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# The dramatic effect of thiophenol on the reaction pathway of ethyl 4-chloromethyl-6-methyl-2-oxo-1,2,3,4-tetrahydropyrimidine-5-carboxylate with thiophenolates: ring expansion versus nucleophilic substitution

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ABSTRACT

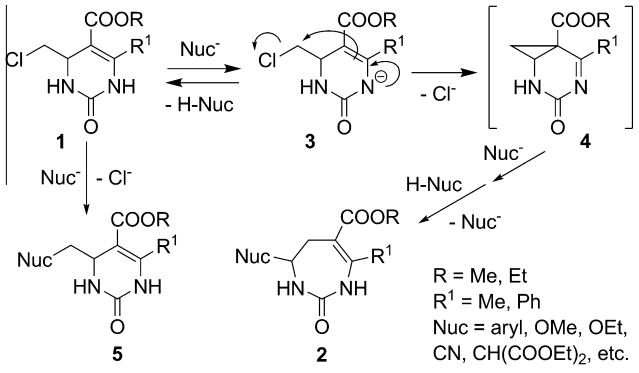
Ethyl 4-methyl-2-oxo-7-phenylthio-2,3,6,7-tetrahydro-1*H*-1,3-diazepine-5-carboxylate and/or ethyl 6-methyl-2-oxo-4-(phenylthiomethyl)-1,2,3,4-tetrahydropyrimidine-5-carboxylate were obtained in the reaction of ethyl 4-chloromethyl-6-methyl-2-oxo-1,2,3,4-tetrahydropyrimidine-5-carboxylate with PhSNa or PhSK with or without PhSH, depending on the reagent ratio, reaction time, or temperature, as a result of ring expansion and/or nucleophilic substitution. The reaction pathway was affected strongly by the basicity–nucleophilicity of the reaction media. The results obtained were confirmed by reactions of 4-mesyloxymethyl-6-methyl-5-tosyltetrahydropyrimidin-2-one with PhSNa/PhSH and ethyl 4-chloromethyl-6-methyl-2-oxo-1,2,3,4-tetrahydropyrimidine-5-carboxylate with NaCN/HCN or $NaCH(COOEt)_2$/$CH_2(COOEt)_2$.



Ring expansion reactions are widely used in organic chemistry,[1] particularly in the synthesis of nitrogen-containing heterocycles.[1,2] An important example of one-carbon ring expansion is the transformation of tetrahydropyrimidines **1** into tetrahydro-1,3-diazepin-2-ones **2** by treatment with nucleophilic reagents (Scheme 1).[3]

It was postulated[3] that diazepinones **2** form via the cyclopropane-containing bicyclic intermediates **4** (Scheme 1) which result from proton abstraction from the N(1)H group under the action of nucleophiles followed by intramolecular nucleophilic substitution of chlorine in anions **3**. Clearly, this reaction depends not only on the nucleophilicity but also on the basicity of the nucleophile. For example, direct nucleophilic substitution of chlorine resulting in pyrimidines **5** cannot be excluded a priori under certain reaction conditions. However, the influence of reaction conditions on the reaction of compounds **1** with nucleophiles remained unexplored.[3] Therefore, study of the effect of the nucleophilicity and basicity of the nucleophile, reagent ratio, solvent, time, and temperature on the reaction of compounds **1** with nucleophiles is interesting. In this research we used the readily available pyrimidinone **6** as the starting material and PhSNa or PhSK as nucleophiles which demonstrate strong nucleophilicity and relatively low basicity.[4] The nucleophiles were generated by the treatment of PhSH with NaH or KOH in an appropriate solvent.

The reaction of **6** with PhSNa (1.08 equiv) in dry MeCN at rt for 7 h yielded diazepinone **7** as the product of ring expansion (Scheme 2). According to the $^1$H NMR spectrum, the crude material contained 3 mol% of tetrahydropyrimidinone **8**, a product of nucleophilic substitution of chlorine in **6** (Table 1, entry 1). Diazepinone **7** formed with complete selectivity under similar conditions in the reaction of **6** with PhSNa (1.10 equiv) in dry THF (rt, 7 h) (entry 2), however, 9 mol% of starting material **6** was recovered. When EtOH was used as the solvent, the rate of the reaction of **6** with PhSK (1.10 equiv) decreased dramatically (conversion of **6** was only 8% after 7 h at rt), and the selectivity also decreased (**7**:**8** = 7:1) (entry 3).




