PHASE TRANSFER CATALYSED OXIDATIVE ARYLTHIOLATION OF 1,3,6-TRIMETHYLURACIL AND ITS 5-BROMO DERIVATIVE

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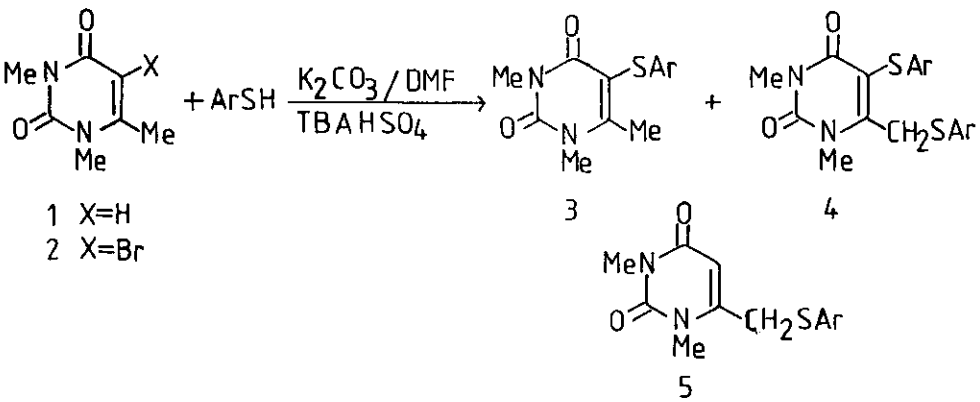
Abstract- Reaction of 1,3,6-trimethyluracil and its 5-bromo derivative with arylthiols under phase transfer catalytic conditions provides C-H substitution products, 5-arylthio-1,3,6-trimethyluracils and 5-arylthio-6-arylthiomethyl-1,3-dimethyluracils.

Uracils substituted with a good leaving group at C-5 or C-6 with mononucleophiles undergo a variety of nucleophilic substitution reactions.[1-6] But in the absence of such a substituent uracil derivatives react with mononucleophiles (viz. alcohol, thiol, amine etc.) in solution phase to form adducts which remain in equilibrium with reactants[1,7,8] and are not isolable. Now we have found that not only 5-bromo-1,3,6-trimethyluracil (2), but 1,3,6-trimethyluracil (1) also react with arylthiols under phase transfer catalytic conditions to provide mainly 5-arylthio-1,3,6-trimethyluracils (3) and 5-arylthio-6-arylthiomethyl-1,3-dimethyluracils (4).

Treatment of 1,3,6-trimethyluracil (1) with phenylthiol on stirring in dimethylformamide containing anhydrous potassium carbonate and tetrabutylammonium hydrogensulphate gave two compounds with 18% recovery of compound (1). The fast moving component, M^+ m/z 370, in its ^1H nmr[9] shows absence of signals for C(6)-CH_3 and C(5)-H protons of compound (1), but shows the presence of C(6)-CH_2S and 10 aromatic H signals.Its off



resonance proton decoupled ^{13}C nmr spectrum[9] shows two quartets due to $2xNCH_3$ and one triplet due to $-CH_2S$ in aliphatic region and twelve signals (six singlets due to 2xC=O, C=C and 2 Ar<u>C</u> and six doublets due ot Ar<u>C</u>H) in low-field region. These data corroborate the structure 1,3-dimethyl-5-phenylthio-6-phenylthiomethyluracil (4, Ar=C_6H_5). The slow moving component,M^+ m/z 262, in its ^1H nmr shows[10] three 3H singlets ($2xNCH_3$ and CH_3-6) along with 5 ArH singlet, but absence of C-5 H. Its off resonance proton decoupled ^{13}C nmr[10] shows three quartets (2x NCH_3, CH_3-6) in aliphatic region and five singlets (2xC=O, C=C and Ar<u>C</u>) and three doublets(3 Ar<u>C</u>H) in low-field region. These data assign the structure 5-phenylthio-1,3,6-trimethyluracil (3, Ar=C_6H_5) to this slow moving component. When the reaction was carried out in the absence of PTC, such C-H substitution reaction did not occur.

