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ON THE INTERACTION OF PROPARGYL MALONATE WITH NUCLEOPHILES IN THE PRESENCE OF MERCURY(II) ACETATE

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The regiochemistry of the reaction of diethyl 2-(prop-2-yn-1-yl)malonate with various nucleophiles in the presence of mercury(II) acetate has been investigated. The derivative of cyclopentadiene and unsaturated ketoesters were isolated depending on the nature of the dicarbonyl compound and the conditions for the reduction of the organomercury intermediates.

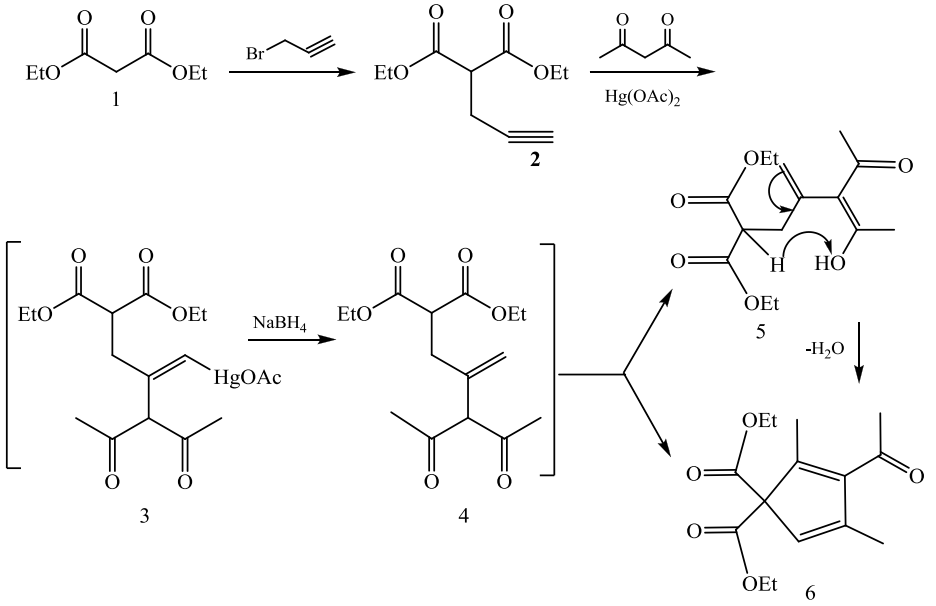
References 6

Earlier, based on the reaction of solvomercuration-demercuration of the terminal triple bond, methods for one-step functionalization were developed and the reasons for obtaining both furan derivatives and the linear products of vinylation were identified [1-4].

Extending the research in this area, diethyl 2-(prop-2-yn-1-yl)malonate **2** synthesized from malonic ester **1** with various CH- and NH-nucleophiles was involved as the substrate in the mercuration-demerculation reaction. The substrate optimally combined model terminal acetylene and dicarbonyl fragments that can influence regiochemistry of the studied reaction.

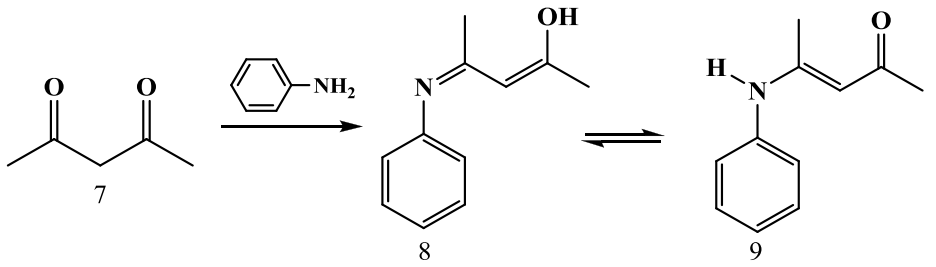
It turned out that the interaction of diethyl 2-(prop-2-yn-1-yl)malonate **2** with sodium acetylacetonate in the presence of mercury(II) acetate in dioxane, followed by demerculation of intermediates **3** and **4** with sodium borohydride, in contrast to alkyl acetylenes, propargyl ethers and proparyl acetate, affords a mixture of diethyl-3-acetyl-2,4-dimethylcyclopenta-2,4-diene-1,1-dicarboxylate **6** and diethyl 2-(3-acetyl-4-hydroxy-2-methylenepent-3-enyl)malonate **5**.

