Chemistry of Heterocyclic Compounds, Vol. 41, No. 7, 2005

REACTION OF 3-ACETYL-4,6,6-TRIMETHYL-5,6-DIHYDRO-2-PYRONE WITH CARBOXYLIC ACID HYDRAZIDES

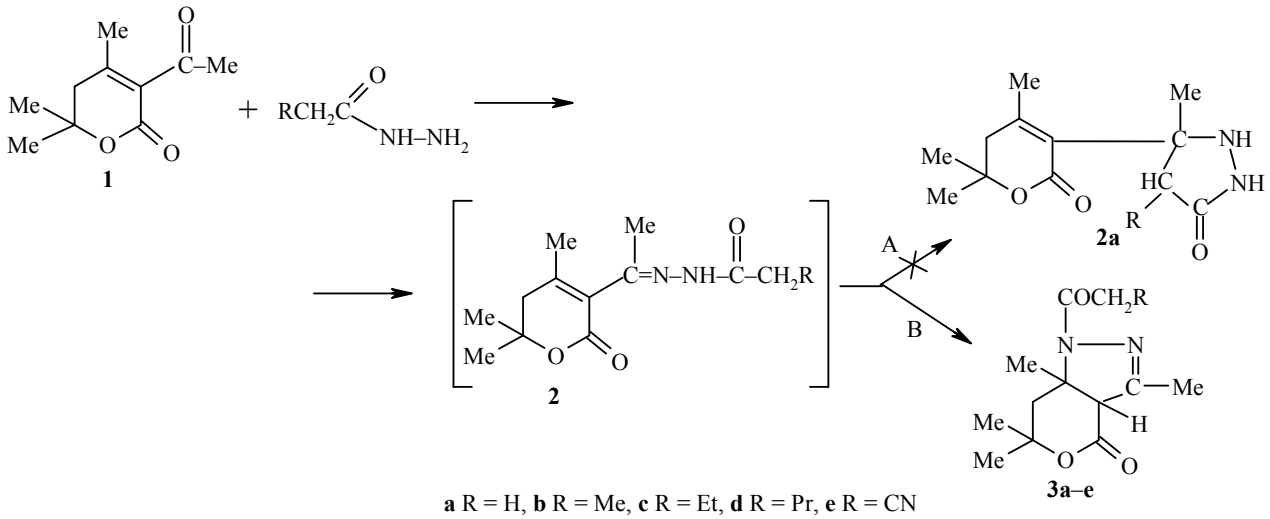
A. A. Avetissian, G. G. Tokmajian, and L. V. Karapetian

The reaction of 3-acetyl-4,6,6-trimethyl-5,6-dihydro-2-pyrone with the hydrazides of a series of carboxylic acids led to the synthesis of 5-alkyl(cyanomethyl)carbonyl-3,5a,7,7-tetramethylpyrazolino-[4,5-c]tetrahydro-2-pyrones, which are the products from cyclization of the intermediately formed alkyl(cyanomethyl)hydrazones of 3-acetyl-4,6,6-trimethyl-5,6-dihydro-2-pyran.

Keywords: 3-acetyl-4,6,6-trimethyl-5,6-dihydro-2-pyrone, hydrazides, hydrazones, 5-alkyl(cyanomethyl)-carbonyl-3,5a,7,7-tetramethylpyrazolino[4,5-*c*]tetrahydro-2-pyrones, cyclization.

In a continuation of researches into the reactions of the hydrazides of carboxylic acids with compounds containing a carbonyl group [1-3] we studied the reaction of 3-acetyl-4,6,6-trimethyl-5,6-dihydro-2-pyrone (**1**) with the hydrazides of a series of carboxylic acids (acetic, propionic, butyric, valeric, and cyanoacetic).