**Scheme 1.** Two possible pathways for the reaction of pyrimidines **1** with nucleophilic reagents: ring expansion or nucleophilic substitution.

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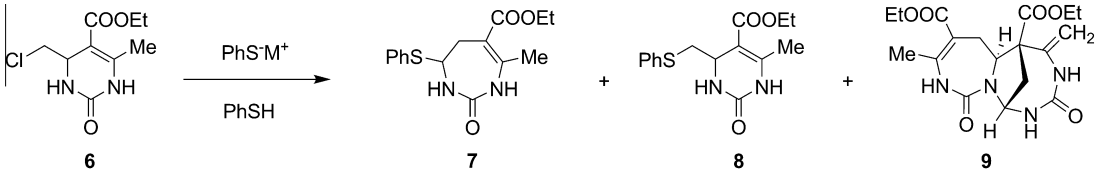



**Scheme 2.** Reaction of pyrimidine **6** with PhSNa or PhSK.

**Table 1**
Reactions of pyrimidine **6** with PhSNa or PhSK

| Entry | Solvent | Base | Molar ratio of **6**:PhSH:base | Molar ratio of **6**:PhSNa:PhSH or **6**:PhSK:PhSH | Conditions | Molar ratio[a] of products **7**:**8**:**6** |
|---|---|---|---|---|---|---|
| 1 | MeCN | NaH | 1.00:1.08:1.09 | 1.00:1.08:0 | rt, 7 h | 97:3:0 |
| 2 | THF | NaH | 1.00:1.10:1.10 | 1.00:1.10:0 | rt, 7 h | 91:0:9 |
| 3 | EtOH | KOH | 1.00:1.13:1.10 | 1.00:1.10:0.03 | rt, 7.5 h | 7:1:92 |
| 4 | MeCN | NaH | 1.00:2.02:1.10 | 1.00:1.10:0.92 | rt, 7 h | 48:43:9 |
| 5 | MeCN | NaH | 1.00:2.21:1.05 | 1.00:1.05:1.16 | rt, 7.2 h | 9:61:30 |
| 6 | MeCN | NaH | 1.00:3.00:1.10 | 1.00:1.10:1.90 | rt, 7 h | 0:35:65 |
| 7 | MeCN | NaH | 1.00:3.00:1.10 | 1.00:1.10:1.90 | Reflux, 7 h | 15:85:0 |
| 8 | MeCN | NaH | 1.00:3.29:1.10 | 1.00:1.10:2.19 | rt, 47.9 h | 1:93:6 |
| 9 | MeCN | NaH | 1.00:3.32:1.10 | 1.00:1.10:2.22 | rt, 72.7 h | 0:97:3 |
| 10 | MeCN | NaH | 1.00:2.24:1.05 | 1.00:1.05:1.19 | rt, 48.2 h | 6:89:5 |
| 11 | MeCN | NaH | 1.00:2.20:1.10 | 1.00:1.10:1.10 | Reflux, 8 h | 33:67:0 |
| 12 | MeCN | NaH | 1.00:3.26:1.08 | 1.00:1.08:2.18 | Reflux, 8.1 h | 16:84:0 |
| 13 | MeCN | NaH | 1.00:4.43:1.10 | 1.00:1.10:3.33 | Reflux, 8.1 h | 11:89:0 |
| 14 | EtOH | KOH | 1.00:2.23:1.10 | 1.00:1.10:1.13 | rt, 7 h | 16:6:78 |
| 15 | MeCN | NaH | 1.00:2.01:2.00 | 1.00:2.00:0.01 | rt, 7 h | 93:7:0[b] |
| 16 | MeCN | NaH | 1.00:3.31:1.10 | 1.00:1.10:2.21 | Reflux, 29 h | 11:89:0 |

[a] According to $^1$H NMR data of the crude products.
[b] 83 mol% of **7** + **8** and 17 mol % of bis-diazepinone **9**.

