PROP-2-IN-1-IL 2-(4-ETILFENOKSI)ASETAT VA AYRIM ALMASHINGAN ARILAZIDLARNING KATALITIK SIKLOBIRIKISH REAKSIYASI

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ANNOTATSIYA

Geterohalqali birikmalar orasida 1,2,3-triazollar – sintez usulining qulayligi, kam zaharliligi va biologik faolligi yuqoriligi sababli hozirgi davrda ko‘plab organik kimyogarlar tomonidan sintezi amalga oshirilmoqda. Ushbu tadqiqot ishida azid-alkin 1,3-bipolyar siklobirikish reaksiyasi asosida yangi 1,2,3-triazol hosilalarining sintez usuli keltirilgan.

Kalit so‘zlar: 1,2,3-triazollar, prop-2-in-1-il 2-(4-etilfenoksi)asetat, aromatik azidlar, 1,3-bipolyar katalitik siklobirikish reaksiyasi.

KIRISH

Jahon miqiyosida olib borilayotgan tadqiqotlar natijasida yallig‘lanishga, sil, saraton, qandli diabet va mikroblarga qarshi, og‘riq qoldiruvchi, isitma tushiruvchi, antivirus, antiepileptik, antimikobakterial, antifungal, antiviral, antiallergik, bakterisid, fungitsid, insektisid va boshqa foydali xususiyatlarga ega bo‘lgan kam zaharli 1,2,3-triazol hosilalarini maqsadli sintez qilish orqali tibbiyot va qishloq ho‘jaligi, hamda sanoatning bir qancha tarmoqlari uchun zarur bo‘lgan turli-tuman preparatlar tayyorlanmoqda.

ADABIYOTLAR TAHLILI VA METODOLOGIYA

1,2,3-Triazol hosilalarining sintezi dunyoning ko‘pgina olimlari tomonidan mukammal tarzda o‘rganilgan bo‘lib, ushbu izlanishlar hozirgi vaqtda jadal rivojlanib bormoqda. Katalitik usulda 1,2,3-triazollarning yangi hosilalarini sintez qilish va ular asosida biologik faol birikmalarni yaratish, sanoat texnologiyalarini ishlab chiqish va qo‘llanilish sohalarini kengaytirishga yo‘naltirilgan ilmiy izlanishlar Huisgen R., Sharpless K., Meldal M., Martinelli M., Lu Yang., Senthil S., Samsonu D., Nino A. D., Albadi J., Singh, R. J., Asgari M. S., Lebeau A., Li P., Wang L., Zheng Z-J., Yuriy M. Sh. va Ilya V.E. kabi olimlar tomonidan izchil olib borilmoqda [1-3].

Mazkur tadqiqot yo‘nalishi bo‘yicha 1H-1,2,3-triazol hosilalarini sintez qilish, kimyoviy xossalari va biologik faolligini o‘rganish bo‘yicha O‘zbekistonlik Maxsumov A.G., Madixonov N., Abdugafurov I.A., Djuraev A.D., Ziyadullaev O.E., Nikbaev A.T., Muxammedova R., Ortikov I.S., Qirg‘izov F.B., Mamajonov J.Sh., Usmanova S.G. va boshqa olimlar tomonidan tizimli ishlar olib borilgan [4,5,6].

Biz ham o‘z tadqiqotlarimizni 1,2,3-triazol hosilalari sintezi, kimyoviy o‘zgarishlari va biologik faolliklarini o‘rganishga bag’ishladik. Buning uchun 1,2,3-triazollarning asosiy sintez usuli bo‘lgan azid-alkin siklobirikish reaksiyasidan foydalanmoqdamiz. Biz ob’ekt sifatida yod sirka kislota propargil efirini (**1**) tanlab oldik. Dastlab yod sirka kislota propargil efirini para-etilfenol (**2**) bilan alkillash reaksiyasi olib borildi va tegishli propargil efir sintez qilindi (**3**). So‘ngra olingan modda bilan ayrim aromatik azidlarni (**4-7**) 1,3-bipolyar siklobirikish reaksiyasi (**8-11**) amalga oshirildi. Reaksiya reagentlarning 1:1 nisbatdagi aralashmasini mis (I) bromid katalizatori ishtirokida toluol eritmasida 110^{o} C (toluolni qaynash harorati) haroratda 6 soat qizdirib olib borildi. Reaksion aralashma sovutildi, tushgan cho’kma filtrlandi, quritildi, etanolda qayta kristallandi va fizik konstantalari o‘rganildi. Katalitik halqalanish natijasida tegishli 1,2,3-triazol hosilalarini 1,4-izomeri hosil bo‘lganligi kuzatildi.