It should be noted that the formation of cyclopentadienyl derivative **6** is a consequence of the prototropic migration of the exomethylene double bond, further dehydration and cyclization according to the following Scheme:

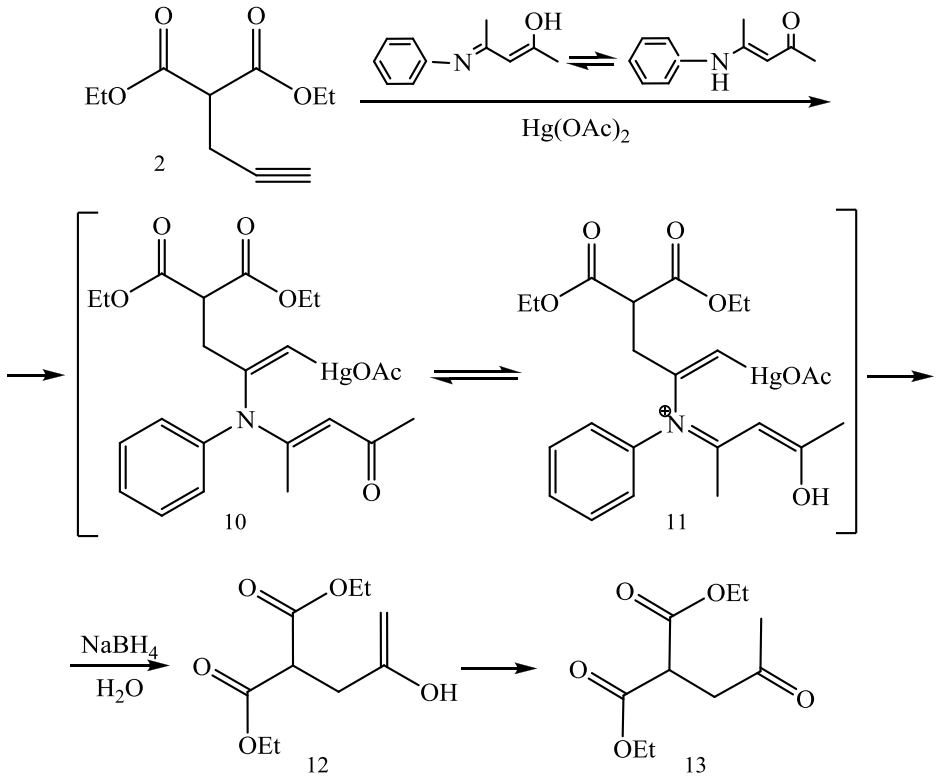


The mixture of linear **5** and cyclopentadienyl **6** derivatives was separated into the individual components by column chromatography.

In this work, we attempted to alkylate diethyl 2-(prop-2-yn-1-yl)malonate **2** with an equilibrium system obtained by condensation of acetylacetone and aniline [5] containing Schiff base **8** and its tautomeric form **9** in a 50: 50 ratio, as per ^{1}H NMR. A characteristic test for the presence of the imine-enamine mixture of **8** and **9** was the ratio of hydrogen atoms of enol **8** (12.4 ppm) and aniline **9** (5.1 ppm).



Similar to the data obtained earlier in [3], after solvolysis with sodium borohydride, products of N-alkylation of the terminal triple bond of diethyl 2-(prop-2- yn-1-yl)malonate were not isolated. It is likely that the reaction proceeded through the intermediate formation of unsaturated amines **10** and **11**, which under demercuration conditions were hydrolyzed to enol **12,** stabilized to diethyl 2-(2-oxopropyl)malonate **13**.



We failed to perform direct hydration (without the participation of amine) in the presence of mercury(II) acetate: only the initial substrate was present in the reaction mixture.

In conclusion, the reactions of diethyl 2-(prop-2-yn-1-yl)malonate with acetylacetone and its derivatives in the presence of mercury(II) acetate have been studied and derivatives of cyclopentadiene and ketoesters were formed.

