

Heterocyclic Transformations Part 4: ^{1a} A Facile Transformation of 3-Alkyl-6-methyl-1,3-oxazine-2,4(3H)-diones to 6-Substituted 5-acetyluracils and 6-Thioxo-1,3,5-triazine-2,4(1H,3H,5H)-diones

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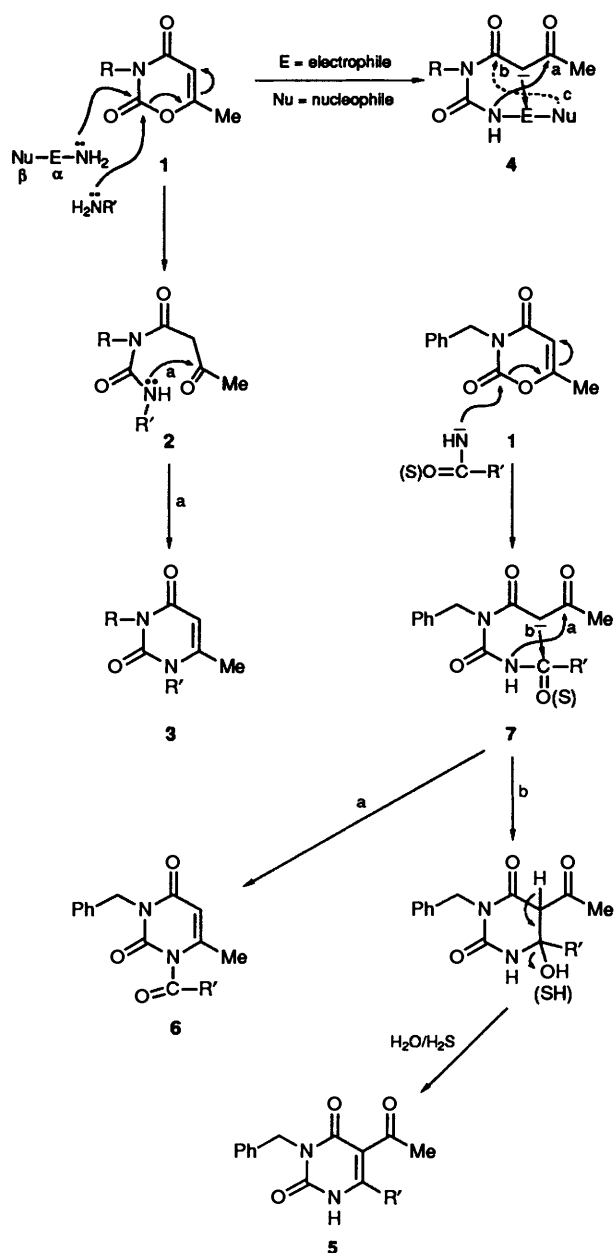
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3-Benzyl-6-methyl-1,3-oxazine-2,4(3H)-dione **1** (R = CH₂Ph) reacts under phase-transfer catalytic conditions with amides and thioamides to give 6-substituted 5-acetyluracils and with malonamide to give a bicyclic pyridopyrimidine system. Similar reactions of **1** with thioureas provide 6-thioxo-1,3,5-triazine-2,4(1H,3H,5H)-diones, but with ureas, the substituents influence the mode of the reaction and the nature of the products. The synthetic scope and utility of these reactions has been examined.

6-Methyl-1,3-oxazine-2,4(3H)-dione **1**, a versatile intermediate, reacts chemoselectively with a variety of nucleophiles¹ in synthetically useful reactions. Alkylamines react at C-2 of **1** to form intermediates **2** which cyclodehydrate (path a) to provide a regioselective synthesis of 1-substituted 6-methyluracils **3**.^{1b} We predicted that if the amine nitrogen carried a substituent with appropriately placed functionality, the intermediate **4**, could undergo alternative cyclizations, regioselectively directed, to provide new synthetic strategies. Here we report that 6-methyl-1,3-oxazine-2,4(3H)-diones **1** react with amides, thioamides, diamides, ureas and thioureas under phase transfer catalytic conditions to give a facile and selective synthesis of a variety of heterocycles.

Results and Discussion

3-Benzyl-6-methyl-1,3-oxazine-2,4(3H)-dione **1** (R = CH₂Ph) with formamide under phase transfer catalytic conditions (DMF-K₂CO₃-tetrabutylammonium hydrogen sulfate) † at 40–50 °C, gave a compound (m.p. 135 °C, M⁺ 244, mol. formula C₁₃H₁₂N₂O₃) the properties of which were consonant with either of the isomeric structures, 5-acetyl-3-benzyluracil **5a** and 3-benzyl-1-formyl-6-methyluracil **6** (R' = H). In its ¹H NMR spectrum, the appearance of one downfield 3 H singlet at δ 2.55 (COCH₃) as compared with a 6-CH₃ signal at δ 2.30 in 6-methyluracil² and the absence of a signal for 5-H (δ 5.7)² of the latter favoured assignment of structure **5a** for this compound. Its ¹³C NMR (APT)³ showed six negative signals (five quaternary- ArC, C-5, 3 × C=O and one methylene) and five positive signals (CH₃, 3 × ArCH, C-6) which further corroborated the structure **5a**. Similarly, **1** (R = CH₂Ph) reacted with acetamide, butanamide, benzamide, *o*-, *m*-, *p*-chlorobenzamide and urethane ‡ to give the respective 5-acetyluracils **5b–h**. It was observed that aliphatic amides formed **5** in better yields than aromatic amides. In case of *o*-chlorobenzamide, the *ortho* substituent adversely affected the yield of product. In a reaction of **1** (R = CH₂Ph) with a heteroaromatic amide-nicotinamide; 3-benzyl-6-methyluracil **3** (R = CH₂Ph, R' = H) was formed along with 5-acetyl-3-benzyl-6-(3-pyridyl)uracil **5i**. 6-Carba-



