Chemistry of Heterocyclic Compounds, Vol. 42, No. 5, 2006

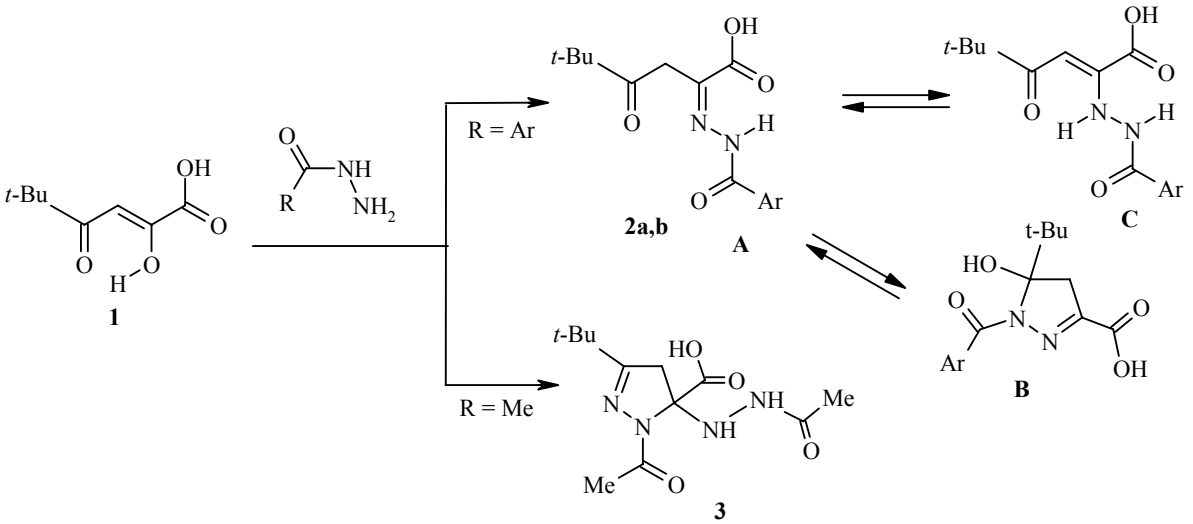
LETTERS TO THE EDITOR

REACTIONS OF PIVALOYLPYROTARTARIC ACIDS WITH ACYLHYDRAZINES IN THE SYNTHESIS OF PYRAZOLINCARBOXYLIC ACIDS

V. O. Kozminykh[1], V. I. Goncharov[2], E. N. Kozminykh[3], and D. B. Oborin[1]

Keywords: 1-aroyl-5-*tert*-butyl-5-hydroxy-4,5-dihydro-1H-pyrazolyl-3-carboxylic acids, 1-acetyl-5-(2-acetylhydrazino)-3-*tert*-butyl-4,5-dihydro-1H-pyrazol-5-carboxylic acid, pivaloylpyrotartaric acid, reactions with acylhydrazines.

It is known that (het)aroylpyrotartaric acids, their esters and amides react with hydrazines to give derivatives of 5-(het)aryl-1H-pyrazol-3-carboxylic acid [1,2]. As the result of the reaction of pivaloylpyrotartaric acid **1** (2-hydroxy-5,5-dimethyl-4-oxo-2-hexenoic acid) the hydrazides of aromatic carboxylic acids under mild conditions we have obtained 2-aroylhydrazono-5,5-dimethyl-4-oxohexanoic acids (**2a,b**, hydrazone form **A**) in preparative yields, together with in solution the minor pyrazoline tautomer – 1-aroyl-5-*tert*-butyl-5-hydroxy-4,5-dihydro-1H-pyrazol-3-carboxylic acids (form **B**). The structures of the latter are in excellent agreement with those of 5-aryl-5-hydroxy-2-pyrazolin-3-carboxamides obtained previously [3].



2 a Ar = 4-MeC_6H_4, **b** Ar = 4-$MeOC_6H_4$

[1] Perm State Pedagogical University, Perm 614990, Russia; e-mail: kvo@perm.ru. [2] Stavropol State Medicinal University, Stavropol 355023, Russia. [3] Moscow Technological and Business State University, Perm Branch, Perm 614065, Russia; e-mail: kvonstu@yahoo.com. Translated from Khimiya Geterotsiklicheskikh Soedinenii, No. 5, 792-794, May, 2006. Original article submitted February 16, 2006.

Apart from the equilibrium structures **A** and **B**, a small amount (up to 7%) of the cyclic enhydrazino-forms of 2-(2-aroylhydrazino)-5,5-dimethyl-4-oxohexenoic acids (**C**) was observed in solutions of compounds **2a,b**. We note that only the NH-chelated form **C**, stabilised by intramolecular hydrogen bonds of the type >N–H···O=C< , occurred in crystals of compounds **2a,b** (absorption bands of pivaloyl and carboxyl carbonyl groups are found in the low frequency region – not above 1698 cm^{-1} – of their IR spectra).

From the reaction of acetylhydrazine with acid **1** we unexpectedly isolated the previously unknown stable cyclic product of the addition of two molecules of the reagent to the α- and γ-carbonyl groups of the substrate **1** – 1-acetyl-5-(2-acetylhydrazino)-3-*tert*-butyl-4,5-dihydro-1H-pyrazol-5-carboxylic acid (**3**).

^{1}H NMR spectra of DMSO-d_6 solutions with TMS as internal standard were recorded on a Bruker AM-300 (300 MHz) instrument, IR spectra of nujol films were recorded with Specord M-80 spectrometer, and mass spectra were obtained with Finnigan MAT INCOS 50 machine.

Reaction of Pivaloylpyrotartaric Acid (1) with Carboxylic Acid Hydrazides. A solution of the hydrazide of *p*-toluic acid (0.75 g, 5 mmol) or the hydrazide of anisic acid (0.83 g, 5 mmol) or of acetic acid hydrazide (0.37 g, 5 mmol) in ethanol (10-15 ml) was added to a solution of pivaloylpyrotartaric acid (**1**) [4] (0.86 g, 5 mmol) in ethanol (10 ml) and the mixture was boiled for 5 min. The precipitate of acids **2a,b** or **3** was filtered off an recrystallized from ethyl acetate or benzene.

2-(4-Methylbenzoyl)hydrazono-5,5-dimethyl-4-oxohexanoic Acid (2a). Yield 1.20 g (79%); mp 182-183°C (benzene). IR spectrum, ν, cm^{-1}: 3187 (NH_{amide}), 1698 (CO_{amide}, $CO_{carboxyl}$), 1638, 1605 ($NH_{chelate}$). ^{1}HNMR apectrum, δ, ppm (*J*, Hz): 1.06 (9H, s, 3 CH_3 in *t*-Bu, pyrazoline form **B**); 1.15 (9H, s, 3CH_3 in *t*-Bu in ring tautomers **A** and **C**); 2.23 (3H, s, CH_3, form **B**); 2.26 (3H, s, CH_3, forms **A** and **C**); 3.02, 3.38 (2H, two d, *J* = 15.0, $C_{(4)}H_2$, form **B**, 15%); 4.08 (2H, s, $C_{(3)}H_2$, form **A**, 78%); 5.74 (1H, s, $C_{(3)}H$, form **C**, 7%); 7.10-7.22, 7.70-7.95 (4H, m, C_6H_4, forms **A**, **B**, and **C**); 11.15 (1H, s, NH, form **A**); 13.35 (1H, br. s, OH in COOH, form **A**). Mass spectrum, *m/z* (I_{rel} %): 305 (2) $[M + 1]^+$, 304 (10) $[M]^+$, 286 (2) $[M - H_2O]^+$, 260 (6), 259 (37) $[M - CO_2 - H]^+$, 247 (8), $[M - (CH_3)_3C]^+$, 220 (4), 202 (2), 175 (5) $[M - CO_2 - (CH_3)_3C\text{-}CO]$, 153 (2), 129 (10), 120 (9), 119 (100) $[4\text{-}CH_3C_6H_4\text{-}C{\equiv}O]^+$, 102 (3), 92 (3), 91 (36) $[CH_3C_6H_4]^+$, 65 (4), 57 (30) $[(CH_3)_3C]^+$, 41 (9). Found, %: C 63.31; H 6.49; N 9.02. $C_{16}H_{20}N_2O_4$. Calculated, %: C 63.14; H 6.62; N 9.20.

5,5-Dimethyl-2-(4-methoxybenzoyl)hydrazono-4-oxohexanoic Acid (2b). Yield 1.40 g (87%); mp 159-160°C (ethyl acetate). IR spectrum, ν, cm^{-1}: 3195 (NH_{amide}), 1692 (CO_{amide}, $CO_{carboxyl}$), 1623, 1604 ($NH_{chelate}$). ^{1}HNMR spectrum, δ, ppm (*J*, Hz): 1.08 (9H, s, 3 CH_3 in *t*-Bu, pyrazoline form **B**); 1.17 (9H, s, 3CH_3 in *t*-Bu in forms **A** and **C**); 2.91, 3.42 (2H, two d, *J* = 15.2, $C_{(4)}H_2$, form **B**, 9% (for comparison, in the spectrum of the *p*-methoxyphenylamide of 5-hydroxy-5-phenyl-4,5-dihydro-1H-pyrazolo-3-carboxylic acid, these signals are found at 3.12 and 3.60, *J* = 15.0 [3]); 3.82 (3H, s OCH_3, form **B**); 3.84 (3H, s, OCH_3, forms **A** and **C**); 4.11 (2H, s, $C_{(3)}H_2$, form **A**, 88%); 5.69 (1H, s, $C_{(3)}H$, form **C**, 3%); 7.06-7.12, 7.66-7.87 (4H, m, C_6H_4, forms **A**, **B**, and **C**); 11.03 (1H, s, NH, form **A**); 13.50 (1H, br. s, OH in COOH, form **A**). Found, %: C 60.35; H 6.48; N 8.57. $C_{16}H_{20}N_2O_3$. Calculated, %: C 59.99; H 6.29; N 8.74.

1-Acetyl-5-(2-acetylhydrazino)-3-*tert*-butyl-4,5-dihydro-1H-pyrazol-5-carbonic Acid (3). Yield 0.45 g (63%); mp 154-155°C (ethyl acetate). IR spectrum (nujol mull, Specord M-80), ν, cm^{-1}: 3185 (NH_{amide}), 1680 (CO_{amide}, $CO_{carboxyl}$), 1615 (NH_{chel}). ^{1}H NMR spectrum (Bruker AM-300, 300 MHz, TMS, DMSO-d_6), δ, ppm : 1.16 (9H, s, 3CH_3 in *t* -Bu); 1.72 (3H, s, CH_3 in $N_{(2')}HCOCH_3$); 2.11 (3H, s, CH_3 in $N_{(1)}COCH_3$); 3.10 (2H, s, $C_{(4)}H_2$); 8.99 (1H, s, $N_{(2')}H$). Mass spectrum (Finnigan MAT INCOS 50), *m/z*, (I_{rel}, %): 239 $[M - CO_2 - H]^+$ (9), 238 (3), 227 $[M - (CH_3)_3C]^+$ (1), 212 (4), 211 $[M - CH_3CONH\text{-}NH]^+$ (32), 197 $[M - CO_2 - CH_3CO]^+$ (2), 181 $[M - CO_2 - H - CH_3CONH]^+$ (2) or $[M - (CH_3)_3C - CO_2 - 2H]^+$, 170 (3), 169 $[M - CH_3CONH\text{-}NH\text{-}CH_2CO]^+$ (36), 153 (4), 151 $[C_8H_{11}N_2O]^+$ (17), 140 (4), 139 $[M - (CH_3)_3C - CO_2 - H - CH_3CO]^+$ (9) or $[C_7H_{11}N_2O]^+$, 125 (3), 124 $[M - CH_3CONH\text{-}NH\text{-}CH_2CO - CO_2 - H]^+$ (7) or [3-*t* -butylpyrazole = $C_7H_{11}N_2]^+$, 113 $[C_4H_5N_2O_2]^+$ (21), 95 $[M - (CH_3)_3C - CO_2 - 2H - 2CH_3CO]^+$ (12), or $[C_4H_3N_2O]^+$, 77 (6), 67 [3-pyrazolyl = $C_3H_3N_2]^+$ (7), 57 $[(CH_3)_3C]^+$ (68), 55 (6), 53 (5), 45 (7), 43 $[CH_3CO]^+$ (100). Found, %: C 50.38; H 6.89; N 19.60. $C_{12}H_{20}N_4O_4$. Calculated, %: C 50.69; H 7.09; N 19.71.

REFERENCES

1. S. G. Perevalov, Ya. V. Burgart, V. I. Saloutin, and O. N. Chupakhin, *Uspekhi Khimii*, **70**, 1039 (2001).
2. V. O. Koz'minykh and E. N. Koz'minykh, *Selected Methods for the Synthesis and Modification of Heterocycles* [in Russian], ed. V. G. Kartsev, IBS PRESS, Moscow, **1**, 255 (2003).
3. V. O. Koz'minykh, N. M. Igidov, E. S. Berezina, E. N. Koz'minykh, and Yu. S. Kasatkina, *Izv. Akad Nauk, Ser. Khim.,* 1564 (2000).