Zagazig J. Pharm. Sci., June, 1996,
Vol. 5, No. 1, pp. 68-74

ISSN 1110-5089

ENHANCED REACTIVITY OF PYRIDIN-3-OL TOWARDS 4-PHENYL-1,2,4-TRIAZOLINE-3,5-DIONE: *FMO* TREATMENT OF THE CYCLOADDITION PROCESS BY *ASED-MO* CALCULATIONS METHOD

Samia A. El-Abbady*[a], Mohamed S. Abdulhalim[a], Mohmed K. Awad[b] and Ahmed H. Moustafa[b]

[a] *Departments of Chemistry, University College for Girls and Faculty of Engineering, Ain Shams University, Cairo, Egypt.*

[b] *Faculty of Applied Sciences, Umm Al-Qura University, Makkah, Saudi Arabia.*

ABSTRACT:

Pyridin-3-ol reacted radily as 4 π electrocyclic component across the 2- and 6-positions of the pyridine ring with the potent azo-dipolarophile: 1,2,4-triazoline -3,5-dione. Structural and configuration assignments were deduced from elemental and spectral evidence. FMO treatment of the enhanced 1,3-dipolar character of pyridin-3-ol towards the cis-azo-dipolarophile was performed using ASED-MO calculations method.

INTRODUCTION

A convincing body of evidence based largely on spectroscopic data[1-5] have confirmed that pyridin-3-ol (1 a) in solutions (in polar solvents) exists to a considerable extent with the unstable mesomeric betaine, pyridinium-3-oxide (l b).

Pyridinium-3-oxides fall within the class of azomethine ylides and are considered as octet-stabilized 1,3-dipoles without an orthogonal double bond. MO calculations[6] and experimental data[7] have confirmed that such type of compounds behave as pericyclic having [4n[π-1,3-dipole across the 2- and 6-positions and/or [4n+2] π-1,3-dipolarophiles across 2- and 4-posiitons.

The reaction of pyridin-3-ol (l a) with acrylic acid, acrylonitrile and methyl acrylate constitute simple one-pot high yield conversions into tropane-like compounds[8]. However, it failed to react as 4 p-1,3-dipole towards many other electron-deficient addends; N-phenyl maleimide, 2-and 4-vinyl pyrine, diethyl maleate and, fumarate, azodiformate, phenyl vinyl and divinely ketone, chalcones, methyl cinnamate, styrene, crotononitrile, methacrylonitrile, methacryaldehyde, phenylpropionate, tetracyanoethylene and fumaronitrile[9].

Now, we wish to describe herein the 1,3-dipole character of pyridin-3-ol towards the potent 1,3-dipolarophile, 4-phenyl- 1,2,4,-triazoline- 3,5-dione.

RESULTS AND DISCUSSION

4-Phenyl-1,2-4-triazoline-3,5-dione having the cis-azo-linkage was proved to be a potent dipolerophile. It reacted rapidly as 2 π-component at low temperature with pyridin-3-ol as 4π-electrocyclic component. When the reaction as carried out in 1:1 molar ratio at -10°C; the only product isolated was identified as 1 (H) -5-phenyl-1,3,5,7-tetrazatricycol [5.3.1.0$^{(3,7)}$] undeca-9-en-4,6,11-trione (2) from the elemental analysis and spectral evidences. IR absorption confirmed the presence of νNH at 3280 cm^{-1}, carbonyl doublet of the fused triazolidine dione ring at 1780 and 1720 cm^{-1} and the charactersitic absorption of δ,β-unsaturated carbonyl groupappeared at 1690 cm^{-1}. ^{1}HNMR spectrum proved the proposed structure for 2. H-2 displayed a doublet at δ 5.5 due to long range W-coupling with H-10 (J= 1.5 Hz); H-10 appeared as a double doublet at 6.2 due to coupling with H-9 ($J_{10,9}$ = 5 Hz and $J_{10,2}$ = 1.5 Hz); the quartet singla at 6.9 is for H-9, resulting from comparable values of $J_{9,10}$ = 5.5 Hz and $J_{8,9}$ = 6 Hz); H-8 displayed a doublet at 5.7 ($J_{8,9}$ = 6 Hz) and the aromatic protons displayed a multiplet at 7.5-7.8. The molecular ion appeared as[M^+-N_2] at m/z 242 a.m.u.

