37, respectively. Separation of this mixture was performed by using flash column chromatography (silica gel stationary phase; gradient elution with 1%-4% ethyl acetate-hexane was employed). A single, pure isomer (2a or 2b) was thereby isolated as a colorless oil (0.16 g, 37% yield): bp 80°C/1 mm; IR (CCl₄) 2950 (s), 2870 (w), 1740 (vs), 1720 (vs), 1450 (w), 1340 (w), 1320 (m), 1300 (m), 1270 (s), 1240 (w), 1210 (w), 1170 (m), 1080 (m) cm⁻¹; ¹H NMR (CDCl₃) 1.41 (d, 1H), 1.69 (d, 1H), 2.41 (s, 2H), 2.59 (m, 2H), 2.88 (m, 4H), 3.22 (t, 1H), 3.67 (s, 3H); ¹³C NMR (CDCl₃) 38.122 (d), 40.718 (d), 42.535 (t), 43.823 (t), 44.080 (d), 46.458 (d), 46.590 (d), 50.856 (d), 52.103 (d), 56.805 (d), 61.049 (s), 171.123 (s), 211.864 (s); mass spectrum (70 eV), m/e (relative intensity) 218.1 (16.7), 190.1 (21.8), 131.1 (32.41), 130.1 (22.5), 125.0 (83.9), 124.0 (17.0), 91.0 (18.3), 66.1 (100.0), 39.0 (32.9).

Anal. Calcd for C₁₃H₁₄O₃: C, 71.54; H, 6.47.
Found: C, 71.34; H, 6.30.

3. Pentacyclo[5,4,0,2.5,03.10,04.8]undecane-10-carboxylic acid 7a

To a 50 ml round-bottom flask equipped with a condenser, were added diethylene glycol (5 ml) and potassium hydroxide (0.34 g, 6 mmol). The resulting mixture was heated with stirring until all of the solid potassium
hydroxide had dissolved. The resulting solution was heated to 80°C, and the mixture of β-keto esters 6a and 6b (0.44 g, 2 mmol) and hydrazine (1.0 g, 31 mmol) were added. The temperature of the reaction mixture was increased to 100-110°C, and the reaction mixture was stirred at this temperature for 5 h. The reaction flask was then fitted with a Dean-Stark tube, and water was removed from the reaction mixture by azeotropic distillation during 3 h. The Dean-Stark trap was then removed, and the temperature of the reaction mixture was increased to 200-210°C. The reaction mixture was heated with stirring at this temperature for 15 h. The solution then was allowed to cool room temperature, and water (10 ml) was added with stirring. The solution was then further cooled to 0°C by application of an external ice bath. Dilute (3%) aqueous hydrochloric acid solution was added dropwise until the pH of the reaction mixture reached 5-6, (ca, 5 ml). The resulting mixture was transferred into a separatory funnel. Water (20 ml) was added, and the resulting mixture was extracted with ether (2 x 30 ml). The organic layer was dried (anhydrous magnesium sulfate) and filtered, and the filtrate was concentrated in vacuo. A crude product mixture 7a and 7b (0.36 g, 95%) was thereby obtained as a viscous yellow oil. The crude product was purified via column chromatography (silica gel stationary phase, 4% ethyl acetate-hexane eluent); a colorless solid was
achieved by recrystallization of the crude solid was achieved by recrystallization from hexane. Pure 7a (0.24 g, 63%) was thereby obtained as a colorless microcrystalline solid: mp 138-139°C; IR (KBr) 2950 (s), 2870 (m), 1680 (vs), 1430 (w), 1330 (w), 1310 (m), 1280 (m) cm⁻¹; ¹H NMR (CDCl₃) 1.42 (m, 2H), 2.10 (m, 3H), 2.47 (d, 3H), 2.72 (m, 2H), 2.88 (m, 1H), 11.40 (b, 1H); ¹³C NMR (CDCl₃) 34.3040 (d), 41.5191 (t), 42.0844 (t), 42.4639 (d), 47.0226 (d), 47.7674 (d), 50.6050 (d), 54.2125 (s), 184.1198 (s); Mass spectrum (70 eV), m/e (relative intensity) 190.05 (29.07), 145.10 (16.36), 112.05 (25.05), 105.05 (93.70), 91.05 (21.93), 80.05 (74.02), 79.05 (100), 78.05 (20.83), 77.05 (49.44), 67.00 (19.41), 66.10 (32.05), 65.10 (20.66), 51.00 (21.34), 45.00 (20.22), 41.00 (22.23), 39.00 (45.45).

Anal. Calcd for C₁₂H₁₄O₂: C, 75.76; H, 7.52.
Found: C, 75.76; H, 7.42.
CHAPTER BIBLIOGRAPHY


4. Thiele, J. *Ber.*, 1901, 34, 68.


Figure 3
The COSY spectrum of 1
Figure 4

The nuclear magnetic double resonance spectrum of 1
Figure 5
The HETCOR spectrum of I
Figure 7

The 13C NMR spectrum of 2a
Figure 9

The nuclear magnetic double resonance spectrum of 2a
Figure 10

The nuclear magnetic double resonance spectrum of 2a
Figure 11

The HETCOR spectrum of 2a
The single crystal X-ray structure of 2a

Figure 12
Figure 15

The $^1$H NMR spectrum of 4
Figure 16
The 13C NMR spectrum of \( \frac{1}{4} \).
Figure 17

The single crystal X-ray structure of 4
Figure 18

The 1H NMR spectrum of II
Figure 19

The $^{13}$C NMR spectrum of II
Figure 20

The 1H NMR spectrum of 5
Figure 21

The $^{13}$C NMR spectrum of 5
Figure 23

The $^{13}$NMR spectrum of 6a and 6b
Figure 24

The 1H NMR spectrum of 6a or 6b
The 13C NMR spectrum of 6a or 6b
Figure 26

The 1H NMR spectrum of 7a
Figure 28

The single crystal X-ray structure of 7a.
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