Scheme 1 a, R' = H; b, R' = Me; c, R' = Pr; d, R' = Ph; e, R' = *o*-ClC₆H₄; f, R' = *m*-ClC₆H₄; g, R' = *p*-ClC₆H₄; h, R' = OEt; i, R' = 3-C₅H₄N

† **1** (R = CH₂Ph) failed to react with formamide when heated (150–160 °C) or in DMF under reflux; with formamide in DMF containing NaH at ambient temperature it mainly decomposed and in MeCN in the presence of Et₃N, it was unchanged; under PTC conditions (MeCN-K₂CO₃-tetrabutylammonium hydrogen sulfate), product **5** was formed in poor yields.

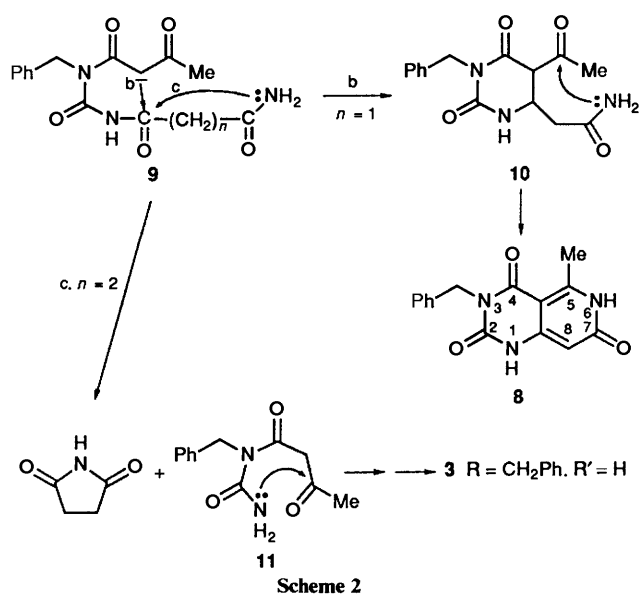
‡ Dehydration has been preferred over the elimination of ethanol from **5** (R = OEt).

moyl-1,3-dimethyluracil with **1** ($R = \text{CH}_2\text{Ph}$) gave only **3** ($R = \text{CH}_2\text{Ph}$, $R' = \text{H}$) (76%). Compound **1** ($R = \text{H}$) due to ease in generation of the anion at N-3 under these PTC conditions, failed to react with amides. Compound **1** ($R = \text{CH}_2\text{Ph}$) failed to react with an unsaturated amide (acrylamide), an *N*-alkylamide (*N*-methylacetamide) and stearamide.

The thioamides, thioacetamide, thiobenzamide and *o*-chlorothiobenzamide with **1** ($R = \text{CH}_2\text{Ph}$) under the above PTC conditions gave **5b**, **5d** and **5e** respectively only in marginally better yields. The reactions of **1** ($R = \text{CH}_2\text{Ph}$) with thioamides in NaH/DMF formed **5** in lower yields (<10%) and **1** ($R = \text{CH}_2\text{Ph}$) decomposed.

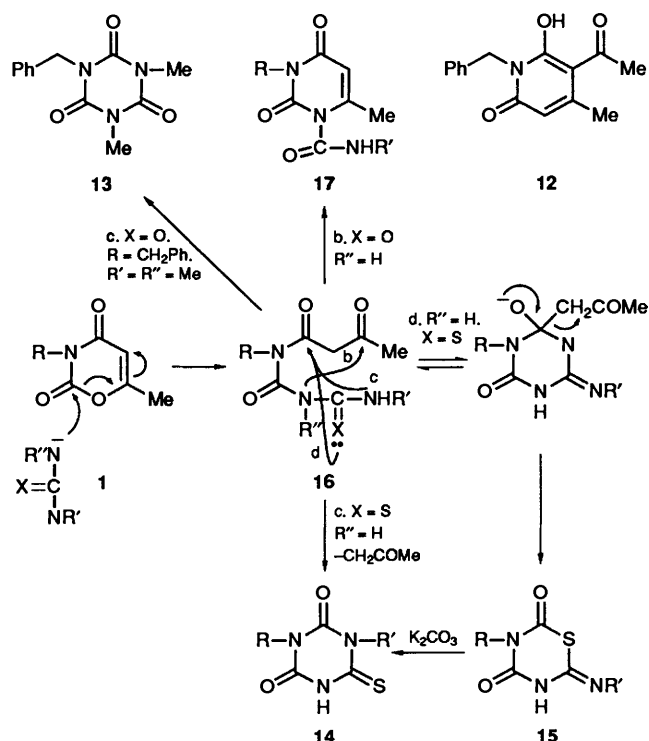
With malonamide under above PTC conditions **1** ($R = \text{CH}_2\text{Ph}$) gave a compound (90%) (m.p. 280 °C, M^+ 283, mol. formula $\text{C}_{15}\text{H}_{13}\text{N}_3\text{O}_3$) the ^1H NMR spectrum of which showed the presence of Me, CH_2Ph and olefinic-H (δ 6.45) and lacked any additional CH_2 signal for CH_2CONH_2 of analogues of structures **5** and **3**. Its ^{13}C NMR (APT)³ showed five positive signals (Me, =CH and $3 \times \text{ArCH}$) and eight negative signals (NCH_2 , ArC, C-4a, C-5, C-8a, $3 \times \text{C}=\text{O}$). From these data, it was assigned the structure, 3-benzyl-5-methylpyrido[4,3-*d*]pyrimidine-2,4,7(1*H*,3*H*,6*H*)-trione **8**. Compound **1** ($R = \text{CH}_2\text{Ph}$) with succindiamide gave **3** ($R = \text{CH}_2\text{Ph}$, $R' = \text{H}$) (60%) and succinimide (25%), m.p. 122–124 °C (lit.,⁴ 123–125 °C), but it did not react with glutaramide.

