TRITSIKLIK XINAZOLONLARDA BORADIGAN BIR REAKTORLI KROSS-BIRIKISH REAKSIYALARI

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Annotatsiya: Ushbu maqolada trisiklik xinazolin alkaloidilarining dastlabki vakili - dezoksipeganin va uning kislorodli analoglarining bromli hosilalarida boradigan Suzuki-Miyaura kross-birikish reaksiyalarini haqida ma'lumot berilgan. Bu reaksiyalarni olib borishdan maqsad, reaksiyalar borishiga substratning va almashingan bor kislotalarining tuzilishi, reaksiya harorati, vaqti va davomiyligining, shuningdek fazoviy (sterik) omillarning ta'sirini atroflicha o'rganish va natijalarni qiyosiy tahlil qilishdan iboratdir. Shu sababli, dastlab biz bromli hosilalarning (**1**, **2**) boshqa aril- va geteril-bor kislotalari bilan kross-birikish reaksiyalarini olib bordik. Hozirgi kunda tannarxi va atrof-muhit omillarini hisobga olgan holda, turli xil kross-birikish reaksiyalari uchun Cu- va Fe asosidagi katalizatorlardan foydalanish sanoat nuqtai-nazaridan yanada rivojlanib bormoqda [4].

Kalit so'zlar: Trisiklik xinazolonlar, bir reaktorli, kposs-birikish, katalizator, arilgalogenidlar.

Аннотация: В этой статье представлена информация о реакциях кросс - сочетания Suzuki-Miyaura, протекающих в бромированных производных дезоксипеганина и его кислородсодержащих аналогах-раннем представителе трициклических хиназолиновых алкалоидов. Целью проведения этих реакций является детальное изучение влияния на ход реакций структуры субстрата и обменных борных кислот, температуры, времени и продолжительности реакции, а также пространственных (стерических) факторов и сравнительный анализ результатов. По этой причине сначала мы провели реакции перекрестного присоединения бромсодержащих производных (1, 2) с другими Арил - и гетерил-борными кислотами. В настоящее время, учитывая стоимость и факторы окружающей среды, использование катализаторов на основе Cu-и Fe для различных реакций кросс - сочетание становится все более продвинутым с промышленной точки зрения [4].

Ключевые слова: трициклические хиназолоны, однореакторный, kposs-сочетание, катализатор, арилгалогениды.

Abstract: This article provides information about the Suzuki-Miyaura cross-coupling reactions that occur in the bromide derivatives of trisyclic xinazolin

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alkaloids and their oxygen-containing analogues. This reaction is composed of the following steps: the formation of the substrate and the unreacted boric acid, the temperature, time, and duration of the reaction, as well as the influence of phase (steric) factors on the reaction. For this reason, we first carried out cross-linking reactions between bromo compounds (1, 2) and other aril- and geteril-boric acids. Today, taking into account the characteristics of tannarx and the surrounding environment, the use of Cu- and Fe-based catalysts for various cross-linking reactions is becoming increasingly important in the industrial sector [4].

Keywords: tricyclic quinazolones, single-reactor, kposs-combination, catalyst, aryl halides.

Kirish

Ma’lumki, kross birikish reaksiyalari – bu zamonaviy organik sintez kimyosining eng muhim yo’nalishlaridan biridir. Ushbu reaksiyalar yordamida turli xil organik substratlar o’rtasida uglerod- uglerod (C-C) yoki uglerod-geteroatom (C-N, C-O, C-S va boshqalar) bog’lari hosil qilinadi. Kross birikish reaksiyalari ko’pincha palladiy (Pd), nikel (Ni) yoki mis (Cu) kabi oraliq metallar ishtirokida katalitik yo’l bilan amalga oshiriladi.

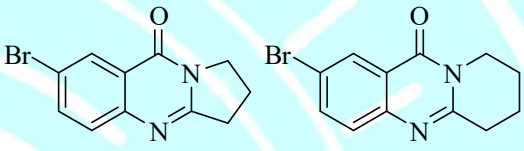
Ferrotsenga bog‘langan biomolekulalar - peptidlar va oqsillar [1], nuklein kislotalar, uglevodlar, porfirinlar [2] va ferrotsen bilding-blokining benzol halqasiga almashingan hosilalari orasida bir qator shishlarga qarshi vositalar mavjud [3]. Hozirgi kunda tannarxi va atrof-muhit omillarini hisobga olgan holda, turli xil kross-birikish reaksiyalari uchun Cu- va Fe asosidagi katalizatorlardan foydalanish sanoat nuqtai-nazaridan yanada rivojlanib bormoqda [4].

Castro va Stephens tomonidan arilatsetilenlar va arilgalogenidlarning o‘zaro kross-birikishi natijasida diarilatsetilenlar hosil bo‘lishi nisbatan pastroq haroratda (piridinda qaynatish) Cu-katalizatorligida muvaffaqiyatli ketishi ko‘rsatib berildi [5]. Keyinchalik, Sonogashira palladiy va misning katalitik miqdordagi ishtirokida terminal alkinlarning aril galogenidlar bilan kross-birikishini kuzatdi [6].

