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A Convenient Method for the Preparation of Furan and Pyrrole Derivatives via Palladium(II)-Catalyzed Intramolecular Cyclization of 3- and 4-Alkenyl Alcohol or Amine Derivatives

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Several furan and pyrrole derivatives were prepared through palladium(II)-catalyzed intramolecular cyclization of 2-(p-toluenesulfonyl)-3-butenols and 2-methanesulfonyl-4-pentenyl alcohol or amine derivatives in good yields.

Allylsulfones are useful synthetic intermediates because of the ability of the sulfonyl group to generate an adjacent carbanion and to act as a leaving group in substitution and elimination reactions.[1)] We have been investigating the preparation and the reactions of allylsufones[2)] and the related vinylsulfones[3)] to extend the synthetic utility of such readily available sulfones.

Recently Tamaru and his co-workers reported that palladium(II) salt catalyzed the inter- and intramolecular di-alkoxycarbonylation of 3-butenols to provide γ-butyrolactone 2-acetic acid esters under 1 atm of carbon monoxide.[4)]

In connection with our interest in palladium catalyzed synthetic reactions using allysulfones, we examined the carbonylation reaction toward the 2-(p-toluenesulfonyl)-3-butenols [2-tosyl-3-butenols, 1] readily available by the reaction of carbanions of allylsulfones and aldehydes. The main product, however, was not the expected inter- and intramolecular di-alkoxycarbonylation product (2a, Eq. 1), but the intramolecular cycloacetalization product (3a, Eq. 2) which is a key intermediate in our original method for the preparation of the substituted furans.[5)] Herein we wish to describe a convenient method for the preparation of furan and pyrrole derivatives via such palladium(II)-catalyzed intramolecular cyclization.

The cycloacetalization was carried out by the use of N,N,N',N'-tetramethyl-

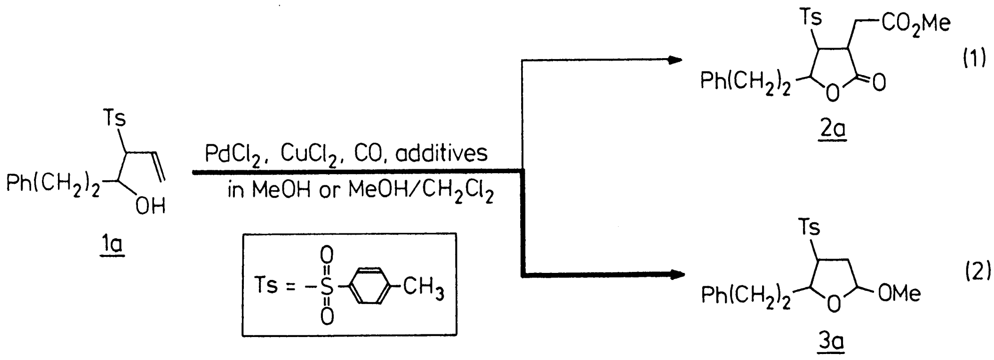
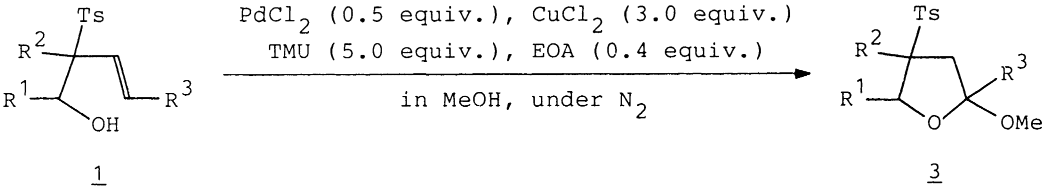


Table 1. Palladium(II)-Catalyzed Intramolecular Cycloacetalization of 2-Tosyl-3-butenols



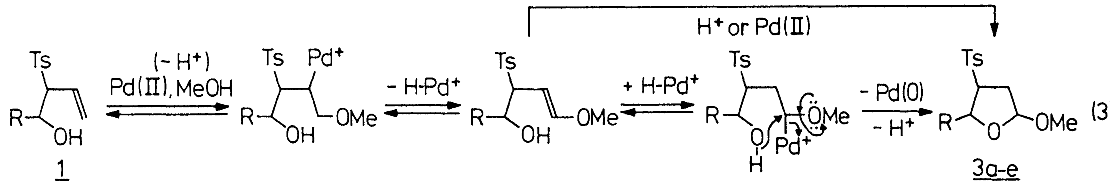
Entry	1a-g[a)]	R^1	R^2	R^3	Conditions	Yield of 3a-g/%[b)]
1	1a	$PhCH_2CH_2$	H	H	reflux, 5 h	95
2	1b	$CH_3(CH_2)_8$	H	H	reflux, 5 h	79
3	1c	$(CH_3)_2CHCH_2$	H	H	reflux, 5 h	81
4	1d	Ph	H	H	reflux, 5 h	69
5	1e	CH_3	H	H	reflux, 5 h	69
6	1f	H	$PhCH_2$	H	reflux, 10 h	23[c)]
7	1g	$PhCH_2CH_2$	H	CH_3	reflux, 20 min	17[d)]
8	1g	$PhCH_2CH_2$	H	CH_3	r.t., overnight	52[e)]

