8-1977

The Preparation and Study of Some Bridged Tropones

Sultan T. Abu-Orabi

THE PREPARATION AND STUDY OF SOME BRIDGED TROPONES

by

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A Thesis
Submitted to the
Faculty of The Graduate College
in partial fulfillment
of the
Degree of Master of Arts

Western Michigan University
Kalamazoo, Michigan
August 1977

ACKNOWLEDGEMENTS

The author would like to express his appreciation and gratitude to Dr. Robert E. Harmon for his great encouragement, guidance, concern and for his numerous helpful suggestions during the period I worked under his supervision. It is acknowledged here that the original ideas for this work were conceived by Dr. Harmon.

Lastly, a deep appreciation is felt toward those who have helped with this work. And my thanks are also to the Chemistry Department of Western Michigan University for providing me with a teaching assistantship.

Sultan T. Abu-Orabi

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TABLE OF CONTENTS

INTRODUCTION

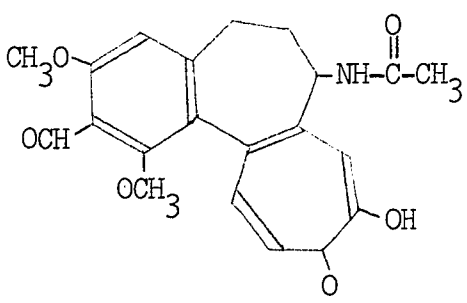
The problem of aromaticity in non-benzoid aromatic compounds has stimulated the synthesis of a variety of tropones and related compounds. Recently the preparation and physical properties of 2,7-polymethylene-4,5-benzotropones and a series of bridged 1- and 2-methylcycloheptapyrazolones have been reported. It has been determined from the infrared and nuclear magnetic resonance spectra that the tropone ring system is planar if the number of methylene groups contained in the bridge equals seven or more. The purpose of this work was to prepare and study a new series bridged of isoxazoletropones and triazoletropones.

HISTORICAL

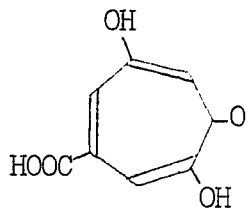
Dewar[1,2,3] proposed the 2-hydroxy-2,4,6-cycloheptatrien-1-one skeleton for colchicine(I) and stipitatic Acid (II). He originated the name of tropolone for 2-hydroxy-2,4,6-cycloheptatrien-1-one(III).

This new type of aromatic ring system, tropolone, was first synthesized in 1950 by Doering and Knox.[4]

Indications of aromaticity in the tropolone ring system directed attention to the need for determining the necessary minimum structural features for aromaticity in a seven membered ring. This prompted Dauben and Ringold[5] to synthesize tropone(IV) in 1951.



I



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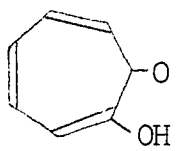

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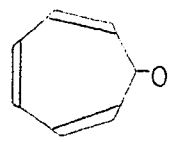
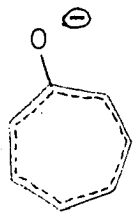
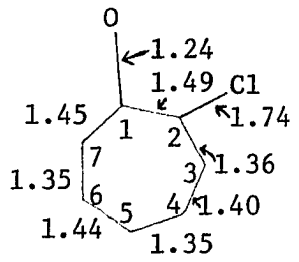


IV

Tropone is generally classified as a non-benzoid aromatic compound,[5,6] possessing aromatic character due to a ground state contribution from the cyclic delocalized six π-electron resonance hybrid structure (V).



V



VI

X-ray crystallographic analysis of 2-chlorotropone (VI) was carried out by Watkin and coworkers,[7,8] who showed that the seven membered ring is planar. The chlorine atom lies close to the plane of the ring and the carbonyl oxygen is displaced out of the plane of the ring.

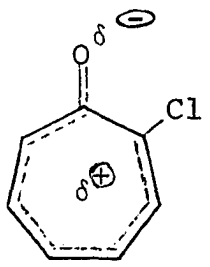
The π-electron system is partially delocalized, the lengths of the C-C double bonds C_2-C_3, C_4-C_5 and C_6-C_7 of 1.36, 1.35 and 1.35Å which are slightly greater than the pure double bond value for ethylene of 1.335Å.[9]

The single bonds C_5-C_6 and C_7-C_1 of 1.44 and 1.45Å are slightly shorter than the length of a theoretically pure single bond between two sp^2 hybridized carbon atoms (1.48-1.50Å).[10,11]

The C_3-C_4 bond at 1.40Å is anomalously short, while C_1C_2 at 1.49Å is longer and corresponds in length to the C_{sp^2}-C_{sp^2} pure single bond values.

The C=O bond length in 2-chlorotropone (1.24Å) agrees closely with the length of this bond determined in the benzotropone (1.24Å). It is, however, somewhat greater than the standard C=O double bond length (1.215Å), and, hence, it maybe concluded that the oxygen atom participates in the π-electron delocalization.

The C-Cl bond length (1.74Å) is in good agreement with lengths commonly found for C_{sp^2}-Cl bond (1.736-1.744Å)[13], but is greater than the value of 1.70Å quoted in reference 12, and, hence, it may be concluded that the chlorine atom is not involved in electron delocalization. The structure based on x-ray data (VII) has partial π-electron delocalization extending from C_2 around to C_1 and onto the oxygen atom. Therefore, the molecule cannot be considered as aromatic, since a completely delocalized pi electron system is not present.[6]



VII

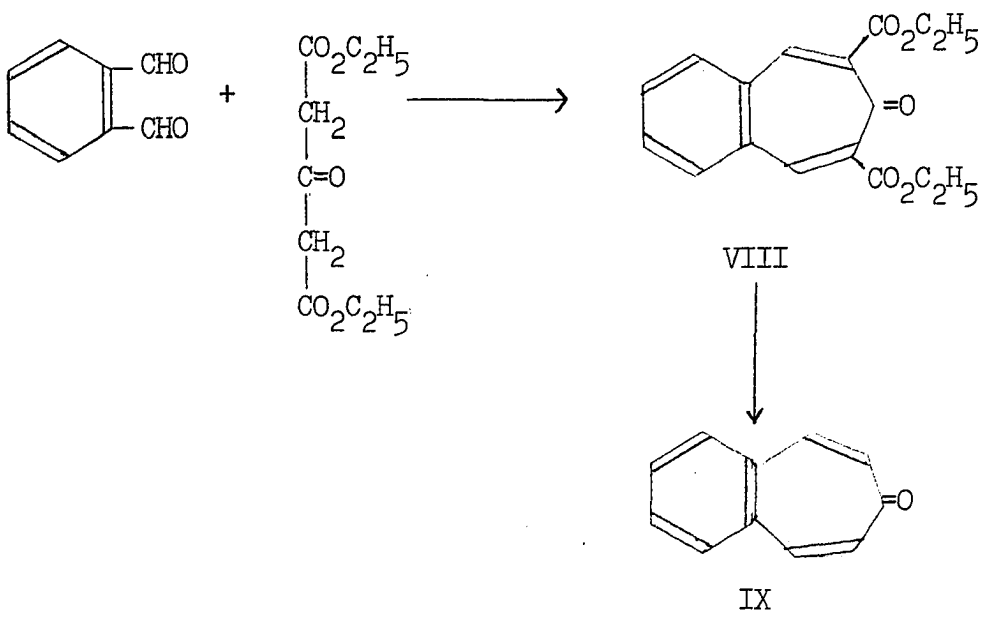
In tropolone[14] itself, the carbon-carbon bond lengths showed no apparent bond alteration as reported for 2-chlorotropone.[8] The average value is 1.407Å which is near to the standard aromatic value of 1.39Å. The C_1-C_2 bond length of 1.452Å is significantly longer than the other C-C bond lengths in this compound reported previously, but the differences between the C_1-C_2 and the other C-C bond lengths are smaller in tropolone itself than in the derivative mentioned above. This indicates that the tropolone is not merely a 2-hydroxy derivative of tropone but is more stabilized by the contribution of the 6π-electron system.

A similar conclusion was reached recently by Bertelli and coworkers,[15] who have reevaluated the question of aromatic character in tropone and related compounds on the basis of dipole moment and n.m.r. measurements.

Veracini and Pietra[16] found when they compared the experimentally observed spectra of tropone with the spectra calculated on the basis of a planar model, that only slight bond differences appeared in the seven membered ring portion.