Experimental Part

^{1}H and ^{13}C NMR spectra (300.07 and 75.46 *MHz* respectively) of the solutions in DMSO-*d6*–CCl4 (1:3) were recorded on a Varian "Mercury-300 VX" spectrometer at 303 K relative to internal TMS. The reaction progress was monitored by TLC using Silufol UV-254 plates, developing with $KMnO_4$ and iodine vapor. GLC analysis was performed using a LHM-80MD instrument (model 3) (1.5 *m* column, AW-NMDC sorbent soaked with 10% Carbovax-20M, rate of carrier gas 40 *mL*/*min*, detector temperature 200°C, evaporator temperature 250°C). Diethyl-2-(prop-2-ynyl)malonate was obtained by reacting sodium malonic ester with propargyl bromide as described in [6]**.**

Diethyl 2-(3-acetyl-4-hydroxy-2-methylenepent-3-enyl)malonate 5, diethyl 3-acetyl-2,4-dimethylcyclopenta-2,4-diene-1,1-dicarboxylate 6. 3.2 *g* of mercury(II) acetate (0.01 *mol*) was dissolved in 50 *ml* of THF, 1.98 *g* (0,01 *mol*) of diethyl 2-(prop-2-yn-1-yl)malonate **2** was added and the mixture was stirred for 1h

at 25 °C. Separately, from 0.23 *g* (0.01 *mol*) of sodium and 1 ml of acetylacetone in 10 *ml* of THF, sodium salt of acetylacetone was obtained, the complex was added and stirred for 12 *h*. Demercuration was carried out by adding 0.2 *g* (0.026 *mol*) of powdered sodium borohydride, the mixture was stirred for another 2 *h*, then the water-ether mixture was added in a 2: 1 ratio, the extracts were dried over magnesium sulfate.

After removal of the solvent, 2.0 *g* of residue was obtained, which was purified by chromatography on a column containing 70 *g* of silica gel (40-100 *μm*). Elution with CCl_4/ether in a 3:1 ratio yielded 0.95 *g* of diethyl 2-(3-acetyl-4-hydroxy-2-methylenepent-3-enyl)malonate **5** with R_f 0.65 (hexane/ether 1:1) and 0.86 *g* of diethyl 3-acetyl-2,4-dimethylcyclopenta-2,4-diene-1,1-dicarboxylate **6** with R_f 0.51 (hexane/ether 1:2).

^{1}H NMR for **5**, (300.07 MHz, DMSO-d6) δ, Hz: 1.77 (t, 3H, CH_3, *J*=7.1), 2.04 (s, 3H, $COCH_3$), 2.71 (ddd, 2H, CH_2, *J*=7.4, 1.5, 1.2Hz), 3.51 (t, 1H, CH, *J*=7,4), 4,15 (q, 2H, OCH_2, *J*=7.1), 5.00 (dt, 2H, =CH_2, *J*=1.5, 1.2), 5.3 (q, 2H, =CH_2, *J*=1.5). Found, %: C 60.79; H 7.39; Calc. for $C_{15}H_{22}O_6$, %: C 60.39; H 7.43.

^{1}H NMR for **6**, (300.07 MHz, DMSO-d6) δ: 1.23 (t, 6H, CH_3), 1.52 (s, 3H, CH_3), 1.95 (s, 3H, CH_3), 2.28 (s, 3H, CH_3), 4.13 (q, 4H, -CH_2CH_3), 5.05 (s, 1H, -C=CH-). Found, %: C 64.71; H 7.2; Calc. for $C_{15}H_{20}O_5$, %: C 64.27; H 7.19.

Reaction of acetylacetone with aniline. 19 *g* (0.2 *mol*) of aniline was dissolved in 160 *ml* of ethanol and 22 *ml* of acetylacetone was added. The reaction mixture was boiled with stirring for 15 *h* [5]. The ethanol was distilled in vacuo, cooled, crystals were separated and washed with ice water, dried under vacuum, heated in a water bath at 45^{o}C. Distillation of the residue in vacuo gave 4 *g* of a mixture of compounds **8** and **9** (the ratio by ^{1}H NMR 50:50).

^{1}H NMR of mixtures **8** and **9**, (400 MHz, DMSO-d6) δ: 1.23 (t, 6H, CH_3), 1.52 (s, 3H, CH_3), 1.95 (s, 3H, CH_3), 2.28 (s, 3H, CH_3), 4.13 (q, 4H, -CH_2CH_3), 5.05 (s, 1H, -C=CH-).

