

Notes

A Synthesis of 5,6-Dihydrouracils in a Sealed-tube and Their Conformational Analysis

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5,6-Dihydrouracil is a type of compound which has great importance in biochemistry as well as in synthetic organic chemistry.¹ Due to its conformational characteristics spectroscopic studies have been widely done.^{2,3} The common practice in preparation of 5,6-dihydrouracils (**2**) is to condense α,β -unsaturated acids with urea⁴ or hydrogenation of uracil derivatives.⁵⁻⁷ Condensation of β -amino acids with isocyanates and subsequent cyclization of the β -ureidopropionic acids is a typical synthetic pathway for N-substituted dihydrouracils (**3**).⁸ The condensation of α,β -unsaturated acids with urea in ethylene glycol seemed to be most straightforward one-step procedure for preparation of **2** although the yields were generally low (e.g., **2a**, 24%; **2b**, 45%; **2h**, 8%).⁴ The yields seems to be worse when pyrophosphoric acid or phosphoric acid is employed.⁹ In addition, the yields in the literature were hardly reproducible in our laboratory when the scale of the reaction was reduced from molar to millimolar amount. The low yield in small scale reaction seemed to be due to ready decomposition of urea at the reaction temperature (190°C). In fact, white solid formed along the wall of the condenser when a mixture of an α,β -unsaturated carboxylic acid and urea in ethylene glycol was heated at ca. 190°C. The solid was biuret and its formation has been known as follow.¹⁰



We report much improved, yet simpler, procedure for the preparation of 5,6-dihydrouracils (**2**) and 5,6-dihydro-1,3-dimethyluracils (**3**), and the interesting spectroscopic properties of them.

Results and Discussion

The key feature in the present procedure is to use a sealed tube made of stainless steel. The inner volume of 40 ml was suitable for the reaction in 0.05-0.1 molar scale. Thus, a mixture of an α,β -unsaturated acid (**1**) and urea (1:1.5-3 by mole) was placed in the tube, sealed, and heated at 195°C for 1-2 h. The reaction mixture was poured into water and the 5,6-dihydrouracil compounds (**2**) separated as solid, which was crystallized from hot water. The yields and the melting points of **2** prepared by this procedure are listed in Table 1.

Preparations of 5,6-dihydro-1,3-dimethyluracil compounds (**3**) were even simpler: heating a mixture of **1** and 1,3-dimethylurea and directly distilling the reaction mixture without

Table 1. Yields and Melting Points of the 5,6-Dihydrouracils (**2**)

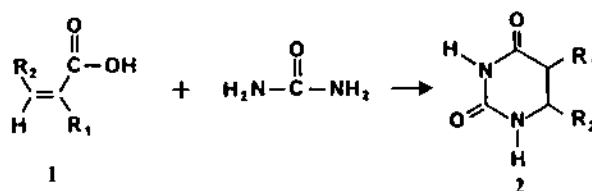
| Compd. | Yield, % ^a | Mp. °C (lit., °C) |
|------------------------|-----------------------|--|
| 2a | 10 | 268 (276-278) ⁴ |
| 2b_{av} | 18 ^b | 216-217 (217-218) ⁴ |
| 2c | 10 | 264-265 (264-265) ¹¹ |
| 2d | 40 | 200-201 (204-205) ¹² |
| 2e | 65 | 194-198 |
| 2f | 30 | 182-188 |
| 2g | 70 | 214-216 |
| 2h | 35 ^c | 206 (220-221) ⁸ , (217-217.5) ¹³ |

^aYields are after recrystallization from water, ^b40% including the mixture (mp. 186-187°C) of **2b_{av}** and **2b_{ax}**, ^c80% when the reaction time was 5 h.