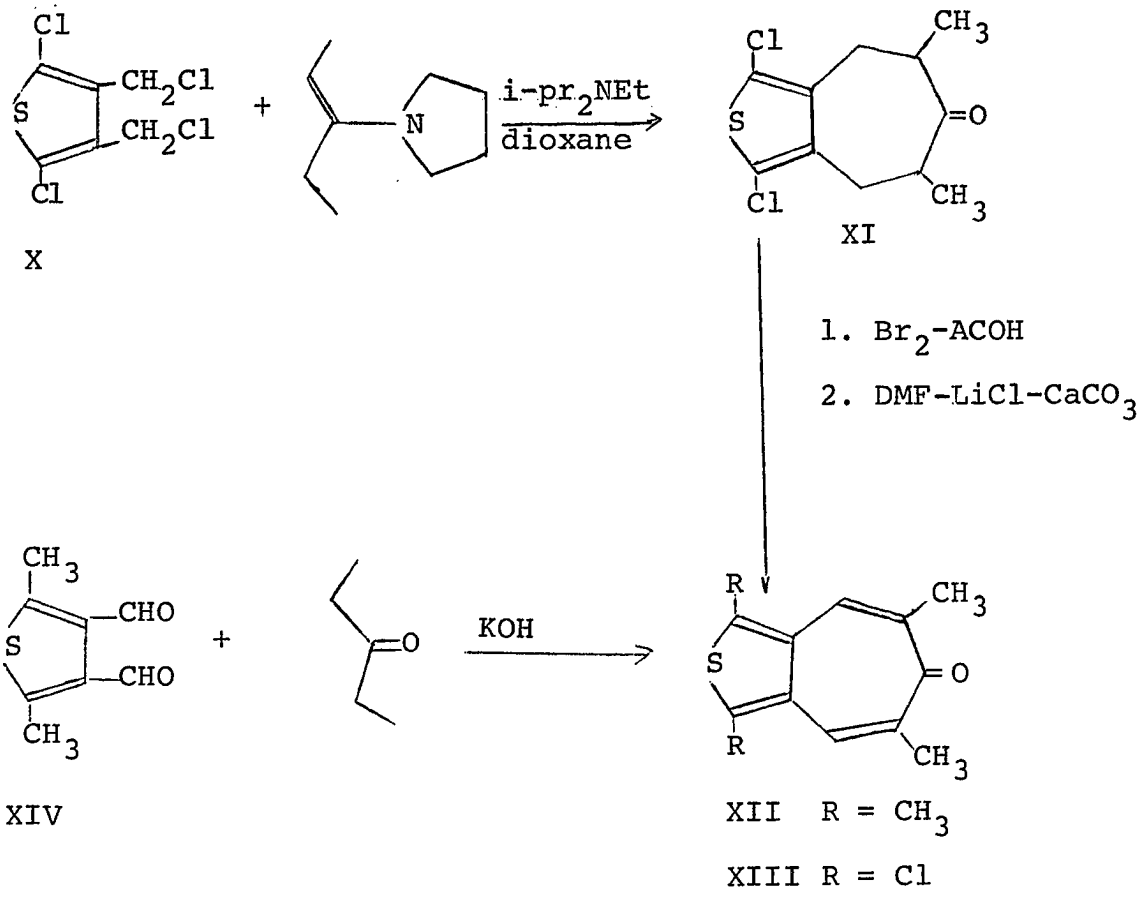
Many fused ring derivatives of the tropone have been synthesized using the aldol condensation reaction. Theile and coworkers,[17,18] have synthesized 4,5-benzotropone(IX) by condensing phthalaldehyde with diethyl

acetone dicarboxylate (Scheme 1) to give 2,7-dicarbethoxy-4,5-benzotropone(VIII) which was hydrolyzed and decarboxylated to give compound IX.



Scheme I

Winn and Bordwell[19] were successful in preparing the analogs of 2-thiaazulen-6-one as shown in Scheme 2. Cyclization of 3,4-bix(chloromethyl)-2,5-dichlorothiophene(X) with the pyrrolidine enamine of 3-pentanone gave 1,3-dichloro-5,7-dimethyl-5,6,7,8-tetrahydro-4-H-cyclohepta[C]-thiophen-6-one(XI) which was converted to dichlorodimethyl-2-thiaazulen-6-one(XIII) by bromination and dehydrobromination. Tetramethyl-2-thiaazulen-6-one(XII) was prepared by cyclization of 2,5-dimethylthiophene-3,4-dicarboxaldehyde(XIV) with 3-pentanone.



X

XI

XIV

XII R = CH_3

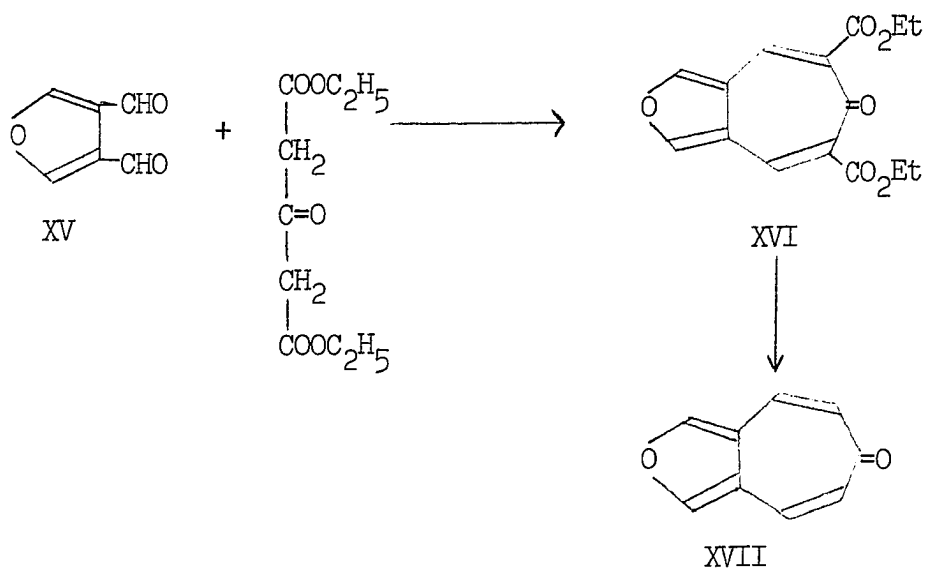
XIII R = Cl

Scheme 2

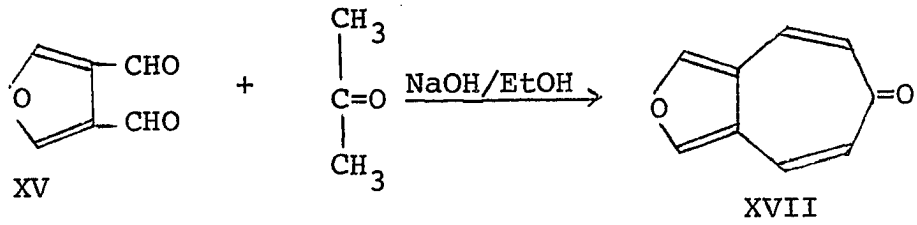
When Winn and Bordwell[19] compared the i.r. spectra for compounds XII and XIII, they found that the carbonyl bands in the infrared were at 1590 and 1630 cm^{-1} respectively. This shows that there is electron delocalization in the molecule and that the electronegative chlorine atoms in XIII hinder delocalization of electrons from sulfur to oxygen relative to the effect of the methyl groups in XII.

In 1968 Cook and Forbes[20] synthesized a new derivative of tropone. They prepared 4,5-furotropone(XVII) using two different procedures. The first one, shown in Scheme 3 was accomplished by the condensing 3,4-furan-dicarboxaldehyde(XV) with diethyl acetone dicarboxylate to give the ester (XVI) which was hydrolyzed and then decarboxylated to give the desired compound(XVII).

The second method, shown in Scheme 4, was more efficient and involved the condensation of 3,4-furan-dicarboxyaldehyde(XV) with acetone using aqueous ethanolic sodium hydroxide. The latter method is believed to be the only reported example of a condensation of dialdehyde with acetone in the presence of base to give seven membered ring.

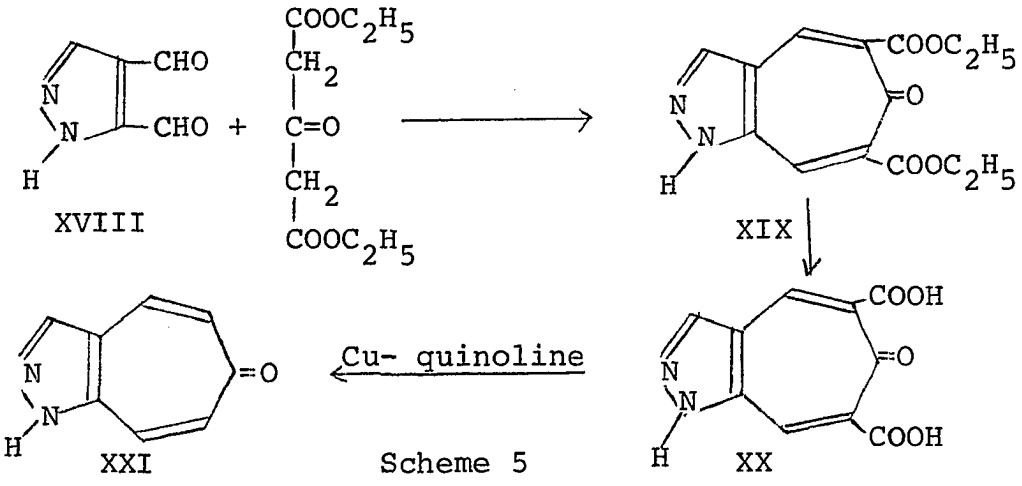


Scheme 3



Scheme 4

Recently Greco and Pesce[21] succeeded in preparing [4,5-c(d)] pyrazolotropone* (or 1,2-diazo-IH-azulen-6-one)(XXI) by the condensation of pyrozole-3(5),4-dicarboxaldehyde(XVIII) with diethyl acetone dicarboxylate to give 2,7-dicarbethoxy [4,5-c(d)] pyrazolotropone(XIX) which was hydrolyzed using sulfuric acid to give 2,7-dicarboxy [4,5-c(d)] pyrozolotropone(XX). Compound XX was decarboxylated using a copper-quinoline mixture to give the parent structure(XXI) (Scheme 5).

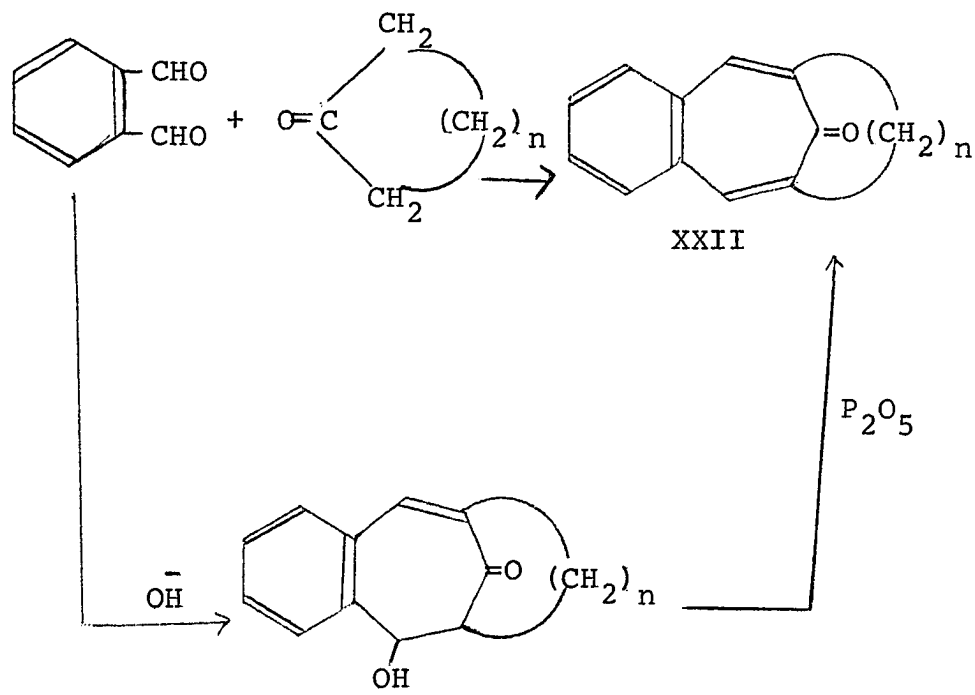


Scheme 5

*The nomenclature employed is analogous to the one accepted for benzotropone and [4,5-c] furotropone[21]: the letters c and d refer to the numbering of the pyrazole ring, the numbers 4 and 5 refer to the side of the tropone ring fused to the pyrozole ring.

