Xudoyberdiyeva A.A.
Sharof Rashidov nomidagi Samarqand davlat universiteti
E-mail: *a.khudoyberdiyeva@mail.ru*
Urunbayeva Z.E.
Samarqand davlat tibbiyot instituti
Saidov A.Sh.
Sharof Rashidov nomidagi Samarqand davlat universiteti
Vinogradova V.I.
O‘zbekiston Respublikasi Fanlar akademiyasi akademik S.Yu. Yunusov nomidagi
O‘simlik moddalari kimyosi instituti

ASETILASETON, GOMOVERATRILAMIN VA BA’ZI AROMATIK ALDEGIDLAR ISHTIROKIDAGI KONDENSATSIYA REAKSIYALARINI O‘RGANISH

Annotatsiya. Ganch sintezi asosida 5-N-((3,4-dimetoksifeniletil)amino)-2,4-diasetil-1-metil-3-fenil-siklogeksen-4-ol-1 yenaminonlarning yangi hosilalari sintezi amalga oshirildi. Gomoveratrilamin, asetilaseton va benzaldegid, p-nitrobenzaldegid, p-gidroksibenzaldegid o‘rtasidagi karbosikllanish reaksiyasi o‘tkazildi. Bir reaktorli uch komponentli [1+1+2] sxema asosida yumshoq, ekologik qulay reaksiya sharoitida mos ravishda siklik yenaminonlar sintez qilindi hamda ularning tuzilishi ^{1}H va ^{13}C YaMR spektrlari natijalari asosida o‘rnatildi.

Kalit so‘zlar: yenaminon, gomoveratrilamin, asetilaseton, p-gidroksibenzaldegid, benzaldegid, *p*-nitroaldegidi, ko‘p komponentli sintez.

Худойбердиева А.А.
Самаркандский государственный университет имени Шарофа Рашидова
E-mail: *a.khudoyberdiyeva@mail.ru*
Урунбаева З.Э.
Самаркандский государственный медицинский университет
Саидов А.Ш.
Самаркандский государственный университет имени Шарофа Рашидова
Виноградова В.И.
Институт химии растительных веществ им. акад. С.Ю.Юнусова Академии Наук
Республики Узбекистан

ИЗУЧЕНИЕ РЕАКЦИЙ ТРЕХКОМПОНЕНТНОЙ КОНДЕНСАЦИИ С УЧАСТИЕМ АЦЕТИЛАЦЕТОН, ГОМОВЕРАТРИЛАМИНА И РЯД АРОМАТИЧЕСКИХ АЛЬДЕГИДОВ

Аннотация. Осуществлен синтез новых производных 5-N-((3,4-диметоксифенилэтил)амино)-2,4-диацетил-1-метил-3-фенилциклогексен-4-ол-1 енаминонов на основе Ганча. синтез. Проведена реакция карбоциклизации между гомовератриламином, ацетилацетоном и бензальдегидом, п-нитробензальдегидом, п-гидроксибензальдегидом. По однореакторной трехкомпонентной схеме [1+1+2] в мягких, экологически чистых условиях реакции синтезированы циклические енаминоны, а их структура установлена по результатам ^{1}H- и ^{13}C-ЯМР-спектров.

Ключевые слова: енаминон, гомовератриламин, ацетилацетон, *p*-гидроксибензальдегид, бензальдегид, *p*-нитробензальдегид, многокомпонентный синтез

Xudoyberdiyeva A.A.
Samarkand State University named after Sharof Rashidov
E-mail: *a.khudoyberdiyeva@mail.ru*
Urunbayeva Z.E.
Samarkand State Medical University
Saidov A.Sh.
Samarkand State University named after Sharof Rashidov
Vinogradova V.I.
The Institute of the Chemistry of Plant Substances named acad. S.Yu.Yunusov of the
Academy of Sciences of the Republic of Uzbekistan

STUDY OF THREE-COMPONENT CONDENSATION REACTIONS INVOLVING ACETYLACETON, HOMOVERATRYLAMINE AND A NUMBER OF AROMATIC ALDEHYDES

Annotation. Synthesis of new derivatives of 5-N-((3,4-dimethoxyphenylethyl)amino)-2,4-diasetyl-1-methyl-3-phenyl-cyclohexen-4-ol-1 enaminones was carried out on the basis of Ganch synthesis. The carbocyclization reaction between homoveratrilamine, acetylacetone and benzaldehyde, *p*-nitrobenzaldehyde, p-hydroxybenzaldehyde was carried out. Based on the one-reactor three-component [1+1+2] scheme, cyclic enaminones were synthesized under mild, environmentally friendly reaction conditions, and their structure was established based on the results of ^{1}H and ^{13}C NMR spectra.