Metod va materiallar. Erituvchilardan asetonitril, etil spirti, geksan, aseton, benzol, toluol, metanol ishlatilgan. Birikmalarning tuzilish natijalari zamonaviy IQ, ^{1}H- va ^{13}C YaMR-spektroskopiyada olingan natijalar asosida ishonchli tarzda tahlil qilingan va tekshirilgan. Reaksiyalarning borishi yupqa qatlamli xromatografiya (YUQX) usulida kuzatib borilgan, elyuent sifatida benzol:metanol - 10:1 (A), etilasetat : petroley efir – 1: 2 (B), geksan : etilasetat – 1:1 (C) nisbatdagi aralashmasi ishlatilgan. Sintez qilingan birikmalarning suyuqlanish haroratlari «MEL-TEMP» (AQSH) priborida aniqlandi.

Prop-2-in-1-il 2-(4-etilfenoksi) atsetat sintezi (3)

Bir og‘izli tubi yumaloq 100 ml li kolbaga 1.22 g (10 mmol) para-etilfenol, 2.46 g (11 mmol) monoyodsirka kislota propargil efiri , 1 g quruq potash, 0.2 g TBAB va 40 ml atsetonitril solindi. Qaytarma sovutgich orqali suv hammomida 80°C da 6 soat qaynatildi. Reaksiya yupqa qatlamli xromatografiya usuli yordamida kuzatib borildi. Reaksion aralashma sovugandan so’ng ustiga 200 ml distillangan suv quyib ikkiga ajratildi. Ustki organik qism ajratgich voronka yordamida ajratildi. Suvli qism 3 marotaba (3*30) efirda ekstraksiya qilinib, organik qismga qo’shildi va suvsiz Na_2SO_4 solib kun davomida quritildi. Efirli qism dekantatsiya usulida qurituvchidan ajratildi va efir oddiy usulda haydab olindi. Qolgan qoldiq vakuum sharoitda 85-86 ^{0}C da (6 mm.sim. ust.) haydaldi. Massasi

1.92 g (88 % unum bilan) mahsulot (**3**) olindi. Suyuqlanish harorati T_{qayn}=48-50°C, R_f 0.7 (sistema A).

(1-(4-bromofenil)-1H-1,2,3-triazol-4-il) metil 2-(4-etilfenoksi) asetat sintezi (8)

100 ml li tubi yumaloq kolbaga 1.00 g (0.005 mol) para-bromfenilazid, 1.09 g (0.005 mol) prop-2-in-1-il 2-(4-etilfenoksi) atsetat, 0.10 g (0,32 mmol) mis(I)bromid va 30.0 ml yangi haydalgan toluol olindi. Kolba moy hammomiga o'rnatilib, qaytarma sovutgichga ulangan xolda, toluolni qaynash haroratida (110^o C) 6 soat davomida qizdirildi. Reaksiyani borishi yupqa qavatli xromatografiya orqali tekshirib turildi. Reaksiya aralashmasida vaqt o‘tishi bilan sariq cho‘kma hosil bo‘la boshladi. 6 soatdan so‘ng reaksiya to‘xtatildi va xona haroratida bir kecha qoldirildi. Tushgan cho‘kma fil’trlandi, quritildi va etanolda qayta kristallandi. Massasi 1.9136 g. 92 % unum bilan mahsulot olindi. T_{suyuq}=118-120^{o}C, R_f 0.6 (sistema B).

^{1}H YaMR (400 MHz, $CDCl_3$): 1.17 (3H, t, J=7.60, -CH_2-CH_3), 2.55 (2H, q, J=7.74, -CH_2-CH_3), 4.64 (2H, s, -OCH_2), 5.41 (2H, s, COO-CH_2-) 6.80 (2H, d, J=8.83, Ar-H- 2,6), 7.08 (2H, d, J=8.71, Ar-H- 3,5) 7.58 (2H, d, J=8.96, Ar-H- 2’, 6’), 7.65 (2H, d, J=9.09, Ar-H- 3’, 5’), 7.96 (1H, s, (1H, s, triazol-H). **^{13}C YaMR** ($CDCl_3$): 169.23, 155.67, 143.27, 137.72, 135.76, 132.98, 128.87, 122.72, 122.27, 121.96, 114.50, 77.23, 65.33, 58.15, 27.94, 15.73,

IQ - spektr (KBr, ν, см$^{-1}$): 3143 (Ar C-H), 2967 (C=C-H), 2931 (CH_2), 1747 (>C=O), 1611 (C=C), 1585 (N=N), 1340 (C-O-), 1211 (C-N), 1176(C-O-C).

