SYNTHESIS OF PYRAZOLES BASED ON FUNCTIONALIZED ALLENOATES

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Abstract – Regiospecific synthesis of pyrazole-3-carboxylate derivatives by 1,3-dipolar cycloaddition of diazomethane with allenates in presence of triethylamine is demonstrated. Reaction of allenates with stearic acid moiety containing diazoketone is explored under ultrasonic conditions. Novel derivatives of pyrazole were achieved in excellent yields.

INTRODUCTION
Among compounds containing nitrogen heterocyclic frameworks, pyrazole is one of most useful building blocks for various biologically active molecules. The biological activities of these compounds have been widely used as antidiabetic, antiviral, antimicrobial, antibacterial, anticancer agents. In addition to their biological importance, pyrazoles play important role as catalysts, molecular magnetic devices and sensors. 1-3 1,3-Dipolar cycloaddition reactions of diazo compounds to double and triple bonds are well known and documented. 4 In contrast, studies including this methodology with regard to allenes have received much less attention. 5 In consideration of biological activity of compounds bearing the pyrazole moiety we planned the synthesis of series of pyrazole derivatives from functionalized allenates.

RESULTS AND DISCUSSION
Allenates 2a-f were obtained from N-phthalyl amino acids 1a-c and fatty acids 1d-f. Thionyl chloride was used to convert acids 1a-f to their corresponding acid chlorides. The reaction of acid chlorides with
triethylamine produced ketenes, followed by treatment with methyl (triphenylphosphoranylidene)acetate afforded allenotes 2a-f (Table 1).

**Table 1. Synthesis of allenotes 2a-f**

<table>
<thead>
<tr>
<th>Entry</th>
<th>R</th>
<th>Isolated yields (%)</th>
</tr>
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<tbody>
<tr>
<td>a</td>
<td>N-Phth</td>
<td>63</td>
</tr>
<tr>
<td>b</td>
<td>N-MePhth</td>
<td>75</td>
</tr>
<tr>
<td>c</td>
<td>N-EtPhth</td>
<td>87</td>
</tr>
<tr>
<td>d</td>
<td>Me(CH₂)₁₅</td>
<td>77</td>
</tr>
<tr>
<td>e</td>
<td>Me(CH₂)₁₃</td>
<td>85</td>
</tr>
<tr>
<td>f</td>
<td>Me(CH₂)₄</td>
<td>66</td>
</tr>
</tbody>
</table>

The allenotes 2a-c were treated by excess diazomethane in the presence of equimolar quantity of triethylamine, which lead to formation of isomeric N-methylpyrazoles 4a-c, 5a-c (Table 2). Formation of N-methylpyrazoles observed even in a small excess of diazomethane but the best results were achieved in a six-fold excess.

**Table 2. 1,3-Dipolar cycloaddition reaction of diazomethane with allenotes 2a-c**

<table>
<thead>
<tr>
<th>Entry</th>
<th>n</th>
<th>Reagents</th>
<th>3</th>
<th>4</th>
<th>5</th>
<th>Isolated yields (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>a</td>
<td>1</td>
<td>CH₂N₂, Et₃N</td>
<td>20</td>
<td>5</td>
<td>3</td>
<td></td>
</tr>
<tr>
<td></td>
<td>1</td>
<td>6×CH₂N₂, Et₃N</td>
<td>-</td>
<td>33</td>
<td>40</td>
<td></td>
</tr>
<tr>
<td>b</td>
<td>2</td>
<td>CH₂N₂, Et₃N</td>
<td>-</td>
<td>10</td>
<td>5</td>
<td></td>
</tr>
<tr>
<td></td>
<td>2</td>
<td>6×CH₂N₂, Et₃N</td>
<td>-</td>
<td>51</td>
<td>24</td>
<td></td>
</tr>
<tr>
<td>c</td>
<td>3</td>
<td>CH₂N₂, Et₃N</td>
<td>-</td>
<td>5</td>
<td>5</td>
<td></td>
</tr>
<tr>
<td></td>
<td>3</td>
<td>6×CH₂N₂, Et₃N</td>
<td>-</td>
<td>27</td>
<td>21</td>
<td></td>
</tr>
</tbody>
</table>
When the reaction of allene 2a with diazomethane was carried out in equimolar quantities, we obtained 3a in 20% yield. The structure of pyrazole 3a was confirmed by X-ray crystallographic analysis (Figure 1). Molecular structure of 3a has some similarities and differences to 4a that we characterized recently.\(^7\)