When the reaction was conducted with two moles of the dipolarophile the only isolated cycloadduct was identified from elemental analysis and spectral evidence as 1-(4-phenyl-1,2,4-triazolidin- 3,5-dione-l-yl) -5-phenyl- 1,3,5,7-tetrazatriclcyo [5.3.1.0$^{(3,7)}$] decaa-9-en-4,6,11-trione (3). I.R spectrum of 3 exhibited νNH cm^{-1}, two carbonyl doublets appeared at 1780, 1725 and 1765, 1715 cm^{-1} assignable for the carbonyl groups of the 1,2,4-triazolidine dione rings. The absorption band

* To whom correspondance should be addressed.

at 1690 cm^{-1} is for δ, β-unsaturated carbonyl group. ^{1}HNMR spectrum of 3 displayed the following signals, δ 5.75 (d, H-2, $J_{2,10}$ = 1.0 Hz); 6.15 (dd., H-10, $J_{10,9}$ = 5.5, $J_{10,2}$ = 1.0Hz) 6.95 (q, H-9, $H_{8,9}$ = 5, J9, 10 = 6 Hz); 5.85 (d, H-8 $J_{8,9}$ = 6 Hz); the aromatic protons appeared as a complex multiplet at 7.0-7.8. [M^+-N_2] at m/z 417 a.m.u.

Meanwhile, the elimination of molecular nitrogen in the ionization chamber led us to investigate the thermal stability of the isolated adducts (2) and (3). Thus, sublimation of (2) and (3) under reduced prssure in air of nitrogen afforded, 1 (H)-4-phenyl-1,4- diazobicyclo [3.3.1] nona-7-en-3,5,9- trione (4) and 1-(4-phenyl-1,2,4-triazolidine -3,5-dione-l-yl)-5phenyl -1,4- phenyl-1,2,4-triazolidine-3,5-dione-l-yl) -5-phenyl-1,4-diazabicyclo [3.3.1]nona-7- en-3,5,9-trione (5) respectively from elemental analysis and spectral evidence. Elemental analysis indicated the loss of molecular nitrogen during the sublimation. This was tentatively established from the mass spectra of (4) and (5) which displayed the expected molecular ions. [M-N_2].

I.R spectrum of (4) exhibited νNH at 3300 cm^{-1}, carbonly doublet at 1760 & 1720 cm^{-1} and δ,β-unsaturated carbonyl group at 1690 cm^{-1}. The chemical shift and multiplicity of (4) confirmed the proposed structure. H-2 appeared as a doublet at δ 5.7 due to the long-range W-coupling with H-8 (J= 1.5 Hz), and the double doublet signal at 5.95 is for H-8 resulting from comparable values of ($J_{8,2}$ = 1.5 Hz, $J_{8,7}$ = 6 Hz); H-6 displayed a doublet at 5.45 ($J_{7,6}$ = 5 Hz), H-7 appeared as a quartet at 7.1 ($J_{7,8}$ = 6 Hz, $J_{7,6}$ = 5 Hz). The aromatic protons displayed a multiplet at 7.6-7.8. The mass spectrum of (4) showed that presence of the molecular ion peak at m/z 242 a.m.u. with the major fragmentation pathway resulting from an intial retrocycloaddition regenerating pyridine-3-ol as the parent peak.

On the other hand, structural assignment of 5 was established on the basis of IR, ^{1}H NMR and mass spectra. The IR spectrum showed a conjugated carbonyl group at 1690 cm^{-1}. The absorption at 3320 & cm^{-1} was due to the νNH group. ^{1}H NMR spectrum displayed H-2 as a doublet at 5.8 due to long range W-coupling with H-8 (J=1.5 Hz), H-8 appeared as a double doublet at 5.9 ($J_{8,2}$ = 1.5 Hz, $J_{8,7}$ = 5.5 Hz); H-6 displayed a doublet 5.75 ($J_{6,7}$ = 6 Hz); H-7 appeared as a quartet at 7.00 ($J_{7,8}$ = 5 Hz and $J_{7,6}$ = 6 Hz), and aromatic portons displayed a multiplet at 7.6-7.8. The mass spectrum displayed the expected molecular ion at m/z (cf. Scheme 1).

In earlier publication, it was reported the high dipolar reactivity of pyridin-3-ol with only monosubstituted acrylic acid addends[9]. Two possible pathways were postulated for the formation of the isolated cycloadducts from these reactions[9] .

(i) Initial reaction of the monomer betaine (1 b) with the monoene to yield the cycloadducts with a NH group which subsequently reacted with an additional molecule of the addend by a Michael-type addition.

(ii) Alternatively, the N-substituted pyridinium -3-oxide (type 7) resulting from the direct reaction between the addend and the nitrogen atom of the pyridin-3-ol, (1 a), with the initially formed Zwitter ions (type 6) undergoing tatutomerisation to the N-substituted pyridinium-3-oxide (7) which reacts with the addend to give the cycloadducts[9].

