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SYNTHESIS OF SOME NEW IMIDAZOLIUM AND PURINIUM SALTS AND THEIR RELATED DERIVATIVES

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ABSTRACT :

Cyclization of 5-amino-1-(4-methoxyphenyl) imidazole-4-carbonitrile **3** with formamide afforded 6-aminopurine derivative **4**. When the latter was reacted with alkyl iodides, the purinium iodide salts **7a-c** were obtained. Upon treating the salts **7a-c** with a - kali, the dequaternized and rearranged products N-alkyl-9-(4-methoxyphenyl)-6-amino-9H-purina **8a-c** were obtained. The 5-(methoxymethylidencamino) imidazole-4- carbonitrile **10** was synthesized by reacting **3** with trimethyl orthoformate. When the imidate **10** reacted with alkylamines, the corresponding 1-alkyl-9- (4-methoxyphenyl)-6-imino-9H-purines **11a-c** were obtained. Rearrangement of the products **11a-c** to their N-alkyl-6-amino-9H-purines **8a-c** was carried out . The 3-alkylimidazolium-4-carbonitrile iodides **12a-e** were synthesized by quaternizing product **3** with alkyl iodides. Treatment of the salts **12a-e** with alkali, afforded the ring-opened products : 2-amino-2-(4-methoxyphenylamino)-1-[N-alkyl formylamino]ethylene-1-carbonitriles **13a-e**, rather than the expected 1-alkyl-4-(4-methoxyphenylamino) imidazole-5-carbonitriles **14a-e**. Products **14a-e** were obtained by cyclization of **13a-e** in acidic medium.

INTRODUCTION

The chemistry of imidazoles has been of considerable biological significance. Imidazolecarbonitriles have been reported as starting materials in the synthesis of some herbicides[1] and fungicides[2]. Compounds 5-aminoimidazole-4-carbonitriles have long been recognized as useful synthetic precursors to purines[3,4] . Whereas, adenosine elicits a number of biological responses through the interaction with at least four cell membrane receptors classified as A_1 , A_{2A} , A_{2B} and A_3 [5-7]. Also, some 6-substituted purine derivatives have been reported for their antitumor activity against Ehrlich Ascities Carcinoma [8-11], antiviral activity[12,13] and as cardiovascular agents[14].

In the present work the synthesis of some new imidazolium, purinium iodides and their related derivatives was attempted for their expected useful biological activity especially in medicinal direction utilizing 5-amino-1-(4-methoxyphenyl) imidazole-4-carbonitrile as a precursor.

RESULTS AND DISCUSSION

Treatment of the 5-amino-1-(4-methoxyphenyl) imidazole-4-carboxamide[15] **1** with N,N-dimethylformamide / phosphorus oxychloride reagent complex afforded the 5-(dimethylaminomethylidene) amino-1-(4-methoxyphenyl) imidazole-4-carbonitrile **2**. When the latter was treated with dilute hydrochloric acid solution, the corresponding 5-amino-1- (4-methoxyphenyl) imidazole-4-carbonitrile[16] **3** was obtained. Cyclization of **3** with formmide gave 6-amino-9-(4-methoxyphenyl)-6-amino-9H-purine **4**[17] .

Alkylation of the 6-aminopurine **4** with methyl-, ethyl- and n-butyl iodides gave the corresponding 1-alkyl derivatives **7a-c** and not the isomeric 3-alkyl **6** or 7-alkyl **5** derivatives.

The structure of **7** was established based on ^{13}C-NMR spectral data. Therefore, comparison of the ^{13}C-NMR spectra (decoupled) of the obtained products with that of compound **4** revealed that, the signals due to C-2 and C-6 of **4** were shifted to higher field after alkylation. These signals appeared in case of the alkylated products at δ : 147.75- 148.13 ppm and 149.91-150.31 ppm regions respectively; on the other hand the corresponding signals of the non-alkylated parent product **4** appeared at δ : 152.99 and 156.26 ppm, respectively (table 1). This finding was found to be in accordance with the previous findings on the ^{13}C-NMR spectra of some pyrrolopyrimidinium [18] and purinium[10] iodide salts. Presumably, such noticeable shielding for C-2 and C-6 of the alkylated products could be explained as being due to incorporation of the alkyl substituents at the N^1-position of the purine ring and thus excluding structures of types **5,6** and suggesting structure of type **7**.

As a complementary support for the proposed structure of type **7**, when the obtained purinium iodide salts **7a-c** were warmed in aqueous sodium hydroxide solution, the dequaternized and rearranged (Dimroth-type[19]) products: N-alkyl-6-amino-(4-methoxyphenyl)-9H-purines **8a-c** were obtained.

The structure of products **8a** and **8b** was confirmed by independent synthesis as previously reported[20] . Product **8c** was also found to be identical in m.p. and mixed m.p. with an authentic sample prepared by unambiguous synthesis from reacting the 6-chloro-9-(4-methoxyphenyl)-9H-purine **9**[21] with n-butylamine.

Reaction of the 5-amino-1-(4-methoxyphenyl)-imidazole-4-carbonitrile **3** with trimethyl orthoformate, catalyzed by trifluoroacetic acid, yieldid the 5-(methoxymethylidene) amino -1-(4-methoxyphenyl) imidazole-4-carbonitrile **10**. Upon reacting the imidate **10** with alkylamines viz., methylamine, ethylamine and

n-butylamine at room temperature, the 1-alkyl-9-(4-methoxyphenyl)-9H-purine-6 (1H)- imines **11a-c** were obtained in good yields .

When **10** was reacted with ammonia solution under the same reaction conditions, the 6-aminopurine derivative **4** was obtained in an excellent yield.

In a previous finding it has been found[22] that the 3-alkyl-7H-pyrrolo[2,3-d] pyrimidin-4(3H)-imines can undergo the Dimroth rearrangement in a polar solvent (boiling water) to give the corresponding 4-alkylamino derivatives. Similarly, when the imino products **11a-c** were heated under reflux for 10 hrs in aqueous ethanol (50%), the corresponding N-alkyl-6-aminopurines **8a-c** were obtained in excellent yields (identical by m.p. and mixed m.p. with the products obtained from the purinium salts **7a-c** and the 6-chloropurine **9**) scheme 1.