![Figure 1. X-Ray crystal structure of 3a](image)

Regioisomeric compounds 4a-c and 5a-c were individually isolated by column chromatography on silica gel. The structure of 4a was determined by X-ray crystallography, and the structure of compound 5a was elucidated by a comparative analysis of the NMR spectra of compounds 4a and 5a using homo- and heteronuclear 2D correlations COSY, NOESY, HSQC, HMBC and \(^1\)H-\(^{15}\)N-HMBC.\(^7\)

1,3-Dipolar cycloaddition reaction of diazoketone, obtained from stearic acid, with allenoates 2a-c was carried out under ultrasonic irradiation in benzene at 65 °C during 20 h. The reaction proceeded regioselectively to provide pyrazole derivatives 6a-c (Scheme 1).

![Scheme 1. Ultrasonic irradiation assisted regioselective synthesis of pyrazoles 6a-c](image)

However, without ultrasonic treatment in benzene at reflux for 40 h, reaction did not proceed at all. Formation of the N-H insertion products were not observed when obtained pyrazoles 6a-c were treated with excess of diazomethane or diazoketone from stearic acid, that is evidenced by the lack of consumption of
the starting materials. It was found that the pyrazoles 7a-c, obtained from allenes 2d-f including stearic, palmitic and caproic acids moieties, behave similarly (Scheme 2).

\[
\begin{align*}
\text{2d-f} & \xrightarrow{6\text{CH}_2\text{N}_2, \text{Et}_3\text{N}} \text{MeO}_2\text{C} & \text{(CH}_2\text{nMe)} \\
7a & n=16 & (60\%) \\
7b & n=14 & (58\%) \\
7c & n=4 & (20\%)
\end{align*}
\]

**Scheme 2.** Synthesis of pyrazoles 7a-c including fatty acids moieties

1,3-Dipolar cycloaddition reaction of diazomethane with allenoates in the presence of triethylamine lead to regiospecific formation of pyrazoles, in case of absence of triethylamine we got the mixture of products that we couldn't isolate and identify. Apparently triethylamine forms complex with diazomethane,\(^8\) which regioselectively attacks electrophilic sp-hybridized central carbon atom with the closure into cycle by the nucleophilic carbon that is in \(\alpha\)-position to an ester group. The mechanism is shown in Figure 2.

**Figure 2.** Mechanism of pyrazole synthesis

Formation of two \(N\)-methylpyrazoles from allenoates 2a-c is explained by the isomerization of pyrazoline into pyrazole derivative that can exist in two tautomeric forms.\(^9,10\) Due to formation of hydrogen bond similar to carboxylic acids\(^11\) pyrazoles produce dimers, which tend to prototropic tautomerism (Figure 3).

**Figure 3**
Polarization of N→H⁺ bond, in the presence of electron acceptor group next to nitrogen atom, promotes N-H insertion of diazomethane similar to known reaction of the O-H insertion of diazomethane in carboxylic acids. In case of stearic, palmitic and caproic acids moieties containing pyrazoles 7a-c, formation of N-methyl derivatives hindered due to steric factor and, on the other hand, being electron donor substituents, fatty acid moieties reduce N→H⁺ polarization.

In conclusion, we have demonstrated that the treatment of 1,2-dienoates with diazomethane in the presence of triethylamine gives pyrazole-3-carboxylate derivatives with good regioselectivity. We have succeeded in developing the 1, 3-dipolar cycloaddition reaction of stearic acid moiety containing diazoketone with allenoates under ultrasonic condition, and a series of novel derivatives of pyrazole were obtained.

**EXPERIMENTAL**

The IR spectra were measured on a Spekord M-80 spectrometer from thin films or suspensions in mineral oil. The ¹H and ¹³C NMR spectra were recorded on a Bruker AM-500 spectrometer at 500.13 and 125.76 MHz, respectively, using tetramethylsilane as internal standard. Correct assignment of signals in the NMR spectra of compounds was achieved using homo- and heteronuclear 2-D correlation techniques: COSY, NOESY, HSQC, HMBC, ¹H-¹⁵N-HMBC. The progress of reactions was monitored by thin-layer chromatography on Sorbfil PTSKh-AF-A plates; spots were detected by UV irradiation, treatment with iodine vapor, or spraying with a solution of ninhydrin or p-methoxybenzaldehyde with subsequent heating to 100–120 °C. The mass spectra were obtained on a Shimadzu LCMS-2010EV instrument. Elemental analysis was carried out using a EURO EA-3000 CHN element analyzer. Ultrasound was generated using a UZDN-2T setup with an operating frequency of 22 kHz. X-Ray diffraction measurements were carried out with Bruker APEX-II CCD diffractometer at 100K. Melting points were measured with a Buetiu apparatus. The products were isolated by column chromatography on silica gel (40–100 and 100–160 μm; Chemapol).

