Synthesis and Structural Studies of 3-Imino-5-Dimethylamino-7-Aryl/Alkylimino-1,2,4,6 –Thiatriazepines

M.R Ugale [1] B.N.Berad [2]

[1]Department of Applied Chemistry, GHRIET, Nagpur, India.
[2]Post Graduate Department of Chemistry, RTMNU, Nagpur, India.
Corresponding Author: manjusha.ugale@raisoni.net

Abstract

The3-imino-5-dimethylamino-7-aryl/alkylimino-1,2,4,6 – thiatriazepines were prepared by the reaction of metformin hydrochloride and N-aryl/alkyl-S chloro isothiocarbamoyl chlorides. The synthesized compounds have been characterized by analytical and IR, NMR and mass spectral studies

Keywords: 3-imino-5-dimethylamino- 7-aryl/alkylimino -1,2,4,6 – thiatriazepines, metformin hydrochloride, N-aryl/alkyl-S chloro isothiocarbamoyl chlorides

Introduction

The 1,2,4,6 thiatriazepine is a seven membered heterocyclic ring consisting of three carbon atoms, three nitrogen atoms and one sulphur atom. Not much work on 1,2,4,6 thiatriazepine is on record. Only one report on 1,2,4,6 thiatriazepines by other method is on record[1]. Work on 1,3,4,6 thiatriazepine has been reported in literature [2-4]. As a part of exercise to find out an alternate method of synthesis of various rings of different sizes we are reporting here thesynthesis of1,2,4,6-thiatriazepines,which is not so common ring, in this paper.

Experimental Work

Melting points are uncorrected and were measured using electro thermal apparatus. FT-IR spectra were recorded with ν max in inverse centimeters. ^{1}H NMR spectra were recorded using tetramethylsilane as internal standard and chemical shifts being reported in parts per million (δ) relative to TMS. The mass spectra were obtained using Waters Q-TOF Micromass instrument. The progress of the reaction was monitored by TLC on Merck Silica Gel 60 F 254 plates with detection by UV light and I_2 vapours as visualizing agent.

Materials and Methods

The chemicals and reagents used in present work were of AR grade and LR grade purchased from SD fine chem. Ltd., and, Loba chem. Ltd., Amines used were aniline, o-toludine, p-toludine ,o-chloro aniline , p-chloro aniline, o-anisidine, p-anisidine, m-chloro aniline etc. The reaction progress was monitored by TLC technique by using suitable mobile phase of solvent. Purification of compounds were done by recrystalization method by using suitable solvent. Determination of melting point was done by using melting point apparatus and are uncorrected. IR spectra recorded on HAPP-GENZEL. ^{1}H NMR spectra on Bruker avance-II 400 NMR spectrometer at 400 MHz in $CDCl_3$ as solvent were recorded. The mass spectra were recorded on TOF MS ES+ 2.77e^3 mass spectrometer

Procedure

Preparation of aryl isothiocyanates: The aryl isothiocyanate are prepared by already known procedure[5]

Preparation of N-aryl-S-chloro isothiocarbamoyl chloride(IIa-i): The required N-aryl-S-chloro isothiocarbamoyl chlorides were prepared by the interaction of aryl isothiocyanates and calculated quantity of chlorine. Details of typical experiment are as follows.

Through a solution of p-tolyl isothiocyanate(1.49 g,10 m Mol in 10 ml $CHCl_3$) pure and dry chlorine gas (0.70 g,10 m Mol) was passed. During the chlorination the temperature of the reaction was maintained below 10 ^{0}C by keeping it in a ice cold condition. The calculated quantity of chlorine gas was passed. The resultant yellow solution was filtered to removesuspended solid impurity and the clear solution was mixed with 25 ml petroleum ether (40-60^0 C) The solvent was then removed by distillation under vacuum. The residual oil was once again diluted with 25 ml petroleum ether and distilled under vacuum. N-p-tolyl-S-chloro isothiocarbamoyl chloride 2.19 g was obtained as pale yellow oil.