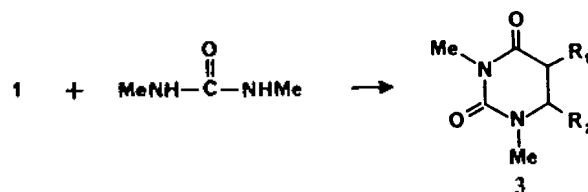
Table 2. Yields and Boiling Points of the 5,6-Dihydro-1,3-dimethyluracils (**3**)

| Compd. | Yield, % ^a | Bp. °C (mmHg) |
|-----------|-----------------------|-----------------------------|
| 3a | 65 | 87-88.5 (0.08) ^b |
| 3b | 80 | 89 (0.07) |
| 3c | 25 | 92 (0.01) |
| 3d | 65 | 86 (0.12) |
| 3e | 60 | 98 (0.08) |
| 3f | 60 | 74 (0.06) |

^aYields are after distillation under vacuum. ^bSolidified after standing: mp. 53°C (lit.⁷ 54-55°C).



| | R ₁ | R ₂ | | R ₁ | R ₂ |
|---|-----------------|---|---|-------------------------------|---------------------------------|
| a | H | H | g | CH ₃ | CH ₂ CH ₃ |
| b | H | CH ₃ | h | H | C ₆ H ₅ |
| c | CH ₃ | H | i | H | COOH |
| d | CH ₃ | CH ₃ | j | H | COOCH ₃ |
| e | H | CH ₂ CH ₃ | k | C ₆ H ₅ | C ₆ H ₅ |
| f | H | CH ₂ CH ₂ CH ₃ | | | |

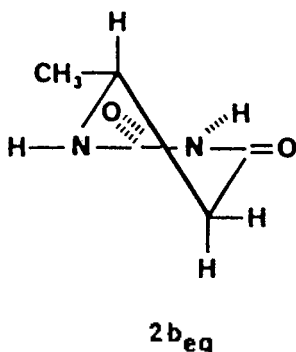


pretreatment with water. The yields with or without the work-up with water were not different noticeably. The yields and the boiling points of **3** are listed in Table 2.

α,β -Unsaturated acids of low molecular weights (**1a-d**) seemed to polymerize substantially under the reaction conditions causing the yields of the hydrouracils (**2a-d**) low (10-40%). Indeed, water insoluble polymeric gum was present in the reaction mixture in each case. Addition of hydroquinone seemed not to be helpful. In cases of **1h** in which a phenyl group is present at β -carbon, *ca.* 50% of the starting material was recovered after the reaction period of 2 h. But prolonged reaction time increased the yield of **2h** significantly (80%).

Hydrouracil has been known to have a half-chair conformation.^{2,3} Therefore, the conformation with the C_6 -substituent equatorial seems to be more favorable than the one with the substituent axial. However, Katritzky *et al.*² studied the NMR spectra of dihydrouracils extensively and suggested the axial arrangement of C_6 -substituents in 5,6-dihydro-6-phenyluracil (**2h**), orotic acid (**2i**) and its methyl ester (**2j**), and 5,6-dihydro-5,6-diphenyluracil (**2k**) in dimethyl sulfoxide. The C_6 -phenyl group of **2h** took equatorial position in trifluoroacetic acid. Their conclusion was based on the values of $J_{1,6}$ and $J_{5,6}$ which were obtained using 60 or 100 MHz spectrometer. Although we were able to reproduce very similar values of chemical shifts and coupling constants for **2h** in dimethyl sulfoxide using 300 MHz instrument we were not able to deduce $J_{1,6}$ value because N_1 -H (as well as N_3 -H) signal appeared as a singlet. Furthermore, H_6 signal collapsed to a singlet-like multiplet which were not resolvable to deduce a reasonable coupling constant in many cases.

In most cases examined in the present study the shapes of N_1 -H and N_3 -H peaks appeared as sharp singlets which were not helpful in calculating $J_{1,6}$ values. Analysis of the peak corresponding to H_6 was not informative due to its complexity arising from the coupling to protons in C_6 -alkyl groups as well as to H_{5ax} and H_{5eq} . Contrastingly, the peaks due to H_{5ax} and H_{5eq} form typical A and B parts of ABX pattern. In spite of this complication we were able to compare the values of the chemical shift and coupling constant and deduced a conclusion that substituents at C_6 and/or C_5 in **2c-h** prepared by the present method may take equatorial position in contrast to axial arrangement of carboxyl and methoxycarbonyl groups in **2i** and **2j**, respectively.



The unambiguous assignment of the conformation of the substituent was possible because we obtained both equatorial and axial conformers of **2b**. When we attempted to prepare **2b** by following the literature (heating a mixture of crotonic

acid and urea in ethyleneglycol at 195°C for 1 h)⁴ we obtained only one conformational isomer, **2b_{eq}**, in low yield (*ca.* 10%) which had identical melting point and IR as well as NMR spectra in the literature.¹⁴ On the other hand, the sealed-tube method (see Experimental section) gave **2b_{eq}** as the first crop upon crystallization from hot water. When the filtrate was kept in a refrigerator (4°C) for 3 days white solid formed as the second crop.