Keywords: enaminone, homoveratrilamine, acetylacetone, p-hydroxybenzaldehyde, benzaldehyde, *p*-nitrobenzaldehyde, multicomponent synthesis

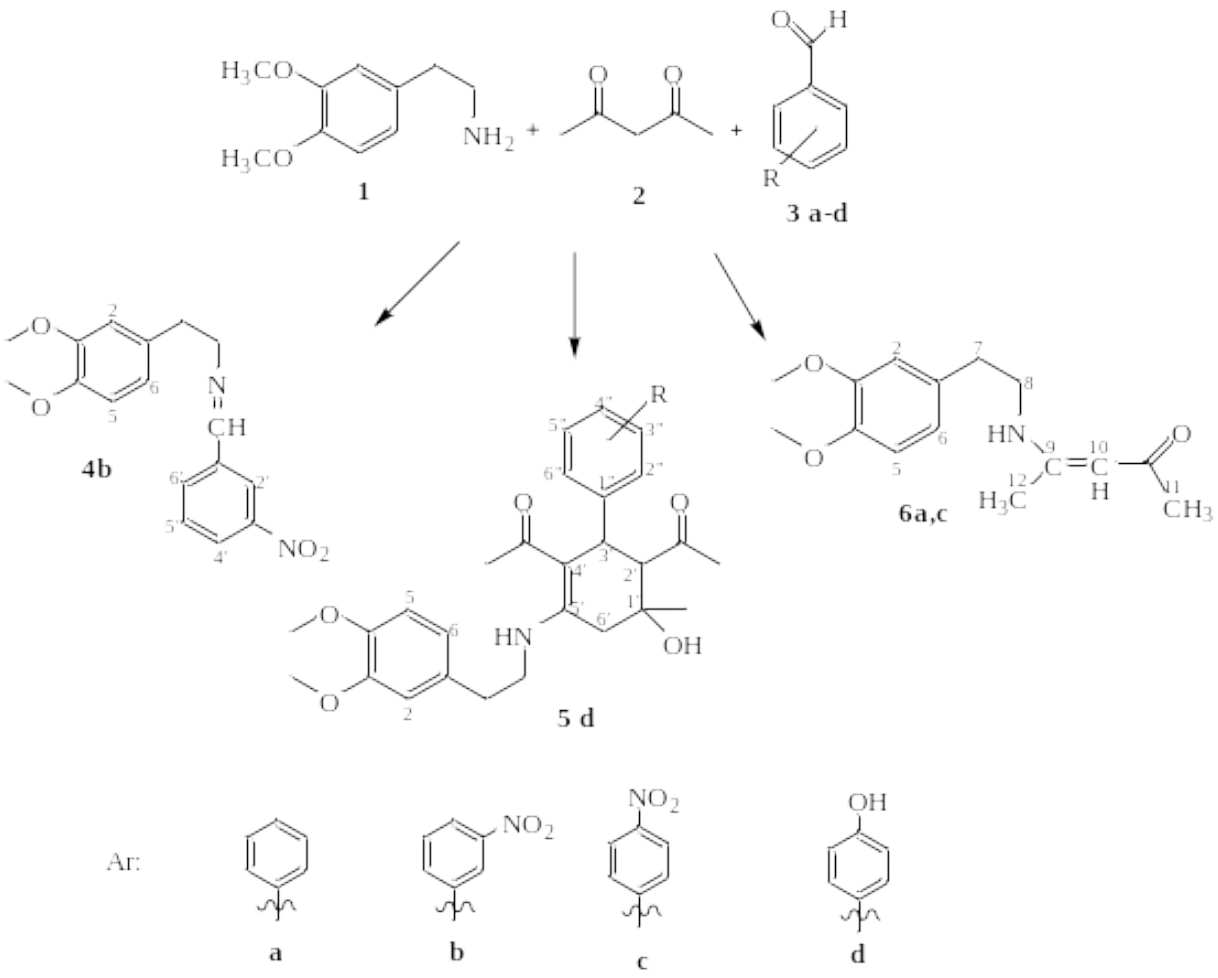
Kirish. Dastlab Ganch sintezi ammiak ishtirokida aldegidlarning etilasetoasetat bilan reaksiyasida o‘rganilgan, bunday reaksiyalar natijasida digidropiridin hosilalari samarali sintez qilina boshlangan. Keyinchalik Sholts [1] va Fillips [2] asetilaseton bilan xuddi shunday sintezlarni amalga oshirdi. Birlamchi aminlar bilan Ganch geterosiklizatsiyasi N-saqlagan digidropirdinlar