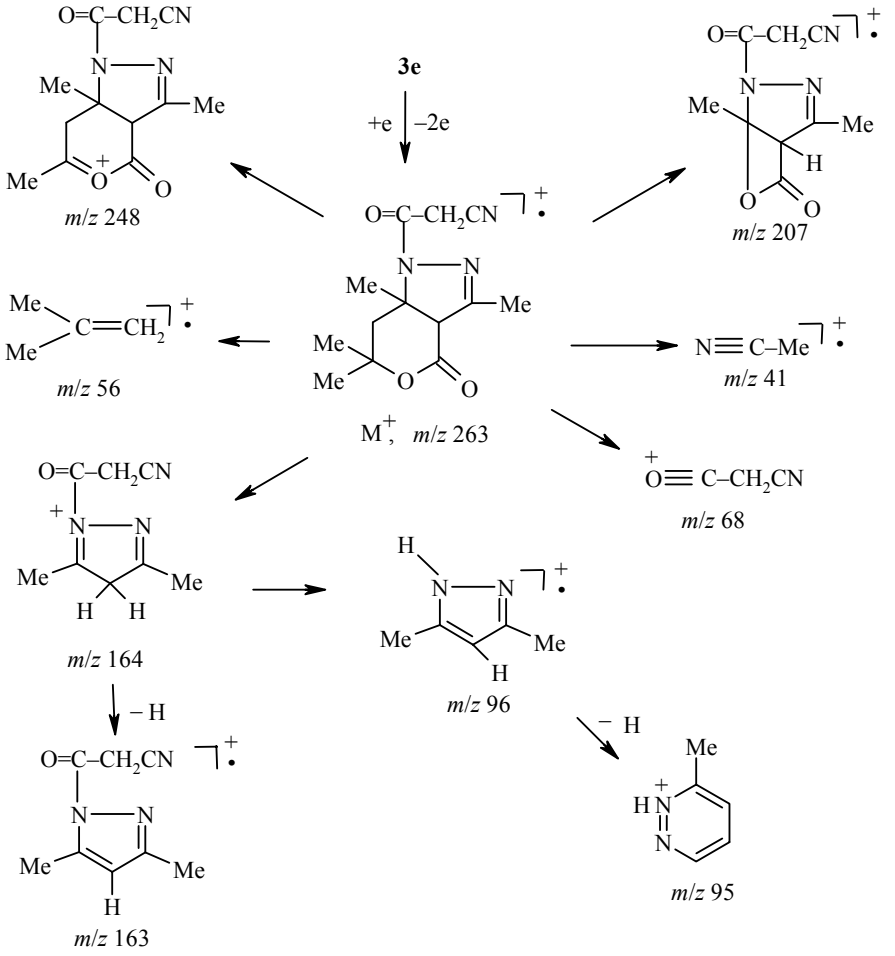
The reaction was conducted by boiling equimolar amounts of the initial components in absolute ethanol for 10-12 h and led to the production of crystalline compounds with good yields (64-71%). It was assumed that both linear products of the initial reaction, i.e., the alkyl(cyano)acetylhydrazones of 3-acetyl-4,6,6-trimethyl-5,6-dihydro-2-pyrone (**2**), and the products from their intramolecular cyclization [which can take place in two directions (A and B)], can be formed.



a R = H, **b** R = Me, **c** R = Et, **d** R = Pr, **e** R = CN

Erevan State University, Erevan 375025, Republic of Armenia; e-mail: kimiakan@sun.ysu.am.
Translated from Khimiya Geterotsiklicheskikh Soedinenii, No. 7, pp. 998-1001, July, 2005. Original article submitted January 25, 2003.

According to the ^{1}H and ^{13}C NMR and IR spectra, the compounds that we obtained are the products from cyclization of the hydrazones **2**, taking place by path B and leading to the condensed heterocyclic system 5-alkyl(cyanomethyl)carbonyl-3,5a,7,7-tetramethylpyrazolino[4,5-*c*]tetrahydro-2-pyrones **3a-e**. In the ^{1}H NMR spectra this is confirmed by the absence of signals for the protons of the NH group and also by the presence of a signal for the proton of the methine group (–CH–) in the region of 3.75-3.95 ppm, depending on the specific compound, and signals of the CH_3 group at the saturated carbon atom (1.0-1.25 ppm).



The mass spectrum was recorded for compound **3e**. It contains a strong peak for the molecular ion, and the nature of its fragmentation confirms the bicyclic **3e** (and not linear **2** or binuclear **2a**) structure of the compound.

Thus, analysis of the EI mass spectra together with the data from the IR and ^{1}H and ^{13}C NMR spectra demonstrates conclusively the structure of the synthesized systems.

EXPERIMENTAL

The IR spectra were recorded on a Specord IR-75 spectrometer in vaseline oil. The ^{1}H and ^{13}C NMR spectra were recorded on a Varian Mercury 300 spectrometer (300 and 75 MHz respectively) with TMS as internal standard. The EI mass spectrum (direct injection) was obtained on an MX-1321A instrument at 50 eV. The purity of the synthesized compounds was monitored by TLC on Silufol plates in the 1:2 acetone–benzene system with development in iodine vapor.

TABLE 1. The Spectra of Compounds **3a-e**

Compound	IR spectrum, ν, cm^{-1}	^1H NMR spectrum (DMSO-d_6), δ, ppm
3a	1120, 1170 (C–O–C), 1625 (C=N), 1640 (C=O), 1710 (C=O lactone)	1.25 (3H, s, CH_3); 1.4 and 1.5 (6H, s, $2CH_3$); 1.9 (1H, d, *J* = 15.2, CH_2); 2.0 (6H, s, $\underline{CH_3}C=N$, $\underline{CH_3}CO$); 3.1 (1H, d, *J* = 15.2, CH_2); 3.75 (1H, s, CH)
3b	1120, 1160 (C–O–C), 1620 (C=N), 1645 (C=O), 1710 (C=O lactone)	1.1 (3H, t, *J* = 7.5, $\underline{CH_3}CH_2CO$); 1.2 (3H, s, CH_3); 1.4 and 1.5 (6H, s, $2CH_3$); 1.9 (1H, d, *J* = 15.2, CH_2); 2.15 (H, s, $\underline{CH_3}C=N$); 2.55 (2H, q, *J* = 7.5, $CH_3\underline{CH_2}CO$); 3.05 (1H, d, *J* = 15.2, CH_2); 3.75 (1H, s, CH)
3c	1120, 1160 (C–O–C), 1625 (C=N), 1645 (C=O), 1710 (C=O lactone)	0.95 (3H, t, *J* = 7.5, $\underline{CH_3}(CH_2)_2CO$); 1.2 (3H, s, CH_3); 1.4 and 1.5 (6H, s, $2CH_3$); 1.6-1.75 (2H, m, $CH_3\underline{CH_2}CH_2CO$); 2.1 (1H, d, *J* = 15.2, CH_2); 2.2 (3H, s, $\underline{CH_3}C=N$); 2.5 (2H, t, *J* = 7.5, $CH_3CH_2\underline{CH_2}CO$); 3.1 (1H, d, *J* = 15.2, CH_2); 3.8 (1H, s, CH)
3d	1120, 1160 (C–O–C), 1620 (C=N), 1645 (C=O), 1710 (C=O lactone)	0.9 (3H, t, *J* = 7.5, $\underline{CH_3}(CH_2)_3CO$); 1.0 (3H, s, CH_3); 1.4 and 1.5 (6H, s, $2CH_3$); 1.6-1.8 (4H, m, $CH_3(\underline{CH_2})_2CH_2CO$); 2.1 (1H, d, *J* = 15.2, CH_2); 2.25 (3H, s, $\underline{CH_3}C=N$); 2.55 (2H, t, *J* = 7.5, $CH_3(CH_2)_2\underline{CH_2}CO$); 3.1 (1H, d, *J* = 15.2, CH_2); 3.9 (1H, s, CH)
3e	1120, 1160 (C–O–C), 1620 (C=N), 1645 (C=O), 1710 (C=O lactone)	1.25 (3H, s, CH_3); 1.42 and 1.55 (6H, s, $2CH_3$); 2.05 (1H, d, *J* = 15.3, CH_2); 2.2 (3H, s, $\underline{CH_3}C=N$); 2.9 (1H, d, *J* = 15.3, CH_2); 3.8 (2H, s, CH_2CN); 3.95 (1H, s, CH)