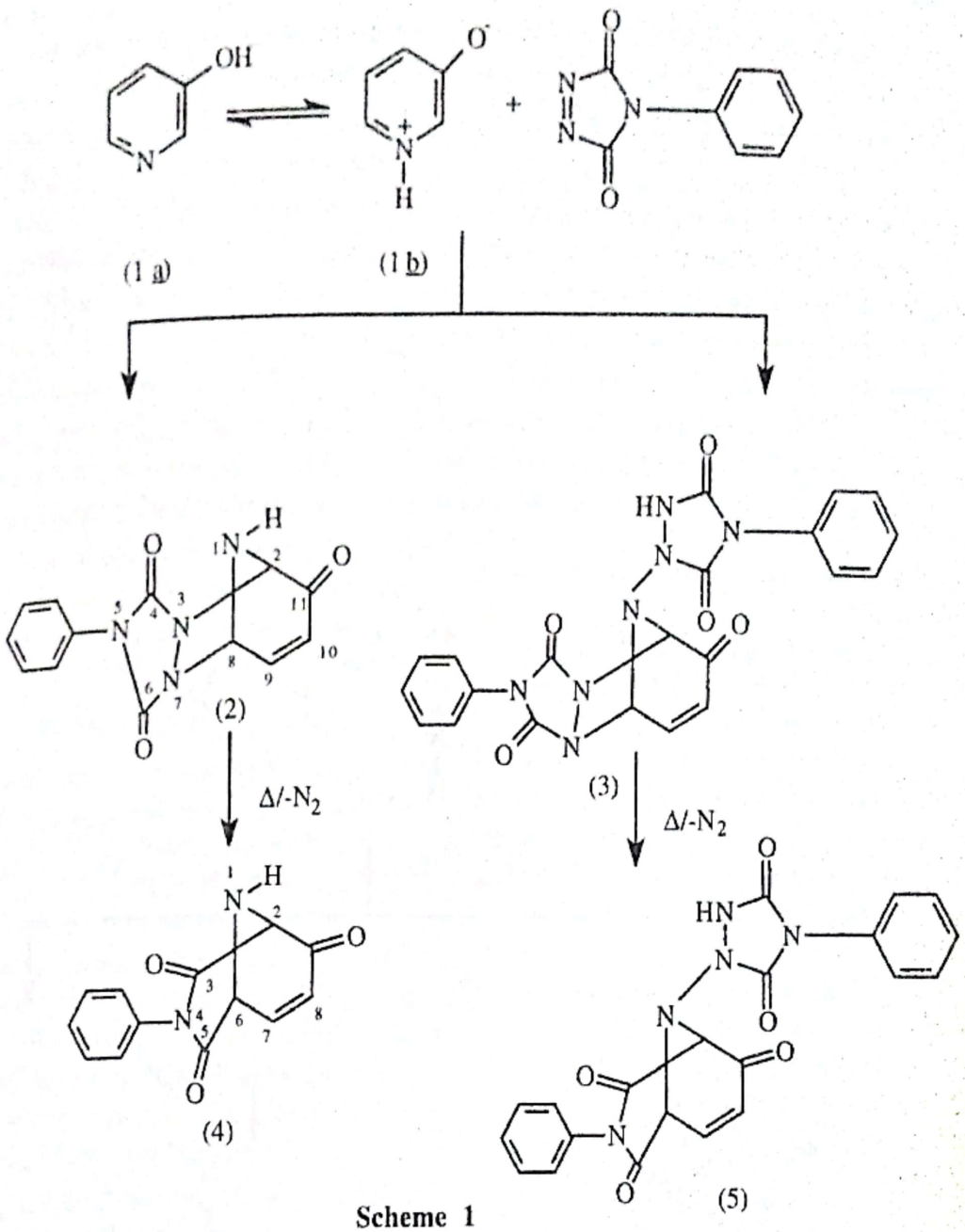
Rescently, we have reproted the lower dipole reactivity of pyridin-3-ol and its 1-methyl and 1-phenylpyridinium-3-oxides with the transdisubstituted olefins, β-nitrostyrenes[10] and benzalace- tophenone[11].

The isolation of the corresponding ether (8) as a major product together with 2,6-chcloadducts (9) as a minor product indicated that the ether (8) obtained resulting from direct reaction between the addend and the nucleophilic oxygen of pyridin-3-ol where as N-substituted pyridinium-3-oxides (6) were produced prior to the cycloaddition process. (pyridine acts with maleic acid[12], acetylenedicarboxylate[13] and p-benzo quinone[14] to produce Zwitter ions). We think that the high dipole reactivity of pyridin-3-ol with acrylic acid addends is in favor with the formation of the reactive Zwitter ions in the first step in order to encourage the latent 1,3-dipole character of the pyridin-3-ol.