The extent of aromaticity of XXI was estimated by comparison of some of its spectral characteristics with data on [4,5-c]-benzotropone(IX) and [4,5-c] furotropone (XVII).[20,21] The n.m.r. data indicates that the three bicyclic tropones can sustain a ring current. A comparison with tropone reveals the bicyclic tropones to be less aromatic. The ultraviolet absorptions[21] indicate the order of aromaticity to be tropone > benzotropone > pyrazolotropone > furotropone.

In 1956 Kloster-Jensen and coworkers[22] prepared 2,7-polymethylene-4,5-benzotropones(XXII) by the condensation of phthalaldehyde with cyclic ketones (Scheme 6).



Scheme 6

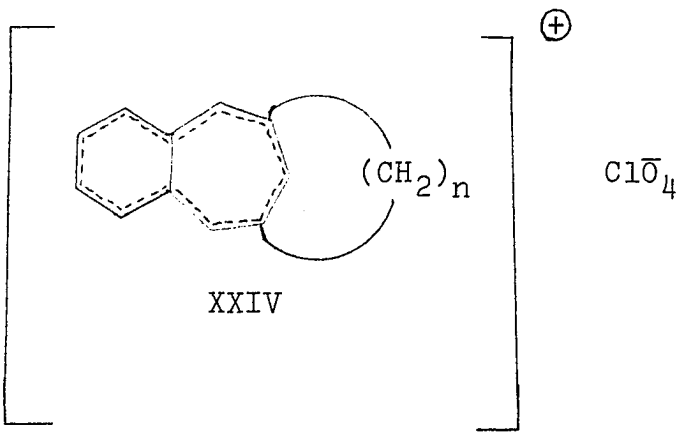
Kloster-Jensen[22] showed that the bridged benzotropones were obtained directly from the condensation reaction when n=7,9,12 or 13. However, if n=4,5,6 or 8 the intermediate (XXIII) had to be dehydrated with phosphorous pentoxide.

On the basis of infrared spectral analysis, Kloster-Jensen and coworkers have postulated that the tropone ring system is planar if the number of methylene groups contained in the bridge equals seven or more. The i.r. spectra of these compounds showed the carbonyl absorption at 1609 cm^{-1}. If the tropone ring is non-planar, electron delocalization is inhibited and the carbonyl absorption should appear at 1650-1700 cm^{-1} indicating increasing double bond character of the carbonyl group.

Harmon and coworkers[23-25] have reached a similar conclusion on the basis of n.m.r. measurements. They found when the number of methylene groups (n) contained in the bridge equals nine, the tropone protons resonated at 7.31 ppm. This downfield shift of the protons in the tropone ring can be attributed to the increased planarity of the system as n is increased above six.

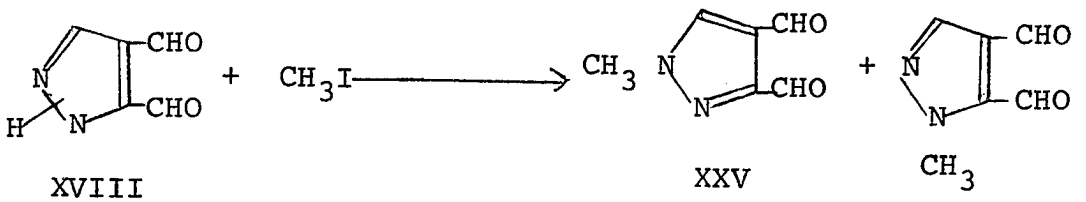
Harmon and coworkers confirmed this further by reduction of the carbonyl function with lithium aluminum hydride to the corresponding alcohols. In these alcohols the seven membered ring system is no longer planar, and the protons resonated at 6.25 ppm.

The n.m.r. spectrum of 2,7-polymethylene-4,5-benzotropylium perchlorate(XXIV), which was obtained by treatment of the alcohols with perchloric acid, showed a further down field shift due to the benzotropylium ion ring protons (9.2 ppm). This shift in resonance peak positions attributed to the delocalized positive charge over both the six and the seven membered ring which decreases the electron density and increases deshielding of the hydrogens on the rings.

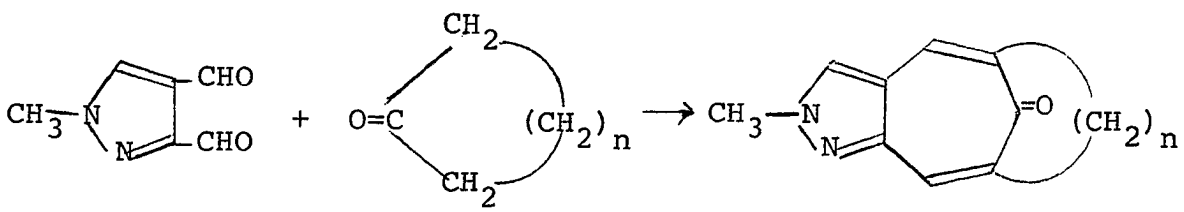


XXIV

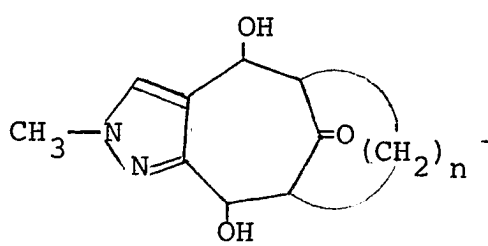
In 1976 Harmon and Larson[26] carried out a similar investigation and they synthesized a series of bridged 2-methyl-6(2H)-cycloheptapyrazolones(XXVII) by condensation of 1-methyl pyrazole-3,4-dicarboxaldehyde(XXV) with cyclic ketones (Scheme 7).



XVIII XXV XXVI



XXV XXVII



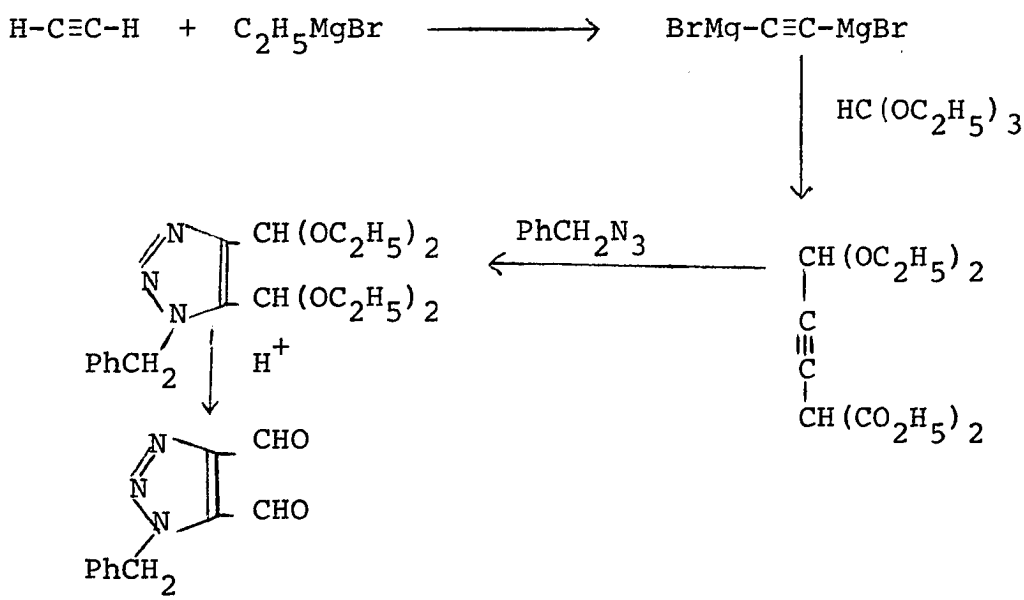
XXVIII

Scheme 7

DISCUSSION

Previous results obtained from studying the poly methylene bridged benzotropones and pyrazolotropones prompted us to attempt the synthesis of the polymethylene triazolotropone in order to see the effect of polymethylene bridges on the aromaticity and planarity of the triazolotropone molecule.

