SYNTHESIS OF AMIDE DERIVATIVES BASED ON GLYCYRETHIC ACID BY EDCI/HOBT ACTIVATION WITH 3-AMINOPROPYL IMIDAZOL

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ABSTRACT: in this work, new amide derivatives were synthesized with 3-aminopropyl imidazole (3-API) by activating the carboxyl group of glycyrrhizic acid (GlC) in the presence of EDCI (1-ethyl-3- (3-dimethylaminopropyl) carbodiimide hydrochloride) and HOBt (1-hydroxybenzotriazole). The reaction was carried out in an inert gas medium, and the synthesis was carried out with a high chemical total (95%). [1] The resulting compound was confirmed using IR and mass spectrometry. The formation of the amide bond was determined by the absorption bands 1642 (C=O) and 3354 cm-1 (N-H). The results show that the EDCI/HOBt system is an effective reagent combination for amide synthesis based on natural triterpenoids.

KEY WORDS: glycyrrhizic acid, 3-aminopropilimidazole, EDCI, HOBt, triterpenoids, imidazole derivatives.

ANNOTATSIYA: ushbu ishda glitsirret kislota (GlK) karboksil guruhi EDCI (1-etil-3-(3-dimetilaminopropil)karbodiimid gidroxlorid) va HOBt (1-hidroksibenzotriazol) ishtirokida faollashtirilib, 3-aminopropil imidazol (3-API) bilan yangi amid hosilalari sintez qilindi. Reaksiya inert gaz muhitida olib borilib, yuqori kimyoviy umum bilan sintez amalga oshirildi (95%). [1] Hosil bo‘lgan birikma IQ va mass-spektrometriya yordamida tasdiqlandi. Amid bog‘ hosil bo‘lishi 1642 (C=O) va

3354 sm^{-1} (N-H) yutilish chiziqlari orqali aniqlangan. Natijalar EDCI/HOBt tizimining tabiiy triterpenoidlar asosida amid sintezi uchun samarali reagentlar kombinatsiyasi ekanligini ko‘rsatadi.

KALIT SO’ZLAR: glitsirret kislota, 3-aminopropilimidazol, EDCI, HOBt**,** triterpenoidlar, imidazol hosilalari.

KIRISH: glitsirret kislota (GlK) shirinmiya (*Glycyrrhiza glabra*) o‘simligidan ajratib olinadigan pentatsiklik triterpenoid bo‘lib, u farmakologik jihatdan juda keng spektrli biofaollikka ega. [2] U yallig‘lanishga qarshi, antiviral, gepatoprotektiv va antitumor xususiyatlari bilan ajralib turadi. Shu sababli, glitsirret kislotasining hosilalarini sintez qilish, ularning farmakologik faolligini o‘rganish hamda yangi dori vositalarini yaratish dolzarb vazifalardan hisoblanadi. 3-aminopropil imidazol (3-API) tarkibida imidazol halqasi mavjud bo‘lib, bu fragment biologik tizimlarda (masalan, histidin qoldig‘i, ferment faol markazlari) muhim rol o‘ynaydi. Imidazol halqasi proton almashinuvi, metall ionlari bilan koordinatsiya va vodorod bog‘lari hosil qilish xususiyatiga ega bo‘lib, biofaollikni sezilarli darajada oshiradi. [3]

Shu sababli GlK va 3-API ni birlashtirish orqali yangi farmakofor tizim yaratish katta ilmiy ahamiyatga ega.

ASOSIY QISM: amid bog‘ hosil qilish uchun karboksil kislotalarni to‘g‘ridan-to‘g‘ri aminlar bilan kondensatsiyalash o‘rniga EDCI/HOBt faollashtiruvchilar ishlatildi.

Reaksiya quyidagi bosqichlarda boradi:

1-bosqich: Karboksil guruhning faollashtirish (EDCI reaksiyasi)
Glitsirret kislota karboksil guruhi EDCI bilan reaksiyaga kirishib, yuqori reaktiv O-asillangan birikmasini hosil qiladi. Bu bosqichda karboksil kislotaning OH guruhi karbodiimid markazi bilan kondensatsiyalanadi. [4]

2-bosqich: HOBt ishtirokida aktiv efir bog’ hosil bo‘lishi
Hosil bo‘lgan O-asillangan oraliq mahsulot beqaror bo‘lib, HOBt bilan reaksiyaga kirishadi. Natijada nisbatan barqaror benzotriazol (OBt-ester) hosil bo‘ladi. Bu bosqich yon reaksiyalar (N-acylurea hosil bo‘lishi)ni sezilarli darajada kamaytiradi. [5]

3-bosqich: Nukleofil hujum va amid bog‘ hosil bo‘lishi 3-aminopropil imidazol tarkibidagi erkin amin guruhi nukleofil sifatida karbonil uglerod atomiga hujum qiladi. Bu jarayon natijasida tetraedrik oraliq kompleks hosil bo‘ladi va keyinchalik HOBt ajralib chiqib, barqaror amid bog‘ (–CONH–) shakllanadi.

NATIJALAR VA MUHOKAMA: sintez qilingan GlK–3API an=mid hosilasi yuqori unum bilan (95%) olindi. IQ spektroskopik tahlil natijalari amid bog‘ hosil bo‘lganini tasdiqladi:

1. 3354 sm^{-1} N-H valent tebranishi (amid)
2. 1642 sm^{-1} C=O (amid karbonil guruhi)
3. 2920–2850 sm^{-1} C–H alifatik tebranishlar

EDCI/HOBt tizimi klassik $SOCl_2$ yoki asilxlorid usullariga nisbatan yuqori selektivlik berishi bilan ajralib turadi. [6]

XULOSA: glitsirret kislota va 3-aminopropil imidazol asosida yangi amid hosilasi EDCI/HOBt yordamida muvaffaqiyatli sintez qilindi. Reaksiya mexanizmi karboksil guruhning O-asillangan va OBt-ester orqali faollashuvi hamda nukleofil amin hujumi orqali amalga oshishi bilan amalga oshirildi. Olingan natijalar ushbu birikmalarni biologik faol moddalarning istiqbolli sinfi sifatida ko‘rib chiqish mumkinligini ko‘rsatadi.

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