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Benzamidoxime-Mediated Crotylation of Aldehydes using Potassium (*Z*) and (*E*)-Crotyltrifluoroborates

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Abstract. A highly diastereoselective protocol for the crotylation reaction of aldehydes using potassium (*Z*) and (*E*)-crotytrifluoroborates was developed. Benzamidoxime was employed as a renewable catalyst, which was easily recovered through a simple extraction process. This method proved to be simple, fast, regio- and chemoselective for different aldehydes. The corresponding homoallylic alcohols were obtained in good to excellent yields without the need of further purification.

Keywords: Crotylation reaction; homoallylic alcohols; benzamidoxime; potassium organotrifluoroborates.

Resumen. Se desarrolló un protocolo altamente diastereoselectivo para la reacción de crotilación de aldehídos usando potasio (*Z*) y (*E*)-crotitrifluoroboratos. La benzamidoxima se empleó como catalizador renovable, que se recuperó fácilmente mediante un proceso de extracción simple. Este método demostró ser simple, rápido, regio- y quimioselectivo para diferentes aldehídos. Los alcoholes homoalílicos correspondientes se obtuvieron con rendimientos buenos a excelentes sin la necesidad de una purificación adicional.

Palabras clave: Reacción de crotilación; Alcoholes homoalílicos; Benzamidoxima; Organotrifluoroboratos de potasio.

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Introduction

The crotylation reaction of carbonyl compounds is a synthetically important reaction, in special due to the formation of new C-C bonds and their interesting reaction mechanisms [1-3]. This reaction leads to the formation of homoallylic alcohols, which are versatile and valuable synthetic intermediates, allowing numerous transformations. As a consequence, these compounds were applied in a variety of synthetic routes toward natural products and biologically active compounds [e.g., (-)-Elisabethadione [4], C9-C20 fragment of tetrafibricin [5], tetrahydrolipstatin [6], (*R*)-argentillactone [7], (*R*)-goniothalamin [7] and an intermediate of fostriecin [8] (Fig. 1)].

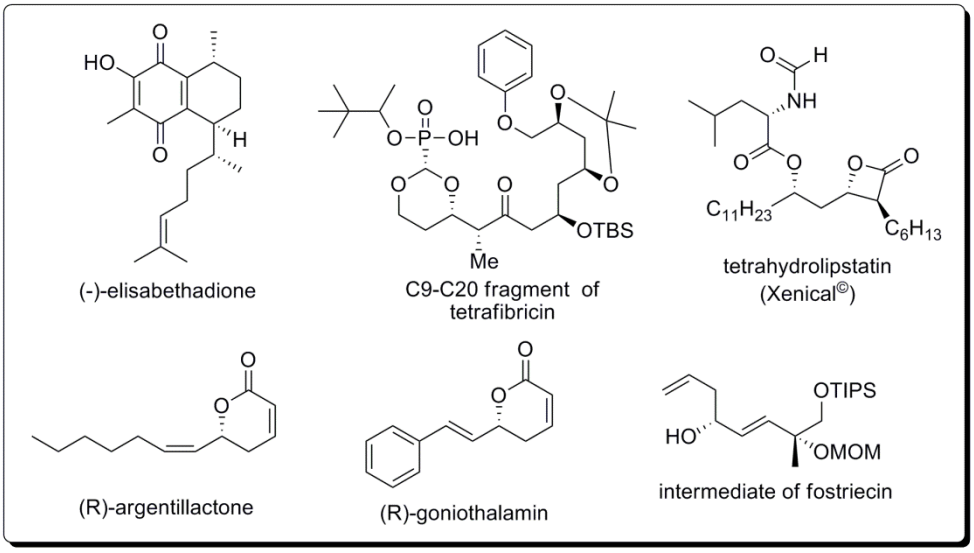

Fig. 1. Natural products and intermediates obtained through crotylation reaction.

Three types of mechanistic proposals for crotylation reactions have been reported in the literature, each one of importance for the understanding relevance for understanding the stereoselectivity inherent to this reaction [9-10].

The commonly methodology employed for crotylation reactions is based on the nucleophilic addition of crotyl-organometallic species (e.g., crotyl-organolithium or crotyl-organomagnesium reagent) on the carbonyl carbon [11, 13]. Nevertheless, the use of these compounds becomes limited, due to their high basicity. In this way the synthesis and manipulation of these reagents is very difficult, in particular because of its instability in the presence of air and moisture. In addition, the loss of chemoselectivity can eventually occurs when a substrate has more than one electrophilic center [14].

To overcome these difficulties, several methods have been developed for crotylation reaction, most of them based on the use of less reactive species. Lewis or Brönsted acid-mediated reactions using compounds based on tin [1, 13, 15], silicon [2, 16, 17] or boron [3, 18] have been reported. The boron-based reagents, specifically the organotrifluoroborates stand out, due to their greater selectivity and stability. They are air and moisture resistant, thermostable and easy to handle. Thus, they can be stored for long periods and their reaction by-products are non-toxic and water-soluble inorganic compounds [19, 20].