The reaction of 5-bromo-1,3,6-trimethyluracil (2) with phenylthiol under PTC conditions provided compounds (3) (Ar=C_6H_5) (38%) and (4) (Ar=C_6H_5) (30%). In this case traces of 1,3-dimethyl-6-phenylthiomethyluracil (5) were also isolated, whose structure was assigned from its ^1H nmr[11] only. Similar, treatment of 1 and 2 with 4-chlorophenylthiol, 2-aminophenylthiol

Table: Reactions of 1,3,6-Trimethyluracils (1) and (2) with Arylthiols.

ArSH	3			4			5		
Ar=	yield* %	M^+ m/z	mp °C	yield* %	M^+ m/z	mp °C	yield* %	M^+ m/z	mp °C
C_6H_5-	37(38)	262	98-99	4(30)	370	35	-(1)	-	-
4-ClC_6H_4-	35(38)	296/298 (1:1)	111-112	3(12)	426/428/430	oil	4(-)	296/298 (1:1)	123
2-$NH_2C_6H_4$-	30(28)	277	148-150	4(20)	388	205-210	-(3)	277	oil
2-C_5H_4N-	10(44)	263	133-137	2(12)	373	oil	-(4)	263	oil

*The yields given in paranthesis corespond to compound (2).

and pyridine-2-thiol gave the corresponding compounds (3) and (4) in moderate yields (see Table).

However, 1 did not react with alkylthiolate ions (benzyl-,propyl-) and 2 with alkylthiolate ions gave respective monoalkylthio derivatives (3) and 6-alkylthiomethyl-1,3-dimethyluracil (5), but corresponding bis(alkylthio) uracils (4) could not be isolated. 1,3-Dimethyluracil did not react with alkyl/arylthiolate ions.

Therefore compound (1) with arylthiolate ions undergoes C-5 H and CH_3-6 substitutions and compound (2) undergoes C-Br and CH_3-6 substitutions to give compounds (3) and (4)*. In literature substitutions of leaving groups present at C-5/C-6 of uracils by nucleophiles are well documented,[1-6] but such C-H substitutions at sp^2 C-5 and sp^3 -CH_3-6 are the first examples.

* The observations that 1 with phenylthiolate ion in the presence of *m*-dinitrobenzene gave 3, but in the presence of *N,N,N',N'*-tetramethyl-*p*-phenylenediamine decomposed, points towards an electron transfer mechanism, which warrants further investigations.

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9. Spectral data: M^+ m/z 370; ^1H nmr ($CDCl_3$): δ 3.34(s, 3H, NCH_3), 3.62(s, 3H, NCH_3), 4.42(s, 2H, CH_2), 7.10(s, 5H, ArH), 7.23-7.55(m, 5H, ArH); ^{13}C nmr($CDCl_3$): δ 28.95(q, N-3CH_3), 33.10(q, N-1CH_3), 35.75 (t, CH_2), 105.67(s, C-5), 127.07(d, ArCH), 128.38 (d, ArCH), 128.78(d, ArCH), 129.28(d, ArCH), 132.55(d, ArCH), 132.42(s, ArC), 135.87 (s, ArC), 151.46(s, C_2=O), 155.82(s, C-6), 160.67(s, C_4=O).
10. Spectral data: M^+ m/z 262; ^1H nmr ($CDCl_3$): δ 2.63(s, 3H, 6-CH_3), 3.36(s, 3H, NCH_3), 3.50(s, 3H, NCH_3), 7.15(s, 5H, ArH); ^{13}C nmr($CDCl_3$): δ 19.26(q, 6-CH_3), 28.99(q, N-3CH_3), 33.38(q, N-1CH_3), 104.03(s, C-5), 128.32(s, ArCH), 128.78(s, ArCH), 129.28(d, ArCH), 136.13(s, ArC), 151.49(s, C=O), 158.18(s, C-6),161.13(s, C_4=O).
11. ^1H Nmr($CDCl_3$): δ 3.28(s, 3H, NCH_3), 3.50(s, 3H, NCH_3), 3.77 (s, 3H, C_6-CH_2), 5.34(s, 1H, C_5-H), 7.33(s, 5H,ArH).

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