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Features on the Way to the Synthesis of 1-Benzoyl-2-Phenyl-3a, 6a-Diazapentalene and 1-Pivaloyl-2-Tert-Butyl-3a,6a-Diazapentalene

Recently discovered 1,3a,6a-triazapentalene systems are among the new fluorophores whose compact and biocompatible structures are suitable for a variety of biological applications. The wavelengths of 1,3a,6a-triazapentalenes vary depending on the nature of the substituents, allowing for the easy synthesis of yellow and red fluorescent reagents for labeling biomolecules. The prototype of the 1,3a,6a-triazapentalene system (without one aza group) is 3a,6a-diazapentalene, which, originally called pyrazolo[1,2-a]pyrazole, which may also exhibit fluorescent activity. However, their research has been limited to a few papers reporting simple and universal principles for synthesizing the 3a,6a-diazapentalene system, one of which involves double alkylation of pyrazole with α-halocarbonyl compounds and treatment of the resulting products with a base. In this work, all stages of the previously performed synthesis of 1-benzoyl-2-phenyl-3a,6a-diazapentalene by the reaction of N-acylalkylation of pyrazole with α-bromoketones through the stages of formation of pyrazolium cation salts are investigated. Based on the studied data, the studied synthesis conditions were first applied by us in stepwise reactions leading to the possible formation of a tert-butyl derivative of 3a,6a-diazapentalene. As a result of the studies, a new, previously undescribed adduct of 3a,6a-diazapentalene, a bicyclic aldol, was obtained. The structure of the substances of the stepwise synthesis was characterized by NMR, IR spectroscopy and mass spectrometry. The mass fragmentation of intermediate N-alkylacylpyrazoles was also considered in detail.

Keywords: 3a,6a-diazapentalenes, pyrazole, N-acylalkylation α-bromoketones, NMR, Aldol, cyclocondensation, quaternization

Introduction

In the chemistry of heterocyclic compounds, a special role belongs to pentalene systems [1]. Recently, a Japanese group [2] of scientists discovered 1,3a,6a-triazapentalene systems, which are among the new fluorophores (Fig. 1).

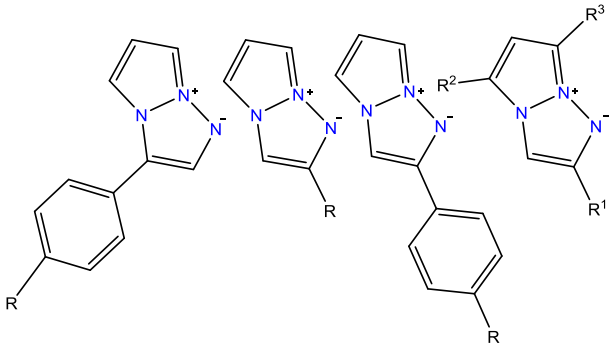

Figure 1. New 1,3a,6a-triazapentalene fluorophores

The compact and biocompatible structure (Fig. 1) of 1,3a,6a-triazapentalene systems exhibits promising spectral properties and is suitable for many biological applications [3, 4]. The wavelengths in them vary depending on the nature of the substituents, which makes it easy to synthesize yellow and red fluorescent reagents for creating labels in biomolecules [3–6].

In recent years, there has been an avalanche-like growth in work on the synthesis and use of 1,3a,6a-triazapentalenes as fluorescent labels [4–9], for example, for various thiols (and in particular, the drug captopril [9]). Methods are being developed for creating unique triazapentalene "wires" to improve the fluorescent properties of materials [10], and their combination with nanomolecular structures [11]. Publications of recent years (on 1,3a,6a-triazapentalenes and benzo- or heterocyclic derivatives) are impressive in their prospects [12–15].

It should be noted that the discovery and selection of such a popular target for fluorescent labels—the triazapentalene system was largely accidental. The prototype of the 1,3a,6a-triazapentalene system (without one aza group) is 3a,6a-diazapentalene [1]. 3a,6a-Diazapentalenes **1** are azaheterocyclic compounds consisting of two five-membered pyrazole rings fused along the N–N bond, having an aromatic 10 π-electron system (Fig. 2), hence the alternative name—pyrazolo[1,2-a]pyrazole.

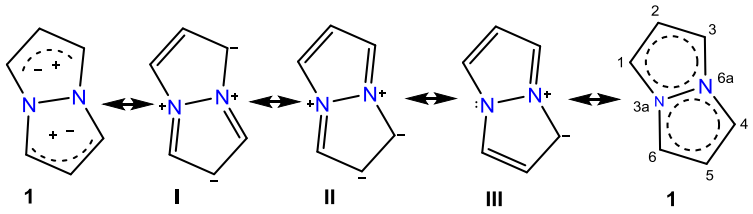

Figure 2. 3a,6a-Diazapentalene **1** and its main resonance forms

The chemistry of these substances froze in the 60–70s of the 20th century and did not develop further [16–20]. These systems are extremely easy to synthesize, but more detailed studies have not been conducted, and no studies of fluorescent properties have been reported. This aspect is undoubtedly a major gap in science that needs to be closed and developed in the scientific community, since 3a,6a-diazapentalene systems carry a huge potential for useful properties and a huge arsenal of scientific discoveries.