**General procedure for the synthesis of the allenoates 2a-f by Wittig reaction** 1 g of an acid was dispersed in 10 mL of anhydrous benzene, five-fold excess of thionyl chloride was added, and the mixture was heated for 3 h under reflux. The solvent and excess thionyl chloride was distilled off on a rotary evaporator, and the residue (phthalimidoacetyl chloride) was used without additional purification. An equimolar amount of triethylamine was added to a solution of methyl (triphenyl-λ5-phosphanylidenecacetate in THF, the mixture was cooled to -10 °C, and a cold solution of phthalimidoacetyl chloride was slowly added dropwise. The mixture was stirred for 0.5 h and kept at 0 °C for 6 h, the precipitate was filtered off, the solvent was distilled off from the filtrate, and the residue was subjected to column chromatography on silica gel using petroleum ether–EtOAc (4 : 1) as eluent.

**Methyl 4-(1,3-dioxo-2,3-dihydro-1H-isooindol-2-yl)buta-2,3-dienoate (2a).** Yield 0.75 g (63%), white crystals, mp 95–97 °C. IR spectrum, ν cm⁻¹: 1782, 1763. ¹H NMR spectrum (CDCl₃), δ ppm: 3.72 s (3H,
Methyl 5-(1,3-dioxo-1,3-dihydro-2H-isoindol-2-yl)pent-2,3-dienoate (2b). Yield 0.88 g (75%), white crystals, mp 87-88 °C. IR spectrum, ν cm⁻¹: 1709, 1771, 1964. ¹H NMR (CDCl₃), δ ppm: 3.63 s (3H, CH₃); 4.36 m (2H, CH₂), 5.64 d.d. (1H, CH, J = 6.2, 2.9, 2.6 Hz), 5.74 m (1H, CH), 7.66-7.81 m (4H, C₆H₄). ¹³C NMR (CDCl₃), δ ppm: 35.09 (CH₂), 52.11 (CH₃), 90.43 (CH_allene), 91.40 (CH_allene), 123.39 (CH_arom.), 131.91 (C_arom.), 134.15 (CH_arom.), 165.36 (C=O), 167.39 (C=O), 212.37 (=C=). MS: m/z 258 [MH]+, 257 [M]+. Anal. Calcd for C₁₄H₁₈NO₄ (257.07): C 65.37; H 4.31; N 5.44; O 24.88. Found: C 65.35; H 4.29; N 5.44.

Methyl 6-(1,3-dioxo-1,3-dihydro-2H-isoindol-2-yl)hexa-2,3-dienoate (2c). Yield 1.01 g (87%), white crystals, mp 102-104 °C. IR, ν cm⁻¹: 1701, 1765, 1952. ¹H NMR (CDCl₃), δ ppm: 2.59 m (2H, CH₂), 3.54 s (3H, CH₃); 3.87 t (2H, CH₂, J = 7 Hz), 5.52 m (1H, CH), 5.65 m (1H, CH), 7.68-7.83 m (4H, C₆H₄). ¹³C NMR (CDCl₃), δ ppm: 26.70 (CH₂), 36.77 (CH₂), 51.76 (CH₃), 88.39 (CH_allene), 91.69 (CH_allene), 123.21 (CH_arom.), 131.97 (C_arom.), 133.93 (CH_arom.), 165.96 (C=O), 168.11 (C=O), 212.44 (=C=). MS: m/z 272 [MH]+, 271 [M]+. Anal. Calcd for C₁₅H₁₉NO₄ (271.27): C 66.41; H 4.83; N 5.16; O 23.59. Found: C 66.39; H 4.81; N 5.16.