Despite the various advantages of using organotrifluoroborates, the amount of papers published reporting the application of these compounds in crotylation reactions is very limited [22]. In addition, this reaction shows some challenges related to the use of green solvents and catalyst control of stereoselectivity.

From a synthetic point of view, amidoximes are versatile building blocks allowing the access to numerous heterocyclic compounds [23-25], and the formation of new C-C bonds in Suzuki [26] and Sonogashira type reactions [27]. In addition, the use of amidoximes as adsorbents and complexing agents was also described in the literature. [28-32]. In particular, the ability of amidoximes to chelate metal ions in aqueous solutions may enable the application of these compounds as phase-transfer agents [33]. In this

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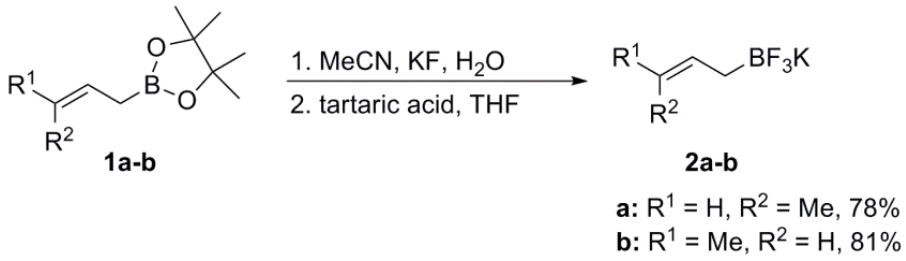
work, we reported the synthesis of different homoalyllic alcohols through the benzamidoxime-mediated crotylation of aldehydes using potassium (*Z*) and (*E*)-crotyltrifluoroborates.

Results and Discussion

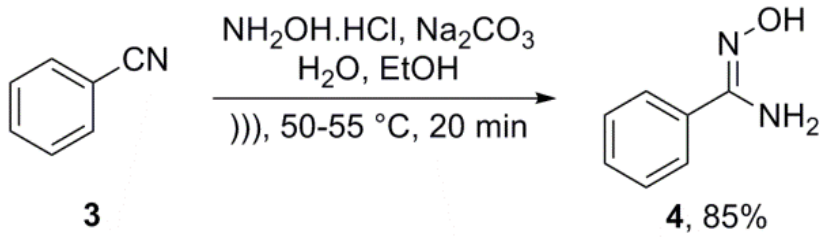
Recently our research group described the allylation of aldehydes mediated by amidoximes [33], and although there are several articles reporting the allylation of carbonyl compounds using organotrifluoroborate salts [34-37], a smaller number of examples of the use of organoboron reagents in crotylation reactions are described [21-22]. This number is even lower when the application of chelating agents is is taken into account.

Our studies began with the transformation of commercially available (*Z*)- and (*E*)-2-(but-2-enyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (**1a-b**) into the respective potassium (*Z*)- and (*E*)-crotyltrifluoroborate (**2a-b**) using the method reported by Lloyd-Jones and co-workers [20] (Scheme 1).



Scheme 1. Synthesis of potassium (*Z*)- and (*E*)-crotyltrifluoroborate (**2a-b**).

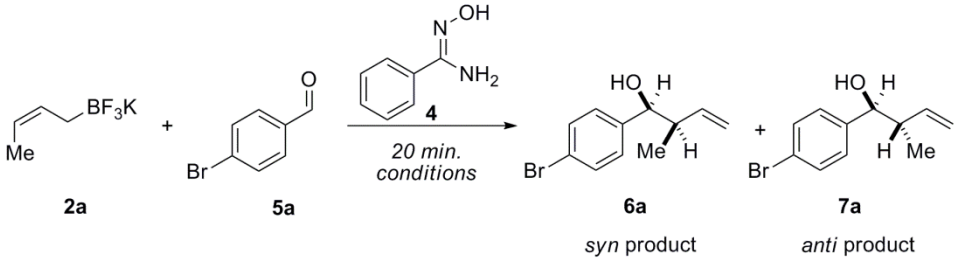
The benzamidoxime (**4**), used as catalyst in the reaction, was synthesized according to a method described in the literature [38] (Scheme 2).



Scheme 2. Synthesis of benzamidoxime (**2**).

After the synthesis of the starting materials, studies on the development of the best conditions for the crotylation reaction were performed. Thus, *p*-bromobenzaldehyde (**5a**) and potassium (*Z*)-crotyl trifluoroborate (**2a**) were used as model substrates. The reaction time was set at 20 minutes and the amount of benzamidoxime (**4**) and the ratio H_2O/CH_2Cl_2 were evaluated. The results are summarized in Table 1.