The formation of **5**, could involve initial attack of amide/thioamide nitrogen* at C-2 of **1** ($R = \text{CH}_2\text{Ph}$) to give the intermediate **7**, which followed path b for cyclization (Scheme 1) and gave 6-substituted 5-acetyluracil derivatives **5**. Formation of 3-benzyl-6-methyluracil **3** ($R = \text{CH}_2\text{Ph}$, $R' = \text{H}$) (m.p. 193–195 °C; lit.⁶ m.p. 194–198 °C) in the reaction of nicotinamide could be ascribed to the competitive formation of 3-benzyl-6-methyl-1-(3-pyridylcarbonyl)uracil **6** ($R = 3\text{-py}$) through path a (Scheme 1) and ease of its subsequent hydrolysis to nicotinic acid (m.p. 235–237 °C; lit.,⁷ m.p. 236–239 °C), which was isolated. In the reaction of **1** ($R = \text{CH}_2\text{Ph}$) with malonamide, initially formed intermediate **9** followed path b to give **10** which further cyclodehydrated to **8**. In the reaction of succindiamide, formation of five-membered ring (path c) **9** dominated over six-membered ring formation (path b) and succinimide was eliminated to give **11**, which cyclodehydrated to **3** (Scheme 2). This mode was further supported by failure of succindiamide to form succinimide under the same PTC conditions.



Urea and **1** ($R = \text{CH}_2\text{Ph}$) under solid-liquid PTC conditions (DMF- K_2CO_3 -tetrabutylammonium hydrogen sulfate) at 40–50 °C gave 3-benzyl-6-methyluracil **3** ($R = \text{CH}_2\text{Ph}$, $R' = \text{H}$) in 44% yield. 1-Methylurea and **1** ($R = \text{CH}_2\text{Ph}$) gave **3** ($R = \text{CH}_2\text{Ph}$, $R' = \text{CH}_3$) (25%) along with another compound (<1%) (m.p. 101–102 °C, M^+ 257), which from its ^1H NMR spectrum was assigned the structure, 3-acetyl-1-benzyl-2-hydroxy-4-methyl-6(1*H*)-pyridone **12**. 1,3-Dimethylurea with **1** ($R = \text{CH}_2\text{Ph}$) under PTC conditions gave a multitude of products (TLC) from which one product (4%), m.p. 137–139 °C (M^+ 247, mol. formula $\text{C}_{12}\text{H}_{13}\text{N}_3\text{O}_3$ from elemental analysis) could be isolated. From its spectral data, this compound could be assigned the structure, 3-benzyl-1,5-dimethyl-1,3,5-triazine-2,4,6(1*H*,3*H*,5*H*)-trione **13**. 1-Phenylurea did not react with **1** ($R = \text{CH}_2\text{Ph}$) probably because of steric constraints.

Thiourea with **1** ($R = \text{CH}_2\text{Ph}$) gave a compound (55%) (m.p. 224–226 °C, M^+ 235, mol. formula $\text{C}_{10}\text{H}_9\text{N}_3\text{O}_2\text{S}$) the ^1H NMR spectrum of which exhibited two singlets at δ 4.95 (2 H) and 7.10 (5 H) due to NCH_2Ph group and a 2 H exchangeable broad signal at δ 12.50. These data suggested either of the isomeric structures, 3-benzyl-6-thioxo-1,3,5-triazine-2,4(1*H*,3*H*,5*H*)-dione **14a** ($R = \text{CH}_2\text{Ph}$, $R' = \text{H}$) and 3-benzyl-6-imino-1,3,5-thiadiazine-2,4-dione **15** ($R = \text{CH}_2\text{Ph}$, $R = \text{H}$) for this compound. Its ^{13}C NMR spectrum showed the presence of only three sp^2 quaternary carbons [δ 134.69 (s, ArC), 146.23 (s, C=O) and 175.34 (s, C=S)] and corroborated the symmetrical structure **14a** in which the two carbonyl carbon signals could overlap. Similarly, **1** ($R = \text{CH}_2\text{Ph}$) with 1-methyl-2-thiourea and 1-ethylthiourea gave 3-benzyl-5-methyl-6-thioxo-1,3,5-triazine-2,4(1*H*,3*H*,5*H*)-dione **14b** (52%, M^+ 249, m.p. 191–192 °C) and 3-benzyl-5-ethyl-6-thioxo-1,3,5-triazine-2,4(1*H*,3*H*,5*H*)-dione **14c** (50%, M^+ 263, m.p. 190–192 °C), respectively. Because of the presence of different substituents at N-1, N-3 and N-5 positions, compounds **14b** and **14c** became unsymmetrical and in their ^{13}C NMR spectra exhibited four quaternary sp^2 hybridised carbons [**14b**: δ 134.55