Methyl icos-2,3-dienoate (2d). Yield 0.88 g (77%), yellow oil. IR, ν cm⁻¹: 1724, 1961, 2852, 2922. ¹H NMR (CDCl₃), δ ppm: 0.88 t (3H, CH₃, J = 7.2); 1.25 m (26H, 13CH₂), 1.63 m (2H, CH₂), 3.73 s (3H, CH₃), 4.45 m (2H, CH₂), 5.57 m (1H, =CH, J = 7.0), 5.63 d (1H, =CH, J = 7.0). ¹³C NMR (CDCl₃), δ ppm: 14.07 (CH₃), 22.66 (CH₂), 27.43 (CH₂), 28.7 (CH₂), 28.95 (CH₂), 29.33 (CH₂), 29.67 (9CH₂), 31.91 (CH₂), 51.83 (CH₃), 87.7 (CH_allene), 95.44 (CH_allene), 167.2 (C=O), 212.41 (=C=). MS: m/z 323 [MH]+, 322 [M]+. Anal. Calcd for C₂₃H₃₈O₂ (322.53): C 78.2; H 11.88; O 9.22. Found: C 78.2; H 11.88.

Methyl octadeca-2,3-dienoate (2e). Yield 0.98 g (85%), yellow oil. IR, ν cm⁻¹: 1961, 61. ¹H NMR (CDCl₃), δ ppm: 0.85 t (3H, CH₃, J = 6.7); 1.14-1.23 m (22H, 2CH₂), 1.38-1.46 m (2H, CH₂), 2.08-2.14 m (2H, CH₂), 3.59 s (3H, CH₃), 5.53 s (1H, =CH), 5.58 s (1H, =CH). ¹³C NMR (CDCl₃), δ ppm: 14.8 (CH₃), 22.62 (CH₂), 25.74 (CH₂), 28.64 (CH₂), 28.79 (CH₂), 28.91 (CH₂), 29.09 (CH₂), 29.3 (CH₂), 29.48 (5CH₂), 31.88 (CH₂), 51.8 (OCH₃), 87.85 (CH_all), 95.45 (CH), 166.58 (C=O), 212.32 (=C=). MS: m/z 295 [MH]+, 294 [M]+. Anal. Calcd for C₁₉H₃₈O₂ (294.47): C 77.5; H 11.64; O 10.87. Found: C 77.51; H 11.65; O 10.84.

Methyl octa-2,3-dienoate (2f). Yield 0.88 g (66%), yellow oil. IR, ν cm⁻¹: 1961, 61. ¹H NMR (CDCl₃), δ ppm: 0.87 t (3H, CH₃, J = 6.5); 1.21-1.48 m (4H, 2CH₂), 2.15 m (2H, CH₂), 3.74 s (3H, CH₃), 5.64 s (1H, =CH), 6.55 s (1H, =CH). ¹³C NMR (CDCl₃), δ ppm: 13.64 (CH₃), 21.82 (CH₂), 25.74 (CH₂), 30.67 (CH₂), 38.09 (CH₃), 52.61 (CH₃), 86.42 (CH₃). MS: m/z 258 [MH]+, 257 [M]+. Anal. Calcd for C₁₇H₃₆O₂ (257.07): C 66.67; H 9.39; O 24.0. Found: C 66.65; H 9.41; O 24.0.
51.86 (OCH₃), 87.78 (=CH₉), 95.36 (CH), 167.8 (C=O), 211.8 (=C=). MS: m/z 155 [MH]+, 154 [M]. Anal. Calc. for C₉H₁₄O₂ (154,21): C 70.10; H 9.15; O 20.75. Found: C 70.12; H 9.15.

**General procedure for the synthesis of the pyrazoles 3a, 4a-c, 5a-c, 7a-c from allenoates 2a-f**

A cold solution (0 °C) of 0.5 g of allenoates 2a-f in 20 mL of CH₂Cl₂ was combined with an equimolar amount of triethylamine, and a six-fold excess of a freshly prepared solution of diazomethane in CH₂Cl₂ was added dropwise. The reaction mixture was stirred on a magnetic stirrer for 6 h at room temperature. The precipitate formed was separated by filtration, the solvent was removed, and the reaction products were separated by column chromatography on silica gel (eluent: petroleum ether/EtOAc 4/1).

**Methyl 4-[1,3-dioxo-1,3-dihydro-2H-isoindol-2-yl]methyl-1H-pyrazole-3-carboxylate (3a).** Yield 0.12 g (20%), mp 196-198 °C. IR, ν cm⁻¹: 1107, 1362, 1377, 1457, 1694. ¹H NMR (d₆-DMSO), δ ppm: 3.86 s (3H, CH₃O); 4.90 s (2H, CH₂), 7.87 s (1H, =CHN), 7.85-7.89 m (2H, C₆H₂), 7.91-7.94 m (2H, C₆H₂), 13.43 s (1H, NH). ¹³C NMR (CDCl₃), δ ppm: 33.24 (CH₂), 51.92 (CH₃O), 119.75 (C), 123.57 (CH₉), 129.69 (=CHN), 132.27 (Cₙ₉N), 134.80 (CH₉), 139.41 (CH=N), 163.35 (O=CO), 168.05 (O=CN). ¹⁵N NMR (CDCl₃), δ ppm: 121 (N), 164 (N₉CO), 213 (NH). MS: m/z 286 [MH]+, 285 [M]. Anal. Calc. for C₁₄H₁₁N₃O₄ (285.25): C 58.95; H 3.89; N 14.73; O 22.44. Found: C 58.95; H 3.89; N 14.73.

**X-Ray diffraction data of 3a.** Monoclinic, space group P2₁/c: a = 12.9491(13)Å, b = 12.6702(13)Å, c = 7.9024(8)Å, β = 90.524(2)°, V = 1296.5(2)Å³, Z = 4, M = 285.26, d(calc) = 1.461 g cm⁻³, wR² = 0.1087 calculated on F² for all 3435 independent reflections with 2θ<58°, (GOF = 1.019 R = 0.0427 calculated on Fhkl for 2711 reflections with I>2σ(I)). Crystallographic data (excluding structure factors) for the structure have been deposited at the Cambridge Crystallographic Data Centre (CCDC) as supplementary publication No. CCDC 858681.

**Methyl 4-[2-(1,3-dioxo-1,3-dihydro-2H-isoindol-2-yl)ethyl]-1-methyl-1H-pyrazole-5-carboxylate (4b).** Yield 0.31 g (51%), mp 110-112 °C. IR, ν cm⁻¹: 1125, 1286, 1396, 1466, 1713. ¹H NMR (CDCl₃), δ ppm: 3.02 t (2H, CH₂, J = 7.6, 7.4 Hz), 3.85 t (2H, CH₂N, J = 7.6, 7.4 Hz), 3.91 s (3H, CH₃O), 4.08 s (3H, CH₃), 7.29 s (1H, CH=N), 7.71-7.75 m (2H, C₆H₂), 7.76-7.79 m (2H, C₆H₂). ¹³C NMR (CDCl₃), δ ppm: 24.40 (CH₂), 38.22 (CH₂N), 40.29 (CH₃N), 51.89 (CH₃O), 122.83 (C), 123.16 (CH₉N), 129.76 (=CN), 131.97 (CH₉N), 133.92 (CH₉N), 138.62 (CH=N), 160.60 (O=CO), 168.10 (O=CN). ¹⁵N NMR (CDCl₃), δ ppm: 19 (N), 163 (N₉CO), 207 (NCH₃). MS: m/z 314 [MH]+, 213 [M]. Anal. Calc. for C₁₆H₁₄N₃O₄ (313.31): C 61.34; H 4.83; N 13.41; O 20.43. Found: C 61.33; H 4.83; N 13.41.

**Methyl 4-[2-(1,3-dioxo-1,3-dihydro-2H-isoindol-2-yl)ethyl]-1-methyl-1H-pyrazole-3-carboxylate (5b).** Yield 0.15 g (24%), mp 153-154 °C. IR, ν cm⁻¹: 1119, 1273, 1385, 1466, 1705. ¹H NMR (CDCl₃), δ ppm: 3.14 t (2H, CH₂, J = 7.6, 7.1 Hz), 3.89 s (3H, CH₃O); 3.91 s (3H, CH₃N); 3.95 t (2H, CH₂N, J = 7.6, 7.1 Hz), 7.33 s (1H, CHN), 7.70-7.73 m (2H, C₆H₂), 7.75-7.78 m (2H, C₆H₂). ¹³C NMR (CDCl₃), δ ppm:
23.38 (CH₂), 38.10 (CH₂N), 39.64 (CH₃N), 51.77 (CH₃O), 121.71 (C), 123.17 (CHₐrom.), 131.00 (CHN), 131.85 (Cₐrom.), 133.88 (CHₐrom.), 140.47 (C=N), 162.81 (O=CO), 168.16 (O=CN). 15N NMR (CDCl₃), δ ppm: 18 (N), 163 (N phthalyl.), 205 (NCH₃). MS: m/z 314 [MH]+, 213 [M]+. Anal. Calcld for C₁₆H₁₅N₃O₄ (313.31): C 61.34; H 4.83; N 13.41; O 13.41.