(1-(2-Bromofenil)-1H-1,2,3-triazol-4-il) metil 2-(4-etilfenoksi) asetat sintezi (9)

Yuqorida keltirilgan usul orqali 1.00 g (0.005 mol) orto -bromfenilazid, 1.09 g (0.005 mol) prop-2-in-1-il 2-(4-etilfenoksi) atsetat, 0.10 g (0,32 mmol) mis(I)bromid va 30.0 ml toluol olindi. Massasi 1.83 g. (88 % unum bilan) mahsulot (**9**) olindi. T_{suyuq}=140-142 ^{o}C. R_f 0.67 (sistema A). **^{1}H YaMR** (400 MHz, $CDCl_3$): 1.17 (3H, t, J=7.60, -CH_2-CH_3), 2.55 (2H, q, J=7.74, -CH_2-CH_3), 4.64 (2H, s, -OCH_2), 5.41 (2H, s, COO-CH_2-) 6.80 (2H, d, J=8.83, Ar-H- 2,6), 7.08 (2H, d, J=8.71, Ar-H- 3,5) 7.58 (2H, d, J=8.96, Ar-H- 2’, 6’), 7.65 (2H, d, J=9.09, Ar-H- 3’, 5’), 7.96 (1H, s, (1H, s, triazol-H). **^{13}C YaMR** ($CDCl_3$): 169.23, 155.67, 143.27, 137.72, 135.76, 132.98, 128.87, 122.72, 122.27, 121.96, 114.50, 77.23, 65.33, 58.15, 27.94, 15.73,

IQ - spektr (KBr, ν, см$^{-1}$): 3153 (Ar C-H), 3045 (C=C-H), 2948 (CH_2), 1760 (>C=O), 1610 (C=C), 1591(N=N), 1510 (Ar-NO_2), 1385 (C-O-), 1201 (C-N), 1175 (C-O-C).

(1-(3,4-Dixlorofenil)-1H-1,2,3-triazol-4-il)metil 2-(4-etilfenoksi)asetat sintezi (10)

Yuqorida keltirilgan usul orqali 0.94 g (0.005 mol) 3.4-dixlorfenilazid, 1.09 g (0.005 mol) prop-2-in-1-il 2-(4-etilfenoksi) atsetat, 0.10 g (0,32 mmol) mis(I)bromid va 30.0 ml toluol olindi. Massasi 1.543g. (76% unum bilan) mahsulot (**45**) olindi. T_{suyuq}=114-115^{o}C, R_f 0.7

(sistema C). **^{1}H YaMR** (400 MHz, $CDCl_3$): 1.17 (3H, t, J=7.60, -CH_2-CH_3), 2.55 (2H, q, J=7.74, -CH_2-CH_3), 4.64 (2H, s, -OCH_2), 5.41 (2H, s, COO-CH_2-) 6.80 (2H, d, J=8.83, Ar-H- 2,6), 7.08 (2H, d, J=8.71, Ar-H- 3,5) 7.58 (2H, d, J=8.96, Ar-H- 2', 6'), 7.65 (2H, d, J=9.09, Ar-H- 3', 5'), 7.96 (1H, s, (1H, s, triazol-H). **^{13}C YaMR** ($CDCl_3$): 169.23, 155.67, 143.27, 137.72, 135.76, 132.98, 128.87, 122.72, 122.27, 121.96, 114.50, 77.23, 65.33, 58.15, 27.94, 15.73,

IQ - spektr (KBr, ν, см$^{-1}$): 3153 (Ar C-H), 3045 (C=C-H), 2948 (CH_2), 1760 (>C=O), 1610 (C=C), 1591(N=N), 1510 (Ar-NO_2), 1385 (C-O-), 1201 (C-N), 1175 (C-O-C).