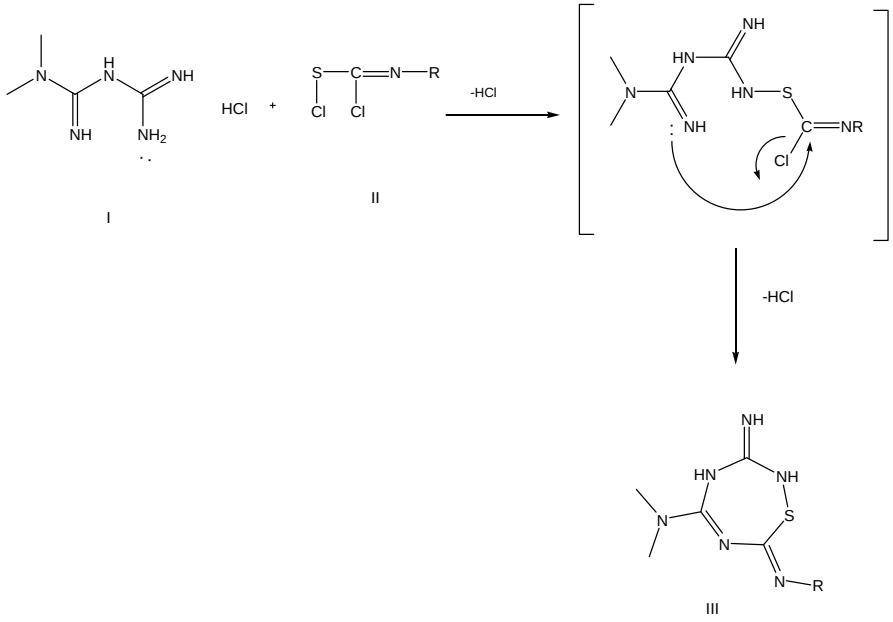
Preparation of 3-imino-5-dimethylamino-7-aryl/alkylimino-1,2,4,6 –thiatriazepines (III).

The metformin hydrochloride (I,1.65 g,10m mole) and N-aryl/alkyl-S-chloro isothiocarbamoyl chlorides(II a-i) (10 m mole) in chloroform (10 ml) were mixed and stirred overnight at room temperature. Then the solvent was allowed to vacuum evaporate to afford solids, crystallized from ethanol to yield 3 imino5-dimethylamino-7-aryl/alkylimino1,2,4,6 thiatriazepines (III a-i)

Results and Discussion

We synthesized a series of 3-imino-5-dimethylamino-7-aryl/alkylimino1,2,4,6 thiatriazepines by the interaction of metformin hydrochloride (I,1.65 g,10m mole) and N-aryl/alkyl-S-chloro isothiocarbamoyl chlorides(II a-i) (10 m mole) in chloroform (10 ml) by mixing and stirring overnight at room temperature. Then the solvent was allowed to vacuum evaporate to afford solids, crystallized from ethanol to yield 3 imino5-dimethylamino-7-aryl/alkylimino1,2,4,6 thiatriazepines (III a-i)

Reaction Scheme



Where R in II, III are
a) p-tolyl b) o-tolyl c) phenyl d) o-chloro phenyle) p-chloro phenyl f) o-anisyl g) p-anisyl h) t-butyl i) m-chloro phenyl.
The structures of the target compounds have been established by IR, ^{1}H-NMR, ^{13}C-NMR and mass structural data.
The other 3-imino-5-dimethylamino-7-aryl/alkylimino1,2,4,6 thiatriazepines (III b-i) were prepared by extending the above reaction to different N-aryl/alkyl-S-chloro isothiocarbamoyl chlorides (II b-h), and the related products were isolated in good yields. (Table 1.1).

Table 1.1 Physical data of 3-imino-5-dimethylamino-7-aryl/alkylimino-1,2,4,6 –thiatriazepines (III)
Reactants :- Metformin hydrochloride (I) and N- aryl/alkyl-S-chloro isothiocarbamoyl chlorides (II)