The isolation of the 1:1 adduct (2) and the 1:2 adduct (3) with 4-phenyl-1,2,4-triazoline-3,5-dione indicated that the cycloaddition process has taken place with the Zwitter ion (1 b) prior to the Michael addition process. Presumably, the energy barrier of the cyclo-addition process is smaller than that for the Michael addition.

The enhanced reactivity of pyridin-3-ol as 4 π electrocyclic component with 1,2,4-triazolin-3,5-dione as 2 component led us to calculate the energy gap between the inter frontier molecular orbital (HOMO and LUMO) energy levels in both reactants using ASED-MO calculations method.

Egypt. J. Pharm. Sci., June, 1996.
Vol. 5, No. 1, PP. 68-74



Scheme 1

The optimization of the 1,2,4-triazolin 3,5-dione has been performed by optimizing its bond lengths, bond angles and dihedral angels.

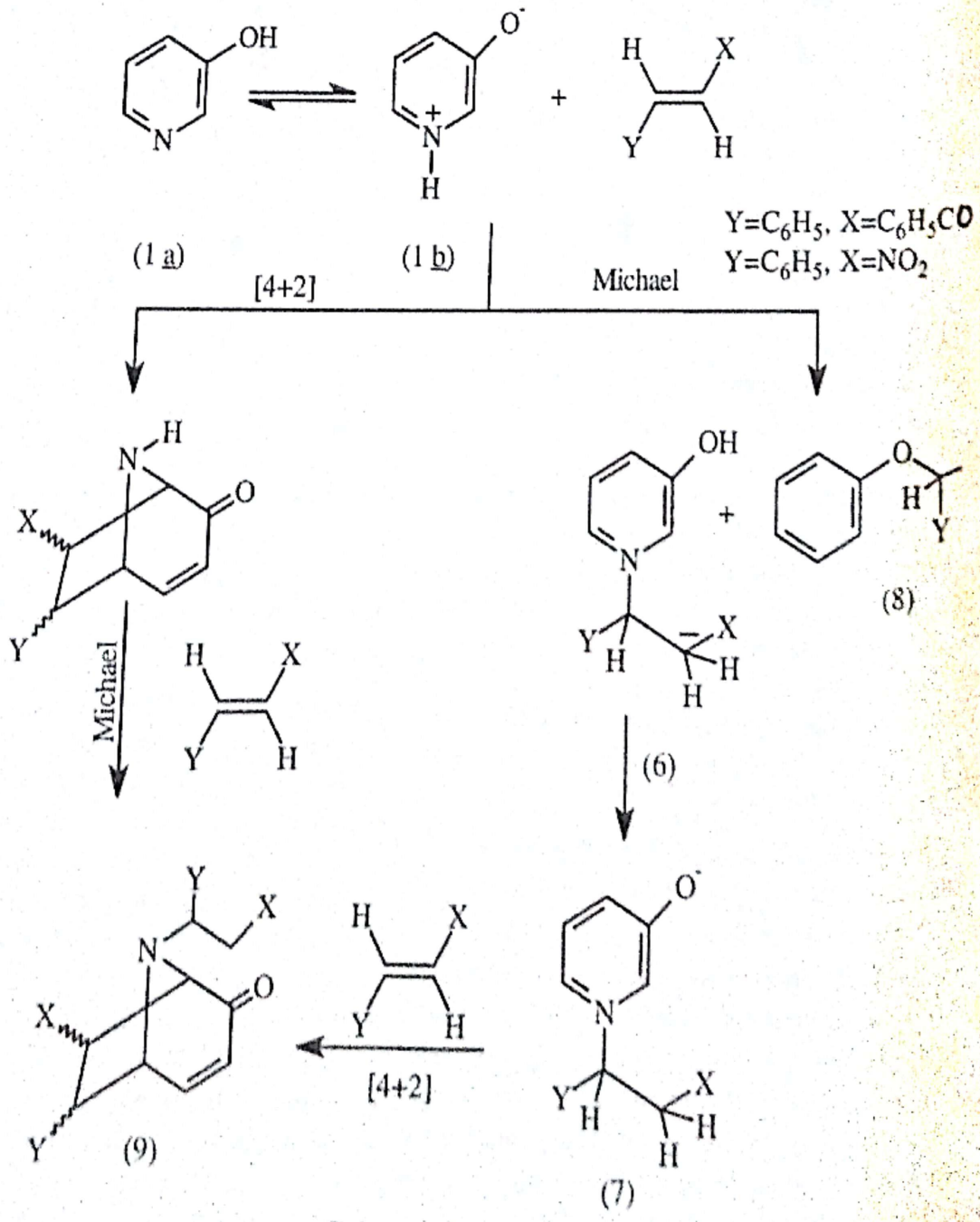
The calculations produce a stable structure with minimum energy when the triazoline ring rotates around C_1-N_7 bond by 53° (Fig. 1).