Thiophenol (PhSH) strongly affected the ratio of **7**:**8** and the rate of the reaction. The amount of pyrimidine **8** increased with a rise in the amount of PhSH in the reaction of **6** with PhSNa (1.05–1.10 equiv) in MeCN at rt for 7 h (entries 1, 4–6). Pyrimidine **8** formed with complete selectivity when 1.90 equiv of PhSH was used (entry 6). However, the reaction rate decreased significantly with an increase in the amount of PhSH (entries 1, 4–6).

The extent of conversion of compound **6** in the reaction with PhSNa in the presence of PhSH (1.90–2.22 equiv) increased with reaction time or temperature. Indeed, the reaction of **6** with PhSNa (1.10 equiv) in refluxing MeCN in the presence of PhSH (1.90 equiv) was complete in 7 h, while the selectivity of the reaction decreased significantly (entry 7). However, the selectivity remained high at rt and over long reaction times (entries 8 and 9).

A relationship between the ratio of **7**:**8** and the amount of PhSH was also observed at rt and over long reaction times (entry 8 vs entry 10), refluxing the reaction mixture (entry 11 vs entry 12 vs entry 13), and when EtOH was used as the solvent (entry 3 vs entry 14).

On using a greater excess of the nucleophile PhSNa (2.00 equiv), bis-diazepinone **9**[5] (17 mol%) formed along with **7** and **8** in the ratio 93:7 (entry 15).

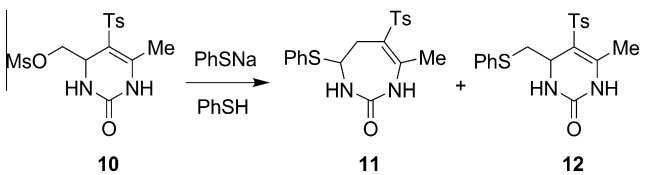
Under the optimal conditions diazepinone **7** was obtained in the reaction of **6** with PhSNa (1.08 equiv) in MeCN at rt for 7 h (entry 1),[6] and pyrimidinone **8** was prepared by the reaction of **6** with PhSNa (1.10 equiv) in the presence of 2.22 equiv of PhSH in MeCN at rt for 73 h (entry 9).[7]

Transformation of **6** into **7** and/or **8** is kinetically controlled. In fact, heating a mixture of **6**, PhSNa, and PhSH in MeCN for 8 or 29 h at reflux resulted in mixtures of **7** and **8** in similar ratios (Table 1, entry 12 vs entry 16). Moreover, reflux of **7**, PhSH, and PhSNa (1.0:1.9:0.1, respectively) in MeCN followed by evaporation of the solvent and aqueous work-up gave only **7** in 88% yield.

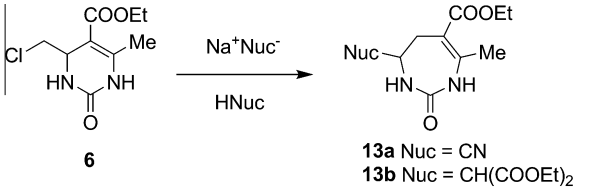
From the results obtained we suggest that the reaction of **6** with PhSNa and PhSK proceeds via two possible mechanisms. In aprotic solvents (MeCN or THF) and highly basic reaction media without PhSH, the thiophenolate-anion acts as a base and abstracts a proton from N(1)H to give anion **3** (R = Et, R$^1$ = Me) (see Scheme 1), which further affords diazepinone **7**. Addition of PhSH inhibits anion **3** formation and therefore causes a decrease in the amount of diazepinone **7**. Probably, in this case, compound **6** reacts with PhSNa via an $S_N2$ mechanism, resulting in pyrimidine **8**. Since chlorine is a rather poor leaving group, the rate of reaction is low, and heating at reflux or a long reaction time is necessary for completion of the reaction. The low rate of reaction of **6** with PhSK in EtOH can be explained by the decreased basicity and nucleophilicity of PhSK in a polar protic solvent.

In continuation of this research we used 4-mesyloxymethyl-5-tosyltetrahydropyrimidine (**10**) as the starting material in a reaction with PhSNa in the presence of PhSH. We found that **10** readily reacted with PhSNa in MeCN to give 4-phenylthio-6-tosyltetrahydro-1,3-diazepinone (**11**) (Scheme 3).[8] As expected, when compound **10** was reacted with PhSNa/PhSH (1:1.08:2.47) in MeCN (rt, 23.7 h), pyrimidinone **12** formed along with diazepinone **11** (**12**:**11** = 56:44). The amount of **12** increased up to 92% in this reaction, when a 1:1.24:3.82 ratio of the reagents was used (MeCN, rt, 42.4 h).[9]

We also attempted to obtain products of direct nucleophilic substitution of the chlorine in the reaction of **6** with other nucleophiles.