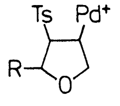
a) Mixture of diastereomers except 1f. Their ratios are given in the following: 1a (55/45), 1b (57/43), 1c (51/49), 1d (64/36), 1e (56/44), 1g (58/42). b) Consist of the four or two (for 3f) diastereomers in the following ratios, determined by 400 MHz PMR: 3a (44/32/15/9), 3b [(45/35/20(two diastereomers)], 3c (37/33/20/10), 3d (37/22/21/20), 3e [62(two diastereomers)/38(two diastereomers)], 3f (53/47), 3g (49/28/14/9). c) 76% of 1f was recovered. d) 13% of 1g was recovered and 47% of furan (7g) was obtained. e) 20% of 7g was obtained.

urea (TMU) as a HCl quencher together with ethyl orthoacetate (EOA) under nitrogen. A typical experimental procedure is described for 1a in the following: The mixture of 1a [a mixture of diastereomers (55 : 45), 83 mg, 0.25 mmol], $PdCl_2$ (22 mg, 0.125 mmol), anhydrous $CuCl_2$ (101 mg, 0.75 mmol), TMU (145 mg, 1.25 mmol), and EOA (16 mg, 0.1 mmol) in methanol (3 ml) was refluxed for 5 h under N_2. After the usual work-up, 3a was obtained in 95% yield as a mixture of possible diastereomers (44 : 32 : 15 : 9) by separation with a preparative TLC (SiO_2, hexane : dichloromethane : ether = 3 : 1 : 1).

The results for the other substrates (1b-g) are summarized in Table 1. The cycloacetalization proceeded even when the α-position of sulfone was alkylated (Entry 6), despite that it was retarded due to the steric hindrance.

The initial formation of 4 is unlikely on the basis of Baldwin's rule (5-Endo-Trig cyclization).[6)] A possible pathway for the cycloacetalization is shown





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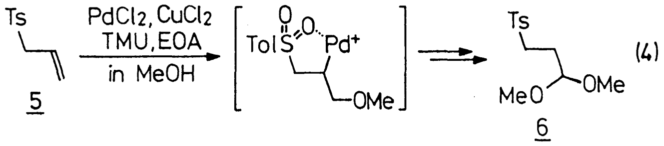
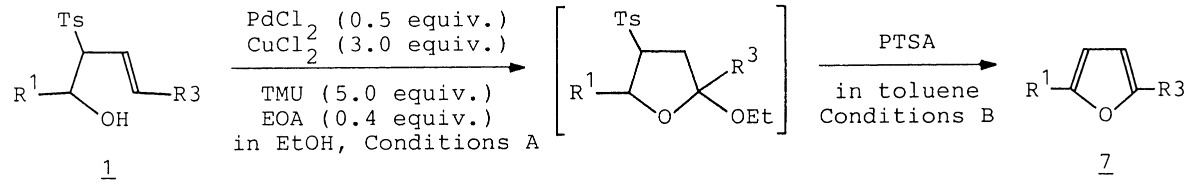


in Eq. 3. The acetalization at the terminal olefinic carbon in contrast to the well-known Wacker process, in which the oxygen nucleophiles attack the nonterminal olefinic carbon,7) may be ascribed to the coordination of the palladium(II) to the tosyl group. This speculation seems to be supported by the fact that the acetalization of allylsulfone (5) carried out under the similar conditions affords the acetal (6) in 80% yield (Eq. 4), in spite of the absence of an electron-withdrawing substituent attached to the olefin.7)

Although conversion of 3a to the corresponding furan (7a) was readily accomplished in 81% yield by refluxing its toluene solution in the presence of a catalytic amount of p-toluenesulfonic acid (PTSA),5) it is recommended for the preparation of a furan to treat the residue containing a cycloacetalization product, obtained by the usual work-up of the initial reaction, with an acid catalyst in refluxing toluene as shown in the following scheme.

