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Pd(II)-Cu(II)-CATALYZED SYNTHESIS OF MONO- AND DIALKENYL-SUBSTITUTED FIVE-MEMBERED AROMATIC HETEROCYCLES[+]

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The Pd-catalyzed one-step alkenylation method of five-membered aromatic heterocycles such as furan or thiophene with olefins has been found. The reaction proceeds regioselectively occurring at the 2-position of the heterocycles and the products have trans-stereochemistry when the substituents on the olefin is bulky.

The aromatic heterocycles like furan and thiophene are important starting materials for synthesis of various biologically and physiologically active compounds.[1] However, these heterocycles are sensitive to acid and base to cause ring opening and/or polymerization. Generally, functionalization of these compounds, especially introduction of alkenyl groups to such heterocycles is very troublesome, and no general method is known for alkenylation. We have developed a new route to alkenylated five-membered aromatic heterocycles. We report here the catalytic one-step mono- and dialkenylations of the five-membered aromatic heterocycles such as furan or thiophene with olefins like acrylonitrile and methyl acrylate by the $\mathrm{Pd(OAc)_2}$-$\mathrm{Cu(OAc)_2}$ catalyst system.[2] Typically, into a 50-ml centrifuge tube containing a magnet stirring bar were added furan (2 mmol), acrylonitrile (2 mmol), $\mathrm{Pd(OAc)_2}$ (0.04 mmol), $\mathrm{Cu(OAc)_2}$ (4 mmol), dioxane (20 ml), and acetic acid (5 ml) and the tube was sealed with a No-Air stopper to avoid evaporation of the volatile furan. Then the mixture was heated with stirring for 8 hr at 100°C. The mixture was filtered and after usual work-up, the products were separated and analyzed by gas (column OV-17) or column (alumina or silica gel) chromatography to give 2-furanacrylonitrile and 2,5-furandiacrylonitrile in 1952% and 1070% yields, respectively (yields are all based on palladium acetate). The total yield reaches to ca. 3000%. Examples are given in the Table.

The new method allows mono- and di-alkenylations of the heterocycles to proceed in high yield without the use of dangerous oxygen pressure. The reaction is regioselective, occurring at the 2-position of the heterocycles. In addition, in the case of methyl acrylate, reaction is trans-stereoselective. This is due to steric effect of the bulky methoxycarbonyl group. The mechanism might involve the electrophilic attack of Pd(II) to the heterocycle to give the intermediate 2-furylpalladium complex, followed by its addition to the olefin and the subsequent elimination of HPdOAc.[2]

By using this method, a large number of alkenyl-substituted furans and thiophenes may be synthesized in just one step. The alkenylated furans and thiophenes may serve as usuful synthetic intermediates.

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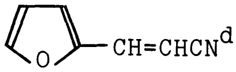
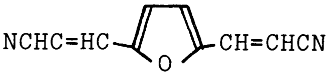
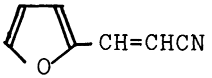
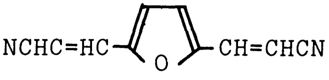
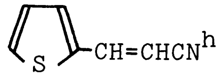
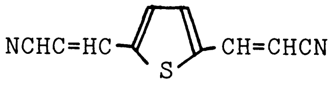
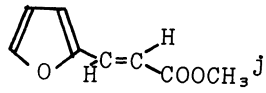
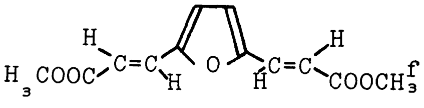
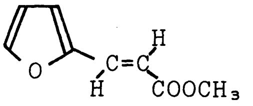
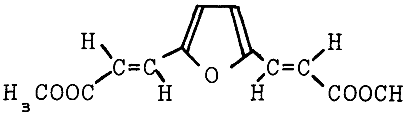
Table. Catalytic Alkenylation of Furan or Thiophene with Olefins by Pd(OAc)$_2$-Cu(OAc)$_2$^{a}

Run	Heterocycle	Olefin	Pd(OAc)$_2$ mmol	Cu(OAc)$_2$ mmol	Product	Yield^{b} %
1	Furan	Acrylonitrile^{c}	0.04	4.0	 [d]	1952
					 [e,f]	1070
2	Furan	Acrylonitrile^{g}	0.04	1.0		1028
						665
3	Thiophene	Acrylonitrile^{c}	0.04	4.0	 [h]	361
					 [f,i]	16
4	Furan	Methyl acrylate^{g}	0.04	4.1	 [j]	1039
					 [f,k]	458
5	Furan	Methyl acrylate^{g}	0.04	0.2		325
						46

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[a] Reactions were carried out at 100°C with stirring for 8 hr using the heterocycle and the olefin(2.0 mmol each), dioxane(20 ml), and acetic acid(5 ml). [b] Yields are based on palladium acetate and determined by glc. [c] Under air. [d] Mixture of 33% cis and 67% trans isomers which were identified by comparison with authentic samples; Org. Syn. Coll. Vol. V, 585 (1973). [e] Mixture of 55% trans,trans and 45% trans,cis isomers. Trans,trans isomer, mp 170-173°C(chloroform-hexane), ^{1}Hnmr(CDCl$_3$)δ 5.89(d,J=17Hz,2H),6.70(s,2H),7.12 ppm(d,J=17Hz,2H). Trans,cis isomer, ^{1}Hnmr(CDCl$_3$)δ 5.40(d,J=12Hz,1H),6.02(d,J=16Hz,1H),6.7-7.4 ppm(m,4H). [f] Satisfactory elemental and mass spectrometric analyses have been obtained for new compounds. [g] Under oxygen. [h] Mixture of 67% trans and 33% cis isomers, identified by comparison with authentic samples; C.A., 68,3854(1968). ^{1}H nmr(CDCl$_3$)δ 5.20(d,J=17Hz),and 6.9-7.1ppm(m). [i] Mixture of 50% trans,trans and 50% trans,cis isomers. Trans,trans isomer, ^{1}Hnmr(CDCl$_3$)δ 5.62(d,J=16Hz,2H),7.10(s,2H),and 7.33 ppm(d,J=16Hz,2H). Trans,cis isomer, ^{1}Hnmr(CDCl$_3$)δ 5.35(d,J=12Hz,1H),5.73(d,J=17Hz,1H),and 7.0-7.7 ppm(m,4H). [j] Identified by comparison with the sample prepared from 2-furylacrylic acid and methanol. ^{1}Hnmr(CDCl$_3$)δ 3.73(s,3H),6.13-6.60(m,3H),7.41(d,J=15.6Hz,1H),and 7.40-7.45 ppm(m,1H). A trace amount of cis isomer was also detected by glc. [k] Mp 142.5-143.5°C(benzene). ^{1}Hnmr(CDCl$_3$)δ 3.79(s,6H),6.38(d,J=16Hz,2H),6.64(s,2H),and 7.40 ppm(d,J=16Hz). A trace amount of the compound thought to be a trans,cis isomer was also detected by glc.

References

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