Although the second crop showed lower melting point (186-187°C) than that of the first crop (217.5-218°C) the melting range was very close indicating that it was a pure compound. However, its IR spectrum showed a remarkable difference from that of the first crop. In addition to peaks at 3180 (m), 1720 (vs), 1690 (vs), 1360 (m), and 1290 (s) cm^{-1} which corresponded to **2b_{eq}**,¹⁴ there were peaks at 3340 (m), 1660 (vs), 1630 (s), and 1150 (m) cm^{-1} which seem to be due to the presence of another compound. Since the elemental analysis data are consistent with $C_5H_8N_2O_2$ of **2b** it seems to be reasonable to assume that the second component in the mixture should be an isomer of **2b_{eq}**. The argument can be supported by interpreting the NMR spectra of both pure **2b_{eq}** (the first crop) and a mixture of **2b_{eq}** and **2b_{ax}** (the second crop).

The key factor in determination of conformation is the observed coupling constant of 9.5 Hz in **2b_{eq}** from the spectrum of the first crop. The value seems to be too large to be $J_{5a,6e}$ or $J_{5e,6e}$ when compared to values observed with dihydroorotic acid (**2i**, 6.9 and 5.1 Hz) and its methyl ester (**2j**, 7.4 and 3.1 Hz) in which the C_6 -substituents are in axial positions. The large value of J should be attributed of $J_{5a,6e}$ from coupling of two axial protons which are *trans* each other. Therefore, the much smaller value of $J_{5e,6e}$ (4.66 Hz) is readily understandable. Furthermore, H_{5e} is likely to lie in the deshielding region of the carbonyl group at C_4 , causing a downfield shift (Table 3). It seems to be in contrast to what observed in methyl dihydroorotate (**2j**) in which H_{5e} peak appeared in the upfield region (δ 2.66 vs δ 2.92 for H_{5a}).²

The NMR spectrum of the second crop clearly showed the presence of two conformers. Furthermore, the peaks arising from the protons in **2b_{ax}** could be identified readily by comparison of the spectrum of **2b_{eq}**. Appearance of two doublets of equal intensities at δ 1.20 and 1.26, respectively, due to 6-methyl group suggests the ratio of the two conformers to be *ca.* 1:1 in deuterium oxide. Interestingly, the ratio changed to 4:3 in dimethyl sulfoxide where the methyl group favors the equatorial arrangement. On the other hand, the equatorial conformer seemed to be mostly present in acetone. With the aid of DEPT spectrum all the peaks in the ¹H-NMR spectrum of the mixture could be assigned unambiguously. Assignments could be readily made for the peaks in ¹³C-NMR spectra similarly (Table 4).

Several attempts were made to separate the conformers of **2b** unsuccessfully. When a mixture was heated in water for 3 h the axial conformer changed to the equatorial one, preventing selective crystallization of **2b_{ax}**. An interesting observation was that the conformational change from the axial form to the equatorial form was irreversible. Thus, when a solution of the first crop (**2b_{eq}**) in water or in dimethyl sulfoxide was heated at 60-70°C for 1 h and examined the NMR spectrum at times, none of **2b_{ax}** was found to be pre-

Table 3. ¹H-NMR Spectral Data (δ) of 5,6-Dihydrouracils (**2**) in Dimethyl Sulfoxide-*d*₆ and 5,6-Dihydro-1,3-dimethyluracils (**3**) in Chloroform-*d* (J, Hz)