TABLE 2. The ^{13}C NMR Spectra of compounds **3b**,**e**

Compound	Chemical shifts (DMSO-d_6/CCl_4, 1:3), δ, ppm*									
	CH_3	$CH_3C=N$	CH_2	CH	N–C	O–C	C=N	C=O	CH_2	R
3a	25.52, 26.17, 29.91	14.57	38.33	59.44	62.67	80.57	149.16	163.91, 170.08	27.25	8.43
3e	25.62, 25.76, 25.81	14.71	38.25	59.49	63.40	80.56	152.66	158.84, 163.63	27.25	113.82

* The signals were assigned on the basis of the two-dimensional correlation ^1H–^{13}C NMR spectra by the HMQC method.

TABLE 3. The Physicochemical Characteristics of Compounds **3a-e**

Compound	Empirical formula	Found, % / Calculated, %				mp, °C	R_f	Yield, %
		C	H	N	O			
3a	$C_{12}H_{18}N_2O_3$	60.65 / 60.50	7.45 / 7.56	11.80 / 11.76	20.10 / 20.17	126	0.42	70
3b	$C_{13}H_{20}N_2O_3$	62.10 / 61.90	7.85 / 7.94	11.00 / 11.11	19.35 / 19.05	136	0.44	71
3c	$C_{14}H_{22}N_2O_3$	63.48 / 63.16	8.10 / 8.27	10.85 / 10.53	17.56 / 18.04	161	0.45	67
3d	$C_{15}H_{24}N_2O_3$	64.33 / 64.28	8.68 / 8.57	10.12 / 10.00	16.97 / 17.14	152	0.49	64
3e	$C_{13}H_{17}N_3O_3$	59.35 / 59.32	6.41 / 6.46	15.99 / 15.97	18.34 / 18.25	122	0.45	68

3-Acetyl-4,6,6-trimethyl-5,6-dihydro-2-pyrone (1). The compound was synthesized by the familiar method [4], and the carboxylic acid hydrazides were obtained by reaction of the ethyl esters of the respective acids with hydrazine hydrate by the methods in [5, 6].

Compounds 3a-e. A mixture of the pyrone **1** (0.45 g, 2.5 mmol), the carboxylic acid hydrazide (2.5 mmol), and absolute ethanol (8 ml) was boiled with a reflux condenser for 10-12 h. After distillation of part of the solvent the crystals that separated were filtered off, washed with ether, recrystallized from alcohol, and dried in air.

Mass spectrum* of compound **3e**, *m/z* (I_{rel}, %): 263 (55), 248 (15), 207 (11), 164 (60), 163 (39), 140 (12), 135 (38), 121 (14), 109 (13), 97 (37), 96 (100), 95 (47), 94 (14), 68 (21), 57 (10), 56 (58), 55 (22), 41 (20), 39(14).

The physicochemical characteristics and the data from the IR and NMR spectra are given in Tables 1-3.

REFERENCES

1. A. A. Avetisyan, A. A. Kagramanyan, Sh. A. Markaryan, and G. S. Melikyan, *Arm. Khim. Zh.*, **41**, 385 (1988).
2. V. V. Ovcharenko, P. B. Terent'ev, A. A. Avetisyan, and A. A. Kagramanyan, *Khim. Geterotsikl. Soedin.*, 1525 (1995).
3. A. A. Avetisyan, G. G. Tokmadzhyan, L. V. Karapetyan, and S. A. Sogomonyan, *Arm. Khim. Zh.*, **55**, 78 (2002).
4. A. A. Avetisyan, B. K. Kasparyan, A. N. Dzhandzhapanyan, and M. T. Dangyan, *Arm. Khim. Zh.*, **35**, 326 (1982).
5. K. A. Kocheshkov (editor), *Organic Reactions* [Russian translation], IL, Moscow (1951), Vol. 3, p. 366.
6. I. Heilbron and H. M. Bunbury, *Dictionary of Organic* Compounds [Russian translation], IL, Moscow (1949), Vol. 1, pp. 6, 372; Vol. 3, p. 517.

* The fragments with intensity greater than 10% are given.