Table 1. Study of the amount of benzamidoxime (**4**) and H_2O/CH_2Cl_2 ratio in the crotylation reaction of *p*-bromobenzaldehyde (**5a**) with potassium (*Z*)-crotyltrifluoroborate (**2a**).



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Entry	(4) (mmol%)	Solvent Ratio (%) H_2O/CH_2Cl_2	Yield (%)[a]	6a:7a (*syn*/*anti*)[b]
1	50	50/50	73	96/4
2	25	50/50	87	95/5
3	10	50/50	88	96/4
4	10	65/35	92	96/4
5	10	100/0	45	92/8
6	10	0/100	0	-
7	-	65/35	8	71/29

[a]Yield of isolated product. [b]Determined by GC.

When the crotylation reaction was performed in the absence of the benzamidoxime (**4**) an incomplete reaction was observed and part of the starting materials was recovered (Table 1, entry 7). A similar result was observed when only H_2O or CH_2Cl_2 was used as reaction solvents (Table 1, entries 5 and 6), which could be justified by the low solubility of the reactants in these solvents. The best result was observed when a 65:35 mixture of H_2O/CH_2Cl_2 and 10 mmol% of benzamidoxime (**4**) were used. In this case, the corresponding homoallylic alcohol (**6a**) was obtained in 92% yield (Table 1, entry 4). It is noteworthy that the use of 25 and 50 mmol% of benzamidoxime (**4**) did not lead to a yield increase (Table 1, entries 1 and 2).

In order to provide evidence that support this hypothesis, a study in the ultraviolet absorption region was carried out. Thus, five 0.001mM aqueous solutions were prepared: benzamidoxime (**4**) - Sol. A, potassium (*Z*)-crotyltrifluoroborate (**2a**) - Sol. B, benzamidoxime (**4**) + potassium (*Z*)-crotyltrifluoroborate (**2a**) - Sol. C, *p*-bromobenzaldehyde (**5a**) - Sol. D and benzamidoxime (**4**) + *p*-bromobenzaldehyde (**5a**) - Sol. E. The results are summarized in Fig. 2.

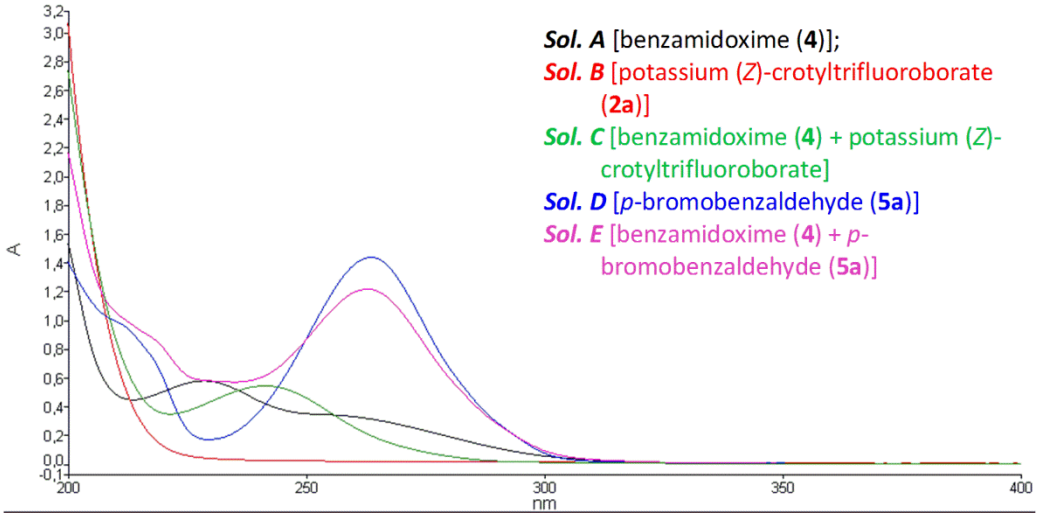

Fig. 2. Absorption spectra in the ultraviolet region.

According to Fig. 2, it was observed that the solution A [benzamidoxime (**4**) - Sol. A] showed two UV absorption bands, π→π* (228 nm) and n→π* (257 nm). On the other hand the solution B [potassium (*Z*)-crotyltrifluoroborate (**2a**) - Sol. B] showed absence of UV absorption bands. Comparing these results with that observed for the solution C [benzamidoxime (**4**) + potassium (*Z*)-crotyltrifluoroborate (**2a**) - Sol. C] was observed a suppression of the transition n→π* (257 nm) and a bathochromic shift of the transition

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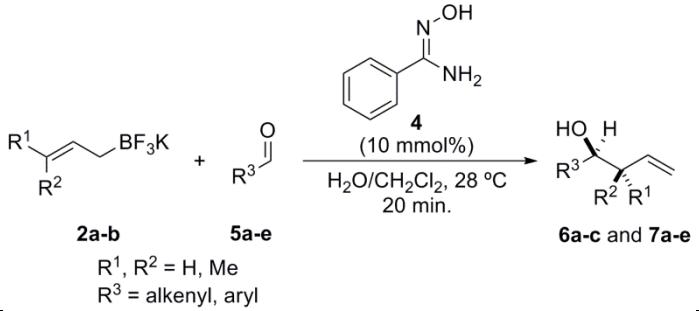
$\pi \rightarrow \pi^*$ of the region from 228 mm to 241 mm. In addition, no interaction between benzamidoxime (**4**) and *p*-bromobenzaldehyde (**5a**) was observed, as shown in Fig. 2 (Sol. D and Sol. E).

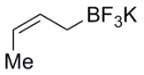
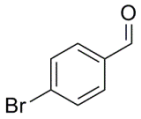
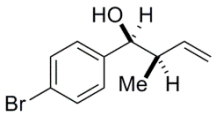
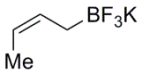
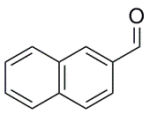
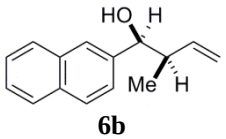
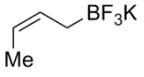
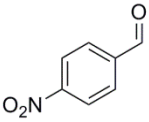
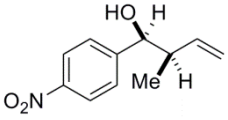
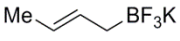
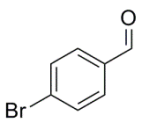
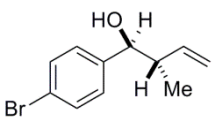
The mechanism for allylation reactions is controversial. Although many authors described that the reaction proceeds through tricoordinate species [39], tetracoordinate trialkylcrotylborate reagents can also add to aldehydes at low temperatures [40].

For the amidoxime-mediated reaction, it would be acceptable that the catalyst would be acting as a phase-transfer catalyst. Although the corresponding difluoroborane or complexed intermediates have not been observed under the reaction conditions, the high diastereoselectivity observed for crotylation reactions suggests a Zimmerman-Traxler transition state [41].

After optimizing the reaction conditions, the crotylation reaction was extended to different aldehydes. The results are summarized in Table 2.

Table 2. Benzamidoxime (**4**) mediated crotylation using potassium (*Z*) and (*E*)-crotyl trifluoroborate (**2a-b**) of different aldehydes (**5a-e**).



Entry	Reactants		Product	Yield (%)[a]
	Trifluoroborate	Aldehyde		
1	 **2a**	 **5a**	 **6a**	92 *syn/anti* (96/4)
2	 **2a**	 **5b**	 **6b**	91 *syn/anti* (97/3)
3	 **2a**	 **5c**	 **6c**	91 *syn/anti* (95/5)
4	 **2b**	 **5a**	 **7a**	89 *syn/anti* (3/97)

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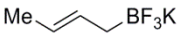
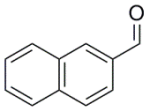
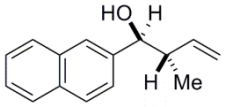
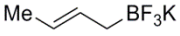
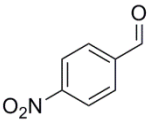
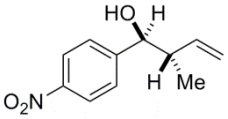
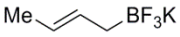
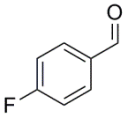
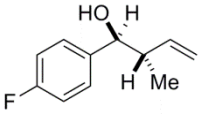
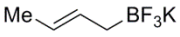
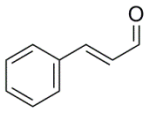
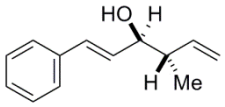
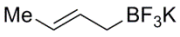
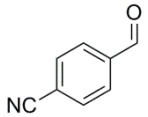
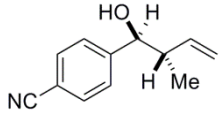
5	 **2b**	 **5b**	 **7b**	91 *syn/anti* (4/96)
6	 **2b**	 **5c**	 **7c**	94 *syn/anti* (5/95)
7	 **2d**	 **5d**	 **7d**	90 *syn/anti* (4/96)
8	 **2b**	 **5e**	 **7e**	85 *syn/anti* (12/88)
9	 **2b**	 **5f**	 **7f**	89 *syn/anti* (4/96)

[a]Yield of isolated product.