An interesting feature of molecule **1** is the impossibility of assigning a covalent structure to it without the participation of dipolar resonance forms, i.e. this molecule is a typical mesoionic structure or, more precisely, a mesomeric betaine [21–23]. According to a detailed analysis [24], the largest contribution (>70 %) is made by only three types of resonance forms (Fig. 2), with structures **I** and **II** with two positive and two negative charges (as well as similar ones and those obtained from them due to the symmetry of system **1**) being preferable, structure **III**, having one positive and one negative charge.

The methods for synthesizing 3a,6a-diazapentalene systems are much simpler, do not require metal catalysts, and are more flexible than those for the 1,3a,6a-triazapentalene system. The authors [16–20] first formulated simple and universal principles for the synthesis of the 3a,6a-diazapentalene system **1** from readily available pyrazoles; one of them is double alkylation of pyrazole with α-halocarbonyl compounds and treatment of the resulting products with a base.

Pyrazoles **2** are five-membered π-electron-excess aromatic heterocyclic compounds that have two linked nitrogen atoms (N–N bond) in the ring structure [25–27], in addition, the pyrazole **2** molecules are planar and strongly associated due to hydrogen bonds [28, 29]. The acid-base properties of pyrazole **2** are due to the presence of pyrrole and pyridine type nitrogen atoms in its structure [30]. Due to the pyridine type nitrogen atom, pyrazole **2** exhibits basic properties (pK_b = 11.5), and due to the pyrrole type nitrogen atom, it exhibits weak acidic properties (pK_a = 2.49) [31].

One of the main ways of creating 3a,6a-diazapentalene compounds is the synthesis of quaternary pyrazolium salts. Only four examples of the synthesis of 1,2-disubstituted pyrazolium salts via repeated alkylation are known in the literature [17], which were then transformed into 3a,6a-diazapentalene structures by treatment with alkaline solutions, through the elimination of water and hydrogen halide and the closure of the second ring of 3a,6a-diazapentalene.

The authors [17] successfully synthesized 4 examples of stable pentalene systems with acceptor substituents, however, these products and their intermediate compounds were not described or characterized spectroscopically.

Taking into account the above, in this study we repeated the previously known synthesis of 3a,6a-diazapentalene, investigated the stepwise route from pyrazole **2** leading to the formation of 3a,6a-diazapentalene compound **8a** through the N-acylalkylation reaction of pyrazole **2** with *α*-bromoketone **3a**, where a series of products were obtained and described. Based on the experience gained and understanding

of the chemistry of the reaction, we have developed and implemented for the first time a similar route aimed at the synthesis of previously unknown *tert*-butyl derivatives of 3a,6a-diazapentalene using unsubstituted pyrazole **2** and 1-brompinacolone **3b** as starting materials.

Experimental

Materials and Methods

Starting materials for the synthesis: pyrazole (98 %) purchased from Acros Organics (Cat. № 13174-0250), phenacyl bromide (98 %) purchased from Sigma-Aldrich (Cat. № 115835), 1-brompinacolone (98 %) purchased from Sigma-Aldrich (Cat. № 414131). Solvents: dioxane (pure grade) and acetone (special purity grade) purchased from EKOS-1; aqueous ammonia solution (analytical grade) purchased from SigmaTec; $NaHCO_3$ (analytical grade) was also used. All reagents were used without further purification.

All reactions and purity were monitored by thin layer chromatography (TLC) on Silufol plates with detection by iodine vapor. Melting and boiling points were determined in open capillaries using a Buchi M560 device.

^1H NMR and ^{13}C NMR spectra were obtained using Agilent 400-MR (400 MHz for ^1H, 100 MHz for ^{13}C) spectrometer in $CDCl_3$ (chemical shift: δ = 7.26 for ^1H, δ = 77.76 for ^{13}C) and DMSO-d_6 (chemical shift: δ = 2.47 for ^1H, δ = 40.03 for ^{13}C). Hexamethyldisiloxane was used as an internal standard. Splitting is reported as s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, br = broad and coupling constants are given in Hz. High resolution mass spectra were recorded on a GC-Mass analysis was performed on an Agilent 7890A gas chromatograph with an Agilent 5975C mass-selective detector on an Rtx DHA-100 column; carrier gas was helium. The samples were dissolved in 1 ml of acetone. The IR spectra were obtained using a FSM 1201 FT-IR spectrophotometer in a KBr tablet in the frequency range: 400–4000 cm^{-1}.