**Scheme 3.** Reaction of pyrimidine **10** with PhSNa/PhSH.




**Scheme 4.** Reaction of pyrimidine **6** with NaCN/HCN or $NaCH(COOEt)_2/CH_2(COOEt)_2$.

However, reaction of **6** with NaCN and HCN (1.00:1.28:2.75) in DMSO (rt, 32 h) resulted in a mixture of diazepine **13a** and starting material **6** in a ratio of 41:59 (Scheme 4). Analogously, diazepinone **13b** formed as a single product in the reaction of **6** with $NaCH(COOEt)_2/CH_2(COOEt)_2$ (1:1.09:2.23) in MeCN (rt, 33.4 h).

Exclusive formation of the products of pyrimidine ring expansion in the reactions of **6** with NaCN/HCN or $NaCH(COOEt)_2/CH_2(COOEt)_2$ versus PhSNa(PhSK)/PhSH could be explained by the higher basicity of NaCN or $NaCH(COOEt)_2$ compared with PhSNa or PhSK.[10]

The structures of **7**, **8**, and **12** were established unambiguously from their $^1H$ and $^{13}C$ NMR spectra. The $^1H$ NMR spectrum of **7** in DMSO-$d_6$ demonstrated long-range couplings between N(1)H and one of the 6-H protons ($^4J_{N(1)H,6\text{-}He}$ = 0.9 Hz) and between 4-$CH_3$ and the other 6-H proton ($^5J_{4\text{-}CH3,6\text{-}Ha}$ = 1.3 Hz). Higher values for the vicinal $^3J_{N(1)H,7\text{-}H}$ and geminal $^2J_{6\text{-}He,6\text{-}Ha}$ coupling constants (6.1 and 15.1 Hz, respectively) for diazepine **7** compared with the corresponding constants for pyrimidines **8** and **12** ($^3J_{N(3)H,4\text{-}H}$ = 3.4–4.1 Hz, $^2J_{CH(A),CH(B)}$ = 13.7–13.8 Hz) were observed. In the $^{13}C$ NMR spectrum of diazepine **7** we observed the chemical shift of the N-CH fragment at 61.32 ppm, while for pyrimidines **8** and **12** these occured at 49.75 and 49.85 ppm, respectively. The 2D NMR spectral data ($^1H,^1H$-COSY, $^1H,^{13}C$-HSQC, $^1H,^{13}C$-HMBC) also confirmed unambiguously the structures of diazepinones **7** and **8**.

In summary, the reaction of 5-functionalized 4-($X–CH_2$)-1,2,3,4-tetrahydropyrimidin-2-ones (X = good leaving group) with nucleophilic reagents resulted in the products of ring expansion (2,3,4,5-tetrahydro-1*H*-1,3-diazepin-2-ones) and/or products of direct substitution of the leaving group (1,2,3,4-tetrahydropyrimidin-2-ones) depending on the reaction conditions. The outcome of the reaction was determined by the nucleophilicity-basicity of the reaction media. Diazepinones **7** and **11** formed in the reaction of **6** and **10** with strong nucleophiles PhSNa or PhSK possessing relatively low basicity ($pK_a$ = 10.3 in DMSO). However, the reaction of **6** and **10** with PhSNa or PhSK in the presence of their conjugate acid (PhSH) gave diazepinones **7** and **11** along with the respective pyrimidines **8** and **12**. An increase in the amount of PhSH led to a significant increase in pyrimidine formation, while the rate of the conversion of starting materials into products decreased. In aprotic solvents, almost pure pyrimidines **8** and **12** were obtained when more than 2 equiv of PhSH were used. However, the reaction of **6** with more basic nucleophiles, NaCN or $NaCH(COOEt)_2$ ($pK_a$ = 12.9 and 15.9, respectively, in DMSO), with or without their conjugate acids yielded only the diazepinones **13a**,**b**.