According to Table 2, the crotyllation reaction led to the formation of the corresponding homoallylic alcohols (**6a-e** and **7a-e**) in good yields and with excellent stereoselectivities. The results also indicate that the nature of the substituent attached to the aromatic ring possess a small influence on the yield and stereoselectivity of the reaction (Table 2). In addition, when an α,β-unsaturated aldehyde was used, the corresponding 1,2-addition product was exclusively obtained, evidencing that this reaction is also regioselective (Table 2, entry 8).

When 4-cyanobenzaldehyde (**5f**) and two equivalents of potassium (*E*)-crotyltrifluoroborate (**2b**) were used in this reaction, only the carbonyl carbon addition product was observed, even after 25 minutes. This fact indicated that the reaction is chemoselective (Table 2, entry 9).

Although the benzamidoxime (**4**) has a higher cost when compared to some promoters or catalysts applied in crotylation reactions, this compound can be easily recovered through a simple extraction process. This procedure was performed using an initially basic and then acidic solution and 85 ± 5% of benzamidoxime (**4**) was recovered after each reaction. The results are summarized on Table 3.

Table 3: Recovery study of the benzamidoxime.

Entry	Benzamidoxime recovered (%)[a]
1	86
2	85

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3	89
4	84
5	80

[a]The percentage refers to the mass (mg) of amidoxime recovered after each extraction.

Conclusion

We have demonstrated an efficient and diastereoselective method for the crotylation of aldehydes using potassium crotyl-trifluoroborates and benzamidoxime as catalyst. The corresponding homoallylic alcohols were synthesized in a short reaction time, in yields ranging from good to excellent using water as the main solvent. The study using ultraviolet spectroscopy indicated an interaction between the benzamidoxime and the organotrifluoroborate during the course of the crotylation reaction. The developed method proved to be regio- and chemoselective, and can be applied in the synthesis of natural products or biologically active compounds.

Experimental Section

General experimental procedures

Commercial solvents were purified according to protocols described in the literature [42]. Hexane and ethyl acetate were purified by distillation, dichloromethane and chloroform were distilled under calcium hydride and ethanol was distilled under magnesium and sublimed iodine. The solvents were removed using a Büchi Rotavapor rotary evaporator model R-114 connected to a KNF Neuberger vacuum pump and the remaining solvent was removed using an Edwards high vacuum pump model RV3. ^{1}H, ^{11}B, ^{13}C and ^{19}F NMR spectra were recorded on a Varian URMNS spectrometer of 400, 128, 100 and 376 MHz, respectively. Deuterated chloroform ($CDCl_3$) and deuterated dimethyl sulfoxide (DMSO-d_6) were used as solvents. Tetramethylsilane (0.00 ppm) was used as an internal reference for ^{1}H and ^{13}C NMR, BF_3•Et_2O (0.00 ppm) was used as an external reference for ^{11}B NMR and CF_3CO_2H (0.00 ppm) was used as an external reference for ^{19}F NMR. All coupling constants (*J*) were described in hertz (Hz). The IR spectra were recorded on a Fourier Spectrum 400 FT-IR/FT-NIR Spectrometer Model Perkin Elmer, the samples being prepared as thin films or KBr pellets. UV spectra were recorded on a PERKIN ELMER Lambda 650 (UV-VIS). The melting points were performed in the Electro-thermal series IA 9100 Digital Melting Point. The application of ultrasound energy was generated in an 8890E-DTH ultrasound bath (with a frequency of 47 kHz and power of 35W; Cole Parmer Co.). The reactions were monitored by thin layer chromatography (TLC) using silica gel plates containing fluorescent indicator F254 from Merck. For visualization, the plates were placed under ultraviolet light and acid solution (EtOH / H_2SO_4, 95: 5).

General Procedure for the synthesis of potassium (*Z*) and (*E*)-crotyltrifluoroborate (2a-b).

In a 25 mL round-bottomed flask containing a solution of **1a-b** (0,15 g; 0,90 mmol) in a MeCN/MeOH (9:1) (4 mL) were added in a solution of KF (0.21 g, 3.60 mmol, 4 eq) in H_2O (0,5 mL). The reaction mixture was stirred until complete solubilization (1 min). Then, a solution of tartaric acid (0.28 g, 1.85 mmol, 2.05 eq) in THF (1.5 mL) was slowly added under vigorous stirring over 5 min. After 1 hour, the reaction mixture was filtered using a Büchner funnel and the filtrate was concentrated through the rotary evaporator under reduced pressure. The obtained white solid was dissolved in hot acetone (3 x 25 mL) followed by the addition of small portions of Et_2O until precipitation of the product. The precipitate was washed with Et_2O to give potassium (*Z*) and (*E*)-crotyltrifluoroborate (**2a-b**).

Potassium (*Z*)-crotyltrifluoroborate (2a): White amorphous powder; 128 mg (78%); ^{1}H NMR (400 MHz, DMSO-d_6) δ 5.48-5.40 (m, 1H, CH=CH), 5.03-4.95 (m, 1H, CH=CH), 1.46 (dd, *J* = 6.8 and 0.8 Hz, 3H, CH_3), 0.84 (brs, 2H, CH_2); ^{13}C NMR (100 MHz, DMSO-d_6) δ 134.2 (CH=CH), 116.5 (CH=CH), 12.4 (CH_3) ^{11}B NMR (128 MHz, DMSO-d_6) δ 4.0 (qua, *J* = 59.8 Hz, BF_3K); ^{19}F NMR (376 MHz, DMSO-d_6) δ -135.9 (qua, *J* = 63.3 Hz, BF_3K). The data match with the previously described compound [43].

Potassium (*E*)-crotyltrifluoroborate (2b): White amorphous powder; 132 mg (81%); ^{1}H NMR (400 MHz, DMSO-d_6) δ 5.43-5.35 (m, 1H, CH), 4.96-4.87 (m, 1H, CH), 1.51 (dd, *J* = 6.4 and 1.2 Hz, 3H, CH_3), 0.80 (brs, 2H, CH_2); ^{13}C NMR (100 MHz, DMSO-d_6) δ 135.2 (CH=CH), 117.8 (CH=CH), 18.2 (CH_3); ^{11}B

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NMR (128 MHz, DMSO-d_6) δ 6.1 (qua, J= 61.4 Hz, BF_3K); ^{19}F NMR (376 MHz, DMSO-d_6) δ -136.3 (qua, J = 63.9 Hz, BF_3K). The data match with the previously described compound [43, 44].

Procedure for synthesis of benzamidoxime (4)

In a 125 mL round-bottomed flask was added hydroxylamine hydrochloride (1.04 g, 15 mmol), sodium carbonate (0.78 g, 7.50 mmol) and water (20 mL). The flask was placed in the ultrasonic bath for 1 minute or until the absence of effervescence. Then, **3** (0.51 mL, 0.51 g, 5.00 mmol) and ethanol (20 mL) were added. The flask was placed back in the ultrasonic bath at 55±5ºC for 20 minutes. After confirming the completion of the reaction by TLC (ethyl acetate), the reaction mixture was concentrated under reduced pressure. To the resulting biphasic system was added ethyl acetate (70 mL) and the organic layer was washed with saturated ammonium chloride solution (2 x 40 mL) and brine (2 x 40 mL). Then the organic layer was dried over anhydrous $MgSO_4$. The solvent was removed using a rotary evaporator and the crude product was crystallized using the chloroform:hexane system (90:10) to afford 578 mg of benzamidoxime (**4**) (85%).

Benzamidoxime (4): white solid, mp 79-80 °C; IR (KBr pellet): ν 3453, 361, 3057, 2369, 2293, 1649, 1529, 1387, 927, 691 cm^{-1}; NMR (DMSO-d_6, 400 MHz): δ 9.63 (s, 1H, OH), 7.69-7.66 (m, 2H, H_{Ar}), 7.37-7.36 (m, 3H, H_{Ar}), 5.80 (brs, 2H, NH_2); ^{13}C NMR (DMSO-d_6, 100 MHz): δ 150.8, 133.3, 128.8, 128.1, 125.4. The data match with the previously described compound [33, 38].

General Procedure for benzamidoxime (4)-mediated crotylation of different aldehydes (5a-f) using potassium (*Z*) or (*E*)-crotytrifluoroborate (2a-b)

In a 25 mL round-bottomed flask containing the appropriate aldehyde **5a-f** (0.25 mmol) in CH_2Cl_2 (1 mL) were added benzamidoxime **4** (6.5 mg, 10% mmol) followed by (*Z*) or (*E*)-crotyltrifluoroborate, **2a-b** (49 mg, 0.3 mmol) and water (2 mL). The resulting biphasic system was stirred for the time described on Table 2. After completion of the reaction, ethyl acetate (20 mL) was added and the organic layer was washed with saturated sodium bicarbonate solution (3 x 20 mL) and brine (20 mL). The organic layer was dried over anhydrous $MgSO_4$ to afford the homoallylic alcohols **6a-c** and **7a-f** without further purification.

(1*S, 2*R**)-1-(4-bromophenyl)-2-methylbut-3-en-1-ol (6a):** Colorless oil; 55.2 mg (92%); ^1H NMR (300 MHz, $CDCl_3$) δ 7.46 (d, J = 8.7 Hz, 2H, H_{Ar}), 7.17 (d, J = 8.7 Hz, 2H, H_{Ar}), 5.74 (ddd, J = 17.4, 10.5 and 6.9 Hz, 1H, C*H*=CH_2), 5.09-5.03 (m, 2H, CH=C*H*$_2$), 4.52 (d, J = 5.4 Hz, 1H, C*H*OH), 2.60-2.49 (m, 1H, C*H*CH_3), 2,03 (brs, 1H, OH), 0.98 (d, J = 6.9 Hz, 3H, CH_3); ^{13}C NMR (75 MHz, $CDCl_3$) δ 141.9, 140.2, 131.5, 128.6, 121.5, 116.4, 76.9, 44.9, 14.2. The data match with the previously described compound [45, 46].

