

Synthesis of New Diazahomoadamantanone and Study the Reactivity of Carbonyl group



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ABSTRACT

In this paper, new diazahomoadamantanone was prepared by condensation of cyclic ketone (cyclododecanone) with 1,3,6,8-tetraazatricyclo[4.4.1.13,8]dodecane and acetic acid in 2-propanol gave new diazahomoadamantanone (13,16-diazatetracyclo-[9.6.1.11,13.111,16]eicosan-18-one) by Mannich,s reaction. Also were studied the reactivity of carbonyl group with various chemical agents like (NaBH₄ , H₂N-NH₂.H₂O and NH₂-OH.HCl). A simplified procedure was developed for the synthesis of 1,3,6,8-tetraazatricyclo [4.4.1.13,8]dodecane from condensation of ethane-1,2-diamine with paraform (Type A) in a very good yield. This new compound was characterized by FT-IR, Mass spectrum, 1H NMR and 13C NMR spectroscopy methods.

Introduction:-

Diazahomoadamantanone (structure A) is a complex polycyclic framework molecule. First one should realize how several simple molecules organize themselves into a larger one. It is well-known that by condensing a cyclic ketone with 1,3,6,8-tetraazatricyclo[4.4.1.13,8]dodecane (1) in 2-propanol in the presence of acetic acid by Mannich,s reaction can give 3,6-diazahomoadamantan-9-one and its derivatives with substituents in the nodal positions [1-6].

We reported the synthesis of new diazahomoadamantanone (13,16-diazatetracyclo [9.6.1.11,13.111,16] eicosan-18-one) (2) (Scheme 1) by similar procedure applying the condensation of cyclic ketone (cyclododecanone) with compound (1). The reactivity of carbonyl group of (a cyclic ketone) diazahomoadamantanone with various chemical agents is common [1-6].



(structure A)

The reactivity of carbonyl group was studied in compound (2) with various chemical agents like (NaBH₄ , H₂N-NH₂.H₂O and NH₂-OH.HCl).We also developed a simplified procedure for the synthesis of 1,3,6,8-tetraazatricyclo[4.4.1. 13,8] dodecane (Scheme 1) [7,8] with a very good yield (85%) from condensing ethane-1,2-diamine with paraform (Type A) replaced paraform (Type C).

Experimental:-

Melting points were recorded using a Gallenkamp melting point apparatus and are uncorrected. FTIR spectra were recorded on a Perkin – Elmer 1720X FTIR spectrometer , KBr disc, (table 1). Mass spectra were recorded on a Finnigan MRT-90 instrument (direct inlet- probe, voltage 5.0 kV, cathode emission current 100 μA, ionizing electron energy 70 eV, ionization chamber temperature 200 °C). Perfluorokerosene was used as a standard. The resolution was $M/\Delta M = 10000$. The injector temperature was 20 °C, (table 2). 1H NMR (table 1) and 13C NMR spectra were recorded on a Bruker WM-250 spectrometer (250.13 and 62.86 MHz) for 2-3% solutions of the compounds under study in CDCl₃, internal reference TMS. The course of the reactions was monitored and the purity of the products was checked by Thin Layer Chromatography (TLC) on Silufol UV-254 plates. Spots were visualized with

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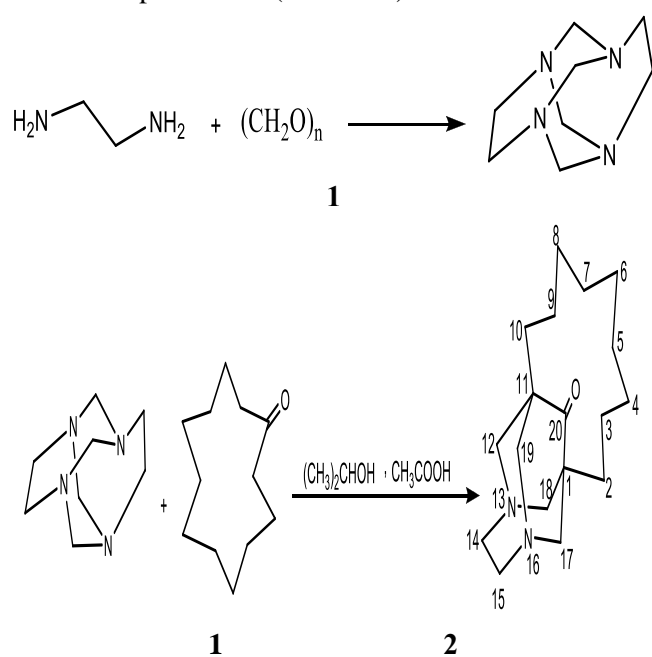
iodine vapor in a moist chamber. The final product was measured in the Republic of the Russian Federation.

