

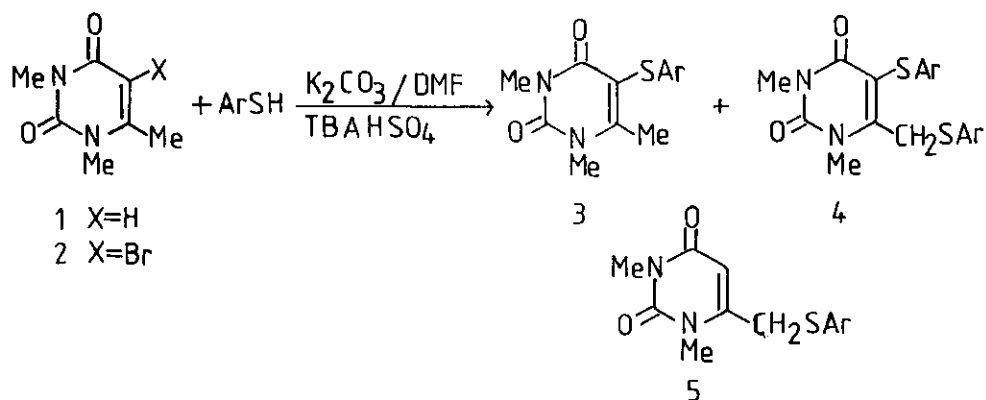
PHASE TRANSFER CATALYSED OXIDATIVE ARYLTHIOLATION OF
1,3,6-TRIMETHYLURACIL AND ITS 5-BROMO DERIVATIVE

Subodh Kumar^{*}, Swapandeep S.Chimni, and Deepika Cannoo
Department of Chemistry, Guru Nanak Dev University,
Amritsar -143 005, India

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 nmr⁹ shows absence of signals for C(6)-CH₃ and C(5)-H protons of compound (1), but shows the presence of C(6)-CH₂S and 10 aromatic H signals. Its off



resonance proton decoupled ^{13}C nmr spectrum⁹ shows two quartets due to $2x\text{NCH}_3$ and one triplet due to $-\text{CH}_2\text{S}$ in aliphatic region and twelve signals (six singlets due to $2x\text{C}=\text{O}$, $\text{C}=\text{C}$ and 2ArC and six doublets due to ArCH) in low-field region. These data corroborate the structure 1,3-dimethyl-5-phenylthio-6-phenylthiomethyluracil (4, $\text{Ar}=\text{C}_6\text{H}_5$). The slow moving component, M^+ m/z 262, in its ^1H nmr shows¹⁰ three 3H singlets ($2x\text{NCH}_3$ and CH_3-6) along with 5 ArH singlet, but absence of C-5 H. Its off resonance proton decoupled ^{13}C nmr¹⁰ shows three quartets ($2x\text{NCH}_3$, CH_3-6) in aliphatic region and five singlets ($2x\text{C}=\text{O}$, $\text{C}=\text{C}$ and ArC) and three doublets (3 ArCH) in low-field region. These data assign the structure 5-phenylthio-1,3,6-trimethyluracil (3, $\text{Ar}=\text{C}_6\text{H}_5$) 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) ($\text{Ar}=\text{C}_6\text{H}_5$) (38%) and (4) ($\text{Ar}=\text{C}_6\text{H}_5$) (30%). In this case traces of 1,3-dimethyl-6-phenylthiomethyluracil (5) were also isolated, whose structure was assigned from its ^1H nmr¹¹ 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		
	yield*	M ⁺	mp	yield*	M ⁺	mp	yield*	M ⁺	mp
Ar=	%	m/z	°C	%	m/z	°C	%	m/z	°C
C ₆ H ₅ -	37(38)	262	98-99	4(30)	370	35	-(1)	-	-
4-ClC ₆ H ₄ -	35(38)	296/ 298	111-112	3(12)	426/ 428/ 430	oil	4(-)	296/ 298	123
		(1:1)						(1:1)	
2-NH ₂ C ₆ H ₄ -	30(28)	277	148-150	4(20)	388	205- 210	-(3)	277	oil
2-C ₅ H ₄ N-	10(44)	263	133-137	2(12)	373	oil	-(4)	263	oil

*The yields given in paranthesis correspond 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 CH₃-6 substitutions and compound (2) undergoes C-Br and CH₃-6 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 sp² C-5 and sp³ -CH₃-6 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.

ACKNOWLEDGEMENTS

We thank CSIR (India) and INSA for financial assistnace ; UGC for COSIST and SAP programmes and CDRI, Lucknow, and TIET, Patiala for mass and elemental studies.

REFERENCES AND NOTES

1. E. G. Sander, "Bioorganic Chemistry" ed. by E. E. Van Tamelen, Academic Press, 1977, 2, 273-297 and references therein.
2. T. K. Bradshaw and D. W. Hutchinson, *Chem. Soc. Rev.*, 1977, 6, 43.
3. S. Kumar and S. S. Chimni, *Heterocycles*, 1988, 27, 2523.
4. S. Kumar and S. S. Chimni, *Ind. J. Chem.*, 1989, 28B, 1079.
5. K. Hirota, Y. Yamada, Y. Kitade and S. Senda, *J. Chem. Soc. Perkin Trans.1*, 1981, 2943.
6. B. C. Pal, *J. Am. Chem. Soc.*, 1978, 100, 5170.
7. I. H. Pitman, M. J. Cho, and G. S. Rork, *J. Am. Chem. Soc.*, 1974, 96, 1840.
8. R. Shapiro, R. E. Servis, and M. Welcher, *J. Am. Chem. Soc.*, 1970, 92, 422.
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-3 CH_3), 33.10(q, N-1 CH_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-3 CH_3), 33.38(q, N-1 CH_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).

Received, 2nd September, 1991