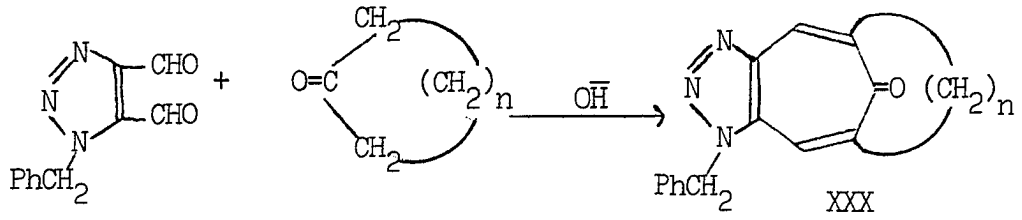
The preparation of 1-benzyl-IH-triazole-4,5-dicarboxaldehyde(XXIX) is shown in Scheme 8. The acetylene dialdehyde bis(diethyl acetal) was prepared according to the procedure reported by Wohl.[27] Treatment of acetylene dicarboxaldehyde bis(diethyl acetal) with benzyl azide prepared from reacting sodium azide with benzyl chloride, followed by acid hydrolysis, affords 1-benzyl-IH-triazole-4,5-dicarboxaldehyde(XXIX).[28]



XXIX

Scheme 8

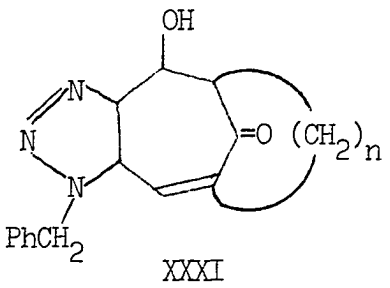
Treatment of 1-benzyl-IH-triazole-4,5-dicarboxaldehyde with cyclic ketones in the presence of alcoholic sodium hydroxide gave a series of polymethylene bridged 1-benzyl-IH-triazoletropones (Scheme 9).



XXX

n = 12

OR



XXXI

n = 7, 8, 9

Scheme 9

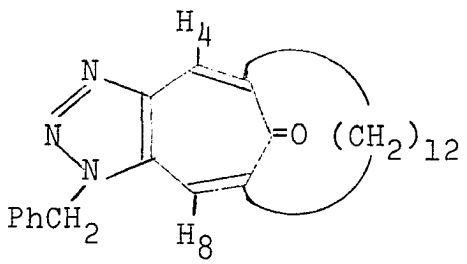
In the case where n=12, the product XXX was obtained, but when n=7,8 or 9 the results of the aldol-type condensations are the monohydroxy ketones XXXI.

These aldol condensations gave results which were analogously different from those reported in the previous work of Harmon and Larson.[26] When they condensed 1-methyl-IH-pyrazole-3,4-dicarboxaldehyde(XXV) with cyclic

ketones (Scheme 7), they found when n=7 or 12 the product XXVII was obtained in one step, but when n=8 or 9 the results of aldol-type condensation the dihydroxy ketones (XXVIII) which were dehydrated to give the product XXVII.

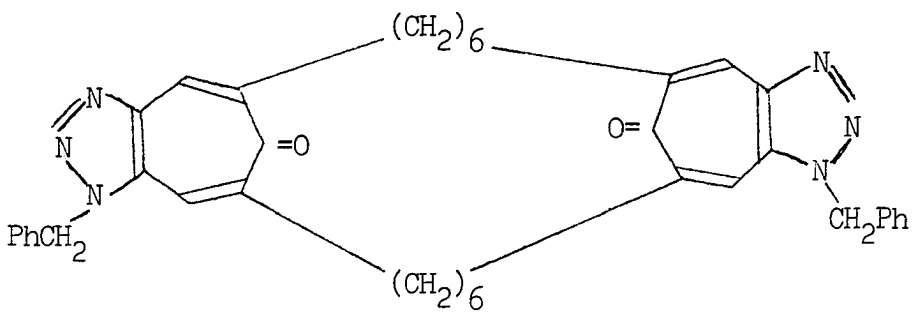
However, the results obtained in this work were similar to those of Kloster-Jensen[22] who found that in the case of 2,7-polymethylene-4,5-benzotropone(XXII) (Scheme 6), the intermediate was not the dihydroxy ketone but rather the monohydroxy ketone.

The nuclear magnetic resonance spectrum of 1-benzyl-5,7-dodecano-6(2H)-cycloheptatriazolone(XXXII) shows the chemical shift of H_4 and H_8 protons is 7.75 ppm. This downfield shift can be attributed to an increase in the planarity of the ring system.



XXXII

The nuclear magnetic resonance spectrum was obtained for 1,1'-dibenzyl-5,5', 7,7'-bis(hexano-6(2H),6'(2H')-cycloheptatriazolone). (XXXIII), which was prepared by condensing 1-benzyl-IH-triazole-4,5-dicarboxaldehyde (2 moles) with 1,10-cyclooctadecanedione (1 mole) in the presence of saturated solution of sodium hydroxide in methanol. The chemical shift of H_4 and H_8 protons is 7.70 ppm. This indicates that the triazolotropones can sustain a ring current and leads to the conclusion that these compounds are aromatic in the tropone ring portion.

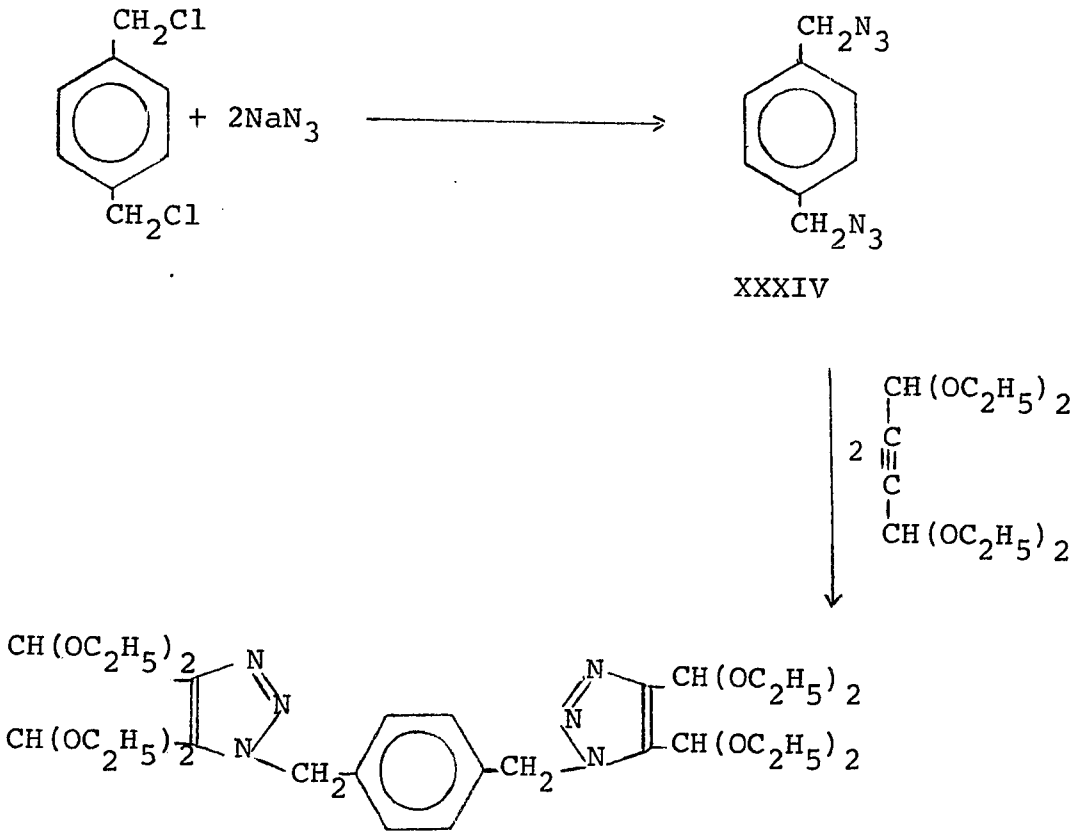


XXXIII

In the case of 4-hydroxy-1-benzyl-4,5-dihydro-5,7-nonano-6(2H)-cycloheptatriazolone(XXXI, n=9), 4-hydroxy-1-benzyl-4,5-dihydro-5,7-octano-6(2H)-cycloheptatriazolone(XXXI, n=8) and 4-hydroxy-1-benzyl-4,5-dihydro-5,7-heptano-6(2H)-cycloheptatriazolone(XXXI, n=7), the chemical shift of H_8 is 6.85-6.90 ppm. These protons resonate at a higher field because these systems cannot

sustain a ring current.

