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REGIOSELECTIVE SYNTHESIS OF ALLYLIC SULFONES BY PALLADIUM-CATALYZED DENITRO-SULFONYLATION OF ALLYLIC NITRO COMPOUNDS

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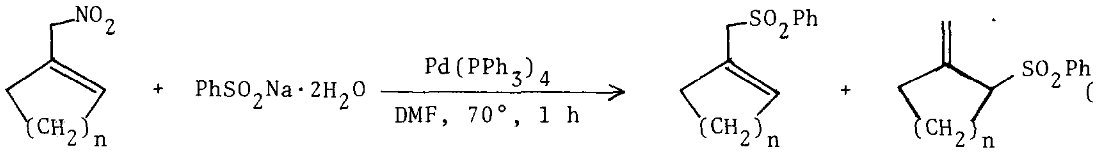
Summary: Allylic nitro compounds undergo denitro-sulfonylation catalyzed by $Pd(PPh_3)_4$ or $Pd(PPh_3)_4$+$NaNO_2$ with $PhSO_2Na\cdot 2H_2O$ to afford allylic sulfones regioselectively.

Allylic sulfones, which have been used as nucleophiles by treatment with base for 1,2 addition to aldehydes[1], 1,4 addition to conjugated carbonyl compounds[2] and simple alkylation[3] and as electrophiles for Pd(0)- and Cu(II)-catalyzed alkylation[4,5], are exceedingly useful intermediates for carbon-carbon bond formation, and utilization of these reactions in conjunction with desulfonylation[6] and elimination of the sulfonyl group[7] has significantly expanded the scope of allylic sulfone chemistry.

Allylic nitro compounds possess the analogous reaction patterns[8], however, the nucleophilic reaction of the carbanion is rather sluggish and less selective than that of allylic sulfones owing to high stability and ambident character of the nitro-stabilized carbanion, respectively , and hence the use of the dianion of allylic nitro compounds is sometimes required to enhance both the reactivity and selectivity[9]. Since some allylic nitro compounds are readily available[10], it is of synthetic value to transform allylic nitro compounds into the corresponding allylic sulfones with high regioselectivity.

Here we wish to report a new and convenient method to prepare allylic sulfones regioselectively from allylic nitro compounds by use of a catalytic amount of palladium(0). 1-Nitromethylcycloalkenes, which are easily prepared from the amine-catalyzed reaction of nitromethane and cycloalkanones[10a], reacted with $PhSO_2Na\cdot 2H_2O$ in the presence of 5 mol% of $Pd(PPh_3)_4$ to produce 1-benzenesulfonylmethylcycloalkenes[11] in fair to excellent yields (eq. 1).

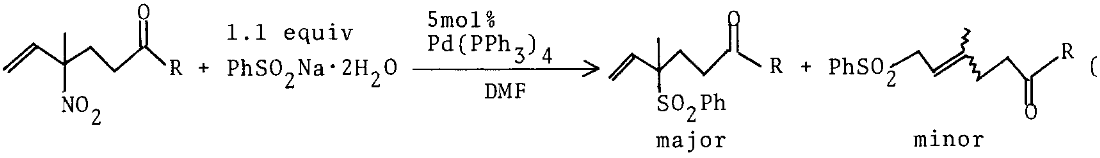


(1)

	yield	endo		exo
n=2	65%	97	:	3
3	85	94	:	6
4	92	100	:	0
5	76	100	:	0

In a typical experiment, a mixture of 1-nitromethylcycloheptene (0.155g, 1.0 mmol), $PhSO_2Na\cdot 2H_2O$ (0.400g, 2.0mmol) and $Pd(PPh_3)_4$ (0.058g, 0.050mmol) in DMF (2.0ml) was stirred under argon at 70° for 1 h. Working up the reaction mixture in the usual way followed by flash column chromatography (silica gel, 4:1 hexane/ethyl acetate) gave pure 1-benzenesulfonylmethylcycloheptene in 92% yield.

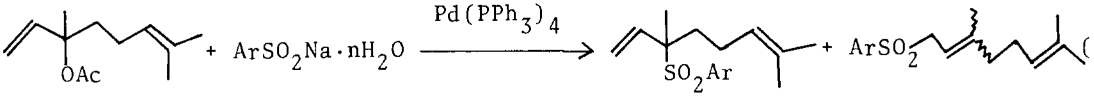
Methyl 4-methyl-4-nitro-5-hexenoate (1) prepared by the base-catalyzed 1,4 addition of 2-nitro-2-butene to methyl acrylate[8a] also underwent palladium (0)-catalyzed denitro-sulfonylation to lead to the allylic sulfones, 4 and 5 in a 77 : 23 ratio, in 82% yield (eq. 2 and entry 1 in Table). A similar ratio of products, 6 and 7[12], was obtained from the reaction of 3-methyl-3-nitro-1-hepten-6-one (2) (eq. 2 and entry 5). This product distribution differs from the result of the reaction catalyzed by $Pd(PPh_3)_4$ of linalyl acetate (3) with $p\text{-}TolSO_2Na\cdot 4H_2O$ in THF and methanol at 25° overnight[13a] or with $PhSO_2Na\cdot 2H_2O$ in DMF at 70° for 3 h, where a mixture of geranyl and neryl aryl sulfones (9) was obtained exclusively as the thermodynamically-controlled product without the formation of linalyl aryl sulfone (8), the kinetically-controlled product (eq. 3 and entry 7)[13a].



(2)

1 R=OMe R=OMe 4 5

2 Me Me 6 7



(3)

3 8 9

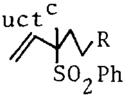
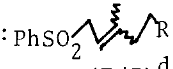
Ar=p-Tol, n=4 THF-MeOH 0 : 100

Ph, 2 DMF

In order to investigate the difference of the regioselectivity described above and to obtain the highly regioselective products, we studied the reaