Preparation and spectral properties of products of the reaction of \(N,N\)-dimethyldihydrazine 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 \(R^1\neq R^2\) \((R^1, R^2 = \text{CO}_2\text{CH}_3, \text{CO}_2\text{CH}_2\text{CH}_3, \text{COCH}_3, \text{CN})\) with \(N,N\)-dimethyldihydrazine. 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: \(N,N\)-dimethyldihydrazine, 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-aminocroclrate and its \(N\)-methyl derivatives (Gatial et al. 2011), vibrational and NMR spectra and conformations of methoxymethylene- and 1-methoxymethylene-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 \textit{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 — \(N,N\)-dimethyldihydrazine 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 corrigration. IR spectra were taken on a FTIR Nicolet NEXUS 470 spectrophotometer using AT-R technique in region 3800—600 cm\(^{-1}\). UV-VIS measurements were recorded on UV-VIS NIR 3600 SHIMADZU spectrophotometer in region 250—700 nm. \(^1\)H NMR spectra were measured in CDCl\(_3\) using spectrophotometer Varian VXR-300 for \(^1\)H NMR 299, 995 MHz and for \(^13\)C NMR 75, 431 MHz at 25 °C. Chemical shifts (\(\delta\)-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 \(N,N\)-dimethyldihydrazine \(2\) (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-
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, Prosyank et al. 1983).

$^1$H NMR (300 MHz, CDCl$_3$), $\delta$ 9.47 (d, 1H, NH$\equiv$CH), 8.26 (d, 1H, NH$\equiv$CH), 3.77 (s, 3H, CO$_2$CH$_3$), 3.70 (s, 3H, CO$_2$CH$_3$), 2.62 (s, 6H, 2×N, N$\equiv$CH$_3$)

$^{13}$C NMR (75 MHz, CDCl$_3$), $\delta$ 169.4, 165.6, 158.7, 87.5, 51.2, 50.9, 48.7

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

UV VIS (DMSO, nm), $\lambda_{\text{max}}$ 299

**Diethyl 2-(2,2-dimethylhydrazinyl)methylene/malonate (3b)**


$^1$H NMR (300 MHz, CDCl$_3$), $\delta$ 9.62 (d, 1H, NH$\equiv$CH), 8.05 (d, 1H, NH$\equiv$CH), 4.09 (2×q, 4H, 2×CO$_2$CH$_2$(CH$_3$)), 2.58 (s, 6H, 2×N, N$\equiv$CH$_3$), 1.18 (2×t, 6H, 2×CO$_2$CH$_3$)

$^{13}$C NMR (75 MHz, CDCl$_3$), $\delta$ 167.9, 166.9, 165.1, 158.0, 87.2, 59.4, 59.2, 48.0, 41.5, 14.7

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

UV VIS (DMSO, nm), $\lambda_{\text{max}}$ 292

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

Yellow solid, ethyl acetate:hexane (1:1), $R_f = 0.22$ (Coqueret et al. 1986, Prosyank et al. 1983).

$^1$H NMR (300 MHz, CDCl$_3$), $\delta$ 11.2 (br, 1H, NH$\equiv$CH), 8.01 (d, 1H, NH$\equiv$CH), 2.66 (s, 6H, 2×N, N$\equiv$CH$_3$), 2.48 (s, 3H, COCH$_3$), 2.26 (s, 3H, COCH$_3$)

$^{13}$C NMR (75 MHz, CDCl$_3$), $\delta$ 200.4, 194.2, 158.8, 109.9, 48.9, 31.9, 27.2

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

UV VIS (DMSO, nm), $\lambda_{\text{max}}$ 317

**2-[(2,2-dimethylhydrazinyl)methylene]malononitrile (3d)**

Light brown crystal (ethyl acetate) (Brown 1967).

$^1$H NMR (300 MHz, CDCl$_3$), $\delta$ 7.63 (s, 1H, —NH$\equiv$CH), 2.66 (s, 6H, 2×N, N$\equiv$CH$_3$)

$^{13}$C NMR (75 MHz, CDCl$_3$), $\delta$ 160.4, 153.3, 114.9, 113.4, 48.4, 46.8

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

UV VIS (DMSO, nm), $\lambda_{\text{max}}$ 300

**E-methyl-2-cyano-3-(2,2-dimethylhydrazinyl)acylate (3e)**

Light yellow solid, CH$_2$Cl$_2$:MeOH (9:1), $R_f = 0.43$.