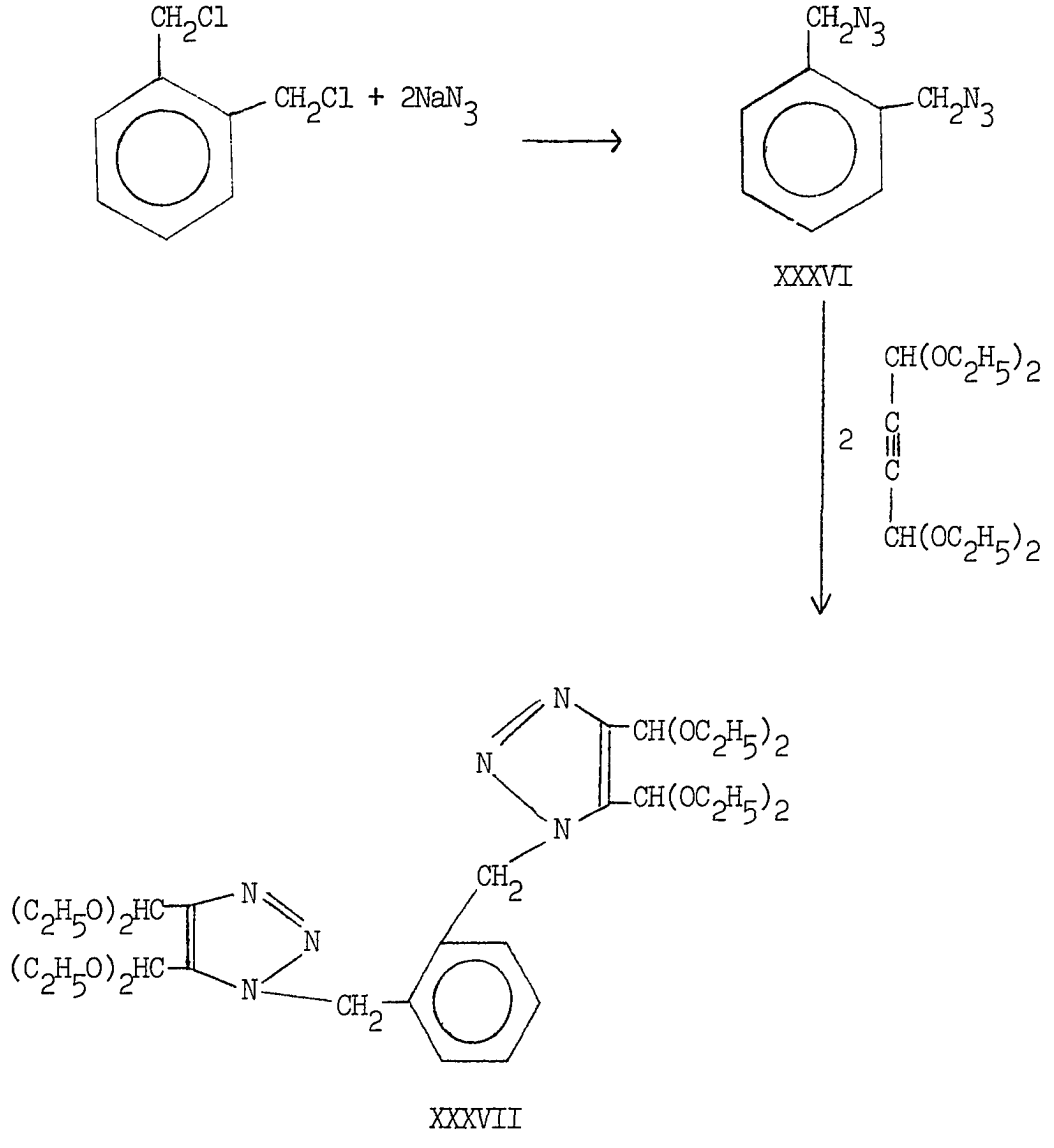
In order to study the effect of bridging on tropone aromaticity when more than one exists in close proximity, linked in one molecule connected through the heteroring portions, we undertook the preparation of 1,1-'-[1,4-phenylenebis(methylene)] bis(triazole-4,5-dicarboxaldehyde tetraethyl acetal)(XXXV), shown in Scheme 10. The α, α'-diazido-p-xylene(XXXIV) was prepared by reacting sodium azide with α, α'-dichoro-p-xylene. Reaction of α, α'-diazido-p-xylene with acetylene dicarboxaldehyde bis(diethyl acetal) (2 moles equivalent) affords 1,1'-[1,4-phenylene bis(methylene)]bis(triazole-4,5-dicarboxaldehyde tetraethyl acetal).



XXXV

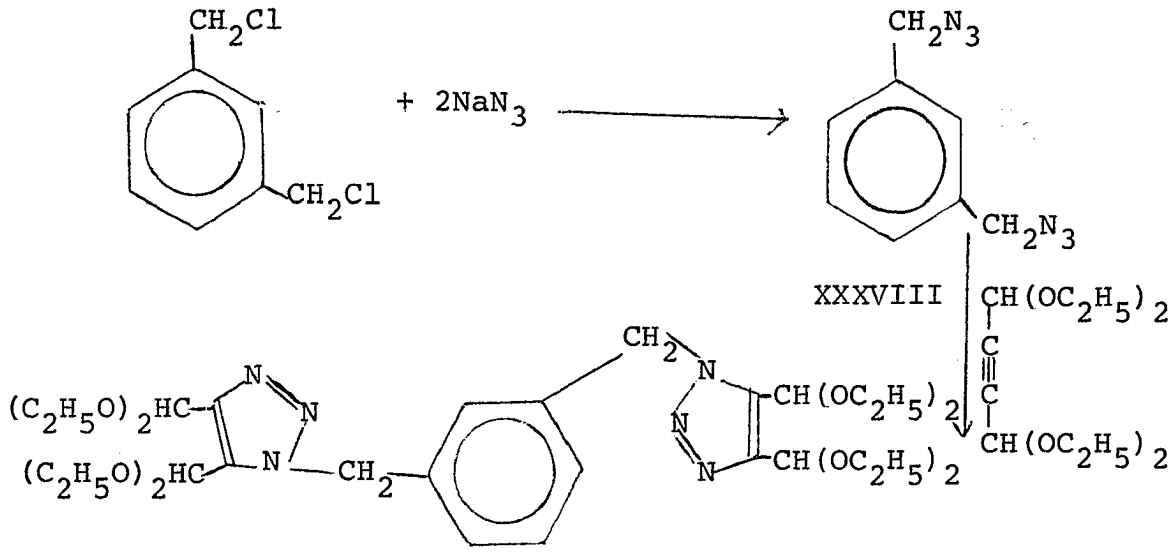
Scheme 10

In a similar procedure 1,1'-[1,2-phenylenebix(methylene)]bix(triazole-4,5-dicarboxaldehyde tetraethyl acetal) (XXXVII) and 1,1'-[1,3-phenylenebix(methylene)] bix(triazole-4,5-dicarboxaldehyde tetraethyl acetal)(XXXIX) were prepared as shown in Schemes 11 and 12.



XXXVII

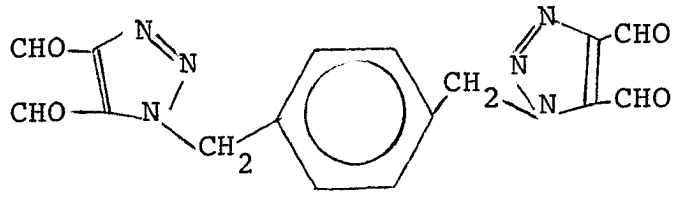
Scheme 11



XXXIX

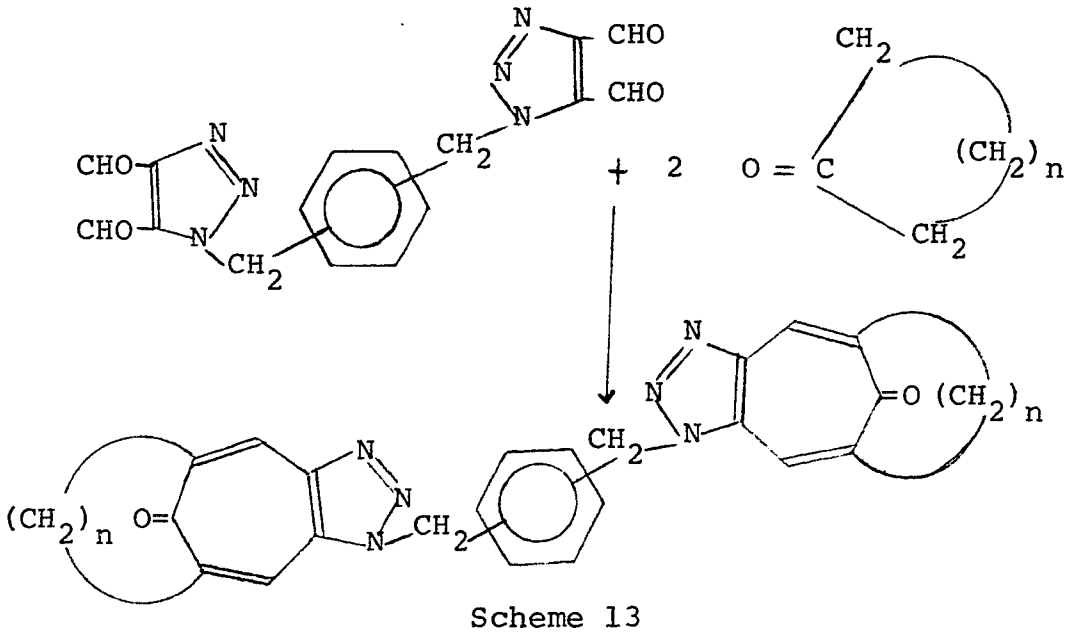
Scheme 12

We were able to hydrolyze 1,1'-[1,4-phenylelenbis-(methylene)]bistriazole-4,5-dicarboxaldehyde tetraethyl acetal)(XXXV) to 1,1'-[1,4-phenylenebis(triazole-4,5-dicarboxaldehyde)(XL).