Experimental Procedure

Synthesis of 1-(2-oxo-2-phenylethyl)-1H-pyrazol-2-ium bromide (4a)

3.4 g (0.05 mol) of pyrazole **2** and 15 ml of dioxane were placed in a 250 ml round-bottomed flask. After 5 minutes, 10 g, (0.05 mol) of phenacylbromide **3a** was added to the mixture. The reaction mixture was stirred for 48 h at room temperature. The precipitated finely dispersed white precipitate of salt **4a** was filtered off and dried in air. The yield of product **4a** is 10.8 g (81 %). Decomposition point over 230 °C (190–193 °C [16]).

Synthesis of 1-phenyl-2-(1H-pyrazol-1-yl)ethan-1-one (5a)

The salt **4a** was treated with 20 ml of aqueous ammonia solution, the precipitated yellow crystals were filtered off and dried in air. The yield of product **5a** is 8.4 g (91 %). M.p. 95 °C (89–92 °C [16]). ^1H NMR ($CDCl_3$) δ (ppm), Hz: 7.95–7.89 (m, 2H, Ph), 7.59–7.52 (m, 2H, Ph), 7.48–7.42 (m, 4H, Ph, Pyr), 6.31 (t, *J* = 4.4, 1H, Pyr), 5.54 (s, 2H, CH_2) (Fig. S1). ^{13}C NMR ($CDCl_3$) δ (ppm): 192.62 (C=O), 139.98 (CH, Pyr), 134.66 (C, Ph), 134.12 (CH, Pyr), 131.03 (C, Ph), 129.03 (CH, Ph), 128.19 (CH, Ph), 106.59 (CH, Pyr), 57.75 (CH_2) (Fig. S2). GC-MS Retention time 17.590 min, m/z (EI) = 186, 158, 105, 77, 51, 41, 28 (Fig. S3). IR ν, cm^{-1} (KBr, neat): 3013 (CH), 2986 (CH_2), 1685 (C=O), 1601 (C=N) (Fig. S4).

Synthesis of 1,2-bis(2-oxo-2-phenylethyl)-1H-pyrazol-2-ium bromide (6a)

3.7 g (0.02 mol) of 1-phenyl-2-(1H-pyrazol-1-yl)ethan-1-one **5a** was dissolved in 15 ml of dry acetone in a 100 ml round-bottomed flask. After the mixture was dissolved, 3.9 g (0.02 mol) of phenacyl bromide **3b** was added. The reaction mixture was capped and stirred for 2 days. If no precipitate formed, the mixture was refluxed for three days. Then the mixture was cooled to room temperature and placed in a cold place. The thickened mass was treated with acetone, which disintegrated into a white fine precipitate **5b**. The precipitate **5b** was washed with hot acetone and isopropyl alcohol and dried in air. The yield of **6a** is 4.8 g. (63 %). M.p. 185 °C (173.5–174 °C [16]). ^1H NMR (DMSO-d_6) δ (ppm), Hz: 8.74 (d, *J* = 3.2, 2H, Ph), 8.47 (d, *J* = 3.1, 2H, Ph), 7.58–7.56 (m, 2H, Ph), 7.49 (t, *J* = 7.6, 2H, Ph), 7.32 (m, 6H, Pyr, Ph), 7.20–7.16 (m, 5H, Pyr, Ph), 6.73 (s, 1H, Pyr), 5.16 (d, *J* = 12.7, 2H, CH_2), 4.88 (d, *J* = 12.8, 2H, CH_2) (Fig. S5). ^{13}C NMR (D_2O) δ (ppm): 191.01 (C=O), 135.42 (Ph), 134.76 (CH, Pyr), 134.06 (Ph), 133.31 (CH, Pyr), 132.45 (Ph), 129.36, 129.21, 128.94, 128.77, 128.62, 128.46, 125.48 (Ph), 112.42 (CH, Pyr), 75.59 (CH_2) (Fig. S6). IR ν, cm^{-1} (KBr, neat): 3078, 1597 (CH), 1693 (C=O) (Fig. S7).

Synthesis of 1-benzoyl-2-phenyl-3a,6a-diazapentalene (8a)