The charge distributions over the whole skeleton of the triazoline system and the bond orders obtained from the calculations are shown in (Fig. 2). The electronic structure of the triazoline system is also investigated using the same method. Considering the frontier molecular orbital energies (HOMO and LUM), the calculations produce a very small energy separation within the triazaolin system, 0.567 eV, which indicates a high reactivity of the molecule (Fig. 3). This is in accord with the experimental observations. The calculations show that the lowest energy transition corresponds to $n \rightarrow \pi^*$ transition which mainly described by one electron excitation from the HOMO level,- 12.208 eV, with considerable contribution form nitrogen's lone-paris, to the low lying LUMO level,-11.641 eV, with complete π^* character. The frontier orbital of the reactive species of pyridin-3-oxide (1 b) was also investigated using the same method in order to decide if the cycloaddition process between pyridinium -3-oxide and the triazoline is HOMO betaine-controlled (Sustmann Type I) or LUMO betaine-controlled (Sustmann Type III) (Fig. 4). The calculations produce a very small energy separation

between the dipole HOMO level and the LUMO level of the dipolarophile, triazoline system with a 0.246 eV compared with that between the LUMO betaine and the HOMO triazoline system, 3.145 eV.

This is clear indication that the cycloaddition of pyridin-3-ol with 1,2,4-triazolin-3,5- dione is HOMO betaine-controlled process (Sustemann Type 1). The HOMO-LUMO energy separations between pyridinium-3-oxide and acrylonitrile was also calculated using the same method in order to correlate the reactivity of pyridin-3-ol with acrylonitrile with that for triazoline dione. It is shown that the energy difference between the dipole HOMO level and the LUMO level of the acrylonitrie, 2.442 eV, is smaller than that of the dipole LUMO and the HOMO of acrylonitrile, 3.678 eV.

Stereoselectivity: N-Phenylmaleimide was reported to react with s triazinyl betaines[15] to yield exclusively the exo-adducts. This is contrary to PMO-FMO theory for $[4\pi_s + 2\pi_s]$ processes which should proceed preferntially via the endotransition state. Dinitrophenyl [16] and nitropyridyl[17] betaines yielded exclusively the endo-adducts. It was assumed that the formation of the exo-adduct is attributed to the long reaction time under



Scheme 2

Egypt. J. Pharm. Sci., June, 1996.
Vol. 5, No. 1, PP 65-74

reflux where the initially formed endo-adduct is converted to the more thermodynamically stable exo-adduct. (cf. addition of furan to maleic anhydride (9).

In our case, it is difficult to assign the configuration of both sp^3-hybridized nitrogen atoms N_3 and N_7 in the isolated cycloadducts (2) and (3). H-2 nd H-8 are the key protons used for the assignment of the stereochemistry of the fused triazolidine ring; each displayed a doublet. It is suspected to assign the endo-configuration for the triazolidine ring in (2) and (3), because the reactions have been completed at low temperautre in few minutes, the reactions may be considered as a fast-stereospecific. This is supported from the calculation of the energy of the frontier orbital of the reactants. The calculations show stabilization of the LUMO level in the dipolarophile which favors the endo-transition state via a secondary orbital overaple.

EXPERIMENTAL

Melting points were determined on a Gallenkamp melting point apparatus and were uncorrected. IR spectra were recorded on a Pye-Unicam model SP 300 IR spectrophotometer and ^1H NMR spectra in $CDCl_3$ on a Varian EM-390 spectrometer using TMs as an internal reference (chemical shifts in δ, ppm). All compounds were purified over a column of alumina neutral (Fluka). Elemental analyses were performed in micro analytical laboratory at Ain Shams University, Cairo. Mass spectra were carried out on FAB MS UMIST MS 50 TC Manchester, U.K.

1 (H)-5-Phenyll1, 1,3,5,,7-tetrazatricyclo [5.3.1.0$^{(3,7)}$] undeca-9-en-4,6,11-trione (2):

4-Phenyl-1,2,4-triazoline-3,5-dione was prepared according to Cookson et al.[19] from the oxidation of 4-phenyl-1,2,4-triazolidine-3,5-dione using t-butylhy pochlorite in dioxan at room temperature. The azo-compound was obtained in high yield. A dioxan solution (25 ml) of pyridin-3-ol (0.95 g, 0.01 mol) was added to a cooled solution of 4-phenyl-1,2,4-triazoline -3,5-dione (1.75g, 0.01 mol) in dioxan (25 ml) at-10°C.