4-(4-((2-(4-etilfenoksi)asetoksi)metil)-1H-1,2,3-triazol-1-il)benzoy kislota sintezi (11)

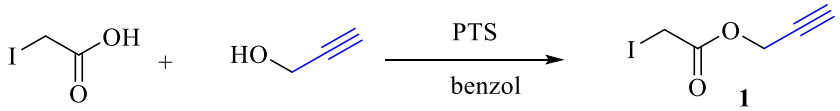
Yuqorida keltirilgan usul orqali 0.815 g (0.005 mol) para-azidobenzoy kislota, 1.09 g (0.005 mol) prop-2-in-1-il 2-(4-etilfenoksi) atsetat, 0.10 g (0,32 mmol) mis(I)bromid va 30.0 ml toluol olindi. Massasi 1.54g. (81 % unum bilan) mahsulot (**48**) olindi. T_{suyuq}=192-194 ^oC, R_f 0.33 (sistema C). **^{1}H YaMR** (400 MHz, $CDCl_3$): 1.18 (3H, t, J=7.87, -CH_2-CH_3), 2.57 (2H, q, J=7.65, -CH_2-CH_3), 4.67 (2H, s, -OCH_2), 5.46 (2H, s, COO-CH_2-) 6.81 (2H, d, J=8.81, Ar-H- 2,6), 7.13 (2H, d, J=8.70, Ar-H- 3,5) 7.89 (2H, d, J=9.05, Ar-H- 2', 6'), 8.29 (2H, d, J=8.93, Ar-H- 3', 5'), 8.08(1H, s, (1H, s, triazol-H). **^{13}C YaMR** ($CDCl_3$): 182.23, 169.23, 155.67, 143.27, 137.72, 135.76, 132.98, 128.87, 122.72, 122.27, 121.96, 114.50, 77.23, 65.33, 58.15, 27.94, 15.73,

IQ-spektr (KBr, ν, sm^{-1}): 2962 (Ar C-H), 2551 (C=C-H), 1749 (>C=O), 1607 (C=C), 1511 (N=N), 1432 (Ar-I), 1255 (C-O-), 1230 (C-N), 1172 (C-O-C).

NATIJALAR MUHOKAMASI

Mazkur tadqiqotimizning asosiy maqsadi, monoyodsirka kislotaning propargil efiri bilan para-etilfenolni alkillash reaksiyasi asosida olingan prop-2-in-1-il 2-(4-etilfenoksi)asetat efirini ayrim arilazidlar bilan o'zaro siklobirikish reaksiyasini amalga oshirish. Reaksiyani borishiga ta'sir etuvchi omillarni aniqlashdan iborat edi. Buning uchun ishni boshlang'ich moddalarni sintez qilishdan boshladik.

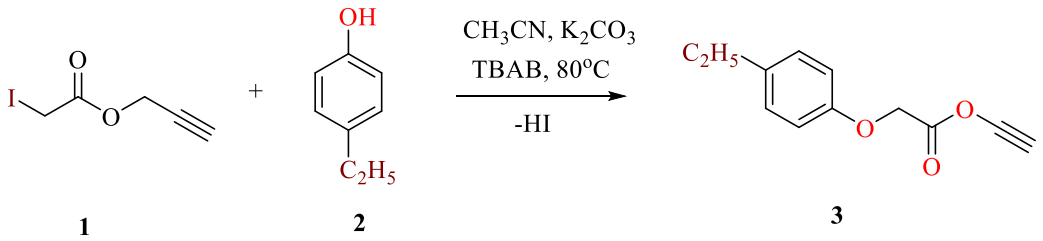
Dastlab monoyodsirka kislota va propargil spirtidan eterifikatsiya reaksiyasi orqali tegishli propargilyodatsetat efiri (**1**) sintez qilib olindi. Reaksiyada suvni tortib oluvchi modda sifatida para-toluolsul'fokislota (PTS) ishlatildi.



1

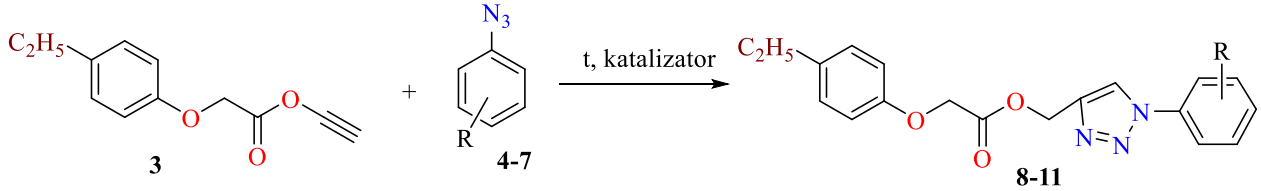
So'ng para-etilfenolni monoyodsirka kislota propargil efiri bilan alkillash reaksiyasi amalga oshirildi. Reaksiya para-etilfenol

va monoyodsirka kislotaning 1:1mol nisbatdagi aralashmasini potash va TBAB katalizatorligida atsetonitril eritmasida qizdirib olib borildi. Natijada yuqori unum bilan prop-2-in-1-il 2-(4-etilfenoksi)asetat (**3**) ajratib olindi. Modda geksanda qayta kristallandi.



