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PREPARATION AND STEREOCHEMISTRY OF SOME HYDRAZONES DERIVED FROM CYCLIC KETONES

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Abstract

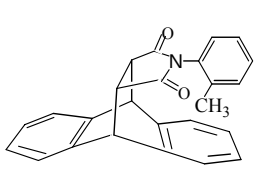
Hydrazones derived from N-aminoimides of anthracene-maleic anhydride adduct, and cyclopentadiene - maleic anhydride adduct with cyclic ketones have been prepared and characterized by IR, ^{1}H NMR spectral data. The magnetic dissymmetric cage moiety has demonstrated restricted rotation about N-N bond and the ketimino group (R_1R_2C=N-) in orthogonal geometry to the succinimidyl plane. The electronic interaction of the lone electron pair of ketimino nitrogen with the cage phenyl ring restricts inversion of nitrogen lone pair electron and provides stability to the stereoisomer.

Hydrazones are important class of organic compounds which have been found of much use in biology and chemistry because of their wide applications. Stereochemical investigations have a great importance in hydrazones where different stereochemical processes like isomerisation about C=N bond, inversion involving the nitrogen atoms (sp^3 and sp^2) and rotation about N-N bond may take place[1]**.** Stereochemistry of hydrazones in various systems have been reported[2-6]. Substituted imines have available a pathway of substantially lower enthalpy of activation for uncatalysed E-Z isomerisation, through the lateral shift mechanism having the transition state of inversion at imino nitrogen[7,8].

Asymmetric cage moieties have been found to be very diagnostic in conformational analysis about N-N and N-C bonds. Two non-planar conformations *syn* (1a) and *anti* (1b) (when the sustituent at the 2'-position of N-phenyl is towards the cage it is named *syn* while in the other case when it is away it is called *anti*) in a 1: 1.1 ratio about the N-C(phenyl) bond in O-toludide derivative (1) have been demonstrated at the ambient temperature, and the high energy barrier to rotation ($\Delta G^{\neq}$=86.1kJmol^{-1}) has been explained on the basis of steric ground[9]**.** The lone- electron pair of pyridyl nitrogen in (2) has a strong repulsion from a phenyl ring of a cage moiety and a preferred non-planar conformation having the pyridyl nitrogen in *anti* – orientation (away from the cage) has been demonstrated[10,11]. Restricted rotation about N-N bond and the lone electron pair of imino nitrogen in *anti* orientation in the solution as well as in solid state has been demonstrated in azomethine (3)[12]. Isomeric hydrazones

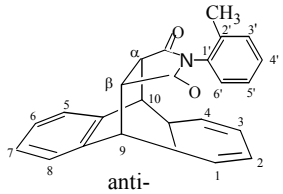
of alkyl aryl ketones have been isolated and characterised by NMR spectroscopy, the sterically crowded conformation has been found to be thermodynamically more stable as compared to its isomeric product, it is all supported by the conformational energy analysis[13].

From the synthetic point of view hydrazones are important synthons for several transformations and their synthesis from various precursors is well documented. Some hydrazones of cyclic ketones have been prepared (I-V) and their stereochemistry has been described in this communication.



syn-

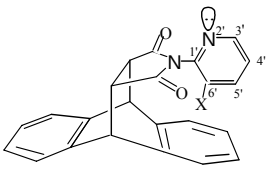
a



anti-

b

1



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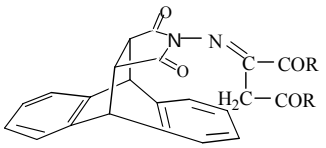

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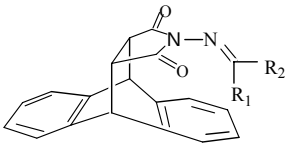
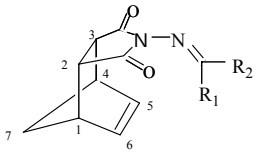