hosil bo‘lishi bilan boradi [3]. Bundan tashqari aminning tabiatiga va mol nisbatiga boo‘liq holda digidropirimidin yenaminon hosilalarining sinteziga erishilgan[4]. Bunday birikmalarning biologik faolligi hamda boshqa tabiiy biologik faol birikmalar sintezida oraliq kaskadlar [5] sifatida ahamiyati yuqoriligidan ularga bo‘lgan qiziqish yildan-yilga oshib bormoqda.

Olingan natijalarning muhokamasi.

Bugungi kunda turli metall-katalizatorlar [6], nanokatalizatorlar [7] ishtirokidagi sintezlar yo‘lga qo‘yilgan. Bundan tashqari ultratovush [8] va mikroto‘lqin [9] ishtirokidagi kam vaqt davomida yuqori unum bilan yenaminonlar sintez qilishga erishilmoqda. Bunday usullarda qo‘llaniladigan katalizatorning sintez qilish usullarining murakkabligi, qimmatligi ko‘pchilik hollarda noqulayliklar keltirib chiqaradi. Shulardan kelib chiqib, ushbu tadqiqot ishida biz ekologik qulay, yumshoq sharoitlarda 5-N-((3,4-dimetoksifeniletil)amino)-2,4-diasetil-1-metil-3-fenil-siklogeksen-4-ol-1 sintezini amalga oshirdik.

Yenaminon hosilalarining sintezini amalga oshirish uchun dastlabki modda sifatida gomoveratrilamin '(**1**), asetilaseton (**2**) va benzaldegid (**3a**), m-nitrobenzaldegid (**3b**), p-nitrobenzaldegid (**3c**), p-gidroksibenzaldegid (**3d**) tanlab olindi. Reaksiyalar xona haroratida 7 sutka davomida olib borildi. Bunda **3a,c** aldegidlari bilan kutilgan mahsulot olishga erishilmadi. Bu ikkala holda kutilgan **5** mahsulot o‘rniga **6** mahsulot 51-59% unumlar bilan hosil bo‘ldi, ularning suyuqlanish haroratlari ham yaqin o‘xshashlikda (81-85℃ oralio‘ida) edi. m-nitrobenzaldegid (**3c**) bilan xuddi shu sharoitda aldegid va amin birlashuvidan imin (**4b**) 57% unum bilan olindi. *p*-gidroksibenzaldegid (**3d**) bilan esa xuddi shu sharoitda olib borilgan reaksiyada esa uch komponentli mahsulotni (**5d**) 74% unum bilan olishga erishildi.



1-Jadval. 6a, 4b, 6c, 5d moddalarning suyuqlanish haroratlari va hosil bo‘lish unumlari.

Moddalar	Vaqt	Unumlar, %	Suyuqlanish harorati, ^oC
6a	7 sutka	51	81-82
4b	7 sutka	57	129-130
6c	7 sutka	59	83-85
5d	7 sutka	74	175-177

Olingan mahsulotlarning **4-6** tuzilishi YAMR-spektrlari ma’lumotlari asosida isbotlandi. **5b** birikmalarning ^1H YaMR-spektrida siklogeksen halqasiga tegishli bo‘lgan metil guruhlariga ($-CH_3$) protonlariga tegishli signallar singlet ko‘rinishida bo‘lib, u 1.77 m.u. va 1,99 m.u. sohada kuzatildi va 6' holatdagi metilen protonlarga tegishli signallar snglet ko‘rinishda aksial va ekvatorial holda 1,91 m.u. va 2,20 m.u. namoyon bo‘ldi, 2' va 3' uglerod atomiga tegishli proton signallari dublet ko‘rinishda J=1.0 Gs 3.80 m.u. va J=2.1 Gs 3.84 m.u. sohada rezonanslashgan. Aminga tegishli α-holatdagi metilen guruhining ($-CH_2-$) protonlariga tegishli signallar triplet ko‘rinishida bo‘lib, u J=6,9 Gs 2.79 m.u. sohada va β holatdagi metilen protonlarga tegishli signallar kvartet ko‘rinishda