The structure of product **10** was infered from its IR spectrum which showed ν C≡N at 2116 cm^{-1} and lacks the absorptions due to NH group. Also, its ^{1}H-NMR spectrum revealed N=CH- proton signal at δ 8.36 [36].

Infrared absorption spectra of products **11a-c** showed typical =N-H stretch vibrations in the 3300-3240 cm^{-1} region and around 1650 cm^{-1} characteristically of a C=N group, whereas the spectra of the N-alkyl-6-aminopurines **8a-c** showed this NH stretching vibrations in the region 3430-3290 cm^{-1}.

In the ^{1}H-NMR spectra of products **11a-c** the singlets appeared in the region δ 7.70-7.76 were assigned to the 2-H protons, whereas these singlets were found to be shifted to lower field (~ 0.66) in the spectra of the correspondings amino compounds **8a-c**. The change in the 2-H protons pattern of products **11a-c** and **8a-c** (δ 8.33-8.41) clearly indicated that, the products obtained from **10** and alkylamines existed in the imino-form of type **11a-c** [24].

Moreover, the behaviour of the 5-aminoimidazole-4-carbonitrile **3** towards some alkyl iodides was also attempted.

Thus, when **3** was heated under reflux with methyl-, ethyl-, n-butyl-, n-pentyl- and n-hexyl- iodides in dimethylformamide, the corresponding 3-alkyl-5-amino-1-(4-methoxyphenyl) imidazolium-4-carbonitrile iodide salts **12a-e** were obtained.

^{1}H-NMR spectra of products **12a-e** revealed remarkable deshielding of 2-H protons, i.e. shifting downfield in δ 9.15-9.20 region relative to that observed for the 2-H protons of their parent non-quaternized imidazole **3**. The signal of the 2-H for each quaternized product showed a sharp singlet in DMSO-d_6 but addition of D_2O caused rapid exchange for the 2-H. This deshielding effect may be equated with an electron deficiency in the imidazole ring, caused by quaternizing at N^3-position [25].

Mass spectra of the purinium **7a-c** and imidazolium salts **12a-e** were characterized by revealing m/z corresponds to M^+ -HI . This observation suggested the splitting of HI in the mass spectrometer. Such finding has been previously reported for some pyrrolopyrimidinium [18] and imidazolium iodide salts [26].

Upon treating the imidazolium iodide salts **12a-e** with aqueous sodium hydroxide solution, no Dimroth-type rearranged products were isolated; instead the 2-amino-1-[N-alkylformyl (amino)]-2-(4-methoxyphenyl)-aminoethylene-1-carbonitriles **13a-e** were smoothly obtained.

The ring opened-structure of compounds of type **13a-e** was confirmed by studying of their IR spectra which showed ν C ≡ N at 2170-2165 cm^{-1} region and a peak at 1660-1650 cm^{-1} region due to the carbonyl absorptions [27] . The ring opened-structure of type **13a-e** was also supported by studying their ^{1}H-NMR which revealed signals at δ 4.70-5.95 and 4.95-6.30 regions due to the NH_2 protons (D_2O exchangeable). The spectra revealed also signals at δ 8.00-8.10 region which corresponds to the CHO protons [28].

Cyclization of products **13a-e** to the Dimroth-type products : 1-alkyl-4-(4-methoxyphenyl) aminoimidazole-5-carbonitriles **14a-e** was successfully carried out by heating under reflux in ethanolic hydrochloric acid solution. ^{1}H-NMR spectra of products **14a-e** revealed, generally, the presence of NH proton signals at δ 6.10-6.35 (D_2O exchangeable) region and the 2-H proton signals were imbedded in the aromatic region. Moreover , the mass spectra of **14a-e** confirmed their proposed structures (scheme 2).

The above-mentioned new imidazolium , purinium iodide salts and their related derivatives are now under investigation for their potential biological activities.