Scheme 3 a, $R = \text{CH}_2\text{Ph}$, $R' = \text{H}$; b, $R = \text{CH}_2\text{Ph}$, $R' = \text{Me}$; c, $R = \text{CH}_2\text{Ph}$, $R' = \text{Et}$; d, $R = \text{Me}$, $R' = \text{H}$; e, $R = \text{Me}$, $R' = \text{Me}$; f, $R = (\text{CH}_2)_3\text{CN}$, $R' = \text{H}$; g, $R = (\text{CH}_2)_3\text{CN}$, $R' = \text{Me}$; h, $R = (\text{CH}_2)_3\text{CO}_2\text{Et}$, $R' = \text{H}$; i, $R = (\text{CH}_2)_3\text{CO}_2\text{Et}$, $R' = \text{Me}$

* Under PTC conditions anion could be generated.⁵

Table 1 Physical and spectral data of compounds 5a-i and 8

Compd. ^a	M.p. (°C) [solvent] ^b	Yield (%)	Reaction temp. (I/°C) time [t/h]	δ H ^c	M ⁺ (m/z) (R.I.)	ν_{\max} (KBr)/ cm ⁻¹	$\lambda_{\max}(\epsilon \times 10^3)/\text{nm}$ (EtOH)
5a	135 [EtOH]	73	40–50 [3]	(TFA) 2.55 (3 H, s, COCH ₃), 5.0 (2 H, s, NCH ₂), 7.10 (5 H, s, ArH), 8.20 (1 H, s, 6-H).	244 (1)	1675, 1610	306.1 (5.76), 249.7 (4.1), 227.7 (4.3), 205.1 (6.3)
5b	157–159 [CHCl ₃]	51 (57) ^c	40–50 [3]	(CDCl ₃) 2.20 (3 H, s, 6-CH ₃), 2.40 (3 H, s, COCH ₃), 4.90 (2 H, s, NCH ₂), 6.80–7.10 (5 H, m, ArH), 10.10 (1 H, br, NH, exchanges with D ₂ O)	258 (97)	1705, 1650	276.5 (11.4), 230.3 (11.2), 208.1 (13.1)
5c	150–152 [CHCl ₃]	48	50–60 [10]	(CDCl ₃) 1.0 (3 H, t, J 6, CH ₃), 1.33–1.90 (2 H, m, CH ₂ CH ₃), 2.40–2.80 (5 H, m, COCH ₃ , 6-CH ₂), 5.0 (2 H, s, NCH ₂), 6.90–7.35 (5 H, m, ArH), 10.50 (1 H, br, NH, exchanges with D ₂ O)	286 (53)	1700, 1680, 1640	276.1 (12.1), 231.3 (11.9), 207.9 (14.2)
5d	210–212 [MeOH]	38 (45) ^c	50–60 [10]	(CDCl ₃ + TFA) 2.15 (3 H, s, COCH ₃), 5.05 (2 H, s, NCH ₂), 7.0–7.25 (10 H, m, ArH)	320 (98)	1685, 1620	282.9 (9.6), 234.1 (15.2), 209.5 (17.3)
5e	170–172 [MeOH]	22 (26) ^c	50–60 [6.5]	(CDCl ₃) 2.40 (3 H, s, COCH ₃), 5.0 (2 H, s, NCH ₂), 7.10–7.40 (9 H, m, ArH), 10.0 (1 H, br, NH, exchanges with D ₂ O)	354 (70)	1690, 1660, 1640	287.1 (13.6), 253.3 (10.4), 214.1 (21.3)
5f	195–197 [MeOH]	31	50–60 [4.5]	(CDCl ₃ + TFA) 2.35 (3 H, s, COCH ₃), 5.10 (2 H, s, NCH ₂), 7.10–7.55 (9 H, m, ArH)	354 (100)	1690, 1630	284.7 (11.1), 230.0 (18.0), 216.1 (23.9)
5g	220–222 [MeOH]	35	50–60 [4.5]	(CDCl ₃ + TFA) 2.35 (3 H, s, COCH ₃), 5.15 (2 H, s, NCH ₂), 7.10–7.50 (9 H, m, ArH)	354 (100)	1690, 1630	285.1 (12.4), 236.9 (20.8), 211.3 (20.7)
5h	164–165 [CHCl ₃]	45	60–70 [8]	(CDCl ₃) 1.30 (3 H, t, J 7, CH ₃), 2.25 (3 H, s, COCH ₃), 4.20 (2 H, q, J 7, OCH ₂ -CH ₃), 4.90 (2 H, s, NCH ₂), 6.85–7.20 (5 H, m, ArH), 10.45 (1 H, br, NH, exchanges with D ₂ O)	288 (75)	1705, 1600	267.7 (10.6), 210.7 (14.9)
5i ^d	188–191 [CHCl ₃]	44	70–80 [8]	(CDCl ₃ [² H ₆]-DMSO), 2.45 (3 H, s, COCH ₃), 5.0 (2 H, s, NCH ₂), 7.0–7.55 (9 H, m, ArH), 8.50 (1 H, br, NH, exchanges with D ₂ O)	321 (100)	1695, 1660	267.7 (10.6), 222.7 (16.2), 210.7 (19.4)
8	280 [MeOH]	90	40–50 [3.5]	(CDCl ₃ + TFA) 2.95 (3 H, s, CH ₃), 5.10 (2 H, s, NCH ₂), 6.45 (1 H, s, 8-H), 7.0–7.30 (5 H, m, ArH)	283 (100)	1680	269.3, 244.1, 209.5