The discharge of colour was instantaneous, striring the reactrion mixture was continued for an additional 1/2 h. The solvent was then removed under reduced pressure and temperature below 40°C till dryness. The obtained solid was chromatographed on a column of alumina using chlroform-light petroleum BP 60080°C. Recrystallisation from ethanol gave 1 (H)-5-phenyl 1-3,5,7-tetrazatricyclo [5.3.1.0$^{(3,7)}$] undeca-9-en-4,6,1 1-trione (2) as yellow needles (1.83 g, yield 68%), m.p 280-300°C with decomposition. IR: 3280 (νNH); 1780 & 1620 cm^{-1} (νC=0 of the triazolidine dione ring), and 1690 cm^{-1} (νC=0, α,β -unsaturated). ^1H, NMR: δ 5.5 (d, 1H, H-2, J2,10=1.5 Hz); 6.9 (q, 1H, H-9, J9,10 = 5.5 Hz, J9,8 = 6Hz), 5.8 (d, 1H, H-8, J8,9 = 6Hz); and 7.5-7.8 (m, 5H, C_6H_5-). (Found: C, 58.12; H, 4.01; N, 20.25. $C_{13}H_{10}H_4O_3$, requires C, 57.77; H, 3.70; N, 20.74%). [M$^+$-N_2] m/z=242 a.m.u.

1-(4-Phenyl-1,2,4-triazolidine-1-yl)-5-phenyl-1,3,5,7-t etrazatricyclo [5.3.1.0$^{(3,7)}$] undeca-9-en-4,6,1 1-trione (3):

A dioxan solution (25) ml of pyridin-3-ol (0.95 g, 0.01 mol) was added to a cooled solution of 4-phenyl-1,2-4-triazoline -3,5-dione (3.5 g, 0.02 mol) at10°C while stirring for 1/2 h. The solvent was removed under reduced pressure at 40°C, whereupon a deep yellow solid was obtained, und purified over a column of alumina using chloroform-light petroleum BP 60-80°C (3:1). A bright yellow solid gave after recrystallisation from ethanol 1-(4-pehnyl-1,2,4-triazoli dine-3,5-dione-1lyl)-5-phenyl-1,3,5,7-tetrazatricyclo [5.3.1.0$^{(3,7)}$]undeca-9-en-4,6,11-trione (3), (3.15 g, 71%), m.p > 320°C with decomposition. IR: 3300 (nNH), 1780, 1725 & 1765, 1715 (two doublets for the carbonyl absorptions of two triazalidinedione rings); and 1690 cm^{-1} (δ,β-unasaturated carbonyl group). ^1H NMR: δ 5.75 (d, 1H, H-2, J2, 10 = 1.0 Hz; 6.15 (dd., 1H, H-10, J10,9 = 5.5 Hz, J10,2 = 1.0 Hz); 6.95 (q, 1H, H-9, J8,9 = 5 Hz, J9,01 = 6 Hz); 5.85 (d, 1H, H-8, J8,9 = 6 Hz); and 7.0-7.8 (m, 10 H, C_6H_5-) (found: C, 56.25; H, 3.45; N, 22.28; $C_{21}H_{15}N_7O_5$, requires C, 56.62;H, 3.37; N, 22.02%). [M$^+$-N_2] m/z 417 a.m.u.

1(H)-4-phenyl-1,4-diazabicyclo [3.3.1] nona-7-en-3,5,9-trione (4):

Sublimation of 2 (0.5 gm, 0.00185 mol), at 180°C under reduced pressure (1.0mm Hg) in nitrogen atmosphere for 1/2 h afforded a pale yellow solid, on the cold finger, 90.1 g, yield 22% , m.p 185-8°C. IR: 3300 (νNH), 1760, 1720 (νC = 0 of cyclic amide), 680 cm^1 (conjugated carbonyl group). ^1H NMR: δ 5.7 (d, 1H, H-2 $J_{2,8}$ = 1.5 Hz); 5.95 (dd, 1H, H-8, $J_{8,2}$= 1.5 Hz. $J_{8,7}$ = 6 Hz); 5.45 (d, 1H, H-6, $J_{6,7}$ = 5 Hz); 7.1 (q, 1H, H-7, $J_{7,8}$ = 6 Hz, $J_{7,6}$ = 5 Hz); 7.6-7..8 (m, 5H, C_6H_5-). (found: C, 64.18; H, 4.49; N, 11.12 $C_{13}H_{10}N_2O_3$ requires: C, 64.46; H, 4.13; N, 11.57%) [M$^+$] m/z = 242 a.m.u.

