ISSN 1070-4280, Russian Journal of Organic Chemistry, 2015, Vol. 51, No. 1, pp. 139–140. © Pleiades Publishing, Ltd., 2015.
Original Russian Text © S.A. Meshcheryakova, 2015, published in Zhurnal Organicheskoi Khimii, 2015, Vol. 51, No. 1, pp. 140–141.

SHORT COMMUNICATIONS

Reaction of Thietane-Containing 2-(6-Methyl-2,4-dioxo-1,2,3,4-tetrahydropyrimidin-3-yl)-acetohydrazides with *N*-Phenylmaleimide

S. A. Meshcheryakova

Bashkir State Medical University, ul. Lenina 3, Ufa, 450000 Bashkortostan, Russia
e-mail: SvetlanaMA@mail.ru

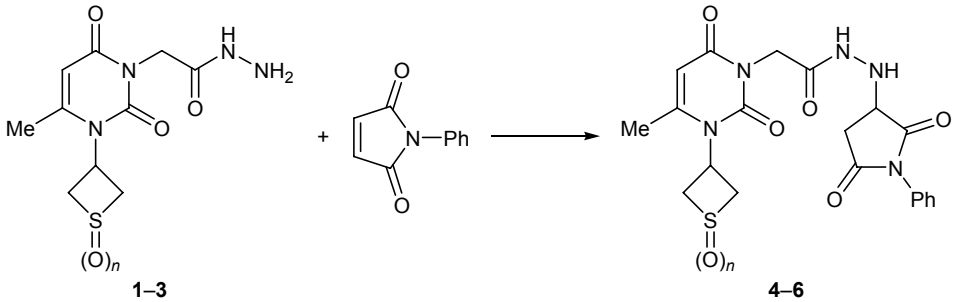
Received May 30, 2014

DOI: 10.1134/S1070428015010285

Heterocyclic carboxylic acid hydrazides are promising building blocks in fine organic synthesis. We previously studied reactions of 2-[6-methyl-2,4-dioxo-1-(thietan-3-yl)-1,2,3,4-tetrahydropyrimidin-3-yl]-acetohydrazide (**1**) with β-dicarbonyl compounds [1] and its condensations with aromatic aldehydes and ketones [2]. Some newly synthesized derivatives of hydrazide **1** were found to exhibit hypotensive [2] and antioxidant activity [3]. In continuation of studies of the reactivity of acetohydrazides containing thietanyl-, 1-oxothietanyl-, and 1,1-dioxothietanylpyrimidine fragments, the present communication reports on their reaction with *N*-phenylmaleimide.

Reactions of hydrazides with maleimides were studied only for aromatic carboxylic acid hydrazides [4]. Despite reduced basicity (pK_a 2.5–3.7), aromatic carboxylic acid hydrazides readily add to the double bond of maleimides on heating in boiling propan-2-ol for 1 h, which is related to the α-effect in hydrazine derivatives. Heating of acetohydrazides **1**–**3** with an equimolar amount of *N*-phenylmaleimide in boiling ethanol for 5 h also led to the formation of the corresponding addition products, hydrazinylsuccinimides **4**–**6**. The ^{1}H NMR spectra of **4**–**6** in DMSO-d_6 confirmed the formation of succinimide ring. Diastereotopic methylene protons resonated as a doublet of doublets at δ 2.68–2.71 ppm and a multiplet at δ 2.96–3.03 ppm (1H each), and the 3-H proton on the asymmetric carbon atom gave a multiplet signal at δ 4.12–4.21 ppm [4].