$^1$H NMR (300 MHz, CDCl$_3$), $\delta$ 9.19 (br, 1H, NH$\equiv$CH), 7.58 (d, 1H, NH$\equiv$CH), 3.76 (s, 3H, CO$_2$CH$_3$), 2.62 (s, 6H, 2×N, N$\equiv$CH$_3$)

$^{13}$C NMR (75 MHz, CDCl$_3$), $\delta$ 168.7, 158.3, 158.1, 118.4, 69.5, 51.9, 51.8, 48.7, 48.5

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

UV VIS (DMSO, nm), $\lambda_{\text{max}}$ 299

**E-ethyl-2-cyano-3-(2,2-dimethylhydrazinyl)acrylate (3f)**

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

$^1$H NMR (300 MHz, CDCl$_3$), $\delta$ 9.17 (d, 1H, NH$\equiv$CH), 7.57 (d, 1H, NH$\equiv$CH), 2.63 (s, 6H, 2×N, N$\equiv$CH$_3$), 4.23 (q, 2H, CO$_2$CH$_2$(CH$_3$)), 1.30 (s, 3H, CO$_2$CH$_2$(CH$_3$)

$^{13}$C NMR (75 MHz, CDCl$_3$), $\delta$ 167.6, 158.1, 118.1, 69.9, 60.8, 48.3, 14.4

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

UV VIS (DMSO, nm), $\lambda_{\text{max}}$ 304

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

Orange solidified oil, CH$_2$Cl$_2$:MeOH (4:1), $R_f = 0.52$.

$^1$H NMR (300 MHz, CDCl$_3$), $\delta$ 11.24 (br, 1H, NH$\equiv$CH), 8.23 (d, 1H, NH$\equiv$CH), 3.78 (s, 3H, CO$_2$CH$_3$), 2.63 (s, 6H, 2×N, N$\equiv$CH$_3$), 2.46 (s, 3H, COCH$_3$)

$^{13}$C NMR (75 MHz, CDCl$_3$), $\delta$ 199.4, 167.0, 158.2, 98.4, 50.9, 48.8, 30.6

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

UV VIS (DMSO, nm), $\lambda_{\text{max}}$ 315

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

Orange solidified oil, (EtOH).

$^1$H NMR (300 MHz, CDCl$_3$), $\delta$ 11.1 (br, 1H, NH$\equiv$CH), 8.15 (d, 1H, NH$\equiv$CH), 4.15–4.08 (q, 2H, CO$_2$CH$_2$(CH$_3$)), 2.58 (s, 6H, N, N$\equiv$CH$_3$), 2.56 (s, 3H, CO$_2$CH$_3$), 2.41 (s, 3H, COCH$_3$), 2.34 (s, 3H, COCH$_3$), 1.23 (t, 3H, CO$_2$CH$_2$(CH$_3$)

$^{13}$C NMR (75 MHz, CDCl$_3$), $\delta$ 197.2, 167.2, 157.8, 99.0, 59.8, 49.0, 30.9, 14.4

UV VIS (DMSO, nm), $\lambda_{\text{max}}$ 313
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, Prosyanik 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 enoether 1e upon E-isomer (3e) has been observed. This fact reflects inversion of configuration during nucleophilic vinylic substitution similarly like in related systems (Salon 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.

Acknowledgement

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References


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

<table>
<thead>
<tr>
<th>No.</th>
<th>R</th>
<th>R1</th>
<th>R2</th>
<th>yield (%)</th>
<th>m.p. (°C)</th>
<th>3a-h:4a-h (E:Z)*</th>
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<tbody>
<tr>
<td>1a</td>
<td>Me</td>
<td>CO2CH3</td>
<td>CO2CH3</td>
<td>96</td>
<td>Oil</td>
<td>no isomers possible</td>
</tr>
<tr>
<td>1b</td>
<td>Et</td>
<td>CO2CH2CH3</td>
<td>CO2CH2CH3</td>
<td>92</td>
<td>Oil</td>
<td>no isomers possible</td>
</tr>
<tr>
<td>1c</td>
<td>Et</td>
<td>COCH3</td>
<td>COCH3</td>
<td>97</td>
<td>83-5</td>
<td>no isomers possible</td>
</tr>
<tr>
<td>1d</td>
<td>Et</td>
<td>CN</td>
<td>CN</td>
<td>81</td>
<td>132-4°</td>
<td>no isomers possible</td>
</tr>
<tr>
<td>1e</td>
<td>Me</td>
<td>CN</td>
<td>CO2CH3</td>
<td>65</td>
<td>61-5</td>
<td>Only E-isomer</td>
</tr>
<tr>
<td>1f</td>
<td>Et</td>
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<td>CO2CH2CH3</td>
<td>70</td>
<td>67, 75°</td>
<td>8:1</td>
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<tr>
<td>1g</td>
<td>Me</td>
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<td>CO2CH3</td>
<td>66</td>
<td>43, 53</td>
<td>12:1</td>
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<tr>
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<td>Et</td>
<td>COCH3</td>
<td>CO2CH2CH3</td>
<td>95</td>
<td>37, 45°</td>
<td>7:1</td>
</tr>
</tbody>
</table>

*Established on the basis of integrated intensity of CH3 signals or —CH= eventually,
°mp 131—134 °C — Brown 1967,
°mp 86 °C — Coqueret et al. 1986,
°mp 68 °C — Emelina et al. 1994.