3,46 m.u. namoyon bo‘ldi. Metoksi (-OCH_3) guruhlariga tegishli protonlarga xos signallar alohida uch protonli singletlar (3H, s) ko‘rinishida 3.81 m.u. va 3.83 m.u. Aromatik halqadagi H-2 protonlari kimyoviy siljish qiymati mos ravishda 6.93 m.u. sohalarda bir protonli dublet shaklida, H-5 va 6 protonga tegishli signallar 6.72 m.u. sohada multiplet ko‘rinishda kuzatiladi. p-gidroksi benzaldegid halqasiga tegishli praton signallari 6.78 (2H, d.d,J=4.5,8.1, H-3",5"), 6.93 (1H, d, J=8.6, H-2"), 7.73 (1H, d, J=8.6, H-6") sohalarda namayon bo‘lgan. OH va NH guruhga taaluqli signallar singlet va keng singlet ko‘rinishda bitta protonli 9.80 m.u. va 10.91 m.u. sohada kuzatilishi aniqlandi.

TAJRIBAVIY QISM.

Birikmalarning unumi va tozaligi Shimadzu LC-20 HPLC (Yaponiya) va C18 (Shimadzu LC-20, Yaponiya) pribori yordamida aniqlandi. IQ spektrlari ATR tizimidan foydalangan holda FT-IR/NIT Spectrum 3 spektrometri yordamida qayd etilgan. YaMR spektrlari JNM-ECZ400R va JNM-ECZ600R spektrometrlarida (Jeol, Yaponiya) 400 va 600 MGts ish chastotalarida, $CDCl_3$ eritmalarida ^1H uchun qayd etilgan. TMS (0 ppm) ^1H NMR spektrlarida ichki standart sifatida ishlatilgan. ^{13}C NMR spektrlarida erituvchining kimyoviy siljishi ($CDCl_3$, TMSga nisbatan 77,16 ppm) ichki standart sifatida ishlatilgan. HR-ESI-MS Agilent Technologies 6420 massa spektrometrida uch karrali LS/MS (elektrospray ionizatsiyasi, ESI TIC Scan va ACQUITY QDa detektorli CAMAG TLC-MS) bilan qayd etilgan. IQ – spektri “FTIR system 2000” priborida (Perkin-Elmer firmasi) KBr tabletkasida olindi. Rf qiymatlari LS 5/40 silikagel plastinkada aniqlandi, harakatchan faza sifatida benzol:metanol (6:1) dan foydlanildi.

Reaksiyaning borishi va hosil bo‘lgan birikmalarning tozaligi Sigma-Aldrich, silufol L/W 10 sm × 20 sm floresan indikator 254 nm (Germaniya) bilan turli erituvchi tizimlarda TLC tomonidan nazorat qilindi. Sintez qilingan barcha moddalarning suyuqlanish temperaturasi mikrostolik Stuart SMP20 apparatida o‘lchandi (1, 2-jadval).

***5-N-((3,4-dimetoksifeniletil)amino)-2,4-diasetil-1-metil-3-fenil-siklogeksen-4-ol-1 yenaminon hosilalarini sintez qilishning umumiy tartibi* (4,5,6 *a-d*).** 0.01 mol gomoveratrilamin, 0.01 mol aromatik aldegid, 0.02 mol asetilaseton aralashmasi (10 ml etanol) 7 sutka davomida magnit aralashtirgich yordamida aralashtirildi. Reaksiyaning borishi yupqa qatlamli xromatogramma usuli bilan nazorat qilib borildi. Reaksiya tugagach erituvchisi uchishi uchun 3 sutkaga qoldirildi. Olingan cho‘kma filtrlandi, qoldiq etanolda qayta kristallandi.

54-((3,4-dimetoksifeniletil)amino)penta-3-en-2-on, $C_{15}H_{21}NO_3$ sintezi (6a). Yuqoridagi usul bilan 0.363 g (0.38 ml, ρ=1.0415 g/ml, 0.003 mol) benzaldegid, 0.342 g (0.7 ml, ρ=0.975 g/ml, 0.006 mol) asetilaseton, 0.62 g (0.61ml, ρ=1.074 g/ml, 0.003 mol) gomoveratrilamin va 10 ml etanol ishtirokida 7 sutka davomida olib borilgan reaksiyadan 0.4 g (51%) mahsulot (**6a**) olindi. Tsuy=81-82°C (xloroform), *Rf*=0.55; (benzol:metanol – 6:1).