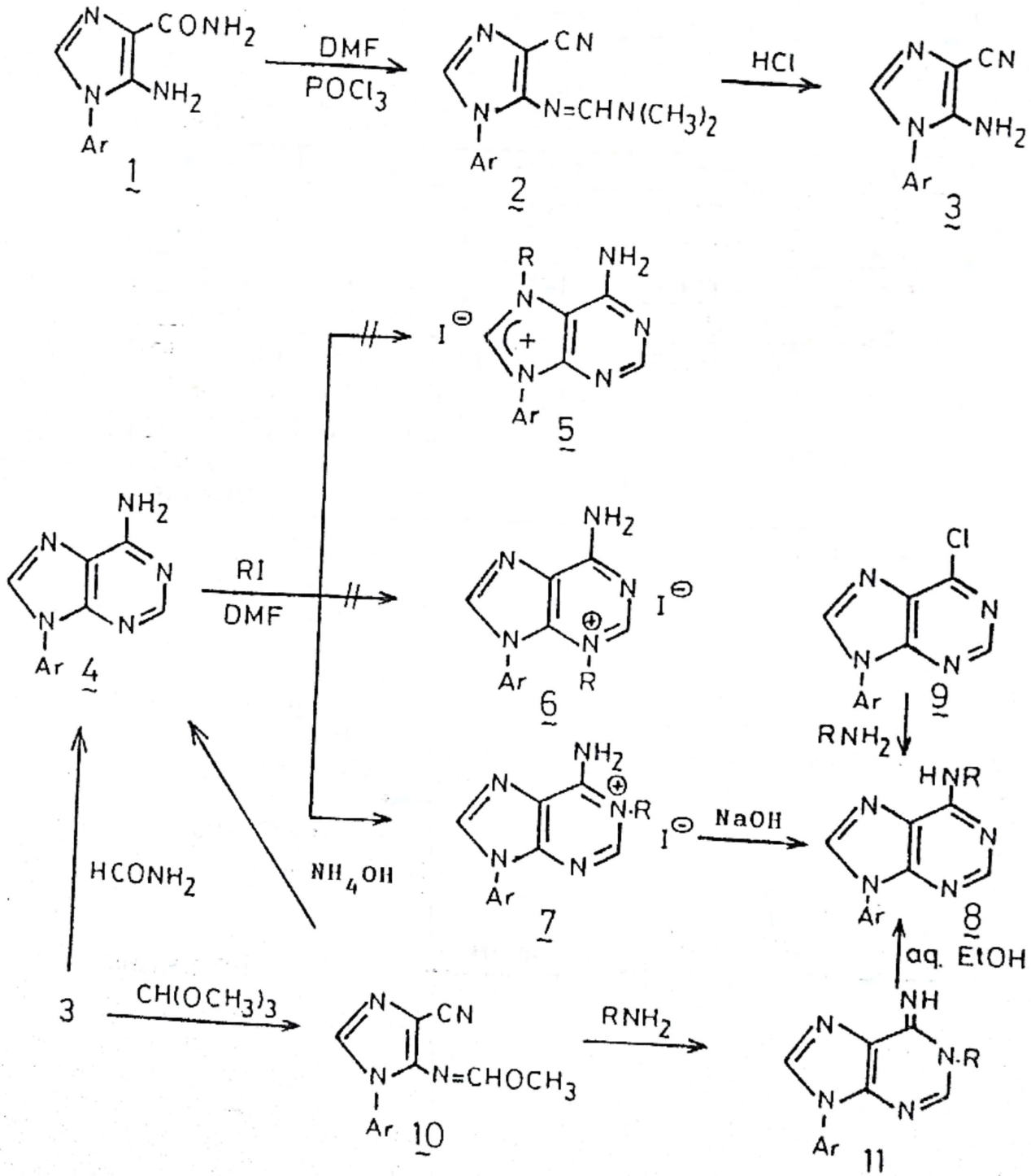
EXPERIMENTAL

Melting points were uncorrected. Microanalyses were carried out in the Microanalytical Center, Cairo University, Egypt. IR spectra (KBr) were recorded on a Jasco FT/IR-300E spectrophotometer. ^{1}H-NMR and ^{13}C-NMR spectra were run on a Jeol Ex 270 MHz and Varian Gemini 200 NMR systems in $CDCl_3$ (or DMSO-d_6 whenever reported) with chemical shift in δ from Me_4Si. Mass spectra were measured by using GCMS QP 100 Ex Schimadzu and Finnigan SSQ 7000 GC/MS spectrometers.

5-(Dimethylamino) methylideneamino-1-(4-methoxyphenyl) imidazole-4- carbonitrile 2 :

To an ice cold N, N-dimethyl formamide/phosphorus oxychloride complex (DMF 15 ml, $POCl_3$ 2.55 g), 5-aminoimidazole-4-carboxamide **1** (0.01 mol) was added in four portions with stirring during 20 min

Zagazig J. Pharm. Sci., December 1997
Vol.6, No. 2, pp. 14-22

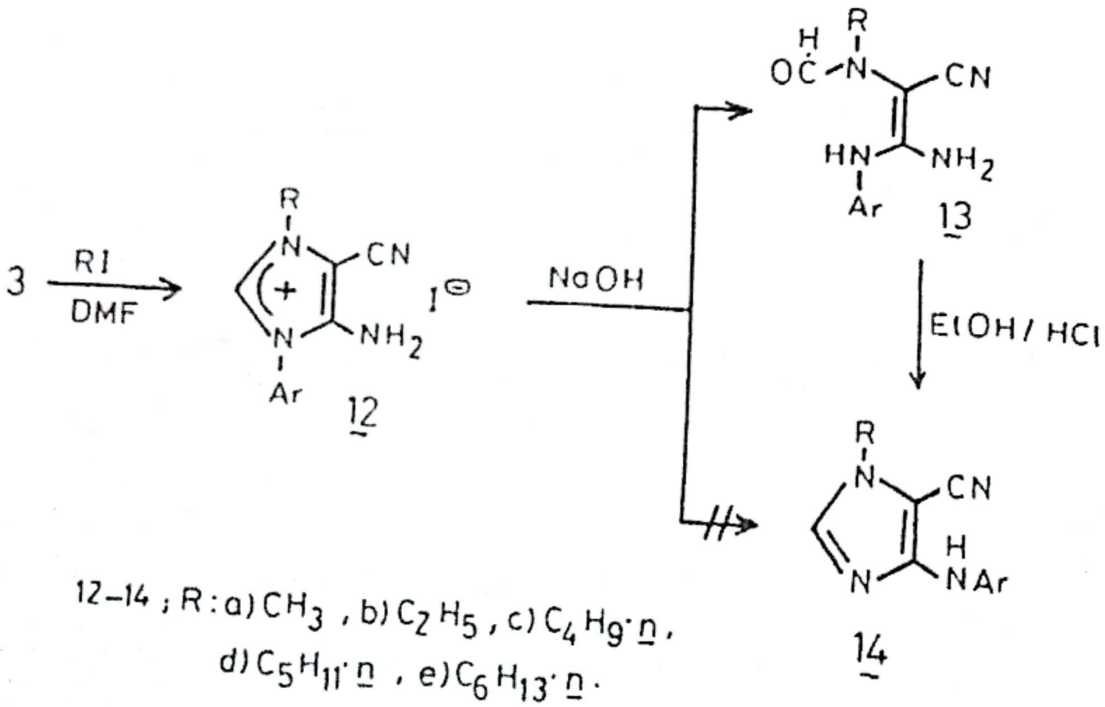


Scheme 1

Table (1) : ^{13}C-NMR* spectra of products **4** and **7a-c**.

Carbon Atom	Compound 4	Compound 7a	Compound 7b	Compound 7c
C-2	152.99	147.96	148.13	147.75
C-4	149.17	146.48	147.00	146.42
C-5	119.09	119.02	119.78	119.27
C-6	156.26	150.76	150.31	149.91
C-8	139.70	143.70	144.30	143.77
C-1'	127.96	126.23	126.77	126.21
C-4'	158.33	159.35	159.91	159.39
C-2', 6'	114.51	114.86	115.36	114.80
C-3', 5'	124.56	125.50	126.12	125.60
Alkyl	OCH_3(55.37)	OCH_3(55.67) NCH_3(38.00)	OCH_3(56.19) CH_3 (14.04) CH_2 (45.92)	OCH_3(55.65) CH_3 (14.00) CH_2 (19.00) CH_2 (30.00) NCH_2(49.65)

* DMSD-d_6



12–14 ; R : a) CH_3 , b) C_2H_5 , c) C_4H_9·n , d) C_5H_{11}·n , e) C_6H_{13}·n .