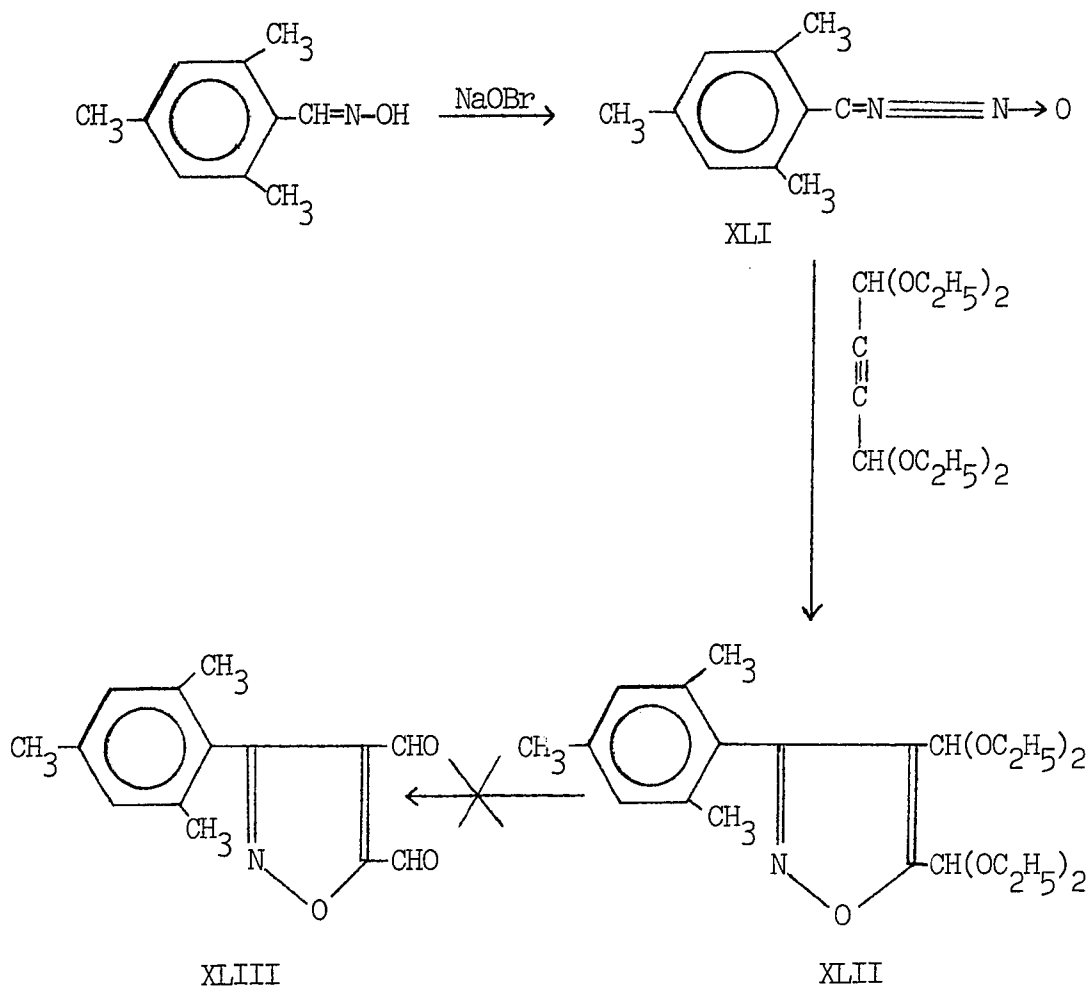
XL

This compound, and also the ortho and meta isomers which could be hydrolyzed in the same procedure, might be condensed with cyclic ketones (Scheme 13) in order to see the effect of polymethylene bridges on the aromaticity and planarity of these tropone molecules. However, available time did not allow completion of this aspect of the problem.



Scheme 13

In an attempt to study the effect of a fused isoxazole ring on the tropone system, 3-mesitylisoxazole-4,5-dicarboxaldehyde bis(diethyl acetal)(XLII) was prepared for the first time by reacting acetylenedicarboxaldehyde-bis(diethyl acetal) with 2,4,6-trimethyl benzonitrile oxide(XLI), prepared by dehydrogenation of 2,4,6-trimethyl benzaldoxime[31] (Scheme 14).

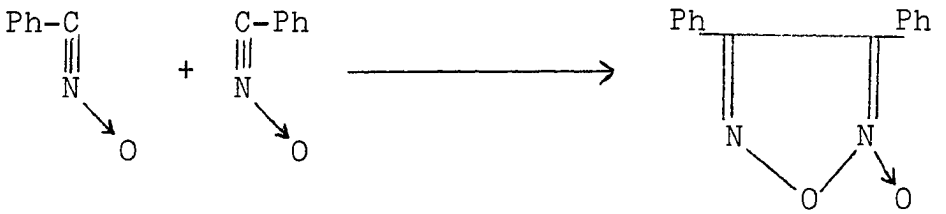


Scheme 14

We were unable to prepare 3-mesitylisoxazole-4,5-dicarboxaldehyde(XLIII) by hydrolysis of compound XLII. No bridged isoxazoletropones were prepared in this investigation since the dialdehyde is an essential starting material for their preparation in our sequence of reactions.

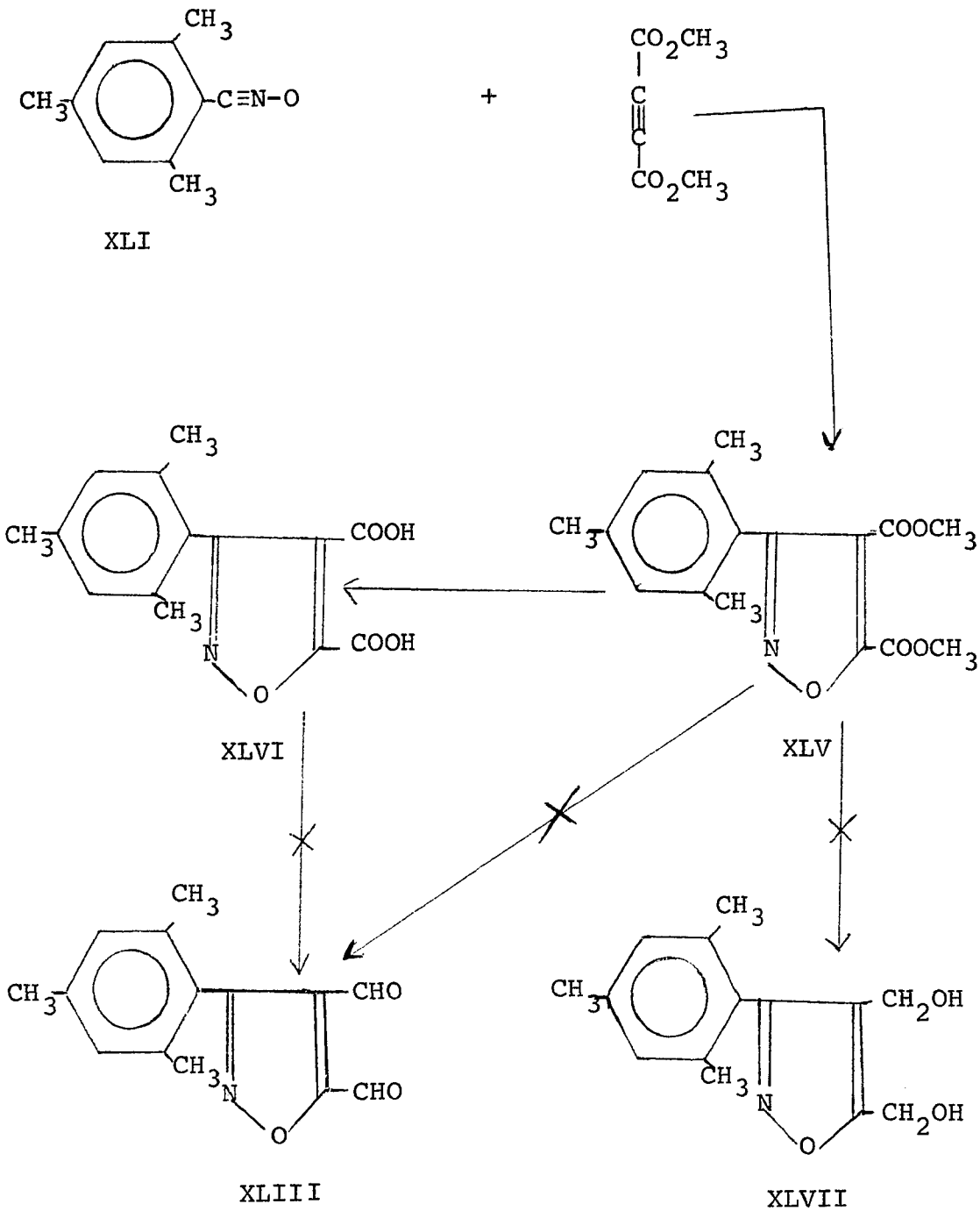
The failure of acetal groups to hydrolyze could be due to steric hindrance introduced by the presence of

the three methyl groups on the phenyl substituent. This sterically hindered benzonitrile oxide was chosen for this work because of its stability. The non-sterically hindered nitrile oxides, e.g. benzonitrile oxide, dimerized spontaneously[32] to the furoxan(XLIV) within less than one hour.



XLIV

Two other methods of preparing 3-mesitylisoxazole-4,5-dicarboxaldehyde(XLIII) were tried (Scheme 15). The first method involved the preparation of dimethyl-3-mesitylisoxazole-4,5-dicarboxylate(XLV) which was synthesized by reacting 2,4,6-trimethylbenzonitrile oxide with dimethyl acetylenedicarboxylate. Compound XLV was treated with diisobutyl aluminum hydride to try to reduce the diester to the dialdehyde(XLIII). However, only unreacted starting material was recovered from the reaction mixture.

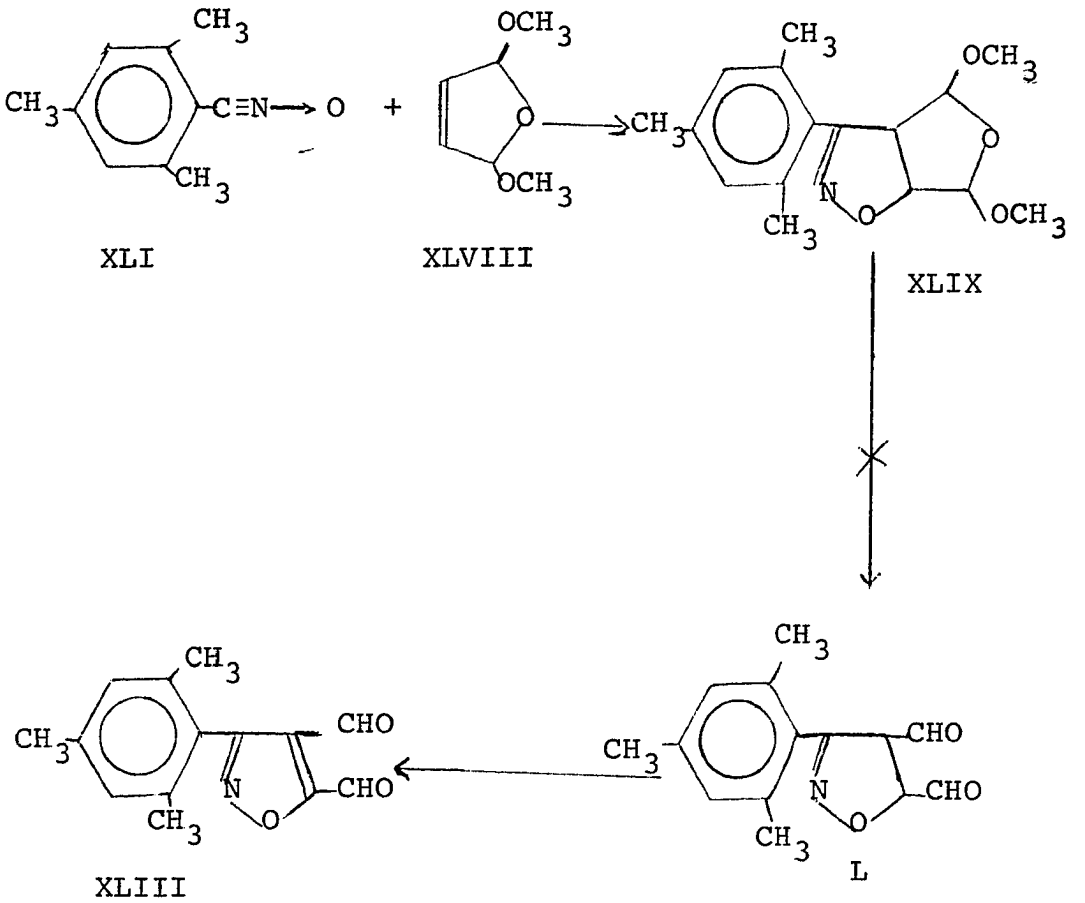


Scheme 15

The diacid(XLVI) was obtained by hydrolysis of the ester(XLV) using 20% sodium hydroxide. Attempts to prepare the dialdehyde(XLIII) from the diacid(XLVI) were unsuccessful. 3-Mesitylisoxazole-4,5-dicarboxylic acid dimethyl ester(XLV) could not be reduced to 3-mesitylisoxazole-4,5-dimethanol(XLVII) using lithium aluminum hydride, (Scheme 15).