We envisage that our findings may be of value for other similar one-carbon ring expansion reactions.[1,2]

## Supplementary data

Supplementary data (experimental procedures for the reactions of **6** with NaCN/HCN and $NaCH(COOEt)_2/CH_2(COOEt)_2$, $^1H$ and $^{13}C$ NMR spectra of **7**, **8** and **12**, and 2D NMR spectra of **7** and **8** ($^1H,^1H$-COSY, $^1H,^{13}C$-HSQC, $^1H,^{13}C$-HMBC) in DMSO-$d_6$) associated with this article can be found, in the online version, at doi:10.1016/j.tetlet.2010.07.098.

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6. *Synthesis of ethyl 4-methyl-2-oxo-7-phenylthio-2,3,6,7-tetrahydro-1H-1,3-diazepin-5-carboxylate* (**7**)*:* To a stirred suspension of NaH (0.036 g, 1.50 mmol) in MeCN (1 mL) was added a solution of thiophenol (0.162 g, 1.47 mmol) in MeCN (2 mL) and the resulting white suspension was stirred at rt for 9 min. Chloromethylpyrimidine **6**[3c] (0.318 g, 1.37 mmol) and MeCN (2.4 mL) were added and the resulting suspension was stirred at room temperature for 7 h. After the reaction was complete the solvent was removed under vacuum, the oily residue was triturated with light petrol (4 mL) and $H_2O$ (4 mL) under cooling until crystallization was complete. The solid was filtered, washed with ice-cold water, light petrol, and dried to give 0.276 g (66%) of a mixture of **7** and **8** in a ratio of 97:3 (Table 1, entry 1). Crystallization from EtOH afforded pure **7**. Mp 169–170 °C (EtOH). $^1H$ NMR (600.13 MHz, DMSO-$d_6$) $\delta$: 8.53 (1H, d, $^4J_{N(3)H,N(1)H}$ = 2.0 Hz, N(3)H), 7.98 (1H, ddd, $^3J_{N(1)H,7\text{-}H}$ = 6.1, $^4J_{N(1)H,N(3)H}$ = 2.0, $^4J_{N(1)H,6\text{-}He}$ = 0.9 Hz, N(1)H), 7.40–7.43 (2H, m, C(2)H and C(6)H in Ph), 7.31–7.35 (2H, m, C(3)H and C(5)H in Ph), 7.25–7.29 (1H, m, C(4)H in Ph), 5.00 (1H, ddd, $^3J_{7\text{-}H,6\text{-}He}$ = 6.2, $^3J_{7\text{-}H,N(1)H}$ = 6.1, $^3J_{7\text{-}H,6\text{-}Ha}$ = 2.0 Hz, 7-H), 3.99–4.08 (2H, m, $OCH_2$), 3.20 (1H, ddd, $^2J_{6\text{-}He,6\text{-}Ha}$ = 15.1, $^3J_{6\text{-}He,7\text{-}H}$ = 6.2, $^4J_{6\text{-}He,N(1)H}$ = 0.9 Hz, 6-He), 2.69 (1H, ddq, $^2J_{6\text{-}Ha,6\text{-}He}$ = 15.1, $^3J_{6\text{-}Ha,7\text{-}H}$ = 2.0 Hz, $^5J_{6\text{-}Ha,4\text{-}CH3}$ = 1.3 Hz, 6-Ha), 2.19 (3H, d, $^5J_{4\text{-}CH3,6\text{-}Ha}$ = 1.3 Hz, 4-$CH_3$), 1.14 (3H, t, $^3J_{CH3,CH2}$ = 7.1 Hz, $CH_3$ in OEt). $^{13}C$ NMR (150.91 MHz, DMSO-$d_6$) $\delta$: 167.40 (C=O in COOEt), 154.08 (C(2)), 147.29 (C(4)), 133.95 (C(1) in Ph), 131.50 (C(2) and C(6) in Ph), 128.91 (C(3) and C(5) in Ph), 127.00 (C(4) in Ph), 105.12 (C(5)), 61.32 (C(7)), 59.46 ($OCH_2$), 33.87 (C(6)), 20.63 (4-$CH_3$), 14.07 ($CH_3$ in OEt). IR (Nujol) $\nu$, $cm^{-1}$: 3324 (m), 3302 (s), 3235 (br s), 3104 (br s) ($\nu$ NH), 1689 (s) ($\nu$ C=O in COOEt), 1673 (s) (amide-I), 1616 (s) ($\nu$ C=C), 1510 (m) ($\nu$ CC in Ph), 1260 (s), 1094 (s) ($\nu$ C–O), 732 (s), 688 (s) ($\delta$ CH in Ph). Anal. Calcd for $C_{15}H_{18}N_2O_3S$: C, 58.80; H, 5.92; N, 9.14. Found: C, 58.47; H, 5.95; N, 9.11.