I, R_1 -C- R_2 = Cyclopentyl

II, R_1- C- R_2 = Cyclohexyl

III, R_1-C- R_2 = 2-Methyl cyclohexyl



IV, R_1-C- R_2 = Cyclopentyl

V, R_1- C- R_2 = Cyclohexyl

RESULTS AND DISCUSSION

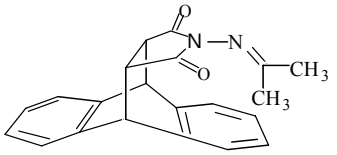
Restricted rotation about N-N bond and ketimine part $–N=C(CH_3)_2$ orthogonal to the succinimidyl plane have been demonstrated in compound (4) through NMR spectroscopy and X-ray crystallography[14]. The two methyl signals of (4) remained sharp and moved slowly on raising the temperature and this could only result from the rotation about C=N bond and an activation energy, $\Delta G^{\neq}$ =28.5 kcal mol^{-1} has been calculated from its VT NMR study. This spectral study clearly illustrate the restricted nitrogen inversion about N-N bond. Condensation of the N-amino-α, β-(9,10-dihydroanthracene–9, 10-

diyl)succinimide with cyclopentanone in ethanol yielded the product (I). ^{1}H NMR spectrum of the compound (I) shows a triplet at δ 1.1 (2H, J = 6.5Hz) for the 5'-methylene protons, a broad multiplet at δ 1.3- 1.7 (4H) for 3, 4'-methylene protons, a triplet at δ 2.55 (2H, J = 6.5 Hz) for 2'-methylene protons along with other resonances. The appearance of the 5'-methylene protons at a shielded position (Δδ ≈1.45ppm) indicates that these protons closely sit over the phenyl ring of the cage. The 3', 4'-methylene protons also appears at somewhat shielded position and experience some anisotropic effect of the cage phenyl ring. Normal resonances of the 2'-methylene protons shows that it is away from the anisotropy of the cage. The spectral pattern of the rigid cyclopentyl moiety indicates that it closely sits over the cage phenyl ring and is orthogonal to the succinmidyl plane. A geometry (5) for compound (I) may be proposed.

Compound (II) obtained by the condensation of N-amino-α, β-(9, 10-dihydroanthracene -9, 10 diyl) succinimide with cyclohexanone in ethanol shows in the ^{1}HNMR spectrum a triplet at δ 0.8 (2H, J = 6.5Hz) for 6'-methylene protons, a broad multiplet at 1.2-1.65 (6H) for 5', 4', 3'-methylene protons, a triplet at δ 2.45 (2H, J = 6.5 Hz) for 2'-methylene protons along with other resonances. The appearance of the 6'-methylene protons as a triplet indicates that these are magnetically equivalent. 6'-Methylene resonances at a shielded position (δ 0.80) and 2'-methylene protons normal resonances indicate that cyclohexyle moiety has a fixed geometry like (5). Resoannces of 3', 4' 5'-methylene protons also show that they are experiencing some anisotropic effect of the cage. As the geometry of the 2'- and 6' – positions are fixed there is no possibility of flipping of the ring and the cyclohexyl moiety assumes a rigid system. The cyclohexyl moiety closely sits over the cage phenyl ring and the cyclohexylimino moiety (-N = C<) is orthogonal to the succinimidyl plane (6) similar to the compound (I).

^{1}H NMR spectrum of the compound (III) which contains a methyl at 2'-position in the cyclohexyl moiety exhibits two broad singlets at δ 0.6 (1H) and 0.8 (1H) for 6'-methylene protons, a doublet at δ1.1 (3H) for the 2'-methyl protons, a multiplet at 1.2-1.9 for 3', 4', 5' -methylene protons, and a multiplate at 2.4 (1H) for 2' methine proton along with the other resonance. The normal resonances of the 2'-methyl protons suggest that it is away from the cage and may acquire a sterically favourable equatorial position. It also indicates the presence of only one isomeric product. 6'-Methylene protons are magnetically non-equivalent and the axial and equatorial protons appear as two broad singlets at δ 0.6 (1H) and 0.8 (1H) respectively. The proton at axial position experiences the maximum interaction of the phenyl ring of the cage as it appears at a shielded position (δ 0.6). Molecular model also supports this observation. The normal resonances of the 2'-methine proton at δ 2.4 and of the 2'-methyl

protons (δ 1.1) indicate that they are *exo* to the cage and the compound (III) assumes the geometry similar to (6) with a rigid conformation of the cyclohexylimino moiety orthogonal to the succinimidyl plane.



