Reference Data

Complete Assignment of the ^{13}C NMR Spectra of Diazinyl-Substituted Ureas and Thioureas

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The total assignment of the ^{13}C NMR spectra of novel diazine derived ureas and thioureas is reported.

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INTRODUCTION

The pyridylurea and pyridylthiourea moieties represent essential substructures of a wide variety of bioactive compounds (e.g. analgesic,[1] acetylcholinesterase inhibitory,[2] anticonvulsant,[3] anti-schemic[4] activity). Considering the reported interesting antitumor activity of *N*-[2-(5-picolyl)]-*N'*-(2-methylphenyl)thiourea (5MTUoT)[5] and the antiviral activity of *N*-[2-(2-pyridylethyl)]-*N'*-[2-(5-bromopyridyl)] thiourea (Trovirdine),[6] we prepared compounds of type **1a–e**, **2a–e** and **3a–e** (Fig. 1) as potential diazine bioisosters.[7] Syntheses and biological activities of compounds **1a–e**, **2a–e** and **3a–e** will be published elsewhere.

Here we report the complete ^{13}C NMR chemical shift assignment of these novel urea derivatives (**1a–e**) and thiourea derivatives (**2a–e** and **3a–e**). Compounds **3a–e** have been claimed in a patent,[8] but there are no reports on their syntheses and spectroscopic data.

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RESULTS

The ^{13}C NMR chemical shifts of **1a–e** and **2a–e** are given in Table 1 and for **3a–e** in Table 2. The ^{13}C chemical shift assignments were made on the basis of chemical shift considerations combined with resonance multiplicities obtained from DEPT[9] spectra and by application of heteronuclear correlation experiments (HETCOR[10]). Quaternary carbon atoms C2′/6′ and C1′ in residue R^2 (compounds **1a–e** and **2a–e**) could be easily distinguished owing to the ratio of their ^{13}C signal intensities of 2:1.

EXPERIMENTAL

^{13}C (50 MHz) NMR spectra were recorded on a Varian GEMINI 200 spectrometer in DMSO-d_6 solutions (40–60 mg ml^{-1}) in 5 mm probe tubes at 30 °C with spectral width 13 000 Hz, 64K data points and 2 s interpulse delay. The center of the solvent signal (DMSO-d_6) was used as an internal standard, which was related to TMS with δ 39.5 ppm (^{13}C). Resonance multiplicities for ^{13}C were established via the acquisition of DEPT[9] spectra. For DEPT sequence, the width of the ^{13}C 90° pulse was 11.7 μs and that of the ^{1}H 90° pulse was 13 μs. The 1/(2*J*) delay was set at 2.8 ms for an average direct CH coupling constant of 180 Hz.

The heteronuclear shift correlation spectra were obtained using the standard Varian HETCOR[10] pulse sequence with an acquisition time

Table 1. ^{13}C NMR chemical shifts (δ, ppm, relative to TMS) of compounds 1a–e and 2a–e

Compound	C-2	C-3	C-4	C-5	C-6	C-1′	C-2′/6′	C-3′/5′	C-4′	C=O/S
1a	—	156.2	116.9	128.6	147.0	134.4	135.2	127.7	126.3	152.3
1b	—	144.2	137.7	114.2	151.3	133.9	134.2	127.8	127.2	151.9
1c	158.2	—	158.1	114.8	158.1	134.9	135.0	127.7	126.2	151.9
1d	157.6	—	158.5	108.3	157.2	134.4	135.2	127.8	126.4	151.9
1e	149.8	135.2	—	137.4	141.3	134.6	135.3	127.8	126.4	151.9
2a	—	156.9	118.6	129.8	147.6	136.4	135.3	127.9	127.3	179.9
2b[a]	—	143.9	146.3	114.7	146.1	135.3	135.6	128.0	127.7	179.2
2c	157.7	—	158.3	115.8	158.3	136.8	135.4	127.8	127.2	179.6
2d	156.6	—	158.1	109.0	157.6	136.5	135.2	127.9	127.3	179.9
2e	149.6	136.2	—	137.6	139.5	136.6	135.4	127.8	127.2	179.8

[a] Compound **2b** represents a hydrochloride.