**Methyl 4-[3-(1,3-dioxo-1,3-dihydro-2H-isodindol-2-yl)propyl]-1-methyl-1H-pyrazole-5-carboxylate (4c).** Yield 0.16 g (27%), mp 74-75 °C. IR, ν cm⁻¹: 1119, 1293, 1614, 1721, 1765. ¹H NMR (CDCl₃), δ ppm: 1.95-1.97 m (2H, CH₂), 2.73 t (2H, CH₂, J = 8.0, 7.3 Hz), 3.73 t (2H, CH₂, J = 6.6, 4.7 Hz), 3.85 s (3H, CH₃O); 4.09 s (3H, CH₃N), 7.37 s (1H, CHN), 7.70-7.72 m (2H, C₆H₂), 7.83-7.85 m (2H, C₆H₂). ¹³C NMR (CDCl₃), δ ppm: 23.38 (CH₃), 30.26 (CH₂), 31.92 (CH₂), 51.93 (OCH₃), 125 (=CHₐlk), 129.88 (=CH), 133.61 (C= N), 162.073 (C=O). MS: m/z 365 [MH]+, 364 [M]+. Anal. Calcld for C₂₀H₂₀N₅O₂ (364.51): C 72.46; H 11.05; N 7.68; O 8.78. Found: C 72.46; H 10.05; N 7.65.

**Methyl 4-heptadecyl-1H-pyrazole-3-carboxylate (7a).** Yield 0.34 g (60%), white oil. IR, ν cm⁻¹: 1697.36, 2868, 2936, 3238. ¹H NMR (CDCl₃), δ ppm: 0.9 t (3H, CH₃, J = 6.7), 1.27-1.38 m (28H, 14CH₂), 1.61 m (2H, CH₂), 2.77 m (2H,CH₂), 3.97 s (3H, CH₃), 7.59 s (1H, =CH), 12.87 s (1H, =N H). ¹³C NMR (CDCl₃), δ ppm: 14.11 (CH₃), 22.69 (CH₂), 24.44 (CH₂), 29.36 (CH₂), 29.43 (CH₂), 29.47 (CH₂), 29.65 (CH₂), 29.69 (8CH₂), 30.42 (CH₂), 31.92 (CH₂), 51.65 (OCH₃), 125.43 (=CHₐlk), 130.5 (=CH), 133.26 (C=N), 162.73 (C=O). MS: m/z 365 [MH]+, 364 [M]+. Anal. Calcld for C₂₂H₄₀N₂O₂ (364.57): C 72.48; H 11.06; N 7.68; O 8.78. Found: C 72.46; H 10.05; N 7.65.

**Methyl 4-pentadecyl-1H-pyrazole-3-carboxylate (7b).** Yield 0.33 g (58%), white oil. IR, ν cm⁻¹: 1697, 2868, 2936, 3238. ¹H NMR (CDCl₃), δ ppm: 0.7 t (3H, CH₃, J = 7.2), 1.25-1.31 m (24H, 12CH₂), 1.60 m (2H, CH₂), 2.75 m (2H, CH₂), 3.97 s (3H, OCH₃), 7.55 s (1H, =CH), 12.85 s (1H, N H). ¹³C NMR (CDCl₃), δ ppm: 14.11 (CH₃), 22.69 (CH₂), 24.05 (CH₂), 29.35 (CH₂), 29.42 (CH₂), 29.60 (CH₂), 29.65 (CH₂), 29.68 (CH₂), 30.26 (CH₂), 31.92 (CH₂), 51.93 (OCH₃), 125 (=CHₐlk), 129.88 (=CH), 133.61 (C= N), 162.073 (C=O). MS: m/z 337 [MH]+, 336 [M]+. Anal. Calcld for C₂₀H₃₆N₂O₂ (336.51): C 71.38; H 10.78; N 8.32 O
Methyl 4-pentyl-1H-pyrazole-3-carboxylate (7c). Yield 0.13 g (20%), yellow oil. IR, ν cm⁻¹: 1691, 61.