7. *Synthesis of ethyl 6-methyl-2-oxo-4-(phenylthiomethyl)-1,2,3,4-tetrahydropyrimidin-5-carboxylate* (**8**)*:* To a stirred suspension of NaH (0.043 g, 1.80 mmol) in MeCN (2 mL) was added a solution of thiophenol (0.596 g, 5.41 mmol) in MeCN (3.2 mL) and the resulting suspension was stirred at room temperature for 22 min. Chloromethylpyrimidine **6** (0.380 g, 1.63 mmol) and MeCN (2.6 mL) were added and the resulting suspension was stirred at room temperature for 72 h 40 min. After the reaction was complete the solvent was removed under vacuum, the oily residue was triturated with light petrol (5 mL) and $H_2O$ (5 mL) under cooling until crystallization was complete. The solid was filtered, washed with ice-cold water, light petrol, and dried to give 0.455 g (91%) of a mixture of **8** and **6** in a ratio of 97:3 (Table 1, entry 9). Crystallization from EtOH afforded pure **8**. Mp 166–168.5 °C (ethanol). $^1H$ NMR (300.13 MHz, DMSO-$d_6$) $\delta$: 9.17 (1H, d, $^4J_{N(1)H,N(3)H}$ = 2.0 Hz, N(1)H), 7.46 (1H, dd, $^3J_{N(3)H,4\text{-}H}$ = 3.6, $^4J_{N(3)H,N(1)H}$ = 2.0 Hz, N(3)H), 7.25–7.37 (4H, m, C(2)H, C(3)H, C(5)H and C(6)H in Ph), 7.13–7.20 (1H, m, C(4)H in Ph), 4.30 (1H, ddd, $^3J_{4\text{-}H,CH(A)}$ = 6.5, $^3J_{4\text{-}H,N(3)H}$ = 3.6, $^3J_{4\text{-}H,CH(B)}$ = 3.6 Hz, 4-H), 3.99 (2H, q, $^3J_{CH2,CH3}$ = 7.1 Hz, $OCH_2$), 3.10 (1H, dd, $^2J_{CH(A),CH(B)}$ = 13.9, $^3J_{CH(A),4\text{-}H}$ = 6.5 Hz, $H_{(A)}$ in $SCH_{(A)}H_{(B)}$), 3.01 (1H, dd, $^2J_{CH(B),CH(A)}$ = 13.9, $^3J_{CH(B),4\text{-}H}$ = 3.6 Hz, $H_{(B)}$ in $SCH_{(A)}H_{(B)}$), 2.08 (3H, s, 6-$CH_3$), 1.11 (3H, t, $^3J_{CH3,CH2}$ = 7.1 Hz, $CH_3$ in OEt). $^{13}C$ NMR (75.48 MHz, DMSO-$d_6$) $\delta$: 165.07 (C=O in COOEt), 152.31 (C(2)), 149.98 (C(6)), 136.27 (C(1) in Ph), 128.90 (C(3) and C(5) in Ph), 128.28 (C(2) and C(6) in Ph), 125.68 (C(4) in Ph), 97.36 (C(5)), 59.22 ($OCH_2$), 49.75 (C(4)), 39.83 ($SCH_2$), 17.83 (6-$CH_3$), 14.15 ($CH_3$ in OEt). IR (Nujol) $\nu$, $cm^{-1}$: 3204 (br s), 3088 (br s) ($\nu$ NH), 1705 (sh) ($\nu$ C=O in COOEt), 1696 (vs) (amide-I), 1637 (s) ($\nu$ C=C), 1580 (m) ($\nu$ CC in Ph), 1227 (vs), 1090 (vs) ($\nu$ C–O), 746 (s), 691 (m) ($\delta$ CH in Ph). Anal. Calcd for $C_{15}H_{18}N_2O_3S$: C, 58.80; H, 5.92; N, 9.14. Found: C, 59.12; H, 6.18; N, 9.15.
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9. *Synthesis of 6-methyl-4-(phenylthiomethyl)-5-tosyl-1,2,3,4-tetrahydropyrimidin-2-one* (**12**)*:* A mixture of **12** and **11** (92:8) (0.366 g, 100%) was prepared (analogously to **8**[7]) from **10**[8] (0.353 g, 0.94 mmol), thiophenol (0.525 g, 4.76 mmol), and NaH (0.028 g, 1.17 mmol) in MeCN (5 mL) (rt, 41 h 26 min). Crystallization from MeCN afforded pure **12**. Mp 221–221.5 °C (dec., MeCN). $^1H$ NMR (300.13 MHz, DMSO-$d_6$) $\delta$: 9.48 (1H, d, $^4J_{N(1)H,N(3)H}$ = 1.9 Hz, $N_{(1)}H$), 7.72 (1H, dd, $^3J_{N(3)H,4\text{-}H}$ = 4.1, $^4J_{N(3)H,N(1)H}$ = 1.9 Hz, N(3)H), 7.61–7.65 (2H, m, C(2)H and C(6)H in Ts), 7.30–7.41 (6H, m, C(3)H and C(5)H in Ts, C(2)H, C(3)H, C(5)H