1 **2** **3**

Olingan prop-2-in-1-il 2-(4-etilfenoksi)asetat efirini ayrim arilazidlar bilan o‘zaro siklobirikish reaksiyasi amalga oshirildi. Azidlar (**4-7**) adabiyotdagi usul orqali sintez qilib olindi [7]. Aromatik azidlardan para-bromfenilazid, orto-bromfenilazid, 3,4-dixlorfenilazid va para-azidobenzoy kislota olindi. Halqalanish reaksiyasi reagentlarning 1:1 nisbatdagi aralashmasini mis(I)bromid katalizatori ishtirokida toluol eritmasida 110°C (toluolni qaynash harorati) haroratda 6 soat qizdirib olib borildi.

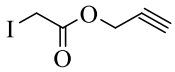
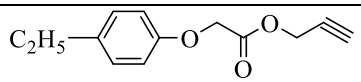
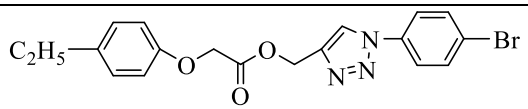


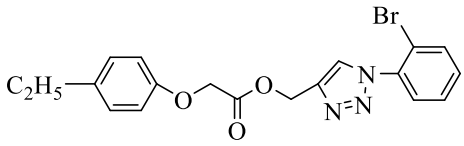
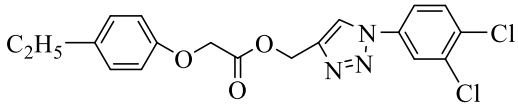
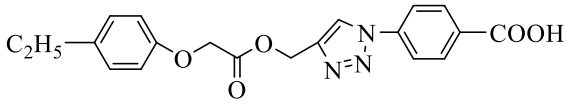
3 **4-7** **8-11**

R= **8**) p-Br; **9**) o-Br; **10**) 3,4-dixlor; **11**) p-COOH

Reaksion aralashma sovutildi, tushgan cho‘kma fil’trlandi, quritildi va fizik konstantalari o‘rganildi. Natijada 1H-1,2,3-triazollarning yangi – 1,4-izomer hosilalari (**8-11**) yuqori unumlar bilan olindi (1-jadval).

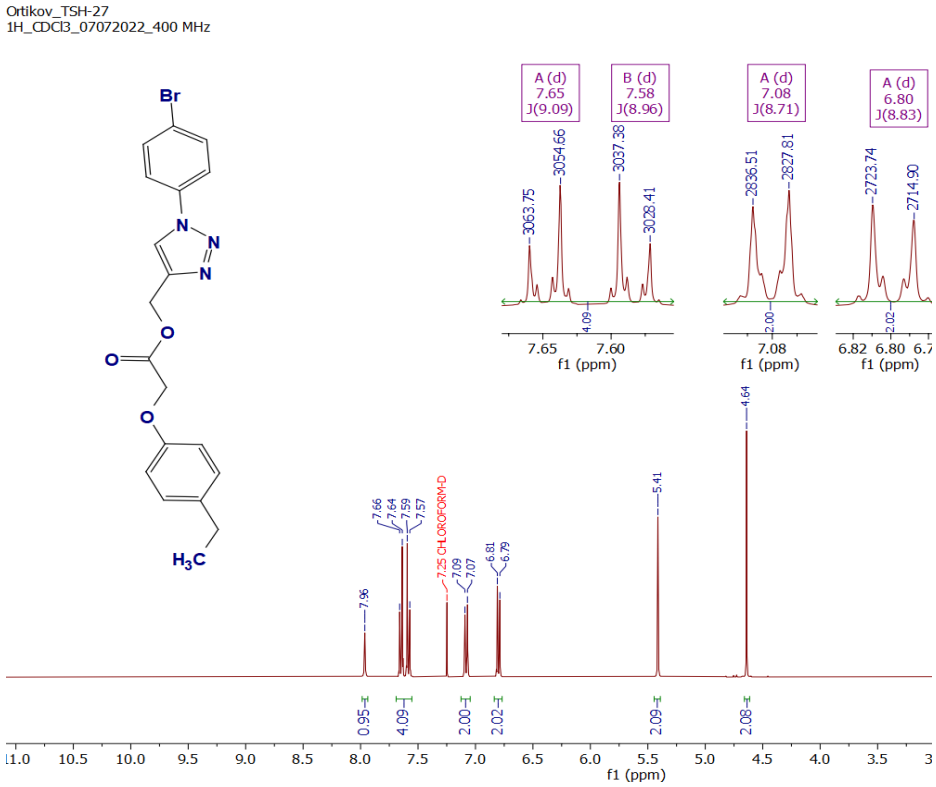
1-Jadval. Sintez qilingan moddalarning unumi, ayrim fizik kattaliklari