¹H NMR (CDCl₃), δ ppm: 0.93 t (3H, CH₃, J = 7.5); 1.46 m (4H, 2CH₂), 1.63 m (2H, CH₂), 2.77 m (2H, CH₂), 3.18 s (3H, OCH₃), 7.57 s (1H, =CH), 9.02 s (1H, NH). ¹³C NMR (CDCl₃), δ ppm: 14.01 (CH₃), 22.42 (CH₂), 24.07 (CH₂), 29.9667 (CH₂), 31.52 (CH₂), 51.78 (OCH₃), 125.1 (=CH₃b), 133.85 (=CH), 135.77 (C=N), 162.1 (C=O). MS: m/z 197 [MH]+, 196 [M]⁻ Anal. Caled for C₁₀H₁₆N₂O₂ (196.25): C 61.20; H 8.22; N 14.27. Found: C 61.22; H 8.21; N 14.23.

1-Diazononadecan-2-one. 1 g (3.5 mmol) of stearic acid, was dispersed in 10 mL of anhydrous benzene, five-fold excess of thionyl chloride was added, and the mixture was heated for 3 h under reflux. The solvent and excess thionyl chloride were removed under vacuum. The stearoyl chloride was dissolved in THF (15 mL), solution was stirred at 0°C and diazomethane, obtained from nitrosomethylurea (26 mmol) in CH₂Cl₂ (26 mL), was slowly added dropwise. The mixture was stirred until gas no longer evolved. The solvent was removed under vacuum. The resulting crude products were purified by column chromatography using CH₂Cl₂ as eluent. Yield 0.89 g (82%), mp 52–53°C. IR, ν cm⁻¹: 1620, 2122, 2849, 2918, 2955. ¹H NMR (CDCl₃), δ ppm: 0.88 t (3H, CH₃, J = 5.7 Hz), 1.15-1.41 m (28H, 14CH₂), 1.59-1.74 m (2H, CH₂), 2.25-2.42 m (2H, CH₂), 5.23 s (1H, CH₂N). ¹³C NMR (CDCl₃), δ ppm: 14.06 (CH₃), 22.65 (CH₂), 25.19 (CH₂), 29.20 (CH₂), 29.33 (CH₂), 29.43 (CH₂), 29.65 (CH₂), 31.90 (CH₂), 41.10 (CH₂), 54.07 (CH₂N), 195.23 (C=O). Anal. Caled for C₁₉H₃₆N₂O: C 73.97; H 11.76; N 9.08. Found: C 74.15; H 11.71; N 9.12.

General procedure for the synthesis of the pyrazoles 6a-c from allenates 2a-c. Dry 50 ml flask was charged with allene (1mmol), 1-diazononadecan-2-one (1 mmol) and benzene (10 mL). The mixture was sonicated at 68°C for 20 h (monitored by TLC). After completion of the reaction, the solvent was removed under vacuum. The resulting crude products were purified by column chromatography using petroleum ether – EtOAc (7:3) as eluent.

Methyl 4-[2-(1,3-dioxo-1,3-dihydro-2H-isoindol-2-yl)methyl]-5-stearoyl-1H-pyrazole-3-carboxylate (6a). Yield 0.28 g (51%), mp 98-99°C, IR, ν, cm⁻¹: 1686, 1709, 2918. ¹H NMR (CDCl₃), δ ppm: 0.92 t (3H, CH₃, J = 6.9 Hz), 1.19-1.40 m (28H, 14CH₂), 1.71-1.79 m (2H, CH₂), 3.09 t (2H, CH₂, J = 7.7 Hz), 3.90 c (3H, CH₃), 5.40 s (2H, CH₂N), 7.73-7.74 m (2H, C₆H₅), 7.83-7.85 m (2H, C₆H₅), 11.82 s (1H, NH). ¹³C NMR (CDCl₃), δ ppm: 14.13 (CH₃), 22.69 (CH₂), 23.59 (CH₂), 29.29 (CH₂), 29.36 (CH₂), 29.50 (CH₂), 29.52 (CH₂), 29.66 (CH₂), 31.70 (CH₂), 31.92 (CH₂), 39.88 (CH₂), 52.63 (CH₂N), 120.05 (CCH₂), 123.17 (CH₆₆m), 132.01 (C₆₆m), 132.02 (CCOOCH₃), 133.83 (CH₆₆m), 149.56 (C-C=O), 159.61 (O=CO), 167.84 (O=CN), 197.43 (C=O). MS: m/z 552 [MH]+, 551 [M]. Anal. Caled for C₃₂H₄₅N₃O₅ (551.72): C 69.66; H 8.22; N 7.62. Found: C 69.68; H 8.20; N 7.62.