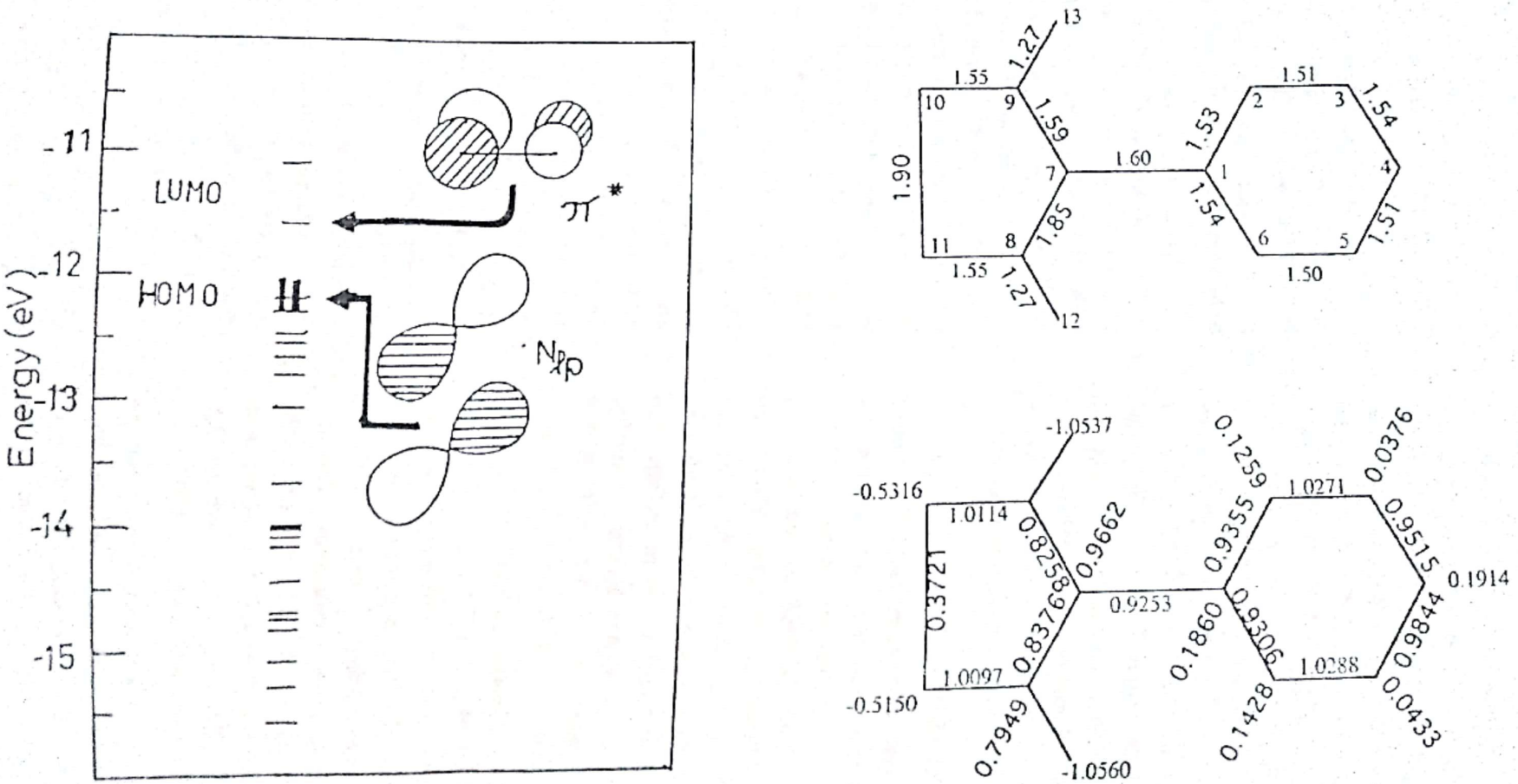


Fig. (1): The calculated electronic structure *of triazoline.*

Egypt. J. Pharm. Sci., June, 1996,
Vol. 37, No. 1, pp. 68-74

1-(4-Phenyl-1,2,4-triazolidine-3,5-dione-1-yl)-4phenyl-1,4diazabicyclo-[3.3.1]nona-7-en-3,5,9-trione (5):

Sublimation of 5 (1.0 g, 0.00239 mol) at 180°C under similar conditions as in the preceding experiment afforded a yellow solid, (0.35 g, yield 37%), m.p 250-2°C. IR: 3320 (νNH), 1775, 1718 and 1760, 1720 cm^{-1} (two doublets for two different cyclic amides). ^1H NMR: δ 5.8 (d, 1H, H-2 J2,8 = 1.5 Hz); 5.9 (dd., 1H, H-8, J8,2 = 1.5 Hz, J8,7 = 5.5 Hz); 5.57 (d, 1H, H-6, J6,7 = 6Hz); 7.000 (q, 1H, H-7, J7,8 = 5 Hz, J7,6 = 6H and 7.6-7.8 (m, 10H, C_6H_5-). (Found: C, 59.84; H, 3.22; N, 13.01 $C_{21}H_{15}N_5O_5$, requires C, 60. 13; H, 3.95 N, 13.42%); [M^+] m/z 417.