Buchvald va Taillefer ham mustaqil ravishda xelatlangan ligandlardan foydalanish orqali Cu-katalizatorligida boradigan kross-birikish reaksiyalarida katta yutuqlarga erishdilar [7]. 2010 yilda Yaponiya va AQSH olimlari: Richard F. Xek, Ei-ichi Negishi va Akira Suzuki murakkab molekulalarni sintez qilish uchun uglerod atomlarini bog‘lashning yangi, yanada samarali usullarini, ya’ni “palladiy bilan katalizlangan kross-birikish reaksiyalarini” ishlab chiqdilar [8].

Tadqiqotlarimiz uchun, biz tarkibida brom atomlari (7-bromdezoksivazitsinon (**1**), 2-brommakinazolinon (**2**) saqlagan substratlarni tanlab oldik:

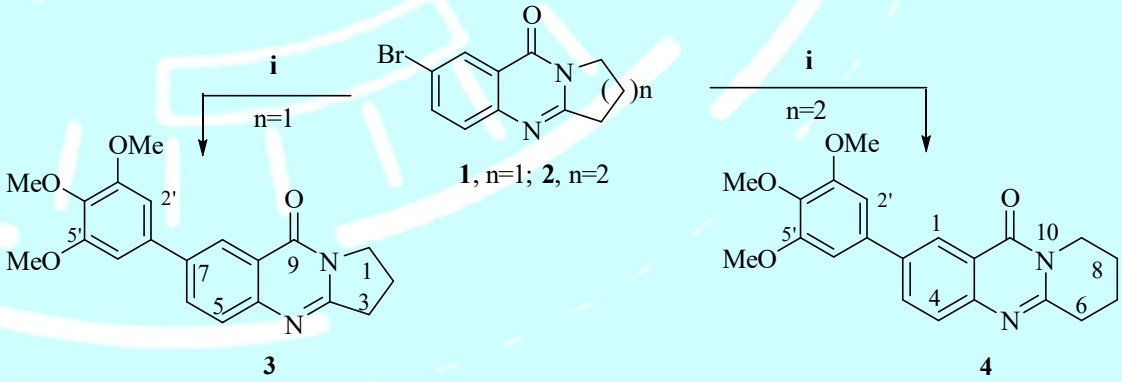
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1 **2**

Bu substratlarni tanlashdan asosiy maqsad, brom-atomi tutgan substratlar (**1**, **2**) ishtirokida Suzuki-Miyaura kross-birikish reaksiyalarini olib borish, hamda olingan natijalarni taqqoslashdan iborat edi. Shu sababli, dastlab biz bromli hosilalarning (**1**, **2**) boshqa aril- va geteril-bor kislotalari bilan kross-birikish reaksiyalarini olib bordik. Bu reaksiyalarni olib borishdan maqsad, reaksiyalar borishiga substratning va almashingan bor kislotalarining tuzilishi, reaksiya harorati, vaqti va davomiyligining, shuningdek fazoviy (sterik) omillarning ta'sirini atroflicha o'rganish va natijalarni qiyosiy tahlil qilishdan iboratdir. Aril- va geteril-bor kislotalari sifatida: 3,4,5-trimetoksifenil bor kislota, 2,4,6-triftorfenil bor kislota va benzotiofen-3-bor kislotalar ishlatildi.

Dastlab, reaksiyalar *mono*-bromxinazolonlarning (**1**, **2**) 3,4,5-trimetoksifenil bor kislotasi bilan atseton va suvli erituvchilar aralashmasida palladiy atsetat katalizatori ishtirokida nisbatan past haroratda o'tkazildi (1-jadval):

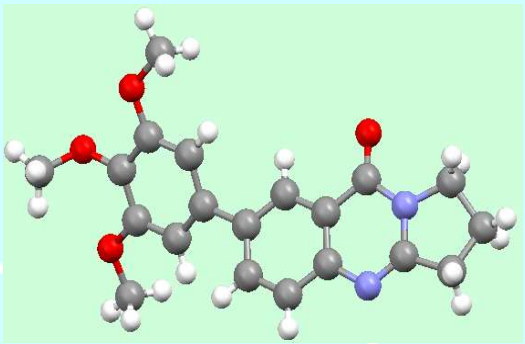


1, n=1; **2**, n=2

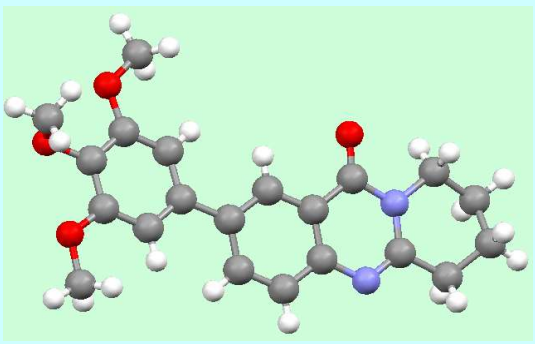
3 **4**

i: $Pd(OAc)_2$ (4.2mol %), 3,4,5-Trimetoksifenil-bor kislota (1.12 ekv.), Na_2CO_3 (1.25 mmol), Atseton/H_2O - 4/2 (v:v), 40-45°C, 30 min(*konversiya 100%*)..

Quyidagi 1- va 2- rasmlarda kross-birikish mahsulotlarining (**3**, **4**) kristaldagi tuzilishlari keltirilgan:



1-Pasm. 3-birikmaning kristaldagi tuzilishi



2-Rasm. 4-birikmaning kristaldagi tuzilishi

Sintez qilingan birikmalarning unumi va ba'zi fizik-kimyoviy kattaliklari

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Birikma	Brutto formula	Unum, %	R_f (sistema)	Suyuqlanish harorati, ^0C
3	$C_{20}H_{20}N_2O_4$	97	0.13 (etilatsetat)	169-170
4	$C_{21}H_{22}N_2O_4$	98	0.30 (etilatsetat)	160-161

Sintez qilingan birikmalarning (**3-4**) spektrlari natijalari

Birikma	**Spektr natijalari**
3	^{1}H YAMR ($CDCl_3$, δ, м.у., *J*, Гs): 2.29-2.37 (2H, м, 2-CH_2), 3.22 (2H, т, *J*=7.8, 3-CH_2), 3.92 (3H, с, OMe-4'), 3.97 (6H, с, $(OMe)_2$-3',5'), 4.25 (2H, т, *J*=7.2, 1-CH_2), 6.88 (2H, с, H-2',6′), 7.72 (1H, д, *J*=8.5, H-5), 7.96 (1H, dd, *J*=2.2, *J*=8.5, H-6), 8.47 (1H, д, *J*=1.9, H-8). ^{13}C YAMR ($CDCl_3$): 161.1 (C-9), 159.4 (C-7), 153.6 (C-8a), 148.3 (C-6), 139.2 (C-5), 135.6 (C-4a), 133.1 (C-3a), 127.3 (C-2',6'), 124.1 (C-3',5'), 120.7 (C-4'), 104.4 (C-1'), 60.9 (C-OMe-4'), 58.3 (C-$(OMe)_2$-3',5'), 46.6 (C-1), 32.5 (C-3), 19.5 (C-2). IQ (ν, $см^{-1}$): 1672 (C=O), 1620 (C=N), 1481 (C-N). TOF MS EI^+ (GCT), m/z (%): 352 ($[M]^+$, 96), 337 ($[M-CH_3]^+$, 100), 309, 279, 223, 175, 139, 111. Hisoblangan: $C_{20}H_{20}N_2O_4$ uchun 352.1423. Topilgan: 352.1422.
4	^{1}H YAMR ($CDCl_3$, δ, м.у., *J*, Гs): 1.97-2.07 (4H, м, 7-CH_2, 8-CH_2), 3.04 (2H, т, *J*=6.7, 6-CH_2), 3.92 (3H, с, OMe-4'), 3.97 (6H, с, $(OMe)_2$-3',5'), 4.13 (2H, т, *J*=6.1, 9-CH_2), 6.88 (2H, с, H-2',6′), 7.67 (1H, д, *J*=8.5, H-4), 7.95 (1H, dd, *J*=2.2, *J*=8.5, H-3), 8.46 (1H, д, *J*=1.9, H-1). ^{13}C YAMR ($CDCl_3$): 162.3 (C-11), 154.9 (C-2), 153.6 (C-11a), 146.6 (C-3), 138.9 (C-1), 137.9 (C-4), 135.6 (C-4a), 133.1 (C-5a), 126.9 (C-2',6'), 124.3 (C-3',5'), 120.5 (C-4'), 104.3 (C-1'), 61.0 (C-OMe-4'), 56.3 (C-$(OMe)_2$-3',5'), 42.5 (C-7), 32.0 (C-8), 22.1 (C-6), 19.3 (C-9). IQ (ν, $см^{-1}$): 1664 (C=O), 1616 (C=N), 1473 (C-N). TOF MS EI^+ (GCT), m/z (%): 366 ($[M]^+$, 100), 351 ($[M-CH_3]^+$, 97), 323, 393, 237, 184. Hisoblangan: $C_{21}H_{22}N_2O_4$ uchun 366.1580. Topilgan: 366.1576.

E'tiborli tomoni shundaki, reaksiyalar juda qisqa vaqt ichida (30 daqiqada) yakunlanadi va konversiya 100% ni tashkil qiladi. Natijada kross-birikish mahsulotlari - **3** (97%) va **4** (98%) yuqori unumlar bilan hosil bo'ladi.

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