The NH protons of the hydrazide fragment were represented by a multiplet at δ 5.81–5.89 ppm and two doublets at δ 9.13–9.15 and 9.84–9.85 ppm. The presence of two sets of signals in the ^{1}H NMR spectra of **4**–**6** indicated that these compounds exist as mixtures of conformational *E* and *Z* isomers due to restricted rotation about the C–N hydrazide bond. The 6-CH_3 and 5-H signals of the pyrimidine fragment and the CONH signal of the *Z* conformer were displaced downfield relative to the corresponding signals of the *E* conformer [1]. The CH_2CO proton signal was also doubled, but the signal from the *Z* isomer was a singlet located upfield from the two asymmetric doublets (^2J = 17.8 Hz, *AB*) belonging to the *E* isomer



1, **4**, *n* = 0; **2**, **5**, *n* = 1; **3**, **6**, *n* = 2.

of **4** and **5**. The corresponding signal of the *E* isomer of **6** was overlapped by the pseudotriplet of the $(CH_2)_2SO_2$ protons in the 1,1-dioxothietane ring. It should be noted that compound **5** displayed in the ^{1}H NMR spectrum only one set of signals from protons in the thietane ring; their position suggests *cis* configuration of the 1-oxothietan-3-yl fragment [5].

Hydrazide **1** was synthesized according to the procedures reported in [1, 6], and hydrazides **2** and **3** were prepared as described in [1, 5].

***N′*-(2,5-Dioxo-1-phenylpyrrolidin-3-yl)-2-[6-methyl-2,4-dioxo-1-(thietan-3-yl)-1,2,3,4-tetrahydropyrimidin-3-yl]acetohydrazide (4).** *N*-Phenylmaleimide, 0.35 g (2 mmol), was added to a solution of 0.54 g (2 mmol) of hydrazide **1** in 20 mL of ethanol, and the mixture was heated for 5 h under reflux. The mixture was cooled, and the precipitate was filtered off, washed with ethanol, and dried. Yield 0.59 g (67%), white crystals, mp 201–203°C (from *i*-BuOH), R_f 0.56 (EtOH). ^{1}H NMR spectrum, δ, ppm: 2.04 s (3H, 6-CH_3, *E*), 2.15 s (3H, 6-CH_3, *Z*), 2.70 d.d (1H, 4′-H, *J* = 18.0, 3.8 Hz), 2.97–3.02 m (1H, 4′-H), 3.05–3.11 m (2H, CH_2S), 4.15–4.21 m (3H, 3′-H, CH_2S), 4.47 s (2H, 3-CH_2, *Z*), 4.76 d and 4.88 d (1H each, 3-CH_2, *J* = 17.8 Hz), 5.63 s (1H, 5-H, *E*), 5.66 s (1H, 5-H, *Z*), 5.82–5.87 m (1H, NH), 6.02–6.08 m (1H, NCH), 7.27–7.32 m (2H, H_{arom}), 7.41–7.50 m (3H, H_{arom}), 9.13 d (1H, NH, *J* = 5.1 Hz, *E*), 9.85 d (1H, NH, *J* = 5.1 Hz, *Z*). *Z*/*E* ratio 75:25. Found, %: C 54.06; H 4.63; N 16.00. $C_{20}H_{21}N_5O_5S$. Calculated, %: C 54.17; H 4.77; N 15.79.

Compounds **5** and **6** were synthesized in a similar way.

***N′*-(2,5-Dioxo-1-phenylpyrrolidin-3-yl)-2-[6-methyl-2,4-dioxo-1-(1-oxo-λ^4-thietan-3-yl)-1,2,3,4-tetrahydropyrimidin-3-yl]acetohydrazide (5).** Yield 0.58 g (63%), light yellow crystals, mp 170°C (decomp., from *i*-PrOH), R_f 0.25 (EtOH). ^{1}H NMR spectrum, δ, ppm: 2.07 s (3H, 6-CH_3, *E*), 2.18 s (3H, 6-CH_3, *Z*), 2.71 d.d (1H, 4′-H, *J* = 18.0, 3.8 Hz), 2.96–3.03 m (1H, 4′-H), 3.35–3.41 m and 3.89–3.97 m (2H each, CH_2S), 4.12–4.19 m (1H, 3′-H), 4.48 s (2H, 3-CH_2, *Z*), 4.75 d and 4.87 d (1H each, 3-CH_2, *J* = 17.8 Hz, *Z*), 5.68 s (1H, 5-H, *E*), 5.72 s (1H, 5-H, *Z*), 5.81–5.86 m (1H, NH), 6.21–6.27 m (1H, NCH), 7.25–7.28 m (2H, H_{arom}), 7.42–7.50 m (3H, H_{arom}), 9.14 d (1H, NH, *J* = 5.2 Hz, *E*), 9.84 d (1H, NH, *J* = 5.2 Hz, *Z*). *Z*/*E* ratio 67:33. Found, %: C 52.37; H 4.78; N 15.13. $C_{20}H_{21}N_5O_6S$. Calculated, %: C 52.28; H 4.61; N 15.24.