Table 2. ^{13}C NMR chemical shifts (δ, ppm, relative to TMS) of compounds 3a–e

Compound	C-2	C-3	C-4	C-5	C-6	N-CH_2	CH_2	C-2′	C-3′	C-4′	C-5′	C-6′	C=S
3a	—	156.6	118.1	129.3	147.2	44.2	35.9	158.7	123.2	136.5	121.5	149.1	179.3
3b	—	144.6	139.4	114.0	150.4	43.3	35.7	158.6	123.3	136.7	121.6	148.9	180.0
3c	157.4	—	157.9	115.5	157.9	44.2	35.8	158.8	123.4	136.5	121.6	149.1	179.2
3d	156.2	—	158.0	108.7	157.3	44.2	35.7	158.7	123.4	136.6	121.6	149.1	179.5
3e	149.6	136.1	—	137.5	139.5	44.3	36.0	159.0	123.7	137.0	122.0	149.3	179.5

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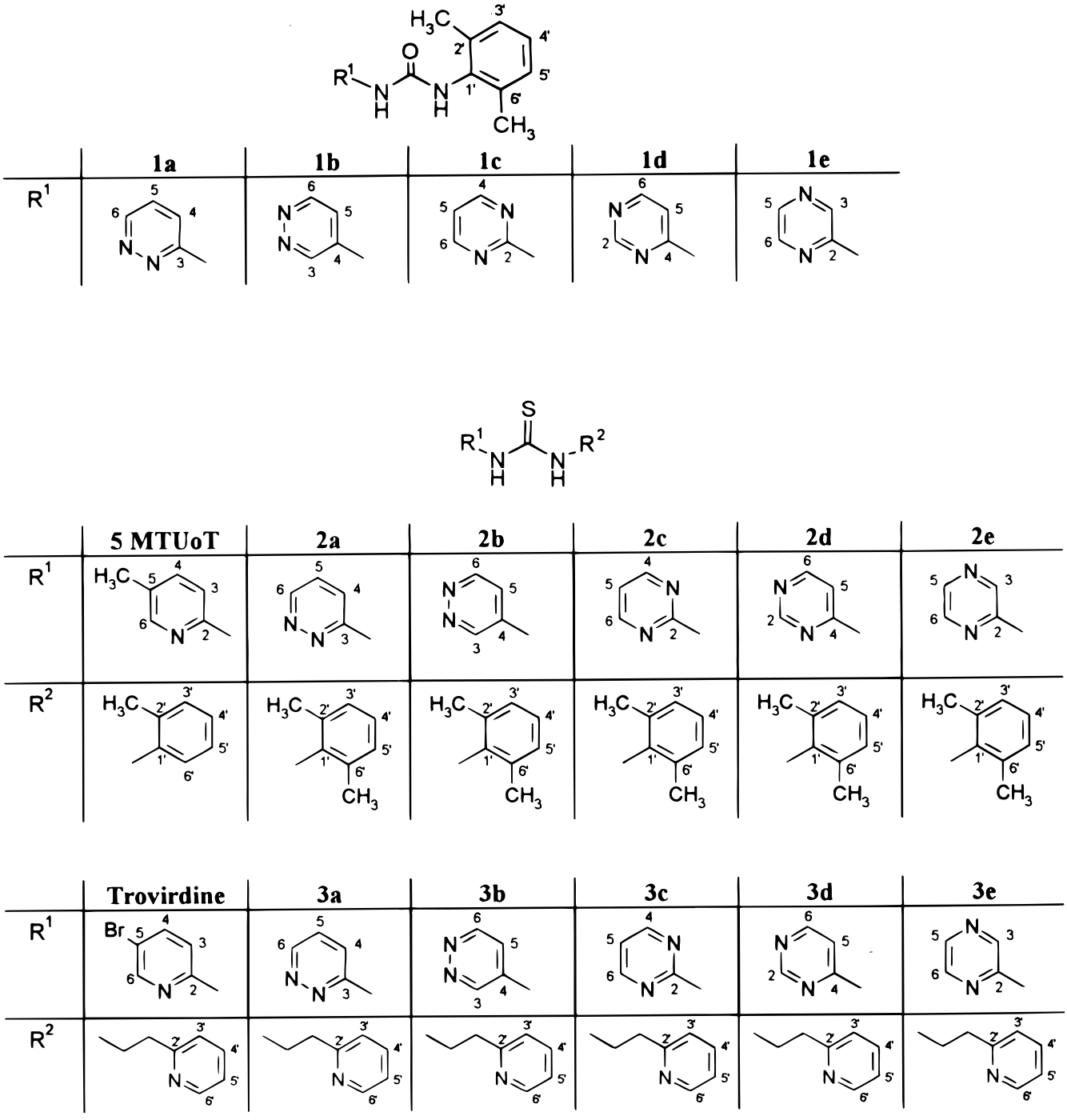