Methyl 4-[2-(1,3-dioxo-1,3-dihydro-2H-isoindol-2-yl)ethyl]-5-stearoyl-1H-pyrazole-3-carboxylate
Yield 0.38 g (67%), mp 66-67 °C. IR, ν cm⁻¹: 1672, 1715, 2851. ¹H NMR (CDCl₃), δ ppm: 0.86 t (3H, CH₃, 3J = 6.5 Hz), 1.12-1.32 m (28H, 14CH₂), 1.53-1.61 m (2H, CH₂, 3J = 7.5 Hz), 3.44 t (2H, CH₂, 3J = 7.5 Hz), 3.74 s (3H, CH₃), 4.00 t (2H, CH₂N, 3J = 6.5 Hz), 7.64-7.66 m (2H, C₆H₂), 7.71-7.73 m (2H, C₆H₂), 11.78 s (1H, NH). ¹³C NMR (CDCl₃), δ ppm: 14.12 (CH₃), 22.68 (CH₂), 22.90 (CH₂), 23.88 (CH₂), 29.28 (CH₂), 29.35 (CH₂), 29.52 (CH₂), 29.69 (CH₂), 31.90 (CH₂), 35.12 (CH₂), 39.58 (CH₂CO), 52.25 (CH₃), 123.04 (CHarom.), 124.06 (CCH₂), 132.03 (C₆H₂), 132.95 (C₆H₂), 133.73 (CHarom.), 148.85 (CC=O), 160.03 (O=CO), 168.19 (O=CN), 197.49 (C=O). MS: m/z 566 [MH]^+ 565 [M]^-. Anal. Calcd for C₃₃H₄₇N₃O₅ (565.74): C 70.06; Н 8.37; N 7.43; О 14.14. Found: C 69.98; Н 8.35; N 7.42.

Methyl 4-[3-(1,3-dioxo-1,3-dihydro-2H-isooindol-2-yl)propyl]-5-stearoyl-1H-pyrazole-3-carboxylate (6c). Yield 0.25 g (43%), mp 60-61 °C. IR, ν cm⁻¹: 1689, 1724, 2925. ¹H NMR (CDCl₃), δ ppm: 0.90 t (3H, CH₃, 3J = 6.9 Hz), 1.18-1.40 m (28H, 14CH₂), 1.68-1.74 m (2H, CH₂), 2.01-2.03 m (2H, CH₂), 3.04 t (2H, CH₂, 3J = 7.5 Hz), 3.16 t (2H, CH₂, 3J = 7.7 Hz), 3.81 t (2H, CH₂, 3J = 7.0 Hz), 3.89 s (3H, CH₃), 7.74-7.76 m (2H, C₆H₂), 7.88-7.89 m (2H, C₆H₂), 11.77 s (1H, NH). ¹³C NMR (CDCl₃), δ ppm: 14.13 (CH₃), 21.02 (CH₂), 22.70 (CH₂), 23.91 (CH₂), 28.99 (CH₂), 29.31 (CH₂), 29.36 (CH₂), 29.54 (CH₂), 29.71 (CH₂), 31.92 (CH₂), 37.83 (CH₂N), 39.67 (CH₂CO), 52.25 (CH₃), 123.17 (CHarom.), 123.21 (C₆H₂), 123.54 (C₆H₂), 127.05 (CCH₂), 133.80 (CHarom.), 148.43 (CC=O), 160.14 (O=CO), 168.46 (O=CN), 197.09 (C=O). MS: m/z 580 [MH]^+ 579 [M]^-. Anal. Calcd for C₃₃H₄₇N₃O₅ (579.77): C 70.44; Н 8.52; N 7.25; О 13.80. Found: C 70.42; Н 8.55; N 7.25.

ACKNOWLEDGEMENTS
This study was performed under financial support by the President of the Russian Federation (program for support of leading scientific schools, project no. NSh-7014.2012.3) and by the Russian Foundation for Basic Research Competition «a» 14-03-00180.

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