

Preparation and spectral properties of products of the reaction of *N,N*-dimethylhydrazine with selected enolethers/alkoxymethylene systems

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Abstract: There were studied series of activated enolethers (alkoxymethylene derivatives of malonic or 3-oxobutanoic acids derivatives of general formula $R-O-CH=C(R^1, R^2)$ where $R^1 = R^2$ / $R^1 \neq R^2$ ($R^1, R^2 = CO_2CH_3, CO_2CH_2CH_3, COCH_3, CN$) with *N,N*-dimethylhydrazine. They smoothly provided products of nucleophilic vinylic substitution reaction – dimethyl hydrazinyl methylene derivatives of malonic or 3-oxobutanoic acids (enhydrazines), respectively from 20 minutes to 2 hours at room temperature.

Keywords: *N,N*-dimethylhydrazine, enolethers, nucleophilic vinylic substitution reaction, enhydrazines

Introduction

The study of the nucleophilic vinylic substitution reaction has been the main area of interest of authors (Milata, Gatial) for a long time. There were reported different kinds of measurements, detail analysis such as isomerizational and conformational study of methyl-2-cyano-3-methoxyacrylate and methyl-2-cyano-3-aminoacrylate and its *N*-methyl derivatives (Gatial et al. 2011), vibrational and NMR spectra and conformations of methoxymethylene- and 1-methoxyethylidene- propanenitrile including solvent effect calculations (Gatial et al. 2004) or isomers and conformers of some push-pull enamines studied by vibrational and NMR spectroscopy and by *ab initio* calculations (Pigošová et al. 2005) and other papers including substituted/non substituted hydrazines with push-pull alkoxymethylene systems (Milata et al. 1997, Gróf et al. 2009).

Materials and methods

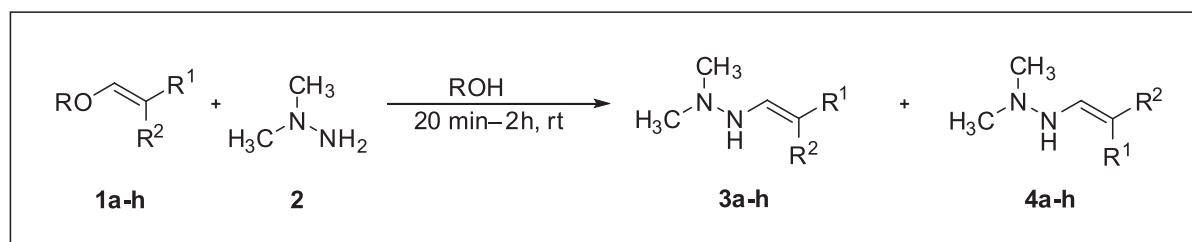
Reagents – *N,N*-dimethylhydrazine and enolethers – alkoxymethylene systems – dimethyl and diethyl methoxymethylene malonate were commercially available (Sigma Aldrich®, Acros Organics®,

Alfa-Aesar®). Commercially available ethoxymethylene malononitrile was recrystallized from 2-propanol before use. Melting points were determined using Kofler hot plate without further corrigation. IR spectra were taken on a FTIR Nicolet NEXUS 470 spectrophotometer using AT-R technique in region $3800-600\text{ cm}^{-1}$. UV-VIS measurements were recorded on UV-VIS NIR 3600 SHIMADZU spectrophotometer in region 250–700 nm. ^1H NMR spectra were measured in CDCl_3 using spectrophotometer Varian VXR-300 for ^1H NMR 299, 995 MHz and for ^{13}C NMR 75, 431 MHz) at 25 °C. Chemical shifts (δ -scale) are quoted in parts per million and following abbreviations are used: s = singlet; d = doublet; t = triplet; q = quartet.