and C(6)H in Ph), 7.19–7.25 (1H, m, C(4)H in Ph), 4.04 (1H, ddd, $^{3}J_{4\text{-H,CH(A)}}$ = 7.9, $^{3}J_{4\text{-H,N(3)H}}$ = 4.1, $^{3}J_{4\text{-H,CH(B)}}$ = 2.7 Hz, 4-H), 3.16 (1H, dd, $^{2}J_{CH(A),CH(B)}$ = 13.8, $^{3}J_{CH(A),4\text{-H}}$ = 2.7 Hz, $H_{(A)}$ in $SCH_{(A)}H_{(B)}$), 3.11 (1H, dd, $^{2}J_{CH(B),CH(A)}$ = 13.8, $^{3}J_{CH(B),4\text{-H}}$ = 7.9, $H_{(B)}$ in $SCH_{(A)}H_{(B)}$), 2.36 (3H, s, $CH_3$ in Ts), 2.17 (3H, s, 6-$CH_3$). $^{13}$C NMR (75.48 MHz, DMSO-$d_6$) $\delta$: 151.91 (C(2)), 148.89 (C(4)), 143.63 (C(4) in 4-$MeC_6H_4$), 139.67 (C(1) in 4-$MeC_6H_4$), 135.54 (C(1) in Ph), 129.97 (C(3) and C(5) in 4-$MeC_6H_4$), 129.04 (C(3) and C(5) in Ph), 128.71 (C(2) and C(6) in Ph), 126.26 (C(2) and C(6) in 4-$MeC_6H_4$), 125.97 (C(4) in Ph), 105.39 (C(5)), 49.85 (C(4)), 40.39 ($SCH_2$), 21.02 ($CH_3$ in Ts), 16.55 (6-$CH_3$). IR (Nujol) $\nu$, $cm^{-1}$: 3219 (s), 3089 (s), 3058 (m) ($\nu$ NH), 1712 (s) (amide-I), 1646 (s) ($\nu$ C=C), 1595 (m), 1583 (m), 1482 (m) ($\nu$ CC in Ph and $C_6H_4$), 1303 (s) ($\nu_{as}$ $SO_2$), 1152 (s) ($\nu_s$ $SO_2$), 810 (s) ($\delta$ CH in $C_6H_4$), 737 (s) 690 (s) ($\delta$ CH in Ph). Anal. Calcd for $C_{19}H_{20}N_2O_3S_2$: C, 58.74; H, 5.19; N, 7.21. Found: C, 58.87; H, 5.34; N, 7.41.


10. For PhSH, HCN, and $CH_2(COOEt)_2$ the equilibrium acidities ($pK_a$) in DMSO are 10.3,[4,11] 12.9,[11] and 15.9,[12] respectively.
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