^1H YaMR spektri: (600 MHz, $CDCl_3$, δ, m.u., J/Hz): 1.71 (3H, s, H_3-12), 1.91 (3H, s, H_3-11), 2.81 (2H, t, J=7.0, H-7), 3.42 (2H, kv, J=7.0, H-8), 3.9 (3H, s,

OCH_3), 3.8 (3H, s, OCH_3), 4.9 (1H, s, H-10), 6.7 (1H, d, J=2.0, H-2), 6.71 (1H, dd, J=2.0, 10.1, H-6), 6.79 (1H, d, J=8.1, H-5).

N-(3,4-dimetoksifeniletil)-1-(3-nitrofenil)metanimin, $C_{17}H_{18}N_2O_4$ sintezi (4b). Yuqoridagi usul bilan 0.44 g (0.003 mol) *m*-nitrobenzaldegid, 0.59 g (0.6 ml, ρ=0.975 g/ml, 0.006 mol) asetilaseton, 0.5 g (0.49 ml, ρ=1.074 g/ml, 0.003 mol) gomoveratrilamin va 10 ml etanol ishtirokida 7 sutka davomida olib borilgan reaksiyadan 0.43 g, (57%) mahsulot (**4b**) olindi. Tsuy=129-130 °C (xloroform), *Rf*=0.71 (benzol:metanol – 6:1).

^{1}H YaMR spektri: (600 MHz, $CDCl_3$, δ, m.u., J/Hz): 2.97 (2H, t, H-α), 3.80 (3H, s, OCH_3), 3.83 (3H, s, OCH_3), 3.88 (2H, t, J=8.2, H-β), 6.73 (1H, s, H-2), 6.75 (1H, d, J=1.8, H-6), 6.77 (1H, d, J=8.0, H-5), 7.56 (1H, t, J=7.9, H-5'), 8.0 (1H, d, J=7.6, H-6'), 8.17 (1H, s, CH), 8.24 (1H, dd, J=2.1, 8.1, H-5'), 8.53 (1H, t, J=1.8, H-2').

4-((3,4-dimetoksifeniletil)amino)penta-3-en-2-on, $C_{15}H_{21}NO_3$ sintezi (6c). Yuqoridagi usul bilan 0.45 g (0.44 ml, ρ=1.0415 g/ml, 0.003 mol) *p*-nitrobenzaldegid, 0.7 g (0.71 ml, ρ=0.975 g/ml, 0.006 mol) asetilaseton, 0.522 g (0.51 ml, ρ=1.074 g/ml, 0.003 mol) gomoveratrilamin va 10 ml etanol ishtirokida 7 sutka davomida olib borilgan reaksiyadan 0.49 g, (59 %) mahsulot (**6c**) olindi. Tsuy=83-85°C (xloroform), *Rf*=0.57 (benzol:metanol – 6:1).

^{1}H YaMR spektri: (400 MHz, $CDCl_3$, δ, m.u., J/Hz): 1.74 (3H, s, H_3-12), 1.97 (3H, s, H_3-11), 2.78 (2H, t, J=7.1, H-7), 3.4 (2H, kv, J=7.1, H-8), 3.84 (3H, s, OCH_3), 3.84 (3H, s, OCH_3), 4.89 (1H, s, H-10), 6.69 (1H, d, J=1.8, H-2), 6.73 (1H, dd, J=8.0, 1.8, H-6), 6.79 (1H, d, J=8.1, H-5).

5-N-((3,4-dimetoksifeniletil)amino)-2,4-diasetil-1-metil-3-*p*-gidroksifenil-siklogeksen-4-ol-1, $C_{27}H_{33}NO_6$ sintezi (5d). Yuqoridagi usul bilan 0.377 g (0.003 mol) p-gidroksibenzaldegid, 0.62 g (0.63 ml, ρ=0.975 g/ml, 0.006 mol) asetilaseton, 0.56 g (0.55 ml, ρ=1.074 g/ml, 0.003 mol) gomoveratrilamin va 10 ml etanol ishtirokida 7 sutka davomida olib borilgan reaksiyadan 0.98 g, (74 %) mahsulot (**5d**) olindi. Tsuy=175-177°C (xloroform), *Rf*=0.67 (benzol:metanol – 6:1).