Experimental

General procedure for preparation of **3a-h** + **4a-h**

To a stirred solution of *N,N*-dimethylhydrazine **2** (8.3 mmol) in (m)ethanol (according to alkoxy group) was added dropwise alkoxymethylene derivatives **1a-h** (8.3 mmol) dissolved in appropriate solvent. Reaction mixture was stirred from 20 minutes to 2 hours at room temperature. Then was solvent removed by vacuum evaporator. Thus were obtained crude prod-



Scheme 1. General scheme for preparation of **3a-h** + **4a-h** (R^1 and R^2 are given in Table 1).

ucts which were recrystallized from ethyl acetate/hexane or purified by column chromatography.

Dimethyl 2-[2,2-dimethylhydrazinyl)methylene]malonate (3a)

Light yellow oil, ethyl acetate:hexane (2:1), $R_F = 0.23$ (Coqueret et al. 1986, Prosyanič et al. 1983)

^1H NMR (300 MHz, CDCl_3), δ 9.47 (d, 1H, $\text{NH}=\text{CH}$), 8.26 (d, 1H, $\text{NH}=\text{CH}$), 3.77 (s, 3H, CO_2CH_3), 3.70 (s, 3H, CO_2CH_3), 2.62 (s, 6H, $2\times\text{N}$, $\text{N}-\text{CH}_3$), $\text{N}-\text{CH}_3$)

^{13}C NMR (75 MHz, CDCl_3), δ 169.4, 165.6, 158.7, 87.5, 51.2, 50.9, 48.7

IR (cm^{-1}), ν 3239, 2990, 1698, 1651, 1439, 1249, 1078, 797

UV VIS (DMSO, nm), λ_{max} 299

Diethyl 2-[2,2-dimethylhydrazinyl)methylene]malonate (3b)

Clear yellow oil, ethyl acetate:hexane (2:1) $R_F = 0.35$ (Coqueret et al. 1986, Prosyanič et al. 1983, Brown 1967)

^1H NMR (300 MHz, CDCl_3), δ 9.62 (d, 1H, $\text{NH}=\text{CH}$), 8.05 (d, 1H, $\text{NH}=\text{CH}$), 4.09 (2 \times q, 4H, $2\times\text{CO}_2\text{CH}_2\text{CH}_3$), 2.58 (s, 6H, $2\times\text{N}$, $\text{N}-\text{CH}_3$), 1.18 (2 \times t, 6H, $2\times\text{CO}_2\text{CH}_2\text{CH}_3$)

^{13}C NMR (75 MHz, CDCl_3), δ 167.9, 166.9, 165.1, 158.0, 87.2, 59.4, 59.2, 48.0, 41.5, 14.7

IR (cm^{-1}), ν 3220, 2980, 1646, 1606, 1220, 1071, 1029, 797

UV VIS (DMSO, nm), λ_{max} 292

3-[(2,2-dimethylhydrazinyl)methylene]pentane-2,4-dione (3c)

Yellow solid, ethyl acetate:hexane (1:1), $R_F = 0.22$,

^1H NMR (300 MHz, CDCl_3), δ 11.2 (br, 1H, $\text{NH}=\text{CH}$), 8.01 (d, 1H, $\text{NH}=\text{CH}$), 2.66 (s, 6H, $2\times\text{N}$, $\text{N}-\text{CH}_3$), 2.48 (s, 3H, COCH_3), 2.26 (s, 3H, COCH_3)

^{13}C NMR (75 MHz, CDCl_3), δ 200.4, 194.2, 158.8, 109.9, 48.9, 31.9, 27.2

IR (cm^{-1}), ν 3190, 2968, 2874, 1617, 1578, 1239, 1222, 1017, 626

UV VIS (DMSO, nm), λ_{max} 317

2-[(2,2-dimethylhydrazinyl)methylene]malonitrile (3d)

Light brown crystal (ethyl acetate) (Brown 1967)

^1H NMR (300 MHz, CDCl_3), δ 7.63 (s, 1H, $-\text{NH}=\text{CH}$), 2.66 (s, 6H, $2\times\text{N}$, $\text{N}-\text{CH}_3$)