In 50 ml of 5 % aqueous $NaHCO_3$ solution 1 g (0.003 mol) of salt **6a** (1,2-bis(3,3-dimethyl-2-oxobutyl)-1H-pyrazol-2-ium bromide) was dissolved, the mixture was stirred and gradually heated to 50 °C. Upon reaching the temperature, copious release of orange precipitate began to be observed on the water sur-

face. The reaction was carried out with intensive stirring for 2–3 days. Control was carried out by TLC. The yellow precipitate **8a** was extracted with chloroform, dried over anhydrous sodium sulfate, then evaporated on a rotary evaporator. Precipitate **8a** was dried in air. The yield of **8a** is 0,71 g (74 %) M.p. 92 °C. ^{1}H NMR (DMSO-d_6) δ (ppm), Hz: 7.90 (s, 1H, Pyr), 7.83 (d, *J* = 6.3, 1H, Pyr), 7.52 (d, *J* = 5.5, 4H, Ph), 7.26 (q, *J* = 6.8, 2H, Ph), 7.10 (dd, *J* = 13.3, 6.6, 4H, Ph), 6.29 (s, 1H, Pyr), 5.82 (s, 1H, CH) (Fig. S8). ^{13}C NMR (DMSO-d_6) δ (ppm): 176.10 (C–O), 140.69, 132.76, 129.92 (Ph), 129.66 (CH, Pyr), 129.55 (CH, Pyr), 129.40, 128.68, 128.07, 127.61, 127.54 (Ph), 113.02 (CH), 109.36 (C=), 104.87 (CH, Pyr). (Fig. S9).

Synthesis of 1-(3,3-dimethyl-2-oxobutyl)-1H-pyrazol-2-iumbromide (4b)

2 g (0.0294 mol) of pyrazole **2** and 15 ml of dioxane were placed in a 100 ml round-bottomed flask. After 5 minutes, 3.95 ml (5.3 g, 0.0294 mol) of 1-brompinacolone **3b** was added to the mixture. The reaction mixture was stirred for 48 h at room temperature. The formed precipitate of salt **4b** was filtered off and dried in air. The yield of product **4b** is 6 g (84 %). M.p. 175 °C.

Synthesis of 3,3-dimethyl-1-(1H-pyrazol-1-yl)butan-2-one (5b)

Then salt **4b** was treated with 20 ml of aqueous ammonia solution, the precipitated yellowish crystals **5a** were filtered off and dried in air. The yield of product **5b** is 3.2 g (65 %).M.p. 56 °C. ^{1}H NMR ($CDCl_3$) δ (ppm), Hz: 8.54 (d, *J* = 3.0, 1H, Pyr), 8.08 (d, *J* = 6.8, 1H, Pyr), 6.71 (t, *J* = 3.0, 1H, Pyr), 4.67 (s, 2H, CH_2), 1.28 (s, 9H, $C(CH_3)_3$) (Fig. S10). ^{13}C NMR ($CDCl_3$) δ (ppm): 205.92 (C=O), 139.34 (CH, Pyr), 129.81 (CH, Pyr), 107.48 (CH, Pyr), 56.53 (CH_2), 43.89 ($\underline{C}(CH_3)_3$), 26.34 ($C(\underline{CH_3})_3$) (Fig. S11). GC-MS Retention time 11.759 min, m/z (EI) = 166, 151, 138, 109, 85, 81, 57, 41, 29, 28 (Fig. S12). IR ν, cm^{-1} (KBr, neat): 2959 (CH_3), 1716 (C=O), 1597 (C=N) (Fig. S13).

Synthesis of 1,2-bis(3,3-dimethyl-2-oxobutyl)-1H-pyrazol-2-ium bromide (6b)

1.43 g (0.009 mol) of 3,3-dimethyl-1-(1H-pyrazol-1-yl)butan-2-one **5b** was dissolved in 15 ml of dry acetone in a 100 ml round-bottomed flask. After the mixture was dissolved, 1.6 g (0.009 mol) of brompinacolin **3b** was added. The reaction mixture was capped and stirred for 2 days. If no precipitate formed, the mixture was refluxed for three days. Then the mixture was cooled to room temperature and placed in a cold place. The thickened mass was treated with acetone, which disintegrated into a white fine precipitate **6b**. The precipitate **6b** was washed with hot acetone and isopropyl alcohol and dried in air. The yield of **6b** is 2.5 g. (82 %). M.p. 190 °C. ^{1}H NMR (D_2O) δ (ppm), Hz: 8.19 (d, *J* = 2.9, 1H, Pyr), 8.00 (d, *J* = 3.0, 1H, Pyr), 6.84 (t, *J* = 2.9, 1H, Pyr), 4.98 (d, *J* = 12.8, 2H, CH_2), 4.70 (d, *J* = 12.8, 2H, CH_2), 1.17 (s, 9H, t-Bu), 0.86 (s, 9H, t-Bu) (Fig. S14). ^{13}C NMR (D_2O) δ (ppm): 212.34 (C=O), 132.01 (CH, Pyr), 130.67 (CH, Pyr), 112.58 (CH, Pyr), 45.13 (CH_2), 38.23 (C, t-Bu), 24.78 (t-Bu), 23.21 (t-Bu) (Fig. S15). IR ν, cm^{-1} (KBr, neat): 2970 (CH_3), 1724 (C=O), 1612 (C=N) (Fig. S16).