^a Elemental analyses: 5a (Found: C, 64.7; H, 4.75; N, 11.2. C₁₃H₁₂N₂O₃ requires C, 64.93; H, 4.91; N, 11.47%); 5b (Found: C, 64.8; H, 5.35; N, 10.6. C₁₄H₁₄N₂O₃ requires C, 65.11; H, 5.42; N, 10.85%); 5c (Found: C, 66.85; H, 6.25; N, 9.5. C₁₆H₁₈N₂O₃ requires C, 67.13; H, 6.29; N, 9.79%); 5d (Found: C, 70.86; H, 4.92; N, 8.52. C₁₉H₁₆N₂O₃ requires C, 71.25; H, 5.00; N, 8.75%); 5e (Found: C, 64.3; H, 4.25; N, 7.9. C₁₉H₁₅ClN₂O₃ requires C, 64.31; H, 4.21; N, 7.89%); 5f (Found: C, 64.75; H, 4.25; N, 7.4. C₁₉H₁₅ClN₂O₃ requires C, 64.31; H, 4.21; N, 7.89%); 5g (Found: C, 64.4; H, 4.3; N, 7.8. C₁₉H₁₅ClN₂O₃ requires C, 64.31; H, 4.21; N, 7.89%); 5h (Found: C, 62.3; H, 5.45; N, 9.5. C₁₅H₁₆N₂O₄ requires C, 62.50; H, 5.55; N, 9.72%); 8 (Found: C, 63.8; H, 4.4; N, 14.5. C₁₅H₁₃N₃O₃ requires C, 63.60; H, 4.59; N, 14.84%). ^b Solvent of the crystallization. ^c Yields in the reactions of thioamides. ^d Another product isolated—3-benzyl-6-methyluracil 3 (14%), m.p. 193–195 °C (CHCl₃); *m/z* 216 (100); δ_{H} (CDCl₃ + [²H₆]-DMSO), 2.0 (3 H, s, CH₃), 4.85 (2 H, s, NCH₂), 5.35 (1 H, s, 5-H), 6.75–7.20 (5 H, m, ArH), 10.20 (1 H, br, NH, exchanges with D₂O); $\nu_{\max}/\text{cm}^{-1}$ 1740 (C=O) and 1630 (C=O); $\lambda_{\max}(\text{MeOH})/\text{nm}$ 260.5 (9.9 × 10³) of 209.7 (14.1 × 10³). ^e 5a: δ_{C} (CDCl₃ + [²H₆]-DMSO)(APT) 29.98 (+ve, CH₃), 42.35 (-ve, CH₂), 107.22 (-ve, ArC), 126.20 (+ve, ArCH), 127.43 (+ve, ArCH), 127.82 (+ve, ArCH), 139.37 (-ve, C-5), 160.03 (-ve, C=O), 162.25 (+ve, 6-H), 163.92 (-ve, C=O), 193.78 (-ve, C=O); 5i: δ_{C} (CDCl₃ + DMSO) 31.15 (q, CH₃), 42.96 (t, CH₂), 112.76 (s, ArC), 122.31 (d, PyC₅), 126.88 (d, ArCH), 127.65 (d, ArCH), 128.07 (d, ArCH), 135.31 (d, PyC₄), 135.45 (s, C=C), 147.52 (d, PyC₆), 150.22 (s, PyC₃), 150.48 (d, PyC₂), 152.12 (s, C=O), 154.72 (s, C=C), 160.79 (s, C=O), 196.74 (s, C=O); 5h: δ_{C} (CDCl₃) 14.19 (q, OCH₂CH₃), 18.11 (q, COCH₃), 43.97 (t, NCH₂), 61.54 (t, OCH₂), 106.43 (s, ArC), 127.78 (d, ArCH), 128.39 (s, ArCH), 128.92 (d, ArCH), 136.17 (s, C-5), 152.10, 153.70 (s, C=O, C-6), 160.08 (s, C=O), 164.31 (s, C=O); δ_{C} (INEPT): 14.20 (+ve, CH₃), 18.14 (+ve, COCH₃), 43.97 (-ve, OCH₂), 61.57 (-ve, NCH₂), 127.78 (+ve, ArCH), 128.39 (+ve, ArCH) and 128.92 (+ve, ArCH).