^{13}C NMR (75 MHz, CDCl_3), δ 160.4, 153.3, 114.9, 113.4, 48.4, 46.8

IR (cm^{-1}), ν 3181, 2883, 2840, 2220, 2205, 1311, 1242, 892, 708

UV VIS (DMSO, nm), λ_{max} 300

E-methyl-2-cyano-3-(2,2-dimethylhydrazinyl)acrylate (3e)

Light yellow solid, $\text{CHCl}_3:\text{MeOH}$ (9:1), $R_F = 0.43$,

^1H NMR (300 MHz, CDCl_3), δ 9.19 (br, 1H, $\text{NH}=\text{CH}$), 7.58 (d, 1H, $\text{NH}=\text{CH}$), 3.76 (s, 3H, CO_2CH_3), 2.62 (s, 6H, $2\times\text{N}$, $\text{N}-\text{CH}_3$)

^{13}C NMR (75 MHz, CDCl_3), δ 168.7, 158.3, 158.1, 118.4, 69.5, 51.9, 51.8, 48.7, 48.5

IR (cm^{-1}), ν 3226, 3187, 2957, 2204, 1703, 1621, 1260, 1230, 764

UV VIS (DMSO, nm), λ_{max} 299

E-ethyl-2-cyano-3-(2,2-dimethylhydrazinyl)acrylate (3f) + Z-ethyl-2-cyano-3-(2,2-dimethylhydrazinyl)acrylate (4f)

Yellowish solid, ethyl acetate:hexane (2:1), $R_F = 0.35$,

^1H NMR (300 MHz, CDCl_3), δ 9.17 (d, 1H, $\text{NH}=\text{CH}$), 7.57 (d, 1H, $\text{NH}=\text{CH}$), 2.63 (s, 6H, $2\times\text{N}$, $\text{N}-\text{CH}_3$), 4.23 (q, 2H, $\text{CO}_2\text{CH}_2\text{CH}_3$), 1.30 (s, 3H, $\text{CO}_2\text{CH}_2\text{CH}_3$)

^{13}C NMR (75 MHz, CDCl_3), δ 167.6, 158.1, 118.1, 69.9, 60.8, 48.3, 14.4

IR (cm^{-1}), ν 3213, 2981, 2882, 2371, 2210, 1678, 1622, 1234, 1018, 778, 715

UV VIS (DMSO, nm), λ_{max} 304

E-methyl-2[(2,2-dimethylhydrazinyl)methylene]-3-oxobutanoate (3g) +

Z-methyl-2[(2,2-dimethylhydrazinyl)methylene]-3-oxobutanoate (4g)

Orange solidified oil, $\text{CHCl}_3:\text{MeOH}$ (4:1), $R_F = 0.52$,

^1H NMR (300 MHz, CDCl_3), δ 11.24 (br, 1H, $\text{NH}=\text{CH}$), 8.23 (d, 1H, $\text{NH}=\text{CH}$), 3.78 (s, 3H, CO_2CH_3), 2.63 (s, 6H, $2\times\text{N}$, $\text{N}-\text{CH}_3$), 2.46 (s, 3H, COCH_3)

^{13}C NMR (75 MHz, CDCl_3), δ 199.4, 167.0, 158.2, 98.4, 50.9, 48.8, 30.6

IR (cm^{-1}), ν 3189, 2953, 2868, 1695, 1630, 1579, 1234, 1076, 778

UV VIS (DMSO, nm), λ_{max} 315

E-ethyl-2[(2,2-dimethylhydrazinyl)methylene]-3-oxobutanoate (3h) +

Z-ethyl-2[(2,2-dimethylhydrazinyl)methylene]-3-oxobutanoate (4h)