Synthesis of 2-(tert-butyl)-2-hydroxy-1-pivaloyl-2,3-dihydro-1H-pyrazolo[1,2-a]pyrazol-4-ium bromide (7b)

In 50 ml of 10 % aqueous $NaHCO_3$ solution 1 g (0.003 mol) of salt **6b** (1,2-bis(3,3-dimethyl-2-oxobutyl)-1H-pyrazol-2-ium bromide) was dissolved, the mixture was stirred and gradually heated to 50 °C. Upon reaching the temperature, copious release of orange precipitate began to be observed on the water surface. The reaction was carried out until the formation of precipitate **7b** ceased. Precipitate **7b** was filtered off and dried in air. The yield of **7b** is 0.71 g (74 %). M.p. 90 °C. ^{1}H NMR (DMSO-d_6) δ (ppm), Hz: 8.36 (d, *J* = 2.9, 1H, Pyr), 8.21 (d, *J* = 2.9, 1H, Pyr), 6.89 (t, *J* = 2.9, 1H, Pyr), 6.54 (s, 1H, OH), 6.49 (s, 1H), 4.98 (d, *J* = 12.5, 1H, CH_2), 4.18 (d, *J* = 12.5, 1H, CH_2), 1.12 (s, 9H, t-Bu), 0.77 (s, 9H, t-Bu) (Fig. S17).^{13}C NMR (DMSO-d_6) δ (ppm): 210.05 (C=O), 132.59 (CH, Pyr), 131.55 (CH, Pyr), 112.54 (CH, Pyr), 90.16 (C-OH), 65.32 (CH), 53.72 (C, t-Bu), 45.14 (C, t-Bu), 39.37 (CH_2), 25.97 (CH_3, t-Bu), 24.25 (CH_3, t-Bu) (Fig. S18).

Results and Discussion

Thus, we obtained 1-benzoyl-2-phenyl-3a,6a-diazapentalene **8a** (74 %), the step-by-step synthesis of which is as follows: pyrazole **2** reacts with phenacyl bromide **3a** (Fig. 3) in dioxane to form salt **4a** (81 %), which, when treated with an aqueous ammonia solution, gives 1-phenacylpyrazole **5a** with a yield of 91 %.

Subsequent alkylation of compound **5a** with a second equivalent of phenacyl bromide **3a** in acetone leads to the formation of 1,2-diphenacylpyrazolium bromide **6a** in 63 % yield. The resulting dialkylated salt **6a** is a colorless crystalline water-soluble substance.

When salt **6a** was treated with 10 % aqueous $NaHCO_3$ solution upon heating to 50 °C for a long time (24 h), 1-benzoyl-2-phenyl-3a,6a-diazapentalene **8a** was formed as a yellow fine powder in good yield (74 %).

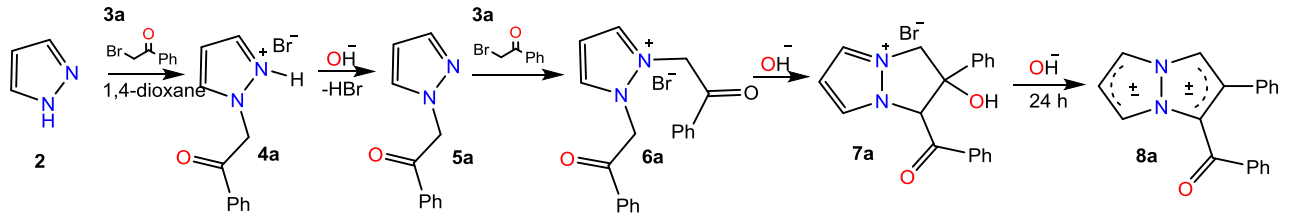

Figure 3. Scheme of the step-by-step synthesis of diaryl-3a,6a-diazapentalene **8a**

The fact that the condensation of carbonyl compounds occurs through the formation of aldols is well known [32], however, in this case, we could not quantitatively observe the formation of aldol **7a**, similar to the 4-fluoro-substituted compound that was previously also obtained and described by X-ray diffraction [33].

The structure of the stepwise synthesized products **4a**, **5a**, **6a**, **8a** was characterized by NMR, IR spectroscopy and mass spectrometry.