(ArC), 145.32 (C=O), 147.35 (C=O), 176.32 (C=S); 14c: δ 134.55 (ArC), 145.12 (C=O), 146.57 (C=O), 175.32 (C=S)] with two very closely placed carbonyl signals. Compound 1 (R = CH₂Ph) with 1,3-dimethyl-2-thiourea gave a multitude of products (TLC) from which only compound 12 could be isolated in < 1% yield. 1-Phenylthiourea failed to react with 1 (R = CH₂Ph) probably because of steric constraints.

To investigate the effect of substituents of 1, in their reactions with thioureas, 3-substituted-1,3-oxazine-2,4(3H)-diones 1 [R = Me, (CH₂)₃CN, (CH₂)₃CO₂Et] were obtained from 6-methyl-1,3-oxazine-2,4(3H)-dione and appropriate halides. Compound 1 [R = Me, (CH₂)₃CN, (CH₂)₃CO₂Et] with thiourea and 1-methylthiourea gave corresponding 6-thioxo-1,3,5-triazine-2,4(1H,3H,5H)-dione 14d–i in 42–57% yields.

Thus, contrary to the effect of substituents in thioureas in their reactions with 1, the N-3 substituents in 1 had no adverse effect in these reactions.

Initially, in the reactions of ureas and thioureas with *N*-alkyl-6-methyl-1,3-oxazine-2,4(3H)-diones 1, the NH₂ group of ureas/thioureas attacks 1 at C-2 to give the intermediate 16 which could follow three pathways b, c, d for cyclization (Scheme 3). In reactions of urea and 1-methylurea, 16 mainly cyclized through path b to give 17 (R = CH₂Ph) which then lost isocyanate to form 3-benzyl-6-methyluracil 3. The isocyanates were trapped in ammonia solution and their respective ureas were isolated. In the reaction of 1,3-dimethylurea where cyclization route b in 16 was hindered, it followed path c to form 3-benzyl-1,3,5-triazine-2,4,6(1H,3H,5H)-trione 13. In the

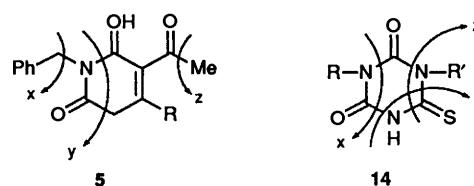
Table 2 Physical and spectral data of compounds **13** and **14a-i**

Compd. ^a	M.p. (°C) [solvent] ^b	Yield (%)	Reaction temp. (I/°C) time [t/h]	δ H ^c	M ⁺ (m/z) (R.I.)	ν_{\max} (KBr)/ cm ⁻¹	$\lambda_{\max}(\epsilon \times 10^3)/\text{nm}$ (MeOH)
13	137–139 [CHCl ₃]	4	40–50 [8]	(CDCl ₃) 3.15 (6 H, s, 2 × NCH ₃), 4.80 (2 H, s, NCH ₂), 6.85–7.15 (5 H, m, ArH)	247 (100)	1700, 1675	208.7 (10.3)
14a	224–226 [MeOH]	55	40–50 [2.5]	(CDCl ₃ + [2H ₆]-DMSO) 4.95 (2 H, s, NCH ₂), 7.10 (5 H, s, ArH), 12.50 (2 H, br, 2 × NH, exchanges with D ₂ O)	235 (79)	1740, 1655	269.9 (27.3), 207 (12.6)
14b	191–192 [MeOH]	52	50–60 [5]	(CDCl ₃ + [2H ₆]-DMSO) 3.50 (3 H, s, NCH ₃), 4.85 (2 H, s, NCH ₂), 7.0–7.35 (5 H, m, ArH), 12.65 (1 H, br, NH, exchanges with D ₂ O)	249 (92)	1740, 1660	267.9 (25.8), 208.3 (12.5)
14c	190–192 [MeOH]	52	50–60 [5]	(CDCl ₃ + TFA) 1.34 (3 H, t, CH ₃), 4.40 (2 H, q, CH ₂), 5.12 (2 H, s, NCH ₂), 7.37–7.41 (5 H, m, ArH)	263 (95)	1760, 1900	270.7 (20.4), 207.7 (9.7)
14d	252 [MeOH]	57	70–80 [5]	(CDCl ₃ + TFA) 3.40 (3 H, s, NCH ₃)	159 (34)	1750, 1675	268.9 (21.4), 204.9 (5.7)
14e	209–210 [MeOH]	55	70–80 [6]	(CDCl ₃ + TFA) 3.35 (3 H, s, NCH ₃), 3.70 (3 H, s, NCH ₃)	173 (100)	1740, 1685	267.3 (17.1), 206.1 (5.2)
14f	209 [MeOH]	49	70–80 [8]	(CDCl ₃ + TFA), 2.10–2.70 (4 H, 2 × CH ₂), 4.25 (2 H, t, J 7, NCH ₂)	212 (25)	2250, 1745, 1700	270.3 (20.3), 206.9 (6.95)
14g	169 [MeOH]	48	70–80 [8]	(CDCl ₃ + TFA) 2.0–2.80 (4 H, m, 2 × CH ₂), 3.80 (3 H, s, NCH ₃), 4.25 (2 H, t, J 7, NCH ₂)	226 (86)	2240, 1735, 1680	167.5 (22.2), 228.5 (3.4)
14h	89–90 [MeOH]	42	70–80 [8]	(CDCl ₃ + TFA), 1.35 (3 H, t, J 7, OCH ₂ CH ₃), 1.90–2.70 (4 H, m, 2 × CH ₂), 3.90–4.50 (4 H, m, NCH ₂ and OCH ₂)	259 (56)	1715, 1680	270.1 (12.6)
14i	89–90 [CHCl ₃]	42	70–80 [7]	(CDCl ₃) 1.30 (3 H, t, J 7, OCH ₂ CH ₃), 1.80–2.50 (4 H, m, 2 × CH ₂), 3.60 (3 H, s, NCH ₃), 3.80–4.30 (4 H, m, NCH ₂ and OCH ₂), 10.0 (1 H, br, NH, exchanges with D ₂ O)	273 (63)	1730, 1670	267.5 (20.8), 228.9 (3.0)