REFERENCES

1. D.E. Metzler and EE. Snell, **J. Am. Chem. Soc.**, 77, 2341, (1977).
2. A Albert and J. N. Philips, **J. Chem. Soc**., 1942, (1956).
3. S.F. Mason, **J. Chem. Soc.**, 5010, (1957).
4. P. Sense and G.G. Gallo, **Ann. Chime** (Rome), 44, 232, (1957)
5. W. Baker and W.D. Ollis, **Quart. Rev**. (London), 11, 15, (1957).
6. A. Rams den, **Adv. Heterocycl. Chem**., 26, 1, (1980).
7. Denies, A. R. Katritzky and Y. Takeuchi, Angew. Chem., 15, 1 and the references therein, (1970).
8. A.R. Katritzky and Y. Takeuchi, **J. Chem Soc**., C 847, **J. Chem. Soc** , C 878 (1971).
9. J. Banerji, N. Dennis, J. Frank, A.R. Katritzky and T. Matsuo, **J. Chem. Soc**., Perkin 1, 2334, (1976).
10. S. A. El-Abbady, A.A.Al-Ahmady and A.H. Moustafa, **Indian. J. Chem** , 31 B, 24, (1992).
11. S.A. El-Abbady, Indian. **J. Heterocyclic Chem** , 3, 25, (1993).
12. Lutz, Beer., 43, 2636 (1910).
13. R.M. Acheson, **Adv. Heterocyclic. Chem.**, 1, 125, (1963).
14. E. deBarry Baronet, J. W. Cook and E.P. Driscoll, **J. Chem. Soc** , Perkin 1, 1930, (1977).
16. N. Dennis, B. Ibrahim, A. R. Katritzky, I. G. Taulov and Y. Takeuchi, **J. Chem., Soc., Perkin 1**, 1883 (1974).
17. N. Dennis, B. Ibrahim, and A.R. Katritzky, **J. Chem. Soc**., Perkin 1, 2307 (1976).
18. N. Entwistle; "Orbital Symmetry Correlation's in Organic Chemistry". A Guide to the Woodward-Hoffmann Rules, Van No strand Reinhold Co., London, p 33, (1972).
19. R.C. Cookson, S. S. Gilani and I.D.R. Steven's. **J. Chem. Soc., (C)**. 1905, (1967).

نشاط بيريدين -٣- أول المتزايد تجاه ٤-فنيل - ١، ٢، ٤- ترايازولين-٣ ، ٥- داى أون :

تفسير عملية الإضافة الحلقية بنظرية FMO بإستخدام طريقة ASED فى حساب المدارات الجزيئية

سامية عبداللطيف العبادى- محمد سعيد عبد الحليم *
قسم الكيمياء - كلية البنات -* وقسم الكيمياء بكلية الهندسة - جامعة عين شمس - القاهرة - مصر
محمد خالد عوض- احمد حشمت مصطفى
قسم الكيمياء - جامعة ام القرى- مكة المكرمة - السعودية

يتفاعل مركب بيزيدين -٣- أول كمكون حلقى إلكترونى يحتوى على ٤ إلكترونات باى بسرعة كبيرة مع الباحث عن ثنائى القطب ٤-فنيلى- ١، ٢، ٤- ترايازولين- ٣، ٥ داى أون بنسبة مولية متكافئة معطيا ناتج الإضافة الحلقية الذى أمكن إثبات التركيب الجزيئى له على ضوء نتائج التحليل العنصرية الدقيقة بجانب دراسة طيف كل من الأشعة تحت الحمراء والرنين النووى المغناطيسى للبروتون وكذلك طيف الكتله.

وعند إعادة التفاعل بإستخدام نسبة مضاعفة للباحث عن ثنائى القطب تم عزل ناتج الإضافة الحلقى من تفاعل ٢ جزئ من الباحث عن ثنائى القطب. يثبت ذلك أن تفاعل بدء بالإضافة الحلقية متبوعا بإضافة من نوع مايكل وذلك يؤيد أن فرق الطاقة بين أعلى مدار مشغول HOMO لمركب بيريدين -٣- أول وأقل مدار غير مشغول LUMO للباحث عن ثنائى القطب صغير. وفى الحقيقة تم حساب هذا الفرق بطريقة ASED حيث تبين أن هذا الفرق يساوى 0.246eV وهذه القيمة تعتبر صغيرة جداً مما يكسب مركب بيريدين-٣- أول نشاط تفاعليا كبيرا جداً تجاه هذا الباحث عن ثنائى القطب. والمركبات الناتجة تبدو لها أهمية تخليقية كبيرة فى مجال تخليق حلقات سباعية تحتوى على ذرتين نيتروجين.