We repeated the studied conditions in reactions of synthesis of *tert*-butyl derivatives of pyrazole, in order to obtain a new 3a,6a-diazapentalene (Fig. 4)

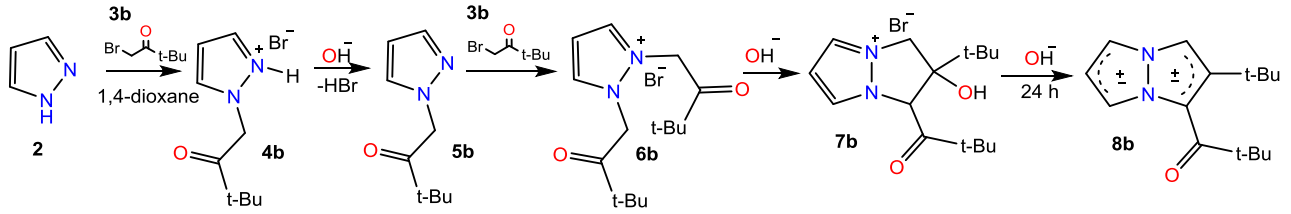

Figure 4. Scheme of the step-by-step synthesis of di(*tert*-butyl)-3a,6a-diazapentalene **8b**

Thus, the N-acylalkylation reaction of unsubstituted pyrazole **2** with 1-bromopinacolone **3b** was carried out in dioxane to form salt **4b** (84 %), which is a colorless crystalline substance soluble in water and polar organic solvents. Upon further treatment of salt **4b** with a base, *tert*-butyl-1-(pyrazol-1-yl)butan-2-one **5b** is formed—low-melting light-yellow crystals, with a total yield of the final product of 65 % (Fig. 4).

The yield of product **5b** decreases due to the increased solubility of the initial salt **4b** in an aqueous medium. And it is more expedient to carry out this reaction in organic solvents, in the presence of anhydrous bases. Thus, we have experimentally established that the reaction in acetone in the presence of K_2CO_3 gives product **5b** with yields of up to 90 %. The potassium carbonate used in parallel with the N-alkylation reaction "One-pot" neutralizes the released hydrobromide with the formation of inorganic salts, as well as the target product **5b**.

Next, N-pinacolone pyrazole **5b** was reacted with another equivalent of 1-bromopinacolone **3b** in acetone for a week, where colorless crystals representing the symmetrical salt **6b** were obtained (Fig. 4).

The next step was to treat salt **6b** with 10 % aqueous $NaHCO_3$ solution by heating to 50 °C for 10 hours, which led to the formation of an orange substance in 74 % yield, NMR analysis of which showed that it was cyclic aldol **7b**. It was determined that the molecule **7b** is not dehydrated, chemical shifts of the geminal protons H^a and H^b are present as a doublet pair, as well as a chemical shift of the OH-group (Fig. 5).

To reliably establish the structure of **7b**, we used homonuclear and heteronuclear methods of 2D NMR spectroscopy, where the most convenient and informative is the $^1H–^{13}C$ HSQC spectrum. Describing this spectrum, we can compare protons connected to the corresponding carbon. As well as signals of protons that do not have direct bonds with carbons.

Thus, Figure 5 shows a pair of doublets of geminal protons H^a (δ 4.98 ppm) and H^b (δ 4.18 ppm), which are bound to carbon C_8 (δ 53.72 ppm). The formation of such doublet protons of one CH_2-group indicates the formation of a cyclic structure and a hindered conformation of the methylene group, in which the rotation of the H^a and H^b protons is limited [34]. There is also a broadened chemical shift of the OH-group, the proton of which does not have a direct bond with carbons.

In addition, the chemical shifts of protons and carbons of the pyrazole fragment (δ_H 8.36 ppm – δ_C 132.59 ppm; δ_H 8.21 – δ_C 131.55 ppm; δ_H 6.89 ppm – δ_C 112.54 ppm) and *tert*-butyl groups (δ_H 1.12 ppm – δ_C 25.97 ppm; δ_H 0.77 – δ_C 24.25 ppm) are clearly distinguished; we compared the sequence in the molecule of these groups using $^1H–^{13}C$ HMBC and $^1H–^1H$ COSY spectra (Figures S19, S20).