R in $RNCSCL_2$ (N-aryl/alkyl-S-chloro isothiocarbamoyl chloride)(II)	3-imino-5-dimethylamino-7-aryl/alkylimino-1,2,4,6 – thiatriazepines(III).	Yield %	mp ^{o}C	Elemental analysis Found(cal) (%) N S
p-tolyl (IIa)	3-imino-5-dimethylamino-7-p-tolylimino-1,2,4,6– thiatriazepines(IIIa).	70.06	222	30.35 11.52 (30.41) (11.60)
o-tolyl(IIb)	3-imino-5-dimethylamino-7-o-tolylimino-1,2,4,6– thiatriazepines(IIIb).	57.32	228	30.30 11.55 (30.41)(11.60)
Phenyl	3-imino-5-dimethylamino-7-phenylimino-1,2,4,6– thiatriazepines(IIIc).	70	232	32.07 12.20 (32.04) (12.22)
o-chlorophenyl	3-imino-5-dimethylamino-7-o-chlorophenylimino-1,2,4,6– thiatriazepines(IIId).	74.85	227	28.27 10.77 (28.32) (10.80)
p-chlorophenyl	3-imino-5-dimethylamino-7-p-chlorophenylimino-1,2,4,6 – thiatriazepines(IIIe).	83.83	232	28.25 10.78 (28.32) (10.80)
o-anisyl	3-imino-5-dimethylamino-7-o-anisylimino-1,2,4,6 – thiatriazepines(IIIf).	59	231	28.72 10.89 (28.75) (10.97)
p-anisyl	3-imino-5-dimethylamino-7-p-anisylimino-1,2,4,6 – thiatriazepines(IIIg).	57.50	234	28.70 10.85 (28.75) (10.97)
t-butyl	3-imino-5-dimethylamino-7-t-butylimino-1,2,4,6 – thiatriazepines(IIIh).	75	196	34.60 13.15 (34.68) (13.23)
m-chloro phenyl	3-imino-5-dimethylamino-7-m-chlorophenylimino-1,2,4,6 – thiatriazepines(IIIi).	74.85	227	28.29 10.72 (28.32) (10.80)

3-Imino-5-dimethylamino-7-p-tolyl imino-1,2,4,6 –thiatriazepines (IIIa)
I.R(KBr)cm^{-1} γ max 3329.5(N-H),3173.3(Ar-H), 2938.2(C-H of CH_3), 1686(C=N), 1508.5 (C=C aromatic),736.9(C-S),^{1}H NMR ($CDCl_3$) δ H ppm7.39(s,1H,=NH),6.89 to 6.87 (d,2H,J=8.0Hz, Ar-H),7.19 to7.17(d,2H,J=8.0Hz, Ar-H) ,2.24 (s,3H ,Ar-CH_3), 2.16 (s,2H, 2NH) ,1.62(s,6H, N-$(CH_3)_2$.) C^{13}NMR ($CDCl_3$) 3 carbons Ar-CH_3 21.28 δ ppm, 2 carbons -N $(CH_3)_2$ 30.00 δ ppm,$CDCl_3$ 77.35 to 77.71 δ ppm,1 carbon of thiatriazepine ring (carbon attached to sulphur) 99.99 δ ppm, 6 aromatic carbons 125.56 to 130.14 δ ppm, 2 carbons of thiatriazepine ring 149.00 δ ppm.
Its molecular formula was established as $C_{12}H_{16}N_6S$

3-Imino-5-dimethylamino-7-o-tolyl imino-1,2,4,6 –thiatriazepines (IIIb)
I.R(KBr)cm-1 γ max 3318, (N-H),3179.1 (Ar-H),2972.2 (C-H of CH_3),1626.2 (C=N),1508 (C=C aromatic),736.9 (C-S), ^{1}H NMR ($CDCl_3$) δ H ppm. 7.60 (s,1H, =NH), 7.47 to 6.99 (m,4H,Ar-H),2.28 (s,3H,Ar- CH_3) ,1.47 (s,1H, NH) ,1.43(s,1H, NH),1.25 (s,6H,N-$(CH_3)_2$,), MS (m/z) 276 (M+), 5%
Its molecular formula was established as $C_{12}H_{16}N_6S$.

3-Imino-5-dimethylamino-7-phenylimino-1,2,4,6–thiatriazepines (IIIc)
I.R(KBr)cm^{-1} γ max 3318(N-H), 3179 (Ar-H),1626.2(C=N),1508.5(C=C aromatic),736.9. (C-S).
The molecular formula was established as $C_{11}H_{14}N_6S$.