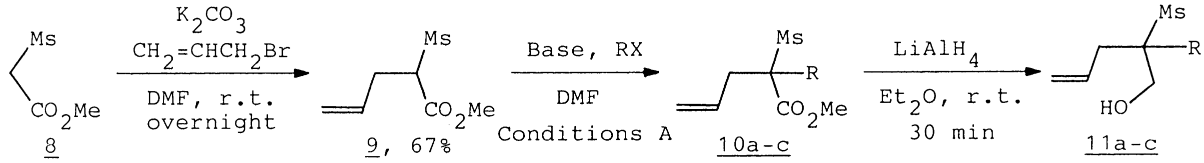


	R^1	R^3	Conditions A	Conditions B	Yield of 7
1a,	$PhCH_2CH_2$	H	reflux, 1 h	reflux, 3.5 h	7a, 81%
1b,	$CH_3(CH_2)_8$	H	reflux, 1 h	reflux, 3.0 h	7b, 71%
1g,	$PhCH_2CH_2$	CH_3	r.t., 3 d†	reflux, 20 min	7g, 78%

†About 30% of the furan (7g) was formed at this stage.

The cycloacetalization of 2-methanesulfonyl-4-pentenol (2-mesyl-4-pentenol) derivatives was next examined. This cyclization seemed to proceed much easier than the above case because of that 5-Exo-Trig cyclization favoured by Baldwin's rule is possible in this case. The starting 4-pentenol derivatives (11a-c) were prepared according to the scheme shown in Table 2. The cycloacetalization of 11a-c and the subsequent transformation to the corresponding furans were carried out in the similar manner described for 1 as shown in the following scheme. The former reaction proceeded readily even at room temperature as expected above, for

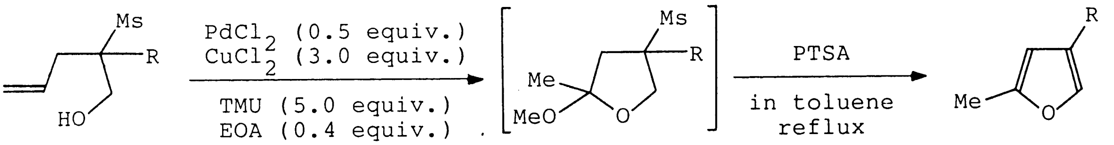
Table 2. Preparation of 2-Mesyl-4-pentenol Derivatives[a)] (Ms = $-SO_2Me$)



RX (equiv.)	Base (equiv.) Additive (equiv.)	Conditions A	Yield of 10a-c/%	Yield of 11a-c/%
$PhCH_2Br$ (1.05)	K_2CO_3 (1.2)	r.t., 9 h	10a, 98	11a, 98
$PhCH_2CH_2Br$ (1.1)	NaH (1.1), NaI (1.1)	50 °C, 27 h	10b, 76	11b, 98
$CH_3(CH_2)_5I$ (1.1)	NaH (1.1)	r.t., 1 d	10c, 64	11c, 97

a) 1.2 equiv. of K_2CO_3 and 1.1 equiv. of allyl bromide were used in the alkylation of 8. All compounds gave satisfactory spectral data.

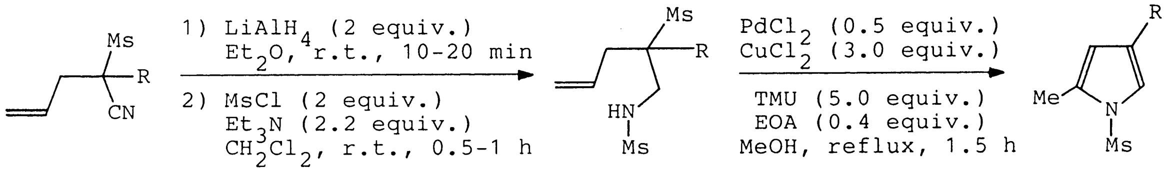
example, the intermediate 12a was isolated in 81% yield accompanied by 7% of furan 13a after reaction in methanol at room temperature for 45 min. Under these conditions, even if the amounts of $PdCl_2$, $CuCl_2$, and TMU were decreased to 0.1, 2.0, and 2.0 equiv., the furan 13a was obtained in 73% yield by reacting for 2.5 h followed by the similar treatment with an acid catalyst.



11a-c 12a-c

1.2 h, 13a, R = $PhCH_2$, 71%
1 h, 13b, R = $PhCH_2CH_2$, 90%
40 min, 13c, R = $CH_3(CH_2)_5$, 75%

It was found that the similar reaction took place for N-mesyl-2-mesyl-4-pentenylamines (15a-c) prepared from mesylacetonitrile derivatives (14a-c) to give the N-mesylpyrroles[8] (16a-c) directly as shown in the following scheme.



14a, R = $PhCH_2$	15a, quant.	16a, 84%
14b, R = $PhCH_2CH_2$	15b, quant.	16b, 65%
14c, R = $CH_3(CH_2)_5$	15c, quant.	16c, 67%

As mentioned above, the present palladium(II)-catalyzed intramolecular cyclization of 2-tosyl-3-butenols and 2-mesyl-4-pentyl alcohol or amine derivatives proved to be useful for the preparation of furan and pyrrole derivatives.

References

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