Diethyl 2-(2-oxopropyl)malonate 13. 4.8 g (0.015 *mol*) of mercury(II) acetate was dissolved in 50 *ml* of THF, 3 g (0.015 *mol*) of diethyl 2-(prop-2-yn-1-yl)malonate **2** was added and the mixture was stirred for 1 h at 25 °C. Separately, from 0.345 *g* (0.015 *mol*) of sodium and 2.6 *g* (0.015 *mol*) of imine-enamine mixture the corresponding salt was obtained, the complex was added and stirred for 15 *h* at 25°C. Demercuration was carried out by adding 0.3 *g* of powdered sodium borohydride with stirring for another 2 *h* and the water/ether mixture in a 2:1 ratio was added, the extracts were dried over magnesium sulfate. After removal of the solvent, 2.5 *g* of the residue was obtained. 1 *g* of this residue was purified by chromatography on a column containing 40 *g* of silica gel (40-100 *μm*). Elution with hexane/ether in a 5:1 ratio yielded 0.8 *g* of diethyl 2-(2-oxopropyl)malonate **13.** ^{1}H NMR (300.07 *MHz*, DMSO-d6) δ, *Hz*: 1.26 (t, 6H, CH_3, *J*=7.1), 2.16 (s, 3H, CH_3), 2.98 (d, 2H, CH_2, *J*=7.2), 3.68 (t, 1H, CH, *J*=7,2), 4.14 (q, 4H, OCH_2, *J*=7.1). ^{13}C NMR **13** (75.46 *MHz*, DMSO-d6) δ: 13.5 (CH_3), 28.9(CH_3), 41.1(CH_2), 46.1(CH), 60.5 (OCH_2), 167.6 (O-CO), 203.2 (CO).

ՊՐՈՊԱՐԳԻԼՄԱԼՈՆԱՏԻ ԵՎ ՆՈՒԿԼԵՈՖԻԼՆԵՐԻ ՓՈԽԱԶԴԵՑՈՒԹՅՈՒՆԸ ՄՆԴԻԿԻ(II) ԱՑԵՏԱՏԻ ՆԵՐԿԱՅՈՒԹՅԱՄԲ

Ն. Գ.ՀՈԲՈՍՅԱՆ, Ք. Վ.ԲԱԼՅԱՆ, Ռ. Ս.ՆԵՐՍԻՍՅԱՆ, Լ. Մ.ՂԱԼԵՉՅԱՆ, Ս. Ա.ՀՈՎԱԿԻՄՅԱՆ, Ռ.Բ.ՍԱՐԳՍՅԱՆ և Ժ. Ա. ՉՈԲԱՆՅԱՆ

Հետազոտվել է դիէթիլ-2-(պրոպ-2-ինիլ)մալոնատի փոխազդեցությունը տարաբնույթ նուկլեոֆիլների հետ մնդիկի (II) ացետատի ներկայությամբ: Դիկարբոնիլային միացության և միջանկյալ միացությունների վերականգնման բնույթից կախված ստացվել են չհագեցած կետոններ և ցիկլոպենտադիենի ածանցյալներ:

О РЕАГИРОВАНИИ ПРОПАРГИЛМАЛОНАТА С НУКЛЕОФИЛАМИ В ПРИСУТСТВИИ АЦЕТАТА РТУТИ (II)

Н. Г.ОБОСЯН, К. В. БАЛЯН, Р. С. НЕРСИСЯН, Л. М. ГАЛЕЧЯН, С. А. ОВАКИМЯН, А. Б. САРГСЯН и Ж. А. ЧОБАНЯН

Исследована региохимия взаимодействия диэтил-2-(проп-2-инил)малоната с различными нуклеофилами в присутствии ацетата (II) ртути. В зависимости от природы дикарбонильного соединения и условий восстановления промежуточных ртутьорганических соединений выделены непредельные кетоны и производное циклопентадиена.

REFERENCES

[1] *Боев В.И., Москаленко А.И., Боев А.М.* // Успехи химии, 1997, т. 66, с. 874 [Russ. Chem. Rev., 1997, 66, 789].

[2] *Баданян Ш.О., Чобанян Ж.А., Тиракян М.Р., Даниелян А.О.* // ХГС, 1998, т. 34, с. 904 [Chem. Heterocycl. Compd., 1998, 34, 781].

[3] *Обосян Н.Г., Балян К.В., Нерсисян Р.С., Саргсян А.Б., Чобанян Ж.А.* // ЖОХ, 2016, т. 86, с 746 [Russ. J. Gen. Chem., 2016, 86, 1011].

[4] *Балян К.В., Генджоян Л.М., Акопян В.В., Обосян Н.Г., Чобанян Ж.А*. // ЖОХ, 2014, т. 84, с. 1800 [Russ. J. Gen. Chem, 2014, 84, 2098].

[5] Adnan dib. // Int. J. Chem. Tech. Res., 2013, v. 5, p. 204.

[6] *Weygand-Hilgetag* Organisch-Chemische Experimentierkunst 3. Neubearbeitete Auflage, Johann Ambrosius Barth /Verlag/Leipzig, 1964, p. 944.