| Compd. | H _{5ar} | H _{5eq} | H _{6ar} | H _{6eq} | H ₁ | H ₃ |
|------------------------------------|--------------------------------|--------------------------------|---|--|--------------------------|--------------------------|
| 2a | 2.44 (6.60) | 2.44 (6.60) | 3.20 (6.60) | 3.20 (6.60) | 7.49 (s) | 9.95 (s) |
| 2b_{ar} | 2.06 (14.20, 7.44) | 2.22 (14.13, 5.71) | 1.02 ^a (d, 6.54) | 3.85 (m) | 5.89 (s) | 7.33 (s) |
| 2b_{eq} | 2.23 (16.11, 9.50) | 2.48 (16.00, 4.66) | 3.54 (m) | 1.10 ^a (d, 6.37) | 7.55 (s) | 10.00 (s) |
| 2b_{ar}^b | 2.43 (7.47) | 2.43 (7.47) | 1.20 ^a (d, 6.48) | 4.02 (m) | — | — |
| 2b_{eq}^b | 2.49 (16.91, 9.65) | 2.74 (16.91, 4.96) | 3.82 (m) | 1.26 ^a (d, 6.64) | — | — |
| 2b_{eq}^c | 2.32 (16.40, 9.84) | 2.59 (16.40, 4.61) | 3.75 (m) | 1.25 ^a (d, 6.42) | 6.73 (s) | 8.97 (s) |
| 2c | 2.54 (m) | 10.5 ^e (d, 6.90) | 2.95 (t, 11.00) | 3.24 (ddd, 11.00, 6.10, 4.00) | 7.53 (s) | 9.93 (s) |
| 2d | 2.21 (dq, 7.00, 9.63) | 1.06 ^a (d, 7.00) | 3.22 (dq, 6.30, 9.63) | 1.13 ^a (d, 6.30) | 7.52 (s) | 10.00 (s) |
| 2e | 2.27 (16.39, 8.58) | 2.54 (16.37, 5.01) | 3.35 (m) | 1.49 ^{a, d} (7.46) 1.39 ^{a, d} (7.00) 0.86 ^a (t, 3 H, 7.39) | 7.59 (s) | 9.99 (s) |
| 2e^b | 2.35 (16.96, 8.10) | 2.60 (16.96, 5.53) | 3.45 (m) | 1.45 ^{a, d} (7.10) 1.39 ^{a, d} (7.00) 0.76 ^a (t, 3 H, 7.46) | — | — |
| 2f | 2.26 (15.99, 8.01) | 2.55 (15.99, 5.14) | 3.43 (m) | 1.33 ^a (m, 4 H) 0.87 ^a (t, 3 H, 7.50) | 7.60 (s) | 10.00 (s) |
| 2f^b | 2.67 (16.96, 7.90) | 2.90 (16.96, 5.58) | 3.84 (m) | 1.60 ^a (m, 4H) 1.06 ^a (t, 3 H, 7.50) | — | — |
| 2g | 2.30 (quintet, 7.10) | 1.10 ^a (d, 7.10) | 3.07 (m) | 1.35 ^a (m, 2 H) 0.86 ^a (t, 3 H, 7.40) | 7.57 (s) | 9.97 (s) |
| 2h | 2.62 (16.30, 6.87) | 2.85 (16.30, 5.78) | 4.67 (app. s) | 7.35 ^a (s, 5 H) | 8.07 (s) | 10.20 (s) |
| 2h^b | 2.94 (17.66, 9.28) | 3.07 (17.32, 5.94) | 4.94 (m) | 7.49 ^a (m, 5 H) | — | — |
| 3a | 2.68 (m) | 2.68 (m) | 3.32 (m) | 3.32 (m) | 2.99 ^a (s) | 3.11 ^a (s) |
| 3b | 2.78 (16.41, 6.39) | 2.39 (16.41, 2.73) | 1.09 ^a (d, 6.67) | 3.41 ^a (6.69, 6.58, 2.73) | 2.90 ^a (s) | 3.04 ^a (s) |
| 3c | 1.23 ^a (d, 6.70) | 2.74 (m) | 2.95 (m, overlapped) | 3.27 (m) | 3.02 ^a (s) | 3.13 ^a (s) |
| 3d | 1.10 ^a (d, 6.50) | 2.50 (7.10, 2.08) | 1.20 ^a (d, 7.14) | 3.28 (6.36, 2.08) | 2.95 ^a (s) | 3.07 ^a (s) |
| 3e | 2.78 (16.50, 6.65) | 2.58 ^f (16.51) | 1.64 ^a (1 H ^g) 1.47 ^a (1 H ^g) 0.87 ^a (t, 7.43) | 3.19 (m) | 3.00 ^a (s) | 3.10 ^a (s) |
| 3f | 2.75 (16.36, 7.35) | 2.49 (16.48) | 1.18-1.57 ^a (m, 4 H) 0.87 ^a (t, 7.10) | 3.25 (m) | 2.96 ^a (s) | 3.06 ^a (s) |

^aChemical shifts corresponding to alkyl or aryl substituents. ^bIn deuterium oxide. ^cIn acetone-*d*₆. ^dTotal 2 H. Two apparent octet overlapped in part. ^eApparent doublet of quintet. ^fApparent doublet. ^gApparent octet.

sent. It was not possible to observe an axial conformer in any other compounds than in **2b**.