(Ar = $C_6H_4OCH_3$·4)

Scheme 2

The resulting mixture was stirred while cooling for 30 min., then for 1 hr. at room temperature. The resulting solution was poured onto crushed ice (50 g) and adjusted to pH 6 with aqueous ammonia solution. The solid product obtained was filtered off, washed with water and recrystallized from methanol to give 2 (86%), m.p 145-7 °C. IR ν/cm-1 : 2205 (C ≡ N) . ^{1}H-NMR δ : 2.92 (s,3H, NCH_3); 3.06 (s, 3H, NCH_3); 3.83 (s, 3H, OCH_3); 6.94 (d, 2H, ArH); 7.31 (d, 2H, ArH); 8.31 (s, 1H, 2-H).

Anal. Calc. for $C_{14}H_{15}N_5O$: C, 62.45; H, 5.58; N, 26.02%. Found : C, 62.65; H, 5.40; N, 26.30%.

5-Amino-1-(4-methoxyphenyl) imidazole-4-carbonitrile 3 :

A suspension of 2 (0.01 mol) in hydrochloric acid solution (2%, 150 ml) was warmed on a steam-bath for 2 hr. After cooling, the solution was treated with aqueous ammonia solution till pH 3.5 . The solid product obtained was filtered off, washed with water, dried and recrystallized from ethanol to give 3 (62%), m.p. 213-5 °C.

9-(4-methoxyphenyl)- 6-amino-9H-purine 4:

A mixture of 3 (5 g) and formamide (50 ml) was heated at 180-90 °C (oil-bath) for 1 hr. After coolling , the solid product obtained was filtered off, dried and crystallized from n-butanol to give 4 (71%), m.p. 226-8 °C [Lit.[17] m.p. 225-7°C] .

IR ν/ cm^{-1}: 3290, 3110 (NH) . ^{1}H-NMR (DMSO-d_6) δ : 3.84 (s, 3H, OCH_3); 7.15 (d, 2H, ArH); 7.40 (br, 2H, NH_2, D_2O-exchangeable); 7.75 (d, 2H, ArH); 8.22 (s,1H, 8-H); 8.50 (s, 1H, 2-H). Mass m/z : 241 (M^+).

1-Alkyl-6-amino-9-(4-methoxyphenyl)-9H-purinium iodides 7a-c :

General procedure :

A mixture of 4 (0.01 mol) and the desired alkyl iodide (0.013 mol) in N,N-dimethyl formamide (30 ml) was heated under reflux for 1 hr. The reaction mixture was concentrated and then treated with dry acetone. The solid product obtained was filtered off, dried and recrystallized from ethanol (95%) to give 7a-c .

1- Methyl-6-amino-9- (4-methoxyphenyl)-9H-purinium iodide 7a :

Yield (72%), m.p. 314-6 °C. IR ν/ cm^{-1} : 3180 (NH). ^{1}H-NMR (DMSO-d_6) δ : 3.85 (d, 6H, $2CH_3$); 7.20 (d, 2H, ArH); 7.70 (d, 2H, ArH); 8.73(s, 1H, 8-H); 8.85(s, 1H, 2-H); 9.25(br, 1H, NH, D_2O-exchangeable); 10.00 (br, 1H, NH, D_2O-exchangeable). Mass m/z : 255 (M^+-HI).

Anal. Calc. for $C_{13}H_{14}IN_5O$: C, 40.73; H, 3.66; N, 18.28%. Found : C, 40.90; H, 3.90; N, 18.50%.

1-Ethyl-6-amino-9-(4-methoxyphenyl)-9H-purinium iodide 7b :

Yield (61%), m.p. 309-11 °C. IR ν/ cm^{-1} : 3210 (NH). ^{1}H-NMR (DMSO-d_6) δ : 1.40(t, 3H, CH_3) ; 3.85(s, 3H, OCH_3) ; 4.35(q,2H, CH_2) ; 7.20(d, 2H, ArH); 7.70(d, 2H, ArH); 8.77(s, 1H, 8-H) ; 8.85(s, 1H, 2-H); 9.35(br, 1H, NH, D_2O exchangeable) ; 10.00 (br, 1H, NH, D_2O exchageable). Mass m/z : 269 (M^+-HI).

Anal. Calc. for $C_{14}H_{16}IN_5O$: C, 42.32; H, 4.03. N, 17.63%. Found : C, 42.30; H, 3.90; N, 17.40%.

1-(n-Butyl)-6-amino-9-(4-methoxyphenyl)-9H-purinium iodide 7c :

Yield (57%), m.p. 270-2 °C.. IR ν/cm-1 : 3180 (NH). ^{1}H-NMR (DMSO-d_6) δ : 0.98 (t, 3H, CH_3); 1.40(m, 2H, CH_2); 1.75(m, 2H, CH_2); 3.85(s, 3H, OCH_3); 4.32(t, 2H, NCH_2); 7.20(d, 2H, ArH); 7.72(d, 2H, ArH); 8.77(s, 1H, 8-H); 8.87(s, 1H, 2-H); 9.33(br,1H, NH, D_2O exchangeable); 10.02 (br, 1H, NH, D_2O exchangeable). Mass m/z : 297(M^+-HI).

Anal. Calc. for $C_{16}H_{20}IN_5O$: C, 45.18; H, 4.71; N, 16.47%. Found : C, 45.20; H, 4.70; N, 16.20%.

N-Alkyl-9-(4-methoxyphenyl)-6-amino-9H-purines 8a-c :

Method A :

Rearrangement of purinium iodide salts 7a-c :

To a solution of 7 (1.0 g) in water (100 ml) was added sodium hydroxide solution (2 ml, 1N). The reaction mixture was heated on a steam-bath for 1-3 hr. and then left to cool. The solid product obtained was filtered off and recrystallized from the proper solvent to give 8a-c.