^{1}H YaMR spektri: (600 MHz, $CDCl_3$, δ, m.u., J/Hz): 1.77 (3H, s, -CH_3), 1.91 (1H, s, H-6'a), 1.99 (3H, s, -CH_3), 2.20 (1H, s, H-6'e), 2.79 (2H, t, J=6.9, H-α), 3.46 (2H, kv, J=6.9, H-β), 3.80 (1H, d, J=1.0, H-2'), 3.81 (3H, s, -OCH_3), 3.83 (3H, s, -OCH_3), 3.84 (1H, d, J=2.1, H-3'), 6.68 (1H, d, J=2.0, H-2), 6.72 (2H, m, H-5,6), 6.78 (2H, d.d,J=4.5,8.1, H-3",5"), 6.93 (1H, d, J=8.6, H-2"), 7.73 (1H, d, J=8.6, H-6"), 9.8 (1H, s, OH), 10.91 (1H, keng s. NH).

Xulosa. Yenaminonlarning yangi hosilalari sintez qilish maqsadida olib borilgan ushbu tadqiqot ishida uch komponenetli reaksiyalar yordamida *p*-gidroksibenzaldegid bilan 5-N-((3,4-dimetoksifeniletil)amino)-2,4-diasetil-1-metil-3-*p*-gidroksifenil-siklogeksen-4-ol-1 (74%), benzaldegid va *p*-nitrobenzaldegid bilan 4-((3,4-dimetoksifeniletil)amino)penta-3-en-2-on (51-59%) alisiklik yenaminon hosilalari va *m*-nitrobenzaldegid bilan N-(3,4-dimetoksifeniletil)-1-(3-

nitrofenil)metanimin (57%) olishga erishildi**.** Olingan mahsulotlarning tuzilishi ^{1}H va ^{13}C YaMR spektrlari natijalari asosida o‘rnatildi.

Foydalanilgan adabiyotlar ro‘yxati

1. Tajbakhsh M. et al. Old reagent, new results: Aromatization of Hantzsch 1, 4-dihydropyridines with supported bismuth nitrate under microwave irradiation in solventless system //Phosphorus, Sulfur, and Silicon and the Related Elements. – 2003. – T. 178. – №. 4. – C. 773-776.
2. Sommers A. H., Aaland S. E. The Reaction of 1, 5-Dibromopentane with o-Substituted Anilines. The Synthesis of 1-Arylpiperidines1 //Journal of the American Chemical Society. – 1953. – T. 75. – №. 21. – C. 5280-5283.
3. Saleh, A. A concise route to 4-aminomethylpyrazoles and 4-aminomethylisoxazoles from acetylaceton-derived hexahydropyrimidines under mild conditions // Chem. papers 69. – 2015. – Vol. 5. – P. 729-736.
4. Siddiqui Z. N., Khan K., Ahmed N. Nano fibrous silica sulphuric acid as an efficient catalyst for the synthesis of β-enaminone //Catalysis letters. – 2014. – T. 144. – C. 623-632.
5. Sathicq A. G. et al. Preyssler heteropoly acids encapsulated in a silica framework for an efficient preparation of fluorinated hexahydropyrimidine derivatives under solvent-free conditions //Synlett. – 2014. – T. 25. – №. 06. – C. 881-883.
6. J.A. Eremina, E.V. Lider, T.S. Sukhikh, I.V. Eltsov, N.V. Kuratieva, B.A. Zakharov, L.A. Sheludyakova, L.S. Klyushova, E.A. Ermakova, V.V. Dotsenko, Synthesis, crystal structures, spectroscopic, and cytotoxicity study of Cu(II), Co(II), Ni(II) and Pd(II) complexes with 2-anilinomethylidene-5,5-dimethylcyclohexane-1,3-dione. // Polyhedron. – 2020. – T. 178 – C. 114325,
7. Jangir N., Bagaria S.K., Jangid D.K., Nanocatalysts: applications for the synthesis of N-containing five-membered heterocycles // RSC Adv. – 2022. – T.12 – №. 2. C. 19640–19666,
8. Tanhaei M., Mahjoub A. R., Safarifard V. Sonochemical synthesis of amide-functionalized metal-organic framework/graphene oxide nanocomposite for the adsorption of methylene blue from aqueous solution //Ultrasonics sonochemistry. – 2018. – T. 41. – C. 189-195.
9. Lak A. et al. Rapid formation of mono-dispersed hydroxyapatite nanorods with narrow-size distribution via microwave irradiation //Journal of the American Ceramic Society. – 2008. – T. 91. – №. 11. – C. 3580-3584