^a Elemental analyses: **13** (Found: C, 58.1; H, 5.3. C₁₂H₁₃N₃O₃ requires C, 58.29; H, 5.26%); **14a** (Found: C, 51.2; H, 4.0; N, 17.45. C₁₀H₉N₃O₂S requires C, 51.06; H, 3.82; N, 17.87%); **14b** (Found: C, 53.2; H, 4.35; N, 16.4. C₁₁H₁₁N₃O₂S requires C, 53.01; H, 4.41; N, 16.86%); **14d** (Found: C, 30.1; H, 3.05; N, 26.1. C₄H₅N₃O₂S requires C, 30.18; H, 3.14; N, 26.41%); **14e** (Found: C, 34.1; H, 3.9. C₅H₇N₃O₂S requires C, 34.68; H, 4.04%); **14f** (Found: C, 39.4; H, 3.45; N, 26.15. C₇H₈N₄O₂S requires C, 39.62; H, 3.77; N, 26.41%); **14g** (Found: C, 42.2; H, 4.45. C₈H₁₀N₄O₂S requires C, 42.47; H, 4.42%); **14i** (Found: C, 43.6; H, 5.3; N, 15.1. C₁₀H₁₁N₃O₄S requires C, 43.95; H, 5.49; N, 15.38%); ^b Solvent of crystallization. ^c **14a**: δ_{C} (CDCl₃ + DMF) 42.17 (t, NCH₂) 125.71, 126.23, 126.57 (d, ArCH), 134.69 (s, ArCH), 146.23 (s, C=O), 175–134 (C=S); δ_{C} (INEPT)(CDCl₃ + DMF) 42.17 (–ve, CH₂) 125.71, 126.23, 126.57 (+ve, ArCH); **14b**: δ_{C} (CDCl₃ + DMF) 33.18 (q, CH₃), 44.0 (t, CH₂), 126.50, 127.09, 127.32 (d, ArCH), 134.63 (s, ArC), 145.32 (s, C=O), 147.35 (s, C=O), 176.05 (s, C=S); δ_{C} (INEPT)(CDCl₃ + DMF) 33.18 (+ve, CH₃), 44.0 (–ve, CH₂), 126.50, 127.09, 127.32 (+ve, ArCH); **14c**: δ_{C} (CDCl₃ + DMF) 9.86 (q, CH₃), 41.0 (t, CH₂), 43.35 (t, CH₂), 125.85, 126.49, 126.62 (d, ArCH), 134.55 (s, ArC), 145.12 (s, C=O), 146.57 (s, C=O), 175.32 (s, C=S); δ_{C} (INEPT)(CDCl₃ + DMF) 9.83 (+ve, CH₃), 40.99 (–ve, CH₂), 43.37 (–ve, CH₂), 125.84, 126.40, 126.62 (+ve, ArCH); **14g**: δ_{C} (dioxane + CDCl₃) 17.40 (CH₂), 24.06 (CH₂), 34.78 (CH₃), 41.35 (CH₂), 119.31 (C=N), 146.80 (C=O), 148.32 (C=O), 176.31 (C=O), δ_{C} (INEPT)(dioxane + CDCl₃): 14.70 (–ve, CH₂), 24.06 (–ve, CH₂), 34.78 (–ve, CH₃) and 41.35 (–ve, CH₂).

reactions of thioureas with **1** (R = alkyl), the intermediate **16** could straightaway cyclize by route c to form the triazine derivatives **14**. But the absence of this mode in the reactions of **1** with biprotic ureas pointed to the alternative mode involving the participation of sulfur in **16** (Scheme 3; path d) followed by elimination of the CH₂COCH₃ group* to give the thiadiazine **15**, which in the presence of added base (K₂CO₃) could undergo Dimroth rearrangement⁸ to **14**. The observation that S-methylthiourea failed to react with **1** further supported the mode d of reaction.

The mass spectra of 6-substituted 5-acetyl-3-benzyluracils **5**, in general constitute loss of (i) PhCH₂ (path x), (ii) [PhCH=N=C=O]⁺ ion (path y) attended by an additional H-shift and (iii) CH₃ (path z) (Scheme 4). With 6-thioxo-1,3,5-triazine-2,4-(1H,3H,5H)-diones **14**, the major mass spectral fragmentation modes constitute, (i) the loss of SH to generate M⁺ – 33 ions, (ii) the formation of [RNCO]⁺ ions (path x) and (iii) the loss of HNCS to give a peak at M⁺ – 59 (path y) (Scheme 4). However in compounds **14b**, **14e**, **14g** and **14i**, the loss of CH₃N=C=S is not observed (path z).