Method B :

Reaction of 6-chloropurine 9 with n-butylamine :

A mixture of 9 (0.01 mol) and n-butylamine (0.013 mol) in absolute ethanol (20 ml) containing triethylamine (0.2 ml) was heated under reflux for 3 hr. The reaction mixture was then evaporated till dryness under reduced pressure. The lefted residue was triturated with petroleum ether 40-60. The solid product separated out was filtered off and recrystallized from ethyl acetate/pet. ether 40-60 (1 : 1) to give 8c (79%).

N-Methyl-9-(4-methoxyphenyl)-6-amino-9H-purine 8a:

(A 1 hr. 60%), m.p. 185 °C (ethanol) [Lit. [19] m.p. 184-6 °C].

N-ethyl-9-(4-methoxyphenyl)-6-amino-9H-purine 8b:

(A 1 hr. 74%), m.p. 119-20 °C (ethyl acetate) [Lit. [19] m.p. 119-21 °C]. ^{1}H-NMR δ : 1.31 (t, 3H, CH_3); 3.70(q, 2H, CH_2); 3.83 (s, 3H, OCH_3); 6.00 (br, 1H, NH, D_2O exchangeable); 7.02 (d, 2H, ArH); 7.52 (d, 2H, ArH); 7.93 (s, 1H, 8-H); 8.42 (s, 1H, 2-H). Mass m/z : 269.

N-(n-Butyl)-9-(4-methoxyphenyl)-6-amino-9H-purine 8c :

(A 3 hr 67%), m.p. 88-9 °C (ethyl acetate/pet. ether 40-60 1: 1). IR ν / cm^{-1} : 3300 (NH). ^{1}H-NMR δ : 0.92 (t, 3H, CH_3); 1.42(m, 2H, CH_2); 1.62 (m, 2H, CH_2); 3.65(t, 2H, N-CH_2); 3.82 (s, 3H, OCH_3); 6.00 (br, 1H, NH, D_2O exchangeable); 7.01 (d, 2H, ArH); 7.52(d, 2H, ArH); 7.92 (s, 1H, 8-H); 8.41 (s, 1H, 2-H). Mass m/z : 297 (M^+).

Anal. Calc. for $C_{16}H_{19}N_5O$: C, 64.65; H, 6.40; N, 23.57%. Found : C, 64.50; H, 6.60; N, 23.80%.

5-Methoxymethylidene amino-1-(4-methoxyphenyl) imidazole-4-carbonitrile 10 :

A mixture of **3** (0.01 mol) and trimethyl orthoformate (15 ml) containing trifluoroacetic acid ($^1/_2$ ml) was heated under reflux for 5 hr. The reaction mixture was then evaporated till dryness under reduced pressure. The obtained residue was triturated with diethyl ether. The solid product obtained was filtered off and recrystallized from benzene /pet. ether 40-60 (1 : 5) to give **10** (90%) m.p. 106-7 °C. IR ν /cm^{-1} : 2116 (C ≡ N) . ^{1}H-NMR δ : 3.81 (s,3H, OCH_3); 3.86 (s,3H, OCH_3); 6.96 (d, 2H, ArH); 7.28(d, 2H, ArH); 7.50 (s, 1H, 2-H) ; 8.36 (s,1H, N=CH-). Mass m/z : 256 (M^+) .

Anal. Calc. for $C_{13}H_{12}N_4O_2$: C,60.94; H,4.69; N, 21.88%. Found : C, 60.70; H, 4.60; N, 22.10%.

1-Alkyl-9-(4-methoxyphenyl)-9H-purin-6-(1H)-imines 11a-c :

General procedure :

A mixture of **10** (0.01 mol) and the desired alkylamine (0.013 mol) in methanol (20 ml) was stirred at room temperature (25 °C) for 24 hr. The solvent was then evaporated under reduced pressure . The solid ppt obtained was filtered off and crystallized from the proper solvent to give **11a-c**.

Reaction of 10 with ammonia solution :

When **10** (0.01 mol) was left to react with ammonia solution (2 ml) at room temp. for 24 hr. The 6-aminopurine derivative **4** was obtained in 85% yield (m.p. and mixed m.p. with the product obtained from **3** and formamide).

9-(4-Methoxyphenyl) -1-methyl-9H-purin-6(1H)-imine 11a :

Yield (80%), m.p. 148-9 °C (methanol). IR ν/cm^{-1} : 3300 (NH); 1655 (C=N). ^{1}H-NMR δ : 3.55(s, 3H, NCH_3) ; 3.85 (s, 3H, OCH_3); 7.00 (d, 2H, ArH); 7.25 (br, 1H, NH. D_2O exchangeable) ; 7.40 (d, H, ArH); 7.70 (s, 1H, 8-H); 7.75 (s, 1H, 2-H). Mass m/z : 255 (M^+).

Anal. Calc. for $C_{13}H_{13}N_5O$: C, 61.18; H, 5.10; N, 27.45%. Found : C, 61.40; H, 4.80; N, 27.20% .

1-Ethyl-9-(4-methoxyphenyl)-9H-purin-6(1H)-imine 11b :

Yield (85%), m.p. 140-1 °C (ethyl acetate), IR ν/cm^{-1} : 3305 (NH) ; 1651 (C=N). ^{1}H-NMR δ : 1.35 (t, 3H, CH_3); 3.80 (s, 3H, OCH_3); 4.10 (q, 2H, CH_2); 7.00 (d, 2H, ArH); 7.20 (br, 1H, NH, D_2O exchangeable); 7.45 (d, 2H, ArH); 7.65 (s, 1H, 8-H); 7.70 (s, 1H, 2-H). Mass m/z : 269 (m^+).

Anal. Calc. for $C_{14}H_{15}N_5O$: C, 62.45; H, 5.58; N, 26.02%. Found : C, 62.70; H, 5.50; N, 26.30%.