3-Imino-5-dimethylamino-7-o-chlorophenylimino-1,2,4,6–thiatriazepines (IIId)
I.R(KBr)cm^{-1} γ max 3323.8,(N-H),3175.2 (Ar-H),1508.5 (C=C aromatic),1062.9 (Presence of aryl chloride group.),736.9(C-S),),^{1}HNMR ($CDCl_3$) δ H ppm.7.74 (s,1H,=NH),7.48 to7.22 (m,4H,Ar-H),7.96 (s,2H,2NH) ,1.25 (s,6H, N-$(CH_3)_2$).
Its molecular formula was established as $C_{11}H_{13}N_6SCl$

3-Imino-5-dimethylamino-7-p-chloro-phenyl imino-1,2,4,6 –thiatriazepines (IIIe)
I.R(KBr)cm^{-1} γ max 3318, (N-H),3173.3(Ar-H),1205.7(p substitution to benzene ring) , 736.9 (C-S), MS(m/z) 295,297 (M+ -H)Cl35,Cl37 95%,31.6%.
The molecular formula was established as $C_{11}H_{13}N_6SCl$.

Synthesis of 3-Imino-5-dimethylamino-7-o-anisyl imino-1,2,4,6 –thiatriazepines(IIIf)
I.R(KBr)cm^{-1} γ max 3372 (N-H),2970.7 (Ar-H),2936(C-H,CH3),1508.5(C=C), 1061(C-O),736.9 (C-S),^{1}H NMR ($CDCl_3$) δ H ppm.8.13(s,1H,= NH),7.05 to 6.72 (m,4H,Ar-H),7.43(s,2H,2NH) ,3.91(s,3H,OCH_3),1.25(s,6H, N-$(CH_3)_2$) The molecular formula was established as $C_{12}H_{16}N_6SO$.

3-Imino-5-dimethylamino-7-p-anisylimino-1,2,4,6–thiatriazepines (IIIg)
I.R(KBr)cm^{-1} γ max, 3393.2 (-N-H),3173.3 (Ar-H),2936 (C-H of CH_3),1624.3 (C=N),736.9 (C-S), MS(m/z) 260 (M+ -OCH_3 protonated.)5%.
The molecular formula was established as $C_{12}H_{16}N_6SO$.

3-Imino-5-dimethylamino-7-t-butyl imino-1,2,4,6 –thiatriazepines (IIIh)
I.R(KBr)cm^{-1} γ max 3393.2 (-N-H),3173.3(Ar-H), 2936(C-H of CH_3),1624.3 (C=N), ^{1}H NMR($CDCl_3$) δ H ppm 7.26 (s,1H,= NH),1.57 to1.62(s,9H,C-$(CH_3)_3$), 2.17 (s,2H,2NH), 1.25 (s,6H, N-$(CH_3)_2$).
The molecular formula was established as $C_9H_{18}N_6S$.

3-Imino-5-dimethylamino-7- m-chloro-phenyl imino-1,2,4,6 –thiatriazepines (IIIi)

I.R(KBr)cm^{-1} γ max 3372.0 (N-H),3173.3 (Ar-H),1686 (C=N),1593.4(Aromatic C=C),713.7(C-S).

The molecular formula was established as $C_{11}H_{13}N_6SCl$

Conclusion

The presented synthetic procedure is convenient and simple method for the synthesis of the various thiatriazepines. These may prove important intermediate if investigated thoroughly.

Acknowledgement:

The authors acknowledge the help of SAIF Chandigarh for providing the spectral data. MRU is thankful to Raisoni management for encouragement.

References

[1] D.T. Tayade, *Res.J.Chem Environ*. 2012 Dec ;16(4):108-10

[2] B.Beagley, S.F.Moss,R.G.Pritchard,D.R.Taylor, *Acta crystallography and Chemistry* .1981 Feb; 37 Part 2:486-89.

[3] S.F. Moss,D.R.Taylor,*J Chem Soc Perkin Trans1*.1982;1999-2005.

[4] Q.Lin, S.T.Mixon, J.Cioslowski,C.U.Pittman,*New J Of chem*.1995; 19:325-29.

[5] B.S.Furniss, A.J.Hannaford, P.W.G Smith and A.R.Tatchell " Vogel's text book of Practical Organic chemistry",5th edn,Longman,U.K.1989.