The trends in the chemical shifts and coupling constants (Table 3) seem to suggest that 6-phenyl group in **2h** should

have similar arrangements as 6-methyl in **2b_{eq}**, which is equatorial. This seems to be the case with **2e** (C₂H₅) and **2f** (C₃H₇), as well.

5,6-Disubstituted hydrouracils (**2d** and **2g**) seemed to have

Table 4. ^{13}C -NMR Spectral Data (ppm) of 5,6-Dihydrouracils (**2**) in Dimethyl Sulfoxide- d_6 and 5,6-Dihydro-1,3-dimethyluracils (**3**) in Chloroform- d

| | C_4 | C_2 | C_5 | C_6 | Substituents |
|------------------------------------|--------------|--------------|--------------|--------------|--|
| 2a | 171.13 | 153.99 | 30.43 | 35.36 | — |
| 2b_{ax} | 172.61 | 158.01 | 38.69 | 42.33 | 20.87 (6-CH ₃) |
| 2b_{eq} | 170.63 | 153.16 | 37.92 | 42.70 | 20.43 (6-CH ₃) |
| 2b_{ax}^a | 179.20 | 160.10 | 45.15 | 46.77 | 22.87 (6-CH ₃) |
| 2b_{eq}^a | 177.14 | 155.50 | 39.73 | 46.16 | 22.29 (6-CH ₃) |
| 2c | 173.70 | 153.97 | 34.30 | 41.89 | 12.46 (5-CH ₃) |
| 2d | 173.35 | 153.16 | 41.17 | 48.74 | 19.35 (6-CH ₃), 11.84 (5-CH ₃) |
| 2e | 170.68 | 153.62 | 35.42 | 48.06 | 9.34 (CH ₃), 27.21 (CH ₂) |
| 2f | 170.66 | 153.53 | 36.50 | 46.50 | 35.90 (6-CH ₂), 17.82 (CH ₂ CH ₃), 13.80 (CH ₃) |
| 2g | 173.81 | 153.19 | 38.30 | 53.68 | 25.45 (CH ₂), 12.18 (5-CH ₃), 8.59 (CH ₃) |
| 2h | 169.85 | 153.86 | 38.26 | 50.10 | 126.07, 127.67, 128.63, 141.20 (all C ₆ H ₅) |
| 3a | 169.52 | 154.23 | 31.59 | 43.08 | 35.99 (N ₃ -CH ₃), 27.68 (N ₁ -CH ₃) |
| 3b | 169.06 | 153.33 | 38.21 | 49.44 | 34.21 (N ₃ -CH ₃), 27.56 (N ₁ -CH ₃), 17.79 (CH ₃) |
| 3c | 170.00 | 152.21 | 36.02 | 50.04 | 35.75 (N ₃ -CH ₃), 27.94 (N ₁ -CH ₃), 13.48 (CH ₃) |
| 3d | 172.44 | 158.22 | 42.75 | 56.33 | 34.90 (N ₃ -CH ₃), 27.80 (N ₁ -CH ₃), 17.92 (C ₆ -CH ₃), 14.55 (C ₅ -CH ₃) |
| 3e | 169.10 | 153.22 | 35.15 | 55.33 | 35.24 (N ₃ -CH ₃), 27.46 (N ₁ -CH ₃), 25.11 (CH ₃), 10.23 (CH ₂) |
| 3f | 169.18 | 160.34 | 35.61 | 53.86 | 35.21 (N ₃ -CH ₃), 27.46 (N ₁ -CH ₃), 34.27 (C ₆ -CH ₂), 19.14 (C ₂ -CH ₃), 14.07 (CH ₃) |