***N′*-(2,5-Dioxo-1-phenylpyrrolidin-3-yl)-2-[1-(1,1-dioxo-λ^6-thietan-3-yl)-6-methyl-2,4-dioxo-1,2,3,4-tetrahydropyrimidin-3-yl]acetohydrazide (6).** Yield 0.48 g (51%), white crystals, mp 197–198°C (from H_2O), R_f 0.29 (acetone–acetonitrile). ^{1}H NMR spectrum, δ, ppm: 2.07 s (3H, 6-CH_3, *E*), 2.19 s (3H, 6-CH_3, *Z*), 2.68 d.d (1H, 4′-H, *J* = 17.9, 4.5 Hz), 2.97–3.03 m (1H, 4′-H), 4.15–4.19 m (1H, 3′-H), 4.27–4.36 m (2H, CH_2S), 4.50 s (1.5H, 3-CH_2, *Z*), 4.83–4.91 m (2.5H, CH_2S, 3-CH_2, *E*), 5.63–5.69 m (1H, NCH), 5.72 s (1H, 5-H, *E*), 5.75 s (1H, 5-H, *Z*), 5.82–5.89 m (1H, NH), 7.25–7.30 m (2H, H_{arom}), 7.41–7.49 m (3H, H_{arom}), 9.15 d (1H, NH, *J* = 5.1 Hz, *E*), 9.84 d (1H, NH, *J* = 5.1 Hz, *Z*). *Z*/*E* ratio 76:24. Found, %: C 50.36; H 4.61; N 14.81. $C_{20}H_{21}N_5O_7S$. Calculated, %: C 50.52; H 4.45; N 14.73.

The ^{1}H NMR spectra were recorded on a Bruker AMX-300 spectrometer at 300 MHz using DMSO-d_6 as solvent and reference. Analytical TLC was performed on Sorbfil plates; elution with ethanol or acetone–acetonitrile (1:1); development under UV light or by treatment with iodine vapor.

REFERENCES

1. Meshcheryakova, S.A. and Kataev, V.A., *Russ J. Org. Chem*. 2014, vol. 50, p. 711.
2. Meshcheryakova, S.A., Kataev, V.A., Nikolaeva, K.V., Perfilova, V.N., Borodin, D.D., and Tyurenkov, I.N., *Russ J. Bioorg. Chem*., 2014, vol. 40, p. 300.
3. Petrova, I.V., Kataev, V.A., Meshcheryakova, S.A., Nikolaeva, K.V., Munasipova, D.A., and Farkhutdinov, R.R., *Med. Vestn. Bashkort*., 2013, vol. 8, no. 4, p. 64.
4. Orlov, M.A. and Korotkikh, N.I., *Zh. Org. Farm. Khim*., 2009, vol. 7, p. 64.
5. Meshcheryakova, S.A., Kataev, V.A., Munasipova, D.A., and Fattakhova, I.Ya., *Russ J. Gen. Chem*., 2014, vol. 84, p. 865.
6. Kataev, V.A., Meshcheryakova, S.A., Lazarev, V.V., and Kuznetsov, V.V., *Russ J. Org. Chem*., 2013, vol. 49, p. 743.