The second method involved the preparation of compound XLIX by treatment of 2,4-6-trimethyl benzonitrile oxide(XLI) with 2,5-dimethoxy-2,5-dihydrofuran (XLVIII) followed by acid hydrolysis to make the corresponding dialdehyde(L). It was hoped that compound L could then be brominated and dehydrobrominated to form the desired dialdehyde (XLIII). But after attempted hydrolysis of compound XLIX, only unreacted starting material was recovered (Scheme 16).

Again, the failure to obtain the dialdehyde can be attributed to the steric hindrance of the mesityl group.



Scheme 16

EXPERIMENTAL

General Information

Melting points were determined using a Thomas-Hoover Unimelt instrument and are reported uncorrected. The nuclear magnetic resonance spectra were taken on a Varian A-60 Spectrometer using tetramethylsilane as an internal reference, δ's are reported in ppm. A Beckman IR-8 spectrophotometer was used for recording infrared spectra.

Elemental analyses were performed by Galbraith Laboratories, Incorporated, Knoxville, Tennessee, 37921, U.S.A., and by Midwest Micro Laboratory LTD., Indianapolis, Indiana, 46226, U.S.A.

Starting materials

Acetylene dialdehyde bis(diethyl acetal) was prepared from acetylene gas and triethyl ortho formate by the method described by Wohl.[27] Benzyl azide was prepared according to a method described by Weygand[28] for alkyl azides (b.p. for benzyl azide: 84° at 40 mm). 1-Benzyltriazole-4,5-dicarboxaldehydebis(diethyl acetal) and 1-benzyltriazole-4,5-dicarboxaldehyde were prepared by the procedure of Henkel and Weygand.[28] The cyclic ketones and diketone were prepared from the corresponding diacid chlorides using the procedures reported by Blomquist.[29,30]

Synthetic Procedures

1-Benzyl-5,7-dodecano-6(2H)-cycloheptatriazolone(XXXII)

A solution of 2.15g (0.01 mole) of 1-benzyltriazole-4,5-dicarboxaldehyde, 2.24g (0.01 mole) of cyclopentadecanone and 0.25g of KOH in 50 ml of methanol was refluxed on a steam bath for 8 hours; then the mixture was cooled for 2 hours and the precipitate was collected by suction filtration.

Recrystallization from ethanol gave 2.42g (60%) of a white crystalline product: m.p. 205-207°; NMR ($CDCl_3$) δ 7.75(2H,s), 7.22(5H,s), 5.75(2H,s), 2.60-3.0(4H,br), 0.85-1.65(20H,br). Anal. calcd. for $C_{26}H_{33}N_3O$: C,77.38; H,8.24; N,10.41. Found: C,77.11; H,8.31; N,10.29.

1,1'-Dibenzyl-5,5; 7,7'-bix(hexano-6(2H),6'(2H)-Cycloheptatriazolone(XXXIII)

A solution of 0.403g (0.002 mole) of 1-benzyl-triazole-4,5-dicarboxaldehyde, 0.28g (0.001 mole) of 1,10-cycloocta decanedione and 0.4g of KOH in 50 ml of methanol was heated under reflux for 3 hours, then the mixture was cooled and the precipitate was collected by suction filtration and recrystallized from chloroform-petroleum ether to give 0.52g (66%): m.p. 240-242°; NMR ($CDCl_3$) δ 7.70(4H,s), 7.10-7.40(10H,br), 5.75(4H,s), 2.30-3.0(8H,br), 0.90-1.70(16H,br). Anal. calcd. for $C_{40}H_{42}O_2N_6$: C,75.21; H,6.63; N,13.16. Found: C,75.06; H,6.73; N,12.93.

4-Hydroxy -1-benzyl-4,5-dihydro-5,7-heptano-6(2H-cyclo-heptatriazolone(XXXIa)

A solution of 1.075g (0.005 mole) of 1-benzyl triazole-4,5-dicarboxyldehyde, 0.77g (0.005 mole) of cyclodecanone and 0.2g of KOH in 30 ml of methanol was heated under reflux for 9 hours; then the solvent was removed under reduced pressure and a pale reddish oily residue was left.

After drying for 60 hours using the vacuum pump, the product was solidified. Recrystallization from chloroform-petroleum ether gave 0.943g (54%): m.p. 197-199°; NMR ($CDCl_3$-DMSO, d_6) δ 7.28 (5H, br), 6.85 (1H, s, H_8), 5.70 (1H, s, OH), 5.55 (2H, s, benzylic), 4.80 (1H, m, H_4), 3.15 (1H, s, H_5), 0.9-1.90 (14H, br). Anal. Calcd. for $C_{21}H_{25}N_3O_2$:C, 71.77; H, 7.17; N, 11.96. Found: C, 71.42; H, 7.03; N, 11.81.

4-Hydroxy-1-benzyl-4,5-dihydro-5,7-octano-6(2H-cyclo-heptatriazolone(XXXIb)

A solution of 1.075g (0.005 mole) of 1-benzyl triazole-4,5-dicarboxaldehyde, 0.841g (0.005 mole) of cycloundecanone and 0.2g of sodium hydroxide in 30 ml of methanol was heated under reflux for 2.5 hours; then the mixture was cooled and the precipitate was collected by suction filtration. Recrystallization from chloroform-petroleum ether yielded 1.32g (72%): m.p.

205-207° NMR ($CDCl_3$-DMSO, d_6) δ 7.27(5H,s), 6.90(1H,s, H_8), 5.68(1H,s,OH), 5.52(2H,s,benzyl), 4.60(1H,s,H_5), 2.36-2.63(2H,br), 2.0-2.20(2H,br), 1.0-1.35(12H,br). Anal. calcd. for $C_{22}H_{27}N_3O_2$: C,72.30; H,7.45; N,11.50. Found: C,72.35; H,7.60; N,11.52.

4-Hydroxy-1-benzyl-4,5-dihydro-5,7-nonano-6(2H)-cyclo-heptatriazolone(XXXIC)

A solution of 1.075g (0.005 mole) of 1-benzyl-triazole-4,5-dicarboxaldehyde, 1.1g (0.006 mole) of cyclo-dodecanone and 0.2g of KOH in 50 ml of methanol was heated under reflux for 2 hours, then the mixture was cooled and the precipitate was collected and washed with cold methanol. Recrystallization from chloroform-petroleum ether yielded 1.35g (71%): m.p. 217-218°; NMR (DMSO,d_6) δ 7.20(5H,s), 6.90(1H,s,H_8), 5.70(1H,s,OH), 5.57(2H,s, benzyl), 4.68(1H,m,H_4), 3.25(1H,s,H_5), 2.45-2.65(2H,br), 2.11-2.20(2H,br), 0.9-1.30(14H,br). Anal. calcd. for $C_{23}H_{29}N_3O_2$: C,72.79; H,7.70; N,11.07. Found: C,72.70; H,7.90; N,11.29.

α,α'-Diazido-p-xylene(XXXIV)

To a solution of 13.0g (0.2 mole) of sodium azide in 70 ml of water and 70 ml of methanol was added 17.5g (0.1 mole) of α,α'-Diazido-p-xylene. The resulting mixture was heated in a bomb flask at 100° for 25 hours;

then the methanol was removed on a rotary evaporator at diminished pressure. The residue was extracted three times with diethyl ether. The extracts were combined and dried over anhydrous $CaCl_2$. Then the ether was evaporated, and the residue solidified near room temperature yielding a white solid which was purified by distillation to give 17.1g (92%): b.p. 118-120° (1 mm); m.p. 30-32°; NMR (CCl_4) δ 7.22(4H,s), 4.21(4H,s): Anal. calcd. for $C_8H_8N_6$: C,51.06; H,4.28. Found: C,50.32; H,4.10.

α,α'-Diazido-O-xylene(XXXVI)

To a solution of 13.0g (0.2 mole) of sodium azide in 80 ml of water and 300 ml of methanol was added 17.5g (0.1 mole) of α,α'-dichloro-o-xylene. The resulting mixture was heated in a bomb flask at 100° for 48 hours, then the methanol was removed on a rotary evaporator at diminished pressure. The residue was extracted three times with diethyl ether and the combined extracts dried over $CaCl_2$. The ether was evaporated and the remaining liquid was distilled to give 16.5g (88%) of product: b.p. 112-115° (1 mm); NMR (CCl_4) δ 7.22(4H,s), 4.26(4H,s). Anal. calcd. for $C_8H_8N_6$: C,51.06; H,4.28. Found: C,51.41; H,4.44.