^aIn deuterium oxide.**Table 5.** Mass Spectral Data of 5,6-Dihydrouracils (**2**) and 5,6-Dihydro-1,3-dimethyluracils (**3**)

| Compd. | M ⁺ (%) | M ⁺ -R (%) | O=C=N ⁺ =C=O | Others |
|-----------|--------------------|-----------------------|-------------------------|--|
| 2a | 114 (2) | — | 70 (90) | 44 (30), 43 (75), 42 (80) |
| 2b | 128 (13) | 113 (100) | 70 (92) | 44 (29), 43 (81), 42 (36), 28 (41) |
| 2c | 128 (73) | 113 (4) | 70 (4) | 56 (62), 42 (100) |
| 2d | 142 (44) | 127 (35) | 70 (19) | 84 (59), 56 (45), 44 (100), 42 (19) |
| 2e | 142 (2) | 113 (75) | 70 (100) | 43 (40), 42 (9) |
| 2f | 156 (2) | 113 (97) | 70 (100) | 54 (10), 43 (29), 42 (18) |
| 2g | 156 (3) | 127 (71) | — | 84 (100), 56 (25) |
| 2h | 190 (100) | — | 70 (27) | 132 (87), 104 (92), 91 (14), 77 (47) |
| 3a | 142 (68) | — | — | 113 (28), 58 (36), 57 (52), 44 (31), 43 (77), 42 (100) |
| 3b | 156 (8) | 141 (35) | — | 84 (55), 58 (17), 56 (23), 42 (100) |
| 3c | 156 (39) | — | — | 113 (20), 71 (19), 58 (35), 56 (38), 44 (40), 42 (100) |
| 3d | 170 (5) | 155 (24) | — | 100 (27), 98 (32), 55 (100), 42 (39) |
| 3e | 170 (2) | 141 (39) | — | 84 (56), 55 (19), 42 (100) |
| 3f | 184 (15) | 141 (57) | — | 84 (88), 58 (26), 55 (22), 42 (100) |

trans arrangement of the substituents, which were confirmed by the values of the coupling constants $J_{5,6}$ of 9.1–9.6 Hz. The chemical shift values of H₅ and H₆ are in line with

the rationale that the alkyl substituents are in equatorial arrangements.

Presence of methyl groups on both nitrogen atoms such as in **3** seems to cause a change in the conformation of the C₆-substituents. The typical AB parts of an ABX pattern in the NMR spectra of **3** reduced to apparent doublets at δ 2.5 with coupling constants of *ca.* 16 Hz and doublets of doublets at δ 2.7 with *J* values of *ca.* 16 and 6 Hz. The observed coupling constants of 6.39 and 2.73 in **3b** seemed to be consistent with the substituent in axial position. Apparently, the interaction between N₁-methyl and C₆-alkyl substituents seems to cause conformational change so that the distance between them becomes large. 5,6-Dimethyl substituents in **3d** seem to favor axial positions as indicated by small coupling constant for $J_{5,6}$ (2.08 Hz).

Electron-impact (EI) mass spectra of **2** showed interesting correlations. Molecular ion (M⁺) was rather weak in cases of 6-alkyl compounds (**2b**, **2e**, **2f**) and loss of alkyl was significant (Table 5). Furthermore, a fragment of *m/e* 70 was common, which might correspond to O=C=N⁺=C=O. On the other hand, mass spectra of **3** showed *m/e* 42 as the base peak in all but **3d**. The fragment may be due to CH₃-N≡H. The presence of 5-methyl or 6-phenyl group change the fragmentation pattern drastically.

Experimental Section

Melting points were determined on MEL-TEMP capillary melting point apparatus and uncorrected. ^1H -NMR and ^{13}C -NMR spectra were obtained on an IBM-300 MHz FT-NMR spectrometer in specified solvents using TMS as an internal standard. Mass spectra were obtained using AEI 30 mass spectrometer. Elemental analyses were performed by the M-H-W Laboratories, Phoenix, Arizona.

An Illustrative Procedure for Preparation of 2: 5,6-Dihydro-6-methyluracil (2b). In a stainless steel tube

(inner diameter 2.2 cm, inner volume 40 ml) were placed crotonic acid (4.30 g, 50 mmole) and urea (7.50 g, 125 mmole). The tube was sealed and was placed in an oil bath whose temperature was maintained at 195°C for 2 h. After cooling to room temperature the mixture was taken out with aid of warm water (ca. 100 ml) and then heated to result a homogeneous solution. The water-insoluble polymeric gum was filtered off and the solution was decolorized with charcoal. Upon cooling slowly to room temperature white solid mass formed which was collected by filtration and dried under vacuum at 50°C to give **2b_{eq}** (1.17 g, 18%), mp. 217.5–218°C. The filtrate gave second crop after 3 days in a refrigerator, which was a mixture of **2b_{eq}** and **2b_{ax}** (1.44 g, 23%), mp. 186–187°C. Total yields of **2b_{eq}** and **2b_{ax}** were about 40% in several run.