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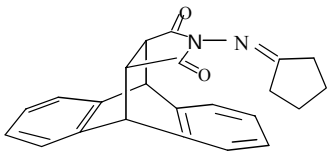

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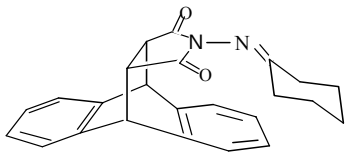

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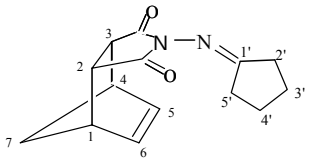

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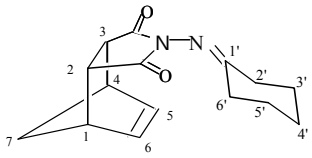

8

[2.2.1] Bicyclo-5-heptene-2, 3-endo-N'-(ketiminyl) dicarboximides (IV,V)

π-Electronic system of an olefinic bond may also have interaction with lone electron pair of nitrogen (sp^2) which may restrict lateral inversion of the imino nitrogen. With this idea, hydrazones have been designed where the imino nitrogen is held over an olefinic bond. The stereochemistry of these hydrazones (IV, V) has been investigated by ^{1}H NMR spectral studies.

Compound (IV) was obtained by the condensation of N-amino [2.2.1] bicyclo--5-heptene-2,3-endo- dicarboximide with cyclopentanone in ethanol. 300MHz ^{1} H NMR spectrum of the compound (IV) is interpreted as follows: δ 1.70 (q, 2H, 7-CH_2), 1.75 (t, 2H, 5'-CH_2), 1.90-2.13 (bm, 4H, 3' and 4'-CH_2), 2.6 (t, 2H, 2'-CH_2), 3.44 (bs, 2H, 2 and 3-H), 3.44 (bs, 2H, 1 and 4-H), 6.17 (bs, 2H, 5, 6-H). Electronic repulsion of the sp^2- hybridized lone electron pair of nitrogen from an olefinic bond similar to an aromatic ring may also be operating in this system. Restricted rotation about the N-N bond and cyclopentylimine moiety orthogonal to the succinimidyl plane is evident from the shielding parameter of 2' and 5'-methylene protons. Appearance of the 5'-methylene

protons at shielded position and also the shielding of 3'-4'-methylene protons reveals that they are *endo* to the olefinic bond and under the anisotropic effect of the olefinic bond (7). 90 MHz ^{1}H NMR spectrum of the compound (V) shows a broad multiplet at δ 1.55-2.15 for 3', 4' 5', 6' -methylene protons, a triplet at δ 2.40 (2H) for 2'-methylenne protons along with the other resonances. The spectral pattern is very much similar to (IV) and a similar geometry having cyclohexyl moiety in *syn* orientation (8) may be proposed.

It is true that the olefinic anisotropic effect is much weaker than the phenyl ring and a smaller shielding parameter has been available for the stereochemical assignment of the hydrazones (IV& V). Comparative shielding data of the methylene protons do provide convincing evidence about the restricted rotation about N-N bond and the *syn* orientation of the cyclopentyl and cyclohexyl moieties

EXPERIMENTAL

Melting points were determined in open capillary tubes and are uncorrected. IR spectra were recorded as neat samples on a Perkin-Elmer Spectrum 100 FT-IR spectrophotometer. Proton nuclear magnetic resonance (^{1}H NMR) spectra were recorded on JOEL AL 300 FT-NMR (300 MHz) spectrometer using chloroform-d as a solvent. Chemical shifts were reported in δ units as parts per million downfield from tetramethylsilane (δ 0.0) used as an internal standard for ^{1}H NMR spectra. Analytical thin layer chromatography was performed using E. Merck silica gel G. Visualization was accomplished with UV light or iodine vapour. Elemental analysis was performed using a Vario-EL elemental analyzer.