1,3,6,8-Tetraazatricyclo[4.4.1.1^{3,8}]-dodecane

(1). To vigorously stirred solution of ethane-1,2-diamine (7.5 ml, 107.5 mmole) small portions (6.5 gm, 215 mmole) of paraform (Type A) were added for 15 min. so that the reaction temperature not above 60°C. The mixture was stirred for 1 h. at room temperature. The mixture was evaporated under a reduced pressure. The crude product was recrystallized from 2-propanol three times. The yield was 10 gm (85 %), white crystals, m.p. 187-188°C (cf. Refs (6,7): m.p. 183-184,181-182°C).

13,16-diazatetracyclo[9.6.1.11,13.111,16]-eicosan-18-one (2).

In round flask (100 ml) was mixed solution of (2.52 gm, 15 mmole) 1,3,6,8-tetraazatricyclo[4.4.1.13,8]-dodecane (1) in (10 ml) 2-propanol, (2.73 gm, 15 mmole) of cyclododecanone in (20 ml) 2-propanol and (2.25 gm, 37.5 mmole) of acetic acid, the reaction mixture was stirred and refluxed for 1.5 hr. The solvent was evaporated under a reduced pressure, then reaction mixture extracted with heptane (3x40 ml). The solvent was distilled off in a vacuum. The crude product was washed with 5 ml of acetone and dried at room temperature, then recrystallized from hexane. The yield compound (2) was 0.4 gm (17 %), white crystals, m.p. 153-154 °C (cf. Refs (2)). FT-IR spectrum, ¹H NMR, ¹³C NMR and Mass spectrum in (Table 1-3).

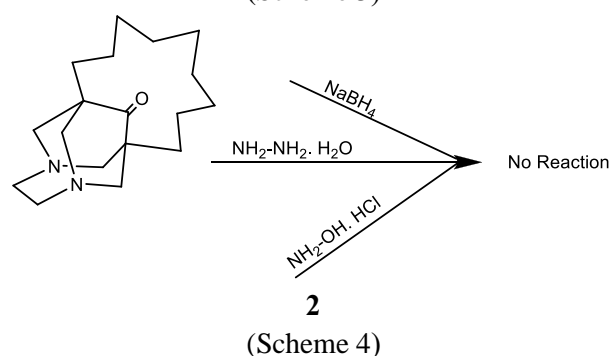
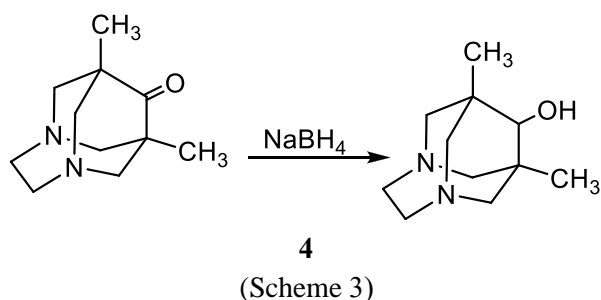
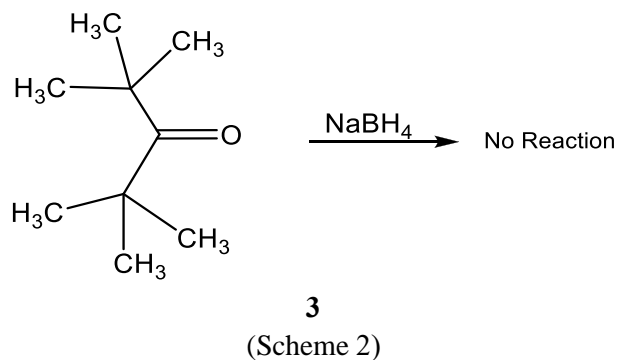


(Scheme 1)

Discussion:-

Synthesis of diazahomoadamantanone and its derivatives were very interesting and perspective compounds. Its known diazahomoadamantanone and its derivatives have biological activity [9]. The present investigation describes the synthesis of new diazahomoadamantanone, containing a substituted aliphatic ring in the nodal positions [1-6]. We prepared 13,16-diazatetracyclo [9.6.1.11,13.111,16] eicosan-18-one (2) by condensing cyclic ketone (cyclododecanone) and 1,3,6,8-tetraazatricyclo[4.4.1.13,8] dodecane (1) in 2-propanol in the presence of acetic acid by Mannich,s reaction capable of producing the major product (2) (Scheme 1) approaching 17% yield. FT-IR spectrum of compound (2) (Table 1) showed band of the stretching vibration due to (C=O) group in region 1715 cm⁻¹. In the ¹H NMR spectrum in (CDCl₃) (Table 1), the protons of (NCH₂C) group for diazahomoadamantan have proved (AB-system), due to doublet-doublet signals with centre (1.80, 3.25 ppm , 2JAB = 14 Hz) respectively. The protons of (NCH₂CH₂N) group appeared as a broad singlet with centre (2.45 ppm) and aliphatic cycle appeared as multiplet (18H, 9CH₂) at range (1.70-0.70). In the ¹³C NMR spectrum (CDCl₃, ppm) (Table 2), we observed the peaks 215.8 (C20); 62.2, 62.1, 60.9, 60.8, 54.7, 52.9 (C12,14,15,17,18,19); 43.5 (C1,11); 29.7, 25.8, 25.3, 24.4, 22.9, 22.6, 22.4, 22.3, 21.9 (C2-10). In the mass spectrum (Table 3) we observed the peak of molecular ion M⁺ with m/z (Irel (%)): 290 (12) [M]⁺, 236 (86), 194 (16), 149 (27), 123 (25), 95 (54), 84 (87), 72 (87), 55 (100), 43 (59).