**Scheme 4****Experimental**

M.p.s were determined in capillaries and are uncorrected. ¹H and ¹³C NMR spectra were recorded on JEOL-JNM (60 MHz) and Bruker AC 200 instruments for solutions in CDCl₃/[2H₆]-DMSO or TFA using TMS as internal standard. IR spectra were recorded for KBr pellets on a Pye-Unicam SP3-300 spectrophotometer and UV spectra on a Shimadzu-UV-240 instrument. Mass spectra were run on JEOL JMS-D-300 and VG micromass 7070F machines operating at 70 eV at CDRI, Lucknow and RSIC, Chandigarh. Thin layer chromatography was performed on precoated TLC plates of silica gel G or silica gel 60 HF₂₅₄. Column chromatography was carried out using silica gel (60-120).

Reactions of 6-Methyl-1,3-oxazine-2,4-(3H)-diones **1** with

* In the reaction of **1** (R = CH₂Ph) with thiourea, the effluent gases were passed through aqueous 2,4-dinitrophenylhydrazine to give acetone 2,4-dinitrophenylhydrazone, m.p. 127 °C (lit.,⁹ m.p. 128 °C).

Amides and Thioamides: General Procedures.—3-Benzyl-6-methyl-1,3-oxazine-2,4(3H)-dione (2.2 g, 0.01 mol), alkane/arene amides/thioamides (0.012 mol), anhydrous K_2CO_3 (3.3 g, 0.024 mol) and tetrabutylammonium hydrogen sulfate (~20 mg) were taken up in DMF (20 cm³) and the mixtures stirred at 40–80 °C. The progress of the reactions was monitored by TLC. After completion of the reaction (3–10 h), the reaction mixture was neutralised with dilute HCl and the suspended solid was filtered off and washed with ethyl acetate. Combined filtrate and washings were evaporated under reduced pressure. The residue was column chromatographed over silica gel with benzene and benzene–ethyl acetate as eluents to give, 5-acetyluracil derivatives (Table 1).

Synthesis of 3-Substituted 6-Methyl-1,3-oxazine-2,4(3H)-dione Derivatives 1 [R = (CH₂)₃CN, (CH₂)₃CO₂Et].—*Method A.* 6-Methyl-1,3-oxazine-2,4(3H)-dione (1.27 g, 0.01 mol), was stirred in acetonitrile (50 cm³) containing anhydrous potassium carbonate (4.1 g, 0.03 mol) and triethylbenzylammonium chloride (~20 mg) for 1 h at ambient temperature. 4-Chlorobutyronitrile/ethyl 4-chlorobutyrate (0.012 mol) was then added and the reaction mixture was stirred. After completion of the reaction (TLC, 18–25 h), the solid was filtered off and washed with acetonitrile. The filtrate and washings were combined and the solvent was distilled off to leave a residue. This was column chromatographed over silica gel using benzene and benzene–ethyl acetate as eluents to give compounds **1** [R = (CH₂)₃CN, (CH₂)₃CO₂Et].

Method B. 4-Chlorobutanonitrile/ethyl 4-chlorobutyrate (0.012 mol) was refluxed in acetone (dry) with sodium iodide (0.013 mol) for 1 h. 6-Methyl-1,3-oxazine-2,4(3H)-dione (0.01 mol) was then added along with anhydrous potassium carbonate (0.03 mol) and the reaction mixture was refluxed. After completion of the reaction (TLC, 8 h), the mixture was worked up as above.

3-(3-Cyanopropyl)-6-methyl-1,3-oxazine-2,4(3H)-dione **1** [R = (CH₂)₃CN]: (A) 18 h (50 °C), (45%); (B) 8 h (55%), m.p. liquid; *m/z* 194 (M⁺, 6); δ_H (CDCl₃) 1.80–2.65 (7 H, m, CH₃ and 2 × CH₂), 4.0 (2 H, t, J 7, NCH₂) and 5.85 (1 H, s, CH); ν_{max} (CHCl₃)/cm⁻¹ 2250 (C=N), 1750 (C=O) and 1700 (C=O); λ_{max} (MeOH)/nm 227.9.

3-(Ethoxycarbonylpropyl)-6-methyl-1,3-oxazine-2,4(3H)-dione **1** [R = (CH₂)₃CO₂Et]: (A) 25 h (50 °C) (35%); (B) 8 h (55%); m.p. 52 °C (CHCl₃); *m/z* 241 (M⁺, 45); δ_H (CDCl₃) 1.25 (3 H, t, J 7, OCH₂CH₃), 1.80–2.50 (7 H, m, 2 × CH₂, CH₃),

3.80–4.40 (4 H, m, NCH₂ and OCH₂) and 5.75 (1 H, s, H); ν_{max} (CHCl₃)/cm⁻¹ 1780 (C=O), 1750 (C=O) and 1720 (C=O); λ_{max} (MeOH)/nm 227.5.

Reactions of 3-alkyl-6-methyl-1,3-oxazine-2,4(3H)-diones 1 with ureas and thioureas. These were performed as those with amides and the data for the products formed are recorded in Table 2.

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