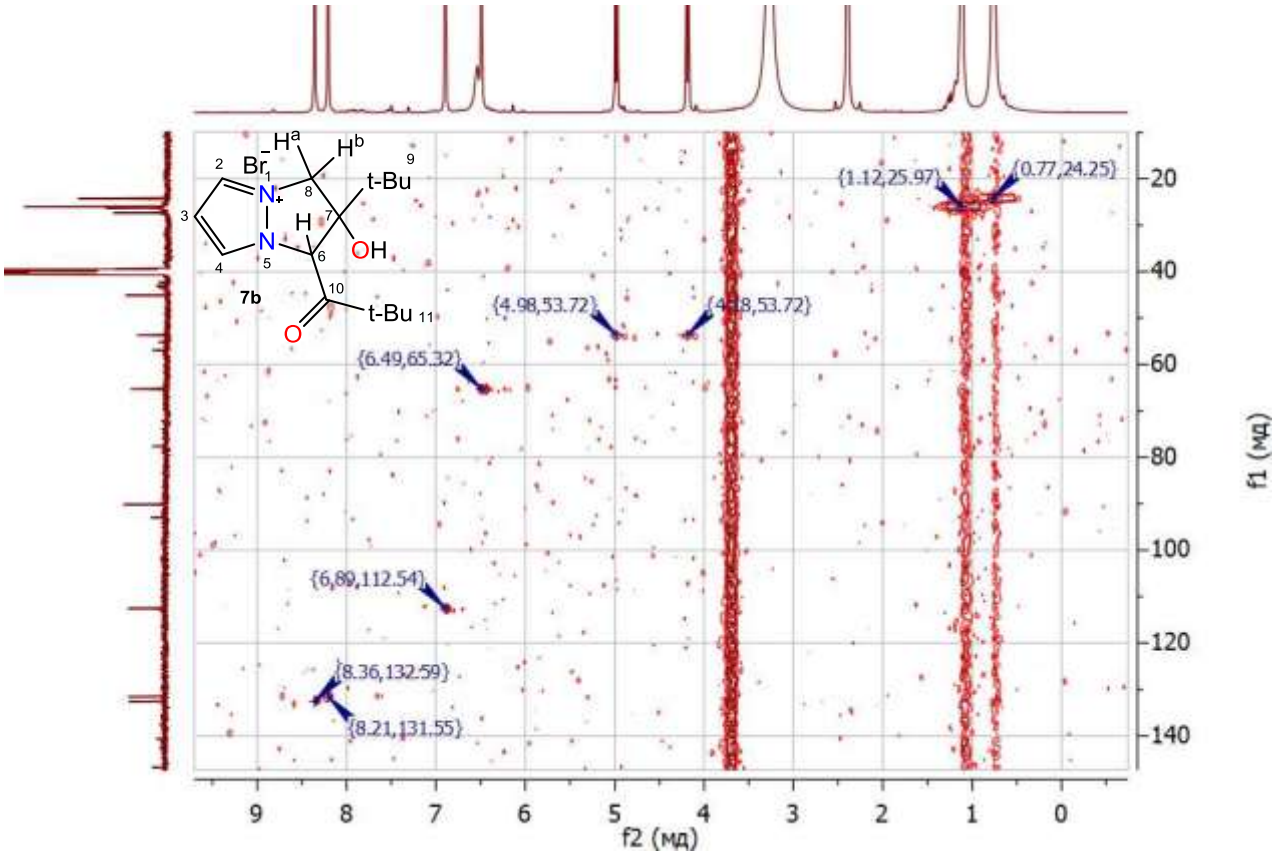

Figure 5. $^{1}H–^{13}C$ HSQC spectrum of aldol **7b** in DMSO-d_6 (δ: 2.50 ppm; 39.5 ppm)

It is known that if the time of treatment with the base of the obtained aldol **7b** is increased from several hours to several days, then 3a,6a-diazapentalene can be obtained [1], however, in the case of *tert*-butyl aldol **7b** we were unable to obtain any pentalene **8b**. The structures of the obtained products **4b**, **5b**, **6b**, **7b** were characterized by IR, NMR spectroscopy and mass spectrometry.

There is no information in the available literature on the features of the fragmentation of N-acylalkyl-pyrazoles, and therefore we examined in detail the features of the ionized decomposition of molecules **5a** and **5b**. Thus, according to the mass spectrometric analysis using Electron ionization, it was determined that the molecular ion of N-pinacolopyrazole **5b** with the value of M^+ = 166.1 m/z has a noticeable intensity. The molecule disintegrates into positively charged ions by the following path (Fig. 6).

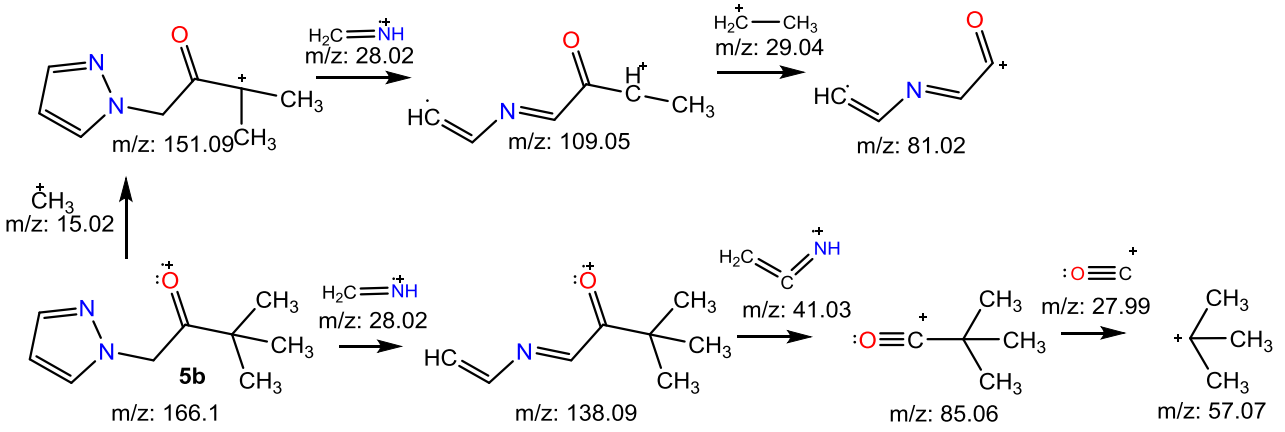

Figure 6. Molecular fragmentation of N-pinacolopyrazole **5b**

The most intense fragment peaks in the mass spectrum of compound **5b** correspond to fragment ions m/z = 29, 57, 81, which is due to the cleavage of the C–C bond adjacent to the oxygen atom, with the charge