It is well-known that carbonyl group in di-tertiary butyl ketone (3) is not active due to the steric effect of methyl group which prevents attack on carbonyl group (Scheme 2), but it is common that carbonyl group of diazahomoadamantanone (4) is active due to the fact that it has bridge structure (aliphatic skeleton) which reduces steric effect of methyl group which allowing attack on carbonyl group like (NaBH₄, H₂N-NH₂.H₂O and NH₂-OH.HCl) (Scheme 3). We studied the reactivity of carbonyl group in compound (2) and observed that this group is absolutely inactive at reaction with all chemical agents like (NaBH₄, H₂N-NH₂.H₂O and NH₂-OH.HCl) due to steric effect of ethylene ring (Scheme 4) which is similar to the effect in compound (3).



Conclusions:-

- 1- Synthesis of new diazahomoadaman-tanone (13,16-diazatetracyclo[9.6.1.11,13.111,16]eicosan-18-one) by the condensation of cyclic ketone (cyclododecanone) with 1,3,6,8-tetraazatricyclo [4.4.1.13,8]dodecane.
- 2- The reactivity of carbonyl group was studied in 13,16-diazatetracyclo[9.6.1.11,13.

111,16]eicosan-18-one with various chemical agents like (NaBH₄, H₂N-NH₂.H₂O and NH₂-OH.HCl), and observed that this group is absolutely inactive due to steric effect of ethylene ring.

- 3- A simplified procedure was developed for the synthesis of 1,3,6,8-tetraazatricyclo-[4.4.1.13,8]dodecane from condensing ethane-1,2-diamine with paraform (Type A).
- 4- The FT-IR, Mass spectrum, ¹H NMR and ¹³C NMR were done successfully to determine the structure of this new compound

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Table 1. Properties of compound (2).

Comp.	M.P./ °C,	Yield %	¹ H NMR spectrum (Chem. Shift , ppm) in CDCl ₃ solvent.			FT-IR spectra , wave number in (cm ⁻¹)
			NCH ₂ CH ₂ N (Sb)	4NCH ₂ C (D) ² J _{AB} =14 Hz	(18H, 9CH ₂) (M)	
2	153-154	17 (white crystals)	2.45	1.80, 3.25	1.70-0.70	C=O (1715)

Sb = broad singlet , D = doublet , M = multiplet , ²J_{AB} = AB system .

Table 2. Properties of compound (2).

Comp.	¹³ C NMR spectrum (Chem. Shift , ppm) in CDCl ₃ solvent.			
	C20	C12,14,15,17,18,19	C1,11	C2,3,4,5,6,7,8,9,10
2	215.8	62.2, 62.1, 60.9, 60.8, 54.7, 52.9	43.5	29.7, 25.8, 25.3, 24.4, 22.9, 22.6, 22.4, 22.3, 21.9

Table 3. Mass spectrum of compound (2).

Comp.	m/z (Irel (%))
2	290 (12) [M] ⁺ , 236 (86), 194 (16), 149 (27), 123 (25), 95 (54), 84 (87), 72 (87), 55 (100), 43 (59).

تحضير مركب ثنائي ازاهوموادامنتانول جديد ودراسة فعالية مجموعة الكربونيل

أحمد حمد شكر كوزنتسوف أ. إ. سيروفا ت. م.

الخلاصة:

في هذا البحث تم تكاثف كيتون حلقي (دوديكانون الحلقي) مع 8,6,3,1-رباعي ازاتلاثي سايكلو [3,81,1,4,4] دوديكان وحامض الخليك في 2-بروبانول ونتاج مركب ثنائي ازاهوموادامنتانول جديد هو 16,13-ثنائي از رباي سايكلو [9.6.1.11,13.111,16] ايكوزان-18-ون من خلال تفاعل مانيج، اضافة الى ذلك تم دراسة فعالية مجموعة الكربونيل اتجاه كواشف كيميائية مختلفة مثل (NaBH₄, H₂N-NH₂.H₂O, NH₂-OH.HCl). كذلك طورت طريقة بسيطة للحصول على المركب 8,6,3,1-رباعي ازاتلاثي سايكلو [3,81,1,4,4] دوديكان من خلال تفاعل الايثان-2,1-ثنائي امين مع البارافورم (نوع A) برفع نسبة الناتج. ان المركب الجديد شخص بواسطة طيف الاشعة تحت الحمراء (FT-IR) وطيف الكتلة (MS), وطيف الرنين النووي المغناطيسي البروتوني (1H NMR) و نظير الكربون 13 (13C NMR).