Figure 1. Structures of the compounds studied.

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of 0.078 s, an average $^{1}J_{CH}$ of 180 Hz, 256 increments with 32 transients per increment, a delay of 1.5 s between transients and data processed as a 2048 × 512 matrix using sine-bell functions for weighting and zero-filling in both domains. Spectral widths of 2 and 7 kHz were employed in the F_1 (^{1}H) and F_2 (^{13}C) dimensions, respectively.

References

1. Y. Ohkubo, K. Nomura and I. Yamaguchi, *Eur. J. Pharmacol.* **204**, 121 (1990).
2. J.-L. Vidaluc, F. Calmel, D. Bigg, E. Carilla, A. Stenger, P. Chopin and M. Briley, *J. Med. Chem.* **37**, 689, (1994).
3. M. R. Pavia, S. J. Lobbestael, C. P. Taylor, F. M. Hershenson and D. L. Miskell, *J. Med. Chem.* **33**, 854 (1990).
4. T. Takemoto, M. Eda, T. Okada, H. Sakashita, S. Matzno, M. Gohda, H. Ebisu, N. Nakamura, C. Fukaya, M. Hihara, M. Eiraku, K. Yamanouchi and K. Yokoyama, *J. Med. Chem.* **37**, 18 (1994).
5. I. H. Hall, K. G. Rajendran, D. X. West and A. E. Liberta, *Anti-Cancer Drugs* **4**, 231 (1993).
6. F. B. Bell, A. S. Cantrell, M. Högberg, S. R. Jaskunas, N. G. Johansson, C. L. Jordan, M. D. Kinnick, P. Lind, J. M., Morin Jr., R. Noreen, B. Öberg, J. A. Palkowitz, C. A. Parrish, P. Pranc, C. Sahlberg, R. J. Ternansky, R. T. Vasileff, L. Vrang, S. J. West, H. Zhang and X.-X. Zhou, *J. Med. Chem.* **38**, 4929 (1995).
7. D. Rakowitz, PhD Thesis, University of Innsbruck (1996).
8. P. Lind, J. M. Morin, Jr. R. Noreen and R. J. Ternansky, *PCT Int. Appl.* WO 93 03 022 (1993); *Chem. Abstr.* **119**, 160110q (1993).
9. D. M. Doddrell, D. T. Pegg and M. R. Bendall, *J. Magn. Reson.* **48**, 323 (1982).
10. (a) A. Bax and G. A. Morris, *J. Magn. Reson.* **42**, 501 (1981); (b) A. Bax, *J. Magn. Reson.* **53**, 512 (1983).