1-(n-Butyl)-9-(4-methoxyphenyl)-9H-purin-6(1H)-imine 11c :

Yield (69%), m.p. 76-7 °C (ethyl acetate /pet. ether 40-60 1 : 1) IR ν/cm^{-1} : 3240 (NH); 1649 (C=N). ^{1}H-NMR δ : 0.95 (t, 3H, CH_3) ; 1.40 (m, 2H, CH_2); 1.82(m, 2H, CH_2); 3.84(s, 3H, OCH_3); 4.05 (t, 2H, NCH_2); 5.00 (br, 1H, NH, D_2O exchangeable); 7.02(d, 2H, ArH); 7.45 (d, 2H, ArH); 7.67 (s, 1H, 8-H); 7.76 (s,1H, 2-H). Mass m/z : 297 (M^+).

Anal.Calc. for $C_{16}H_{19}N_5O$: C, 64.65; H, 6.40; N, 23.57%. Found : C, 64.80; H, 6.40; N, 23.40%.

Rearrangement of Products 11a-c :

General Procedure :

A suspension of **11** (0.5 g) in aqueous ethanol (50 ml, 50%) was heated under reflux for 10 hr. The solid product obtained was filtered off, and recrystallized from the proper solvent to give 95% yield of **8a-c** (m.p. and mixed m.p. with the products obtained from the purinium salts **7a-c** and the 6-chloropurine **9**).

3-Alkyl-5-amino-1-(4-methoxyphenyl) imidazolium-4-carbonitrile iodides 12a-e :

General procedure :

A mixture of **3** (0.01 mol) and the desired alkyl iodide (0.012 mol) in N, N-dimethylformamide (15 ml) was heated under reflux for 3 hr. The dark brown solution was evaporated to a gum, which when dissolved in dioxan yielded a solid product ,which was filtered off and recrystallized from the proper solvent to give **12a-e**.

5-Amino-1-(4-methoxyphenyl)-3-methylimidazolium-4-carbonitrile iodide 12a :

Yield (90%), m.p. 195-7 °C (abs. ethanol). IR ν/cm^{-1} :3110 (NH); 2220 (C≡N). ^{1}H-NMR (DMSO-d_6) δ 3.82(s, 3H, NCH_3); 3.86(s, 3H, OCH_3) ; 7.20(d, 2H, ArH); 7.55(d, 4H, ArH, NH_2); 9.14(s, 1H, 2-H). Mass m/z : 228 (M^+ -HI).

Anal. Calc. for $C_{12}H_{13}IN_4O$: C,40.45; H, 3.65; N,15.73%. Found : C,40.60; H, 3.90; N, 15.50%.

Zagazig J. Pharm. Sci., December 1997
Vol.6, No. 2, pp. 14-22

5-Amino-3-ethyl-1-(4-methoxyphenyl) im dazolium-4-carbonitrile iodide 12b :

Yield (69%), m.p. 187-9 °C (ethanol /dioxan). IR ν/cm^{-1} : 3235 (NH); 2225 (C≡N). ^{1}H-NMR (DMSO-d_6) δ 1.50(t, 3H, CH_3); 3.85(s, 3H, OCH_3); 4.15(q, 2H, CH_2); 7.20(d, 2H, ArH); 7.50(br, 2H, NH_2, D_2O exchangeable); 7.57(d, 2H, ArH); 9.16(s, 1H, 2-H). Mass m/z : 242 (M^+-HI).

Anal. Calc. for $C_{13}H_{15}IN_4O$: C, 42.16; H, 4.05; N, 15.14%. Found : C, 42.20; H, 4.20; N, 15.30%.

5-Amino-3-(n-butyl)-1-(4-methoxyphenyl) imidazolium-4-carbonitrile iodide 12c:

Yield (69%), m.p. 175-7 °C (ethanol/dioxan). IR ν/cm^{-1} :3445, 3135 (NH); 2215 (C≡N). ^{1}H-NMR (DMSO-d_6) δ 0.90(t, 3H, CH_3); 1.40(m, 2H, CH_2); 1.85 (m, 2H, CH_2); 3.85(s, 3H, OCH_3); 4.15(t, 2H, NCH_2); 7.15(d, 2H, ArH); 7.55(t, 4H, ArH, NH_2); 9.20(s, 1H, 2-H). Mass m/z : 270 (M^+-HI).

Anal. Calc. for $C_{15}H_{19}IN_4O$: C,45.23; H, 4.77; N, 14.07%. Found : C, 45.00; H, 4.70; N, 14.00%.

5-Amino-1-(4-methoxyphenyl)-3-(n-pentyl) imidazolium-4-carbonitrile iodide 12d :

Yield (60%), m.p. 138-40 °C (dioxan). IR ν/cm^{-1} : 3375 (NH); 2217 (C≡N). ^{1}H-NMR (DMSO-d_6) δ : 0.90 (t, 3H,CH_3); 1.30 (m, 4H, $2CH_2$); 1.90 (m, 2H, CH_2); 3.85(s, 3H, OCH_3); 4.15(t, 2H, NCH_2); 7.20(d, 2H, ArH); 7.55(d, 4H, ArH,NH_2); 9.20(s, 1H, 2-H). Mass m/z : 284 (M^+ -HI).

Anal. Calc. for $C_{16}H_{21}IN_4O$: C, 46.60; H, 5.10; N, 13.59%. Found : C,46.30; H, 5.00; N, 13.50%.

5-Amino-3-(n-hexyl)-1-(4-methoxyphenyl) imidazolium-4-carbonitrile iodide 12e:

Yield (57%), m.p. 126-8 °C (dioxan). IR ν/cm^{-1} : 3445 (NH); 2225 (C≡N). ^{1}H-NMR (DMSO-d_6) δ : 0.90 (t, 3H, CH_3); 1.35(m, 6H, $3CH_2$); 1.90 (m, 2H, CH_2); 3.85(s, 3H, OCH_3); 4.10(t, 2H, NCH_2); 7.20(d, 2H, ArH); 7.55(d, 4H, ArH, NH_2); 9.19(s, 1H, 2-H). Mass m/z : 298 (M^+-HI).

Anal. Calc. for $C_{17}H_{23}IN_4O$: C,47.89; H, 5.40; N, 13.15%. Found : C,47.70; H,5.20; N, 12.85%.