α,α'-Diazido-m-xylene(XXXVIII)

To a solution of 13.0g (0.2 mole) of sodium azide in 80 ml of water and 399 ml of ethanol was added 17.5g (0.1 mole) of α,α'-dichloro-m-xylene. The resulting mixture was heated in a bomb flask at 100° for 46 hours, then most of the methanol was removed on a rotary evaporator at diminished pressure. The residue was extracted four times with diethyl ether and the combined ether extracts were dried over calcium chloride. The ether was evaporated and the remaining liquid was cautiously distilled to give 16.5g of product*: b.p. 118-120° (1.5 mm); NMR (neat δ 7.18(4H,s), 4.12(4H,s). Anal. calcd. for $C_8H_8N_6$: C,51.06; H,4.28. Found: C,50.84, H,4.37.

1,,'-[1,4-Phenylenebis(methylene)] bix(triazole-4,5-dicarboxaldehyde tetraethyl acetal) (XXXV)

To a solution of 9.2g (0.04 mole) of acetylene dicarboxaldehyde bix(diethyl acetal) in 10 ml of absolute alcohol was added 3.76g (0.02 mole) of α,α'-diazido-p-xylene. The resulting mixture was heated in a bomb flask at 90° for 32 hours. The ethyl alcohol was removed under reduced pressure. The resulting solid residue was recrystallized twice from petroleum ether yielding 5.6g of solid (43%): m.p. 70-71°;

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*α,α'-Diazido-m-xylene was shown to be very explosive.

NMR ($CDCl_3$ δ 7.28(4H,s), 5.89(2H,s), 5.73(4H,s), 5.65 (2H,s), 3.2-3.9(16H,m), 0.95-1.35(24H,m). Anal. calcd. for $C_{32}H_{52}O_8N_6$: C,59.24; H,8.08; N,12.95. Found: C,59.50; H,7.85; N,13.20.

1,1'-[1,2-Phenylenebis(methylene)] bis(triazole-4,5-dicarboxaldehyde tetraethyl acetal) (XXXVII)

To a solution of 13.8g (0.06 mole) of acetylene dicarboxaldehyde bis(diethyl acetal) in 15 ml of absolute alcohol was added 5.64g (0.03 mole) of α,α'-diazido-o-xylene. The resulting mixture was heated in a bomb flask at 100° for 28 hours. The ethyl alcohol was removed under reduced pressure. The resulting product was a viscous liquid which decomposed before reaching the boiling point on attempted distillation at 1 mm. The amount recovered was 14.2g (73%); NMR ($CDCl_3$) δ 7.18(4H,s), 5.99(2H,s), 5.78(4H,s), 5.65(2H,s), 3.25-4.0(16H,m), 0.95-1.35(24H,m). Anal. calcd. for $C_{32}H_{52}O_8N_6$: C,59.24; H,8.08; N,12.95. Found: C,58.95; H,8.06, N,13.4.

1,1'-[1,3-Phenylenebis(methylene)] bis(triazole-4,5-dicarboxaldehyde tetraethyl acetal((XXXIX)

To a solution of 13.8 (0.06 mole) of acetylene dicarboxaldehyde bis(diethyl acetal) in 15 ml of absolute alcohol was added 5.64g (0.03 mole) of α,α'-diazido-m-xylene. The resulting mixture was heated in a bomb flask at 100° for 25 hours. The ethyl alcohol was

removed under reduced pressure. The resulting product was a red viscous liquid, which decomposed before reaching the boiling point on attempted distillation at 1 mm. The amount recovered was 15.5g (78%); NMR ($CDCl_3$) δ 7.20(4H, s), 5.90(2H,s), 5.75(4H,s), 5.65(2H,s), 3.25-3.90(16H,m), 0.95-1.35(24H,m). Anal. calcd. for $C_{32}H_{52}O_8N_6$: C,59.24; H,8.08; N,12.95. Found: C,59.39; H,7.93; N,13.19.

1,1'-[1,4-Phenylenebis(methylene)] bis(triazole-4,5-dicarbosaldehyde) (XL)

To a solution of 19.47g (0.033 mole) of 1,1'-[1,4-phenylenebis(methylene)] bis(triazole-4,5-dicarboxaldehyde tetraethyl acetal) in 30 ml of ethanol was added a solution of 3 ml of concentrated sulfuric acid in 50 ml of water. The resulting mixture was refluxed on a steam bath for 40 minutes; then the solution was diluted by adding 60 ml of water. The product was extracted by using diethyl ether and the ether solution was dried over anhydrous Na_2SO_4. The ether was removed under reduced pressure. The resulting product was a red viscous liquid which has a very high boiling point and it was not further purified. The yield was 8.3g (78%); NMR ($CDCL_3$) δ 10.1 (2H,s), 10.22(2H,s), 7.35(4H,s), 5.90(2H,s).

3-Mexitylisoxazole-4,5-dicarboxaldehyde tetraethyl acetal (XLII)

To a solution of 7.25g (0.045 mole) of 2,4,6-trimethylbenzonitrile oxide in 100 ml of tetrahydrofuran was

added 11.50g (0.050 mole) of acetylenedicarboxaldehyde bis(diethyl acetal). The resulting mixture was heated in a bomb flask at 90° for 3.5 hours, then the solvent was removed under reduced pressure. Distillation of the remaining liquid yielded 13.5g (77%) of product; b.p. 173-177° (1 mm). The product solidified near room temperature; m.p. 44-45°. When the reaction was carried out under atmospheric pressure and in a regular flask the yield was 6.1g (35%). NMR ($CDCl_4$) δ 6.85(2H, s), 5.87(1H,s), 5.13(1H,s), 3.15-3.90(8H,m), 2.32(3H,s, $1CH_3$), 2.10(6H,s,$2CH_3$), 0.93-1.38(12H,m). Anal. calcd. for $C_{22}H_{33}NO_5$: C,67.54; H,8.50; N,3.58. Found: C,67.28; H,8.25; N,3.44.

Dimethyl 3-mesitylisoxazole-4,5-dicarboxylate (XLV)

To a solution of 8.5g (0.05 mole) of 2,4,6-trimethyl benzonitrile oxide in 80 ml of tetrahydrofuran was added 7.81g (0.05 mole) of dimethyl acetylene dicarboxylate. The resulting mixture was heated under reflux for one hour, then the solvent was removed under reduced pressure. Recrystallization of the residue from emthanol-petroleum ether yielded 8.7g (57%) of the product: m.p. 77-78.5°; NMR (CCl_4) δ 7.15(2H,s), 4.0(3H,s,$1CH_3$), 3.7(3H,s,$1CH_3$), 2.30(3H,s,$1CH_3$), 2.10(6H,$2CH_3$). Anal. calcd. for $C_{16}H_{17}NO_5$: C,63.36; H,5.65; N,4.62. Found: C,62.98; H,5.57; N,4.47.

3-Mesitylisoxazole-4,5-dicarboxylic acid (XLVI)

Dimethyl-3-mesitylisoxazole-4,5-dicarboxylate (2g) in 30 ml of 20% NaOH was heated under reflux for 2 hours; then the solution was cooled and acidified with 10 ml of concentrated HCl. The resulting solution was stirred vigorously for about 15 minutes. The mixture was cooled to room temperature. The product was extracted using diethyl ether and the ether solution was dried over anhydrous $CaCl_2$. The ether was removed under reduced pressure leaving a grey solid product; m.p. 212-214°; NMR (DMSO-d_6) δ 10.0(2H,s), 6.90(2H,s), 2.20(3H,s,1CH_3), 1.95(6H,s,2CH_3).

Preparation of Compound (XLIX)

To a solution of 6.0g (0.0375 mole) of 2,4,6-trimethylbenzonitrile oxide in 70 ml of tetrahydrofuran was added 4.9g (0.0375 mole) of 2,5-dimethoxy-2,5-dihydrofuran. The resulting mixture was heated under reflux for one hour. The solvent was removed under diminished pressure. The resulting solid residue was recrystallized from emthanol-petroleum ether yielding 6.13g 9f solid (56%): m.p. 134-135°; NMR (CCl_4) δ 6.90 (2H,s), 5.10(2H,d), 4.80(1H,s), 4.20(1H,d), 3.45(3H,s, 1 methoxy), 3.25(3H,s,1 methoxy), 2.35(3H,s,1CH_3), 2.20 (6H,s,2CH_3). Anal. calcd. for $C_{16}H_{21}O_4N$: C,65.96; H,7.27; N,4.81. Found: C,65.91; H,7.00; N,4.82.

SUMMARY

The previously unreported polymethylene bridged 1-benzyltriazoletropones were made by the condensation of 1-benzyltriazole-4,5-dicarboxaldehyde with cyclic ketones.

Bridged cycloheptatriazolones were obtained when 1-benzyl-IH-triazole-4,5-dicarboxaldehyde was condensed under aldol conditions with cyclopentadecanone and 1,10-cyclooctadecanedione.

When 1-benzyl-IH-triazole-4,5-dicarboxaldehyde was condensed with cyclodecanone, cycloundecanone or cyclododecane, in the presence of base, bridged hydroxytriazolocycloheptanones were obtained.

The bridged cycloheptatriazolones showed aromatic properties, based on n.m.r. spectral evidence, whereas the bridged hydroxytriazolocycloheptanones did not.

It was found that 3-mesitylisoxazole-4,5-dicarboxaldehyde could not be prepared by hydrolysis of 3-mesitylisoxazole-4,5-dicarboxaldehyde tetraethyl acetal. Therefore no bridged isoxazoletropone were prepared in this investigation since the dialdehyde is an essential starting material in the preparation.

1,1'-[1,4-Phenylenebis(methylene)] tetraethyl acetal), 1,1'-[1,2-phenylenebis(methylene)] bis(triazole-4,5-dicarboxaldehyde tetraethyl acetal) and 1,1'-[1,3-phenylenebis(methylene)] bis(triazole-4,5-dicarboxaldehyde tetra-

ethyl acetal) were prepared for the first time by reaction of α, α'-diazidoxylenes with acetylene dicarboxaldehyde bis(diethyl acetal).

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VITA

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