N-(Cyclopentanoneimino)- α, β -*endo*-(9', 10'-dihydroanthracene-9',10'-diyl)succinimide (I) : It was prepared by refluxing the N-aminoimide[15]of the anthracene-maleic anhydride adduct with equimolar amount of cyclopentanone and a catalytic amount of *p*-toluenesulphonic acid in ethanol for 3 hrs. On cooling the reaction mixture, the product separated which was recrystallised from ethanol, showed a single spot on TLC plate (yield 70%); mp 260-62; IR (neat): 1777w, 1705s, 1614m; ^{1}H NMR: δ 1.1 (t, 2H, 5'-CH_2), 1.2-1.65 (m, 4H, 3'& 4'–CH_2), 2.55 (t, 2H, 2'-CH_2), 3.2 (t, 2H, α & β-H), 4.8 (bs, 2H, 9 & 10 -H), 7.04-7.45 (m, 8H, ArH).

N-(Cyclohexenoneimino)- α, β -*endo*-(9',10'-dihydroanthracene-9',10'-diyl) succinimide(II): It was prepared by refluxing the N-aminoimide of the anthracene-maleic anhydride adduct with equimolar amount of cyclohexenone and a pinch of *p*-toluenesulphonic acid in ethanol for 4 hrs. On cooling the reaction mixture, the product separated which was recrystallised from ethanol, showed a single spot on TLC plate (yield 75%); m.p 255-58; IR(neat): 1782w, 1710s, 1612m; ^{1}H NMR: δ 0.8 (t, 2H, 6'-CH_2), 1.2-1.65 (m, 6H, 3', 4' & 5'– CH_2), 2.45 (t, 2H, 2'-CH_2), 3.20(t, 2H, α & β-H), 4.82 (bs, 2H, 9 & 10 -H), 7.1-7.4 (m, 8H, ArH).

N-(2 - Methylcyclohexanoneimino) - α, β – *endo* - (9', 10'-dihydroanthracene-9', 10'-diyl) succinimide (III): It was obtained from N-aminoimide of the anthracene-maleic anhydride adduct with equimolar amount of 2-methylcyclohexanone in the same way repored for (II), showed a single spot on TLC (yield 65%); mp. 220-22^{0}C; IR(neat): 1780w, 1717s, 1610m; ^{1}H NMR: δ 0.6 0.8 (ds, 2H, 6'-CH_2), 1.2-1.9 (m, 6H, 3', 4' & 5'-CH_2), 1.1 (d, 3H, 2'-CH_3), 2.4 (m, 1H, 2'-CH), δ3.29 (t, 2H, α & β-H), 4.80 (t, 2H, 9 & 10 -H), 7.05-7.4 (m, 8H, ArH).

N-(Cyclopentanoneimino) [2.2.1] bicycle – 5 – heptene - 2, 3 - *endo*-dicarboximide (IV): It was prepared by refluxing the N-amino- [2.2.1] bicyclo -5-heptene-2,3-*endo*-dicarboximide with equimolar amount of cyclopentanone and a catalytic amount of *p*-toluenesulphonic acid in ethanol for 12 hrs. On cooling the reaction mixture a pasty solid separated which was recrystallised from benzene- n-hexane (1:1), showed a single spot on TLC plate (yield 60%); m.p 167-69 ^{0}C; IR (neat): 1780w, 1705s, 1614m; ^{1}H NMR: δ 1.70 (q, 2H, 7-CH_2), 1.75 (t, 2H, 5'-CH_2), 1.90-2.13 (bm, 4H, 3' and 4'-CH_2), 2.60 (t, 2H, 2'-CH_2), 3.44 (bs, 2H, 2 and 3-H), 3.44 (bs, 2H, 1 and 4-H), 6.17 (bs, 2H, 5, 6-H).

N-(Cyclohexanoneimino) [2.2.1] bicycle – 5 – heptene - 2,3 - *endo*-dicarboximide (V): It was obtained from N-aminoimide of cyclopentadiene-maleic anhydride adduct with equimolar amount of cyclohexanone in the same way repored for (IV), showed a single spot on TLC plate (yield 65%); m.p 155-58^{0}C; IR(neat): 1782w, 1715s, 1612m; ^{1}H NMR: δ 1.70 (q, 2H, 7-CH_2), 1.55-2.15 (bm, 8H, 3', 4', 5' & 6', -CH_2), 2.4 (t, 2H, 2'-CH_2), 3.44 (bs, 2H, 2 and 3-H), 3.44 (bs, 2H, 1 and 4-H), 6.17 (bs, 2H, 5, 6-H).

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