retained on the resonance-stabilized acylium cations m/z = 85 and 81. In addition, the fragmentation of **5b** is due to the opening of the pyrazole ring with the detachment of ions m/z 28 $NH=CH^+$ and m/z 41 $NH=C=CH^+$, which are also displayed in the mass fragmentation of N-phenacylpyrazole **5a** (Fig. 7).

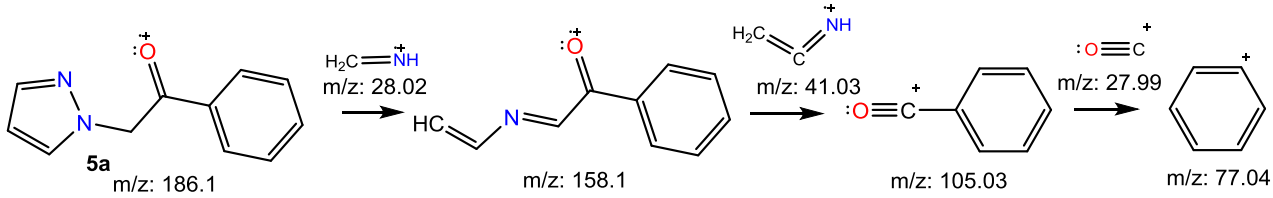

Figure 7. Molecular fragmentation of N-phenacylpyrazole **5a**

The peak of the molecular ion m/z 186.1 of N-phenacylpyrazole **5a** has a noticeable intensity. First of all, the particle m/z 28 $NH=CH^+$ is detached from the pyrazole ring to form a molecular ion m/z 158.1, the high intensity of which is due to the formation of a stable conjugated system of alternating double bonds. Further fragmentation of the m/z 158.1 ion occurs at the bond in the α-position relative to the phenyl ring with the formation of the characteristic Ph-$C=O^+$ fragment (m/z 105), which exhibits maximum intensity along with the phenyl ion m/z 77. The latter is formed when the Ph-$C=O^+$ fragment subsequently loses the $C=O^+$ particle.

Thus, N-alkylacylpyrazoles **5a** and **5b** are substances that are ketones and simultaneously substituted cyclic diamines, the identification of which in the mass spectra can be carried out by the characteristic separation of particles m/z 28 $NH=CH^+$ and m/z 41 $NH=C=CH^+$ and by the presence of fragmentary ions corresponding to the decomposition of aliphatic (**5b**) or aromatic ketones (**5a**).

Conclusions

Thus, in this study, we have thoroughly studied the steps, substances and their structure in the synthesis of 1-benzoyl-2-phenyl-3a,6a-diazapentalene **8a** via the N-acylalkylation reaction of pyrazole **2** with α-bromoketone **3a**. Where substance **8a** was obtained with a good yield of 74 %.

The studied chemistry of the process was used step by step to implement the synthesis route of a similar *tert*-butyl derivative of the 3a,6a-diazapentalene system **8b**. Studies have shown that this step-by-step synthesis of **8b** stopped at the formation of the aldol salt **7b**, and the target 3a,6a-diazapentalene **8b** was not obtained under the studied conditions. The structure of the aldol salt **7b** was characterized by 2D NMR spectroscopy. It is impossible not to note the peculiarity of the influence of the steric factor of phenyl and *tert*-butyl groups, which may require additional study using molecular optimization methods, since in the synthesis of the target phenyl derivative **8a**, the aldol product **7a** was not isolated by us.

The mass fragmentation of N-alkylacylpyrazoles **5a** and **5b** is also considered in detail, the consideration of which will facilitate further study of 3a,6a-diazapentalene structures.

It should be noted that the simplicity and availability of the starting reagents (**2**, **3a**, **b**) in the synthesis of 3a,6a-diazapentalene systems, high yields of intermediate products, simplicity of experiments and conditions for the isolation of target substances open up the possibility of scaling and obtaining significant quantities of derivatives of 3a,6a-diazapentalene structures for the possible creation of functional fluorophore reagents.

Supporting Information

The Supporting Information is available free at https://ejc.buketov.edu.kz/index.php/ejc/article/view/488/301

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Conflicts of Interest

The authors declare no conflict of interest.

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