2-Amino-1-[N-alkylformyl(amino)]-2-[(4-methoxyphenyl) amino] ethylene-1- carbonitriles 13a-e :

General procedure :

Aqueous sodium hydroxide solution (5 ml, 1N) was added to a solution of **12** (0.005 mol) in water (150 ml) at room temperature. The resulting mixture was heated on a steam-bath for 1 hr. The solid product separated out was filtered off (products **13a, b** were obtained by extracting the reaction mixture with chloroform and evaporated till dryness),washed with water and recrystallized from the proper solvent to give **13a-e.**

2-Amino-1-[N-methylformyl (amino)]-2-[(4-methoxyphenyl) amino] ethylene-1- carbonitrile 13a :

Yield (58%), m.p. 153-4 °C (benzene/dioxan). IR ν/cm^{-1} : 3410, 3305 (NH); 2168 (C≡N); 1660 (C=O). ^{1}H-NMR δ :2.95 (s, 3H, NCH_3); 3.80(s, 3H, OCH_3); 4.75(br, 1H, NH, D_2O exchangeable); 5.05(br, 1H, NH, D_2O exchangeable); 6.75-7.50 (m, 5H, ArH, ArNH); 8.05(d, 1H, CHO). Mass m/z : 246 (M^+).

Anal. Calc. for $C_{12}H_{14}N_4O_2$: C,58.54; H, 5.69; N, 22.76%. Found : C, 58.80; H, 5.40; N, 22.60%.

2-Amino-1-[N-ethylformyl amino]-2-[(4-methoxyphenyl) amino] ethylene-1- carbonitrile 13b:

Yield (57%), m.p. 168-9 °C (benzene/dioxan). IR ν/cm^{-1} : 3405, 3290 (NH); 2165 (C≡N); 1655 (C=O). ^{1}H-NMR (DMSO-d_6) δ:1.15(t,3H,CH_3); 3.35(m,2H, CH_2); 3.75(s, 3H,OCH_3); 5.95(br, 1H, exchangeable), 6.30 (br, 1H, NH, D_2O exchangeable); .80-7.20 m, 4H, ArH); 8.00(d, 1H, CHO); 8.25(br, 1H, NH, D_2O exchangeable). Mass m/z, 260(M^+).

Anal. Calc for $C_{13}H_{16}N_4O_2$: C, 60.00; H, 6.15; N, 21.54%. Found : C, 60.30; H, 6.15; N, 21.50.

2-Amino-1-[N(n-butyl)formyl-amino]-2-[(4-methoxyphenyl) animo] ethylene-1-carbonitrile 13c:

Yield (55%) m.p. 156-8 °C (benzene /dioxan). IR ν/cm^{-1} : 3390, 3220 (NH); 2175 (C≡N); 1650 (C=O). ^{1}H-NMR δ 0.90 (t, 3H, CH_3); 1.35 (m, 2H,CH_2); 1.60 (m, 2H, CH_2); 3.40 (m, 2H, NCH_2) 3.80 (s, 3H, OCH_3); 4.75(br, 1H, NH, D_2O exchangeable); 4.95 (br, 1H, NH, D_2O exchangeable). 6.60-7.30(m, 5H, ArH, ArNH); 8.10(d, 1H, CHO). Mass m/z : 288 (M^+).

Anal. Calc. for $C_{15}H_{20}N_4O_2$: C, 62.50; H, 6.94; N, 19.44%. found : C, 62.20; H, 6.80; N, 19.30%.

2-Amino-1-[N-(n-pentyl) formyl amino]-2-[(4-methoxyphenyl)amino]ethylene-1-carbonitrile 13d :

Yield (56%), m.p. 150-2 °C (methanol) IR ν/cm^{-1}: 3425, 3340, 3230 (NH); 2165 (C≡N); 1650 (C=O). ^{1}H-NMR δ 0.85 (t, 3H, CH_3); 1.25 (m, 4H, $2CH_2$); 1.65(m, 2H, CH_2); 3.30 (m, 2H, NCH_2); 3.80 (s, 3H, OCH_3); 4.70(br, 1H, NH, D_2O exchangeable); 4.95(br, 1H, NH, D_2O exchangeable);6.60-7.35 (m, 5H, ArH, ArNH); 8.10(d, 1H, CHO). Mass m/z : 302 (M^+).

Anal. Calc. for $C_{16}H_{22}N_4O_2$: C, 63.58; H, 7.28; N, 18.54% Found : C, 63.30; H, 7.10; N, 18.70%.

2-Amino-1-[N-(n-hexyl) formyl-amino)]-2-[4-methoxyphenyl) amino] ethylene-1-carbonitrile 13e :

Yeild (60 %), m.p. 131-3 °C (benzene). IR ν/cm^{-1} 3375 (NH); 2170 (C≡N); 1650 (C=O) ^{1}H-NMR δ 0.85 (t, 3H, CH_3); 1.25 (m, 6H, $3CH_2$), 1.60 (m, 2H, CH_2); 3.35 (m, 2H, NCH_2); 3.75 (s, 3H, OCH_3); 4.75 (br, 1H, NH, exchangeable); 5.05 (br, 1H, NH, D_2O exchangeable); 6.60-7.50 (m, 5H, ArH, ArNH); 8.05 (d, 1H, CHO). Mass m/z : 316 (M^+).

Anal Calc for $C_{13}H_{24}N_4O_2$: C, 64.56; H, 7.59; N, 17.72% Found. C, 64.80, H, 7.30, N, 18.00%

1-Alkyl-4-(4-methoxyphenyl) amino imidazole-5-carbonitriles 14a-e :

General procedure :

A solution of **13** (0.01 mol) in ethanol (50ml) containing conc. hydrochloric acid (1/2 ml) was heated under reflux for 3 hr. The mixture was then evaporated, the lefted precipitate was treated with cold water, filtered and crystallized from methanol to give **14a-e**.