Anal. **2e**: Calcd for C₆H₁₀N₂O₂: C, 50.69; H, 7.09; N, 19.70. Found: C, 50.88; H, 7.21; N, 20.03. **2f**: calcd for C₇H₁₂N₂O₂: C, 53.83; H, 7.74; N, 17.94. Found: C, 53.60; H, 7.68; N, 18.22. **2g**: Calcd for C₇H₁₂N₂O₂: C, 53.83; H, 7.74; N, 17.94. Found: C, 53.49; H, 7.55; N, 18.27.

An Illustrative Procedure for Preparation of 3: 5, 6-Dihydro-1,3-dimethyluracil (3a). A mixture of acrylic acid (3.6 g, 50 mmole) and 1,3-dimethylurea (3.60 g, 50 mmole) was placed in a stainless steel tube, sealed, and heated at 190°C for 2 h. The liquid mixture was distilled under vacuum to give **3a** (4.65 g, 65%), bp. 88–92°C at 0.08 mm.

Anal. **3a**: calcd for C₆H₁₀N₂O₂: C, 50.69; H, 7.09; N, 19.70. Found: C, 50.46; H, 7.27; N, 19.90. **3b**: calcd for C₇H₁₂N₂O₂: C, 53.83; H, 7.74; N, 17.94. Found: C, 53.62; H, 7.63; N, 17.87. **3c**: calcd for C₇H₁₂N₂O₂: C, 53.83; H, 7.74; N, 17.94. Found: C, 53.68; H, 7.86; N, 18.06. **3d**: calcd for C₈H₁₄N₂O₂: C, 56.45; H, 8.29; N, 16.46. Found: C, 56.66; H, 8.60; N, 16.38. **3e**: calcd for C₈H₁₄N₂O₂: C, 56.45; H, 8.29; N, 16.46. Found: C, 56.23; H, 8.57; N, 16.62. **3f**: calcd for C₉H₁₆N₂O₂: C, 58.67; H, 8.75; N, 15.20. Found: C, 58.38; H, 8.55; N, 15.50.

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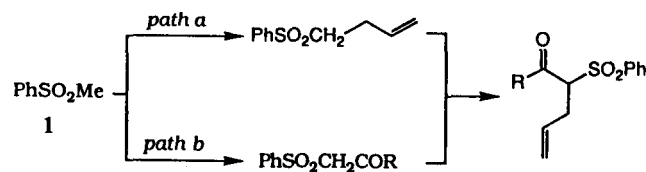
Facile Synthesis of α -Allyl Substituted β -Oxo Sulfoxes

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β -Keto sulfones are important building blocks and are widely used in synthetic organic chemistry.¹ The acidic nature of the methylene protons provides a convenient way of introducing various electrophiles at that position.² In the course of our studies on the reactivity of β -keto sulfones,³ a consequence of our investigation of iodine-induced enoetherification of α -allyl substituted β -keto sulfones⁴ was the requirement of an efficient method for synthesizing these compounds. We were surprised to find that no comprehensive method appear in the literature for the preparation of α -allyl substituted β -oxo sulfones.



We first tried the allylation of methyl phenyl sulfone (1) and subsequent acylation (*path a*). However this reaction gave a problem to give di-allylated product.⁵ Second, we assumed the acylation of methyl phenyl sulfone and subsequent allylation (*path b*). Fortunately β -keto sulfones were obtained in excellent yields from the reaction of acyl halides with 1,1-dilithiomethyl phenyl sulfone (2) which is easily generated by treatment of 2 equiv. of *n*-BuLi to a solution of methyl phenyl sulfone (1) in THF at -30°C .⁶

Therefore we tried *in situ* allylation of enolate (3) which is generated from reaction of acyl halide with 1,1-dilithiomethyl phenyl sulfone (2) (Method A). Only the reaction of allyl bromide with enolate 3 ($\text{R}=\text{NMe}_2$), which is generated *in situ* from *N,N*-dimethylcarbonyl chloride and sulfone di-