№	Birikmalarning tuzilish formulasi	Rf qiymati *	T_{suyuq}, °C	Unum, %
1		0.67 (A)	140	79
3		0.7 (A)	48-50	88
8		0.6 (B)	118-120	92

9		0.67 (A)	140-142	88
10		0.7 (C)	114-115	76
11		0.33 (C)	192-194	81

* A) bbenzol : metanol – 10:1, B) etilasetat : petroley efir – 1: 2, C) geksan : etilasetat – 1:1

Hosil bo‘lgan triazol hosila (1-(4-bromofenil)-1H-1,2,3-triazol-4-il) metil 2-(4-etilfenoksi) atsetatning (**8**) tuzilishi ^{1}H YaMR- va ^{13}C YaMR-spektrlari orqali tahlil qilindi. Uning 1H-YaMR spektrida ($CDCl_3$) fenil guruhi hamda triazol halqasini bog‘lab turuvchi metilen guruhlari protonlari nisbatan kuchsiz sohada – 4.64 va 5.41 m.u. larda ikki protonli singlet holida tegishli kimyoviy siljishga (4.64 2H, s, -OCH_2; 5.41 2H, s, -COO-CH_2) ega bo‘lganini ko'rishimiz mumkin (1-rasm). Molekuladagi benzol halqasi protonlari 6.8 m.u. (2H, d, J=9.09, Ar-H- 2, 6), 7.08 m.u. (2H, d, J=9.09, Ar-H- 3’, 5’), 7.58 m.u. (2H, d, J=9.09, Ar-H- 2’, 6’) ва 7.65 m.u. da (2H, d, J=8.96, Ar-H- 3, 5) holida namoyon bo‘lganligini ko‘rish mumkin. Triazol halqasidagi bitta proton esa 7.96 m.u. da singlet holida kimyoviy siljishga ega bo‘ldi.



1-rasm. (1-(4-bromfenil)-1H-1,2,3-тtriazol-4-il) metil 2-(4-etilfenoksi) atsetatning (**8**) ^{1}H YaMR spektri.

8- Moddaning IQ spektrida tegishli Ar-H, -CH_2-, C-O-C, C=O, C-N, N=N, Ar-Br kabi funksional guruhlariga hos bo‘lgan yutilish chastotalarini ko‘rishimiz mumkin. Olingan spektral natijalarning tahlili **8**-moddaning tuzilishini tegishli strukturaga mos ekanligini to‘liq isbotlaydi. **9-11**-Moddalarning ham tuzilishi ^{1}H YaMR, ^{13}C YaMR va IQ spektrlari orqali o‘rganilgan bo‘lib, tuzilishi isbotlangan.

XULOSA

Para-etilfenolning (**2**) monoyodsirka kislotaning propargil efiri (**1**) bilan yumshoq sharoitda alkillanishidan (atsetonitril) yuqori unumlar bilan izomer prop-2-in-1-il 2-(4-etilfenoksi) atsetat (**3**) sintez qilingan. Olingan prop-2-in-1-il 2-(4-etilfenoksi) atsetatni para-brom, orto-brom, para-karboksil, 3.4-dixlorfenilazidlar bilan o‘zaro halqalash natijasida 1H-1,2,3-triazollarlarning yangi hosilalari (**8-11**) ajratib olingan. Ushbu tadqiqotlarni kelgusida maqsadli sintez reaksiyalarida muvaffaqiyatli qo'llash mumkin. Bu usullarning sodda va qulayligi ularning qator afzalliklarga ega ekanligini bildiradi.

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