4-(4-Methoxyphenyl)amino-1-methylimidazole-5-carbonitrile 14a:

Yield (66%), m.p. 157-8 °C IR ν/cm^{-1} : 3355 (NH); 2190 (C≡N). ^{1}H-NMR δ 3.65(s, 3H, NCH_3); 3.80(s, 3H, OCH_3); 6.15(br, 1H, NH, D_2O exchangeable), 6.85(d, 2H, ArH), 7.20 (d, 3H, ArH, 2-H). Mass m/z : 228 (M^+)

Anal Calc. for $C_{12}H_{12}N_4O$: C, 63.16; H, 5.26; N, 24.56% Found : C, 63.30; H, 5.00; N, 24.60%.

1-Ethyl-4-(4-methoxyphenyl)aminoimidazole-5-carbonitrile 14b:

Yield (54%), m.p. 132-4 °C. IR ν/cm^{-1} : 3340 (NH); 2195 (C≡N) ^{1}H-NMR δ 1.45 (t, 3H, CH_3); 3.75(s, 3H, OCH_3), 3.95 (q, 2H, CH_2), 6.32 (br, 1H, NH, D_2O exchangeable); 6.85 (d, 2H, ArH); 7.25(d, 3H, ArH, 2-H). Mass m/z: 242 (M^+).

Anal Calc. For $C_{13}H_{14}N_4O$: C, 64.46; H, 5.77; N, 23.14%. Found : C, 64.30; H, 5.60; N, 23.20%.

1-(n-Butyl)-4-(4-methoxyphenyl)aminoimidazole-5-carbonitrile 14c:

Yield (67%), m.p. 108-10 °C. IR ν/cm^{-1} : 3330 (NH); 2200 (C≡N) ^{1}H-NMR δ 0.95 (t, 3H, CH_3); 1.35 (t, 2H, CH_2), 1.80 (m, 2H, CH_2); 3.75 (s, 3H, OCH_3); 3.90 (t, 2H, NCH_2); 6.35 (br, 1H, NH, D_2O exchangeable); 6.85 (d, 2H, ArH); 7.20 (d, 3H, ArH, 2-H). Mass m/z : 270 (M^+).

Anal. Calc. for $C_{15}H_{18}N_4O$: C, 66.67; H, 6.67; N, 20.74%. Found : C, 66.90; H, 6.40, N, 21.00%.

4-(4-Methoxyphenyl) amino-1-(n-pentyl)imidazole-5-carbonitrile 14d :

Yield (53%), m.p. 110-2 °C. IR ν/cm^{-1} : 3335 (NH); 2190 (C≡N). ^{1}H-NMR δ 0.90 (t, 3H, CH_3); 1.30 (m, 4H, $2CH_2$); 1.85 (s, 2H, CH_2); 3.75(s, 3H, OCH_3); 3.90 (t, 2H, NCH_2); 6.20 (br, 1H, NH, D_2O exchangeable); 6.85 (d, 2H, ArH); 7.25 (d, 3H, ArH, 2-H). Mass m/z : 284 (M^+).

Anal. Calc. for $C_{16}H_{20}N_4O$: C, 67.61; H, 7.04; N, 19.72%. Found : C, 67.40; H, 6.80, N, 21.00%.

1-(n-Hexyl)-4-(4-methoxyphenyl) aminoimidazole-5-carbonitrile 14e:

Yield (53%), m.p. 112-3 °C. IR ν/cm^{-1} : 3325 (NH); 2210 (C≡N). ^{1}H-NMR δ 0.85 (t, 3H, CH_3), 1.25 (m, 6H, $3CH_2$); 1.80 (m, 2H, CH_2); 3.75(s, 3H, OCH_3) 3.90 (t, 2H, NCH_2); 6.10 (br, 1H, NH, D_2O exchangeable); 6.85 (d, 2H, ArH); 7.20 (d, 3H, ArH, 2-H). Mass m/z : 289 (M^+).

Anal. Calc. for $C_{17}H_{22}N_4O$: C, 68.46; H, 7.38, N, 18.79%. Found : C, 68.60; H, 7.10, N, 18.80%.

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Zagazig J. Pharm. Sci., December 1997
Vol.6, No. 2, pp. 14-22

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تشييد أملاح بعض الاميدازوليم والبيورينيم الجديدة ومشابهاتها

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قسم كيمياء مبيدات الآفات - المركز القومى للبحوث - الدقى-القاهرة-مصر

بحلوقة المركب ٥-امينو-١-(٤-ميثوكس فينيل) اميدازول-٤-كربونيتريل (٣) بواسطة الفورماميد نتج مشتق ٦-امينوبيورين (٤) . عند مفاعلة المركب الأخير مع ايودات الالكيل نتجت أملاح ايودات البيورين (٧أ-جـ) بالقلوى تم الحصول على المركبات ٦-الكيل امينو -٩-(٤-ميثوكس فينل) -٩هـ-بيورين (٨أ-جـ) تم تشييد المركب ٥- (ميثوكس-ميثيلين امينو) اميدازول-٤- كربونيتريل (١٠) من خلال تفاعل (٣) مع ثلاثى ميثيل ارثوفورمات . عند مفاعلة الأميد(١٠) مع بعض امينات الالكيل تم الحصول على المشتقات ١-الكيل -٩-(٤-ميثوكس فينيل) -٩هـ-بيورين -٦- امينات (١١أ-حـ) . تم اجراء اعادة ترتيب التركيب الكيميائى للمركبات (١١أ-حـ) الى قرائنها (٨أ-حـ) . الايودات ٣- الكيل اميدزوليم -٣-كربونيتريلات (١٢أ-هـ) تم تشييدها من خلال تربيع المنتج (٣) بواسطة ايودات الالكيل . عند معاملة الأملاح (١٢أ-هـ) بالقلوى أعطت المركبات : ٢-امينو -٢-(٤- ميثوكس فينيل) امينو-١- (فورميل (الكيل) امينو) ايثيلين -١-كربونيتريلات (١٣أهـ) بدلا من مشتقات ١- الكيل -٤- (٤-ميثوكس فينيل) امينو -٥- كربونيتريلات المقابلة (١٤أ-هـ) المركبات (١٤أهـ) تم الحصول عليها من خلال حلوقة المشتقات (١٣أ-هـ) فى وسط حامضى .