(1*S, 2*R**)-2-methyl-1-(naphthalen-2-yl)but-3-en-1-ol (6b)**: Colorless oil, 48.2 mg (91%); ^1H NMR (400 MHz, $CDCl_3$) δ 7.86-7.82 (m, *3*H, H_{Ar}), 7.77 (brs, 1H, H_{Ar}), 7.50-7.47 (m, *2*H, H_{Ar}), 7.45 (dd, J = 8.4 and 1.6 Hz, H_{Ar}), 5.82 (ddd, J = 17.2, 10.4 and 6.8 Hz, 1H, C*H*=CH_2), 5.12-5.06 (m, 2H, CH=C*H*$_2$), 4.79 (d, J = 5.6 Hz, 1H, C*H*OH), 2.75-2.67 (m, *1*H, C*H*CH_3), 2.11 (brs, 1H, OH), 1.06 (d, J = 6.8 Hz, 3H, CH_3); ^{13}C NMR (100 MHz, $CDCl_3$) δ 140.3, 140.0, 133.1, 132.8, 127.9, 127.7, 127.6, 126.0, 125.7, 125.2, 124 , 6, 115.6, 77.3, 44.5, 13.9. The data match with the previously described compound [46].

(1*S, 2*R**)-2-methyl-1-(4-nitrophenyl)but-3-en-1-ol (6c):** Colorless oil, 47.1 mg (91%); ^1H NMR (400 MHz, $CDCl_3$) δ 8.18 (d, J = 8.4 Hz, 2H, H_{Ar}), 7.48 (d, J = 8.4 Hz, 2H, H_{Ar}), 5.78 (ddd, J = 17.6, 10.4 and 6.8 Hz, 1H, C*H*=CH_2), 5.12 (d, J = 10.4 Hz, 1H, CH=C*H*$_2$), 5.08 (d, J = 17.6 Hz, 1H, CH=C*H*$_2$), 4.77 (d, J = 4.8 Hz, 1H, C*H*OH), 2.64-2.56 (m, 1H, C*H*CH_3), 2.21 (brs, 1H, OH), 0.97 (d, J = 6.4Hz, 3H, CH_3); ^{13}C NMR (100 MHz, $CDCl_3$) δ 149.9, 147.1, 139.3, 127.2, 123.2, 116.6, 76.0, 44.6, 13.3. The data match with the previously described compound [45, 46].

(1*S, 2*S**)-1-(4-bromophenyl)-2-methylbut-3-en-1-ol (7a):** Colorless oil, 53.4 mg (89%); ^1H NMR (400 MHz, $CDCl_3$) δ 7.46 (d, J = 8.4 Hz, 2H, H_{Ar}), 7.21 (d, J = 8.4 Hz, 2H, H_{Ar}), 5.81-5.72 (m, 1H, C*H*=CH_2), 5.21-5.16 (m, 2H, CH=C*H*$_2$), 4.34 (d, J = 7.2 Hz, 1H, C*H*OH), 2.94 (s, 1H, OH) 2.64-2.56 (sext, J = 7.2 Hz, 1H, C*H*CH_3), 0.89 (d, J = 7.2 Hz, 3H, CH_3); ^{13}C NMR (100 MHz, $CDCl_3$) δ 141.4, 140.1, 131.3, 128.5, 121.3, 117.2, 77.1, 44.6, 16.3. The data match with the previously described compound [45, 46].

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(1*S, 2*S**)-2-methyl-1-(naphthalen-2-yl)but-3-en-1-ol (7b):** Colorless oil, 48.2 mg (91%); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.86-7.83 (m, *3*H, H_{Ar}), 7.78 (brs, 1H, H_{Ar}), 7.52-7.47 (m, *3*H, H_{Ar}), 5.92-5.81 (m, 1H, C*H*=CH_2), 5.25 (brd, *J* = 11.7 Hz, 1H, CH=C*H*$_2$), 5.21 (brd, *J* = 3.9 Hz, 1H, CH=C*H*$_2$), 4.55 (d, *J* = 7.8 Hz, 1H, C*H*OH), 2.61 (sext, *J* = 6.6 Hz, 1H, C*H*CH_3), 2.29 (brs, 1H, OH), 0.92 (d, *J* = 6.6 Hz, 3H, CH_3); ^{13}C NMR (75 MHz, $CDCl_3$) δ 140.5, 139.8, 133.1, 133.0 128.1, 127.9, 127.6, 126.0, 125.9, 125.8, 124.6, 116.9, 77.9, 46.2, 16.6. The data match with the previously described compound [46].

