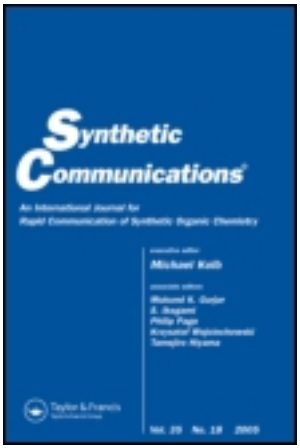

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REGIOSELECTIVE N-METHYLATION OF METHYLTHIO - SUBSTITUTED PYRIMIDINONES AND 1,2,4-TRIAZINONE WITH METHANOL OVER H-Y ZEOLITE.

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Abstract: Liquid - phase methylation of 2-methylthio -4- pyrimidone (4), 6-methyl -2-methylthio -4-pyrimidone (5) and 6-methyl-3-methylthio- 1,2,4- triazine-5- one (6) with MeOH over HY-Zeolite selectively gave 1-methyl- 2-methylthio- 4-pyrimidone (7),1,6-dimethyl- 2-methylthio- 4-pyrimidone (9) and 2,6-dimethyl- 3-methylthio- 1,2,4-triazine- 5-one (11), respectively.

Methyl iodide or dimethyl sulfate have been used as methylating agents for pyrimidines[1-3] and 1,2,4- triazines[4,5]. Alkylation of 2-thiouracil (1) and 6- methyl-2-thiouracil (2) with methyl iodide under basic conditions is known to lead

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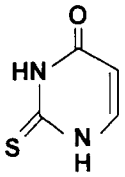

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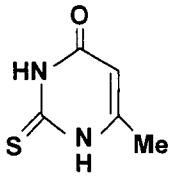

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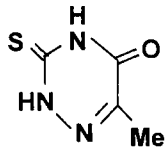

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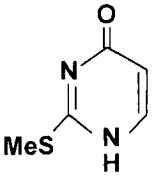

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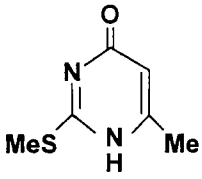

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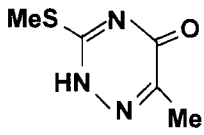

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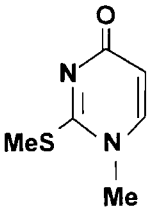

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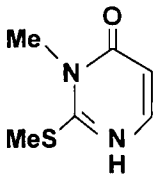

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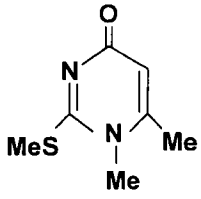

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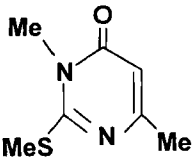

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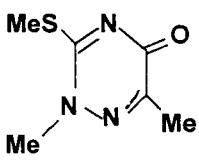

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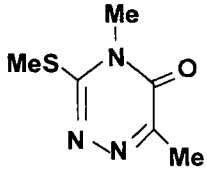

(12)

mainly to S-alkylation to give (4) and (5),respectively. Similary methylation of 6-methyl-3-thioxo- 1,2,4-triazine- 5 - one (3) gives the corresponding 3-methylthio derivative (6).

Methylation of (4) and (5) with methyl iodide under basic conditions gave a mixture of two N-methyl derivatives (7 and 8 and 9 and 10),respectively [2,3] Methylation of (6) under similar conditions afforded a mixture of (11) and (12) [6],although it has been claimed by Gut[4,5] and that methylation by methyl iodide should give the 2N-methyl derivative (11) preferentially.

For studying the tautomerisim in these pyrimidones and triazinones regioselective methylation of these compounds is desirable. The concept of heterocyclic tautomerisim is critical to the structure of DNA[6]. The correct hydrogen bonding between the base - pairs of the nucleotides and hence a specific tautomer is needed for the formation of the double helix[7,8].

In addition methyl halides and dimethyl sulfate , are highly toxic and corrosive,and often more than a stoichiometric amount of strong base such as $MeO^- Na^+$ or NaOH is required.To avoid these disadvantages the liquid phase regioselective N-methylation of (4),(5) and 6) using methanol as the methylating agent and H-Y zeolite as the catalyst was carried out.

Organic transformation catalyzed by zeolites is becoming important in the area of organic synthesis [10-15]. Recently highly efficient para-selective bromination of simple aromatic substrates by means of bromine and a reusable zeolite has been reported[13].