Orange solidified oil, (EtOH),

^1H NMR (300 MHz, CDCl_3), δ 11.1 (br, 1H, $\text{NH}=\text{CH}$), 8.15 (d, 1H, $\text{NH}=\text{CH}$), 4.15–4.08 (q, 2H, $\text{CO}_2\text{CH}_2\text{CH}_3$), 2.58 (s, 6H, N , $\text{N}-\text{CH}_3$), 2.56 (s, 3H, COCH_3), 2.41 (s, 3H, COCH_3), 2.34 (s, 3H, COCH_3), 1.23 (t, 3H, $\text{CO}_2\text{CH}_2\text{CH}_3$)

^{13}C NMR (75 MHz, CDCl_3), δ 197.2, 167.2, 157.8, 99.0, 59.8, 49.0, 30.9, 14.4

UV VIS (DMSO, nm), λ_{max} 313

Tab. 1. Yields and melting points of the products of the reaction of enolethers 1a-h with *N,N*-dimethylhydrazine.

No.	R	R ¹	R ²	yield (%)	m.p. (°C)	3a-h:4a-h (<i>E</i> : <i>Z</i>) [*]
1a	Me	CO ₂ CH ₃	CO ₂ CH ₃	96	Oil	no isomers possible
1b	Et	CO ₂ CH ₂ CH ₃	CO ₂ CH ₂ CH ₃	92	Oil	no isomers possible
1c	Et	COCH ₃	COCH ₃	97	83-5	no isomers possible
1d	Et	CN	CN	81	132-4 ^a	no isomers possible
1e	Me	CN	CO ₂ CH ₃	65	61-5	Only <i>E</i> -isomer
1f	Et	CN	CO ₂ CH ₂ CH ₃	70	67, 75 ^b	8:1
1g	Me	COCH ₃	CO ₂ CH ₃	66	43, 53	12:1
1h	Et	COCH ₃	CO ₂ CH ₂ CH ₃	95	37, 45 ^c	7:1

^{*}Established on the basis of integrated intensity of CH₃ signals or —CH= eventually,

^amp 131–134 °C – Brown 1967,

^bmp 86 °C – Coqueret et al. 1986,

^cmp 68 °C – Emelina et al. 1994.

Results and discussion

In Table 1 are presented data obtained from nucleophilic vinylic substitution of *N,N*-dimethylhydrazine with selected alkoxymethylene derivatives of malonic and 3-oxobutanoic acids derivatives in good to excellent yields. Other physic-chemical and spectral properties of products **3a-h**, **4a-h** are given in experimental part. This method allowed us to prepare eight enhydrazine derivatives **3a-h/4a-h**. Compounds **3a**, **3b**, **3d**, **3f** (Coqueret et al. 1986, Prosyaniak et al. 1983, Brown 1967), **3h** (Emelina et al. 1994) have been prepared before.

We completed other data (¹³C NMR spectra, IR, UV VIS) for complete confirmation and structure elucidation of compounds **3a**, **3d** and **3f**. Enolethers **1a-1d** exist like no isomers due to equality of R¹ and R² groups, respectively. Enolethers derived from cyanoacetic acid (**1e**, **1f**) exist like mixtures of isomers, in which *E*-isomer dominate **1e**. Also enolethers derived from 3-oxobutanoic acid (**1g**, **1h**) exist like mixtures of isomers with dominating *E*-isomer (**1g** 12:1; **1h** 7:1). In ¹H NMR spectra of products derived from enolethers **1f-h** we observed signals not only for *E*- but also for *Z*-isomer in ratios 8:1 for **3f** + **4f**, 12:1 for **3g** + **4g** and 7:1 for **3h** + **4h**. In the case of the reaction of the enolether **1e** solely *E*-isomer (**3e**) has been observed. This fact reflects inversion of configuration during nucleophilic vinylic substitution similarly like in related systems (Saloň et al. 2005) stabilized by intramolecular hydrogen bond of the NH proton with oxygen of the carbonyl group of the acetyl substituent (**1g**, **1h**) or alkoxycarbonyl substituent (**1e**, **1f**).

Thus obtained products will be in used for conformational, isomerizational study, ab initio calculations and kinetic measurements, too.

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