(1*S, 2*S**)-2-methyl-1-(4-nitrophenyl)but-3-en-1-ol (7c):** Colorless oil, 48.7 mg (94%); ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.20 (d, *J* = 8,7 Hz, 2H, H_{Ar}), 7.51 (d, *J* = 8,7 Hz, 2H, H_{Ar}), 5.74 (ddd, *J* = 18.6, 10.5 and 8.1 Hz, 1H, C*H*=CH_2), 5.23-5.14 (m, *2*H, CH=C*H*$_2$), 4,52 (d, *J* = 7.2 Hz, 1H, C*H*OH), 2.53-2.41 (m, 1H, C*H*CH_3), 0.95 (d, *J* = 6.6 Hz, 3H, CH_3); ^{13}C NMR (100 MHz, $CDCl_3$) δ 149.8, 139.1, 127.6, 123.4, 117.9, 76.7, 46.3, 24.8, 16.3. The data match with the previously described compound [45, 46].

(1*S, 2*S**)-1-(4-fluorophenyl)-2-methyl-but-3-en-1-ol (7d):** Colorless oil, 40.5 mg (90%); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.32-7.29 (m, 2H, H_{Ar}), 7.06-7.01 (m, 2H, H_{Ar}), 5.83-5.74 (m, 1H, C*H*=CH_2), 5.22 (brd, *J* = 7,2 Hz, 1H, CH=C*H*$_2$), 5.19 (brs, 1H, CH=C*H*$_2$), 4.35 (d, *J* = 8.0 Hz, 1H, C*H*OH), 2.48-2.41 (m, 1H, C*H*CH_3), 0.86 (d, *J* = 6.8 Hz, 3H, CH_3); ^{13}C NMR (100 MHz, $CDCl_3$) δ 140.7, 128.8, 128.6, 117.5, 115.5, 115.3, 77.5, 46.9, 16.8. The data match with the previously described compound [47]

(3*R, 4*S**, *E*)-4-methyl-1-phenyl-hexan-1,5-dien-3-ol (7e):** Colorless oil, 40 mg (85%); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.33-7.15 (m, 5H, H_{Ar}), 6.53 (d, *J* = 12 Hz, 1H, C*H*=CH), 6.13 (d, *J* = 12 e 5.4 Hz, 1H, C*H*=CH), 5.71 (ddd, *J* = 12.9, 7.8 and 6.0 Hz, 1H, C*H*=CH_2), 5,13-5.09 (m, 2H, CH=C*H*$_2$), 3.98 (t, *J* = 5.1 Hz, 1H, C*H*OH), 2.34-2.26 (m, 1H, C*H*CH_3), 1.55 (brs, 1H, OH), 0,99 (d, *J* = 5.1Hz, 3H, CH_3); ^{13}C NMR (100 MHz, $CDCl_3$) δ 140.1, 136.7, 131.7, 130.1, 128.5, 127.6, 126.5, 116.7, 76.1, 53.4, 44.7, 16.0. The data match with the previously described compound [34]

4-(1*S, 2*S**)-1-hidroxy-2-methyl-but-3-en-1-yl)benzonitrile (7f):** Colorless oil, 41.6 mg (89%); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.64 (d, *J* = 8.8 Hz, 2H, H_{Ar}), 7.45 (d, *J* = 8.8 Hz, 2H, H_{Ar}), 5.74 (ddd, *J* = 18.4, 10 and 8.4 Hz, 1H, C*H*=CH_2), 5.31-5.16 (m, 2H, CH=C*H*$_2$), 4.46 (d, *J* = 7.2 Hz, 1H, C*H*OH), 2.45 (sext, *J* = 7.2 Hz, 1H, C*H*CH_3), 0.93 (d, *J* = 7.2 Hz, 3H, CH_3); ^{13}C NMR (100 MHz, $CDCl_3$) δ 147.8, 139.3, 132.0, 127.5, 118.8, 117.8, 111.4, 77.0, 46.3, 16.3. The data match with the previously described compound [48]

General Procedure for Procedure for Benzamidoxime Recovery:
After performing the crotylation reaction, ethyl acetate (20 mL) was added to the combined aqueous phases and the organic layer was washed with 0.1 M sodium bicarbonate solution (3 x 20 mL). The aqueous phases were then combined and acidified using 0.1 M hydrochloric acid solution. The aqueous phase was then extracted with ethyl acetate (20 mL) and the organic layer was separated and dried over anhydrous $MgSO_4$. Removal of the solvent gave benzamidoxime **4** without further purification.

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Supplementary Data
All NMR spectra are available in PDF format.

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