Here we wish to report that (4),(5) and (6) can be selectively converted into (7),(9) and (11), respectively , by using MeOH over H-Y zeolite. The Na form of Y-zeolite was

ion - exchanged with NH_4 Cl to obtain the NH_4 form which was converted into H-Y by heating at 673 K for 8h,then cooling to 423 K.A solution in MeOH of (4),(5) or (6) was fed into an autoclave reactor and catalyst was added. The temperature of the reactor was raised to 480 K and the pressure reached 24.4 bar.

Only one N-methylation occurred in every case. where is without catalyst no methylation occurred.H-Y zeolite showed much higher activity and selectivity than Na-Y zeolite.

This result showed that the selectivity and reactivity is not determined by the pore structure but by the Bronsted acid strength of the catalyst.A moderately acidic catalyst like H-Y favours the formation of the 1N-methylpyrimidines (7) and (9) and the 2N-methyl- 1,2,4-trazine derivative (11).

Experimental

Products were characterized by MP,IR,NMR and mass spectra and by direct comparison with authentic samples. Reactions were carried out in a Buchi laboratory - autoclave BEP 280/Type 17/3,0 dm3 fitted to work with bds 488.

General Procedure

The methylthio compounds (4),(5) and (6) (0.1 mol),MeOH(200 ml) and HY-zeolite (0.5g) were fed into a laboratory - autoclave , reaching 24.4 bar and 486.15 K in 45 min. The reaction vessel was kept in this condition for 1 hr. The solvent was

evaporated , water was added to the crude mixture and the product was extracted with $CHCl_3$. Chloroform was dried over $Na_2 SO_4$ and evaporated to dryness to give the N-methyl derivative as a single product,(7),(9) and (11), respectively.

7,(85%) as white needles , m.p.166-167 C (lit[3]-168-169 C); ^{1}HNMR,δ($CDCl_3$) 2.55 (3H,S,SCH_3),3.55(3H,S,NCH_3) , 6(1H,d,CH),7.25(1H,d,CH).

9,(90%),m.p.181-182 C(lit [16],180-181),^{1}HNMR δ($CDCl_3$)2.1(3H,S,CH_3),2.5(3H,S,SCH_3) ,3.45 (3H,S,NCH_3),6(1H,S,CH).

11,(93%) Crystallized from benzene/light petroleum(b.p.60-80) m.p.184-185 C (lit[4],187-188),^{1}HNMR δ($CDCl_3$).2.2(S,3H,CH_3),2.65(S,3H,SMe),3.8(S,3H,NCH_3).

References

1- Barrett,H.W. Goodman,I and Dittmer,K, J.Am.Chem.Soc,**1948**,70,1753.

2- Brown,J.D,Hoorger,E and Mason,F.J.Chem.Soc,**1955**,211.

3- Katritzky,A.R,Baykut,G,S;Racwal,Szafran,M, Caster,K.C and Eyler,J.J. Chem. Soc.Perkin Trans II **1989**,1499.

4- Gut,J and Prystas,M,Coll.Czech,Chem. Commun.,**1961**,26,986.

5- Ibid,**974**.

6- Heravi,M.M and Bakavoli,M,Sci.J.I.R.Iran **1992**,3(3,4),107.

7- Elyuero,J,Marzin,C,Katritzky,A.R and Lenda,P,The Tautomerism of eterocycles, Academic Press, London,**1976**.

8- Lehninger,A.L,short Course in Biochemistry Butter worth,New York.**1973**,Ch.21.

9- Katritzky.A.R,Chimia,1970,24, **134**.

10- For reviews see (i) Holderich.W.F. and Van Bekkum,H stud. surf. Sci. Catal.**1991**,58,631; (ii) Venuto.P, Microporouo Mater **1994**,2,297 ; (iii) Feast.S and Lercher. Y.A, Strd. Surf.Sci.Catal.**1996**,102,363.

11- Pavan,T,Ramesh,K. Reddy; and Reddy,R.S.J.Chem.Research(5), **1994**,394.

12- Ono.Y, Izawa.Y and Fu.Z.J.Chem.Soc,Chem,Commun, **1995**,9.

13- Smith.K and Bahzad.D,J.Chem.Soc ,Chem,Commun ,**1996**,467.

14- Kumar,P.Reddy,R.S.Singh,A.P and Pandey,B , Tetrahedron lett,**1992**,33,825.

15- Kumar,P,S.V.N.Rayu,Reddy,R.S and Pandey,B , Ibid,**1994**,35,1289.

16- Shugar,D and Fox,J.J . Bull.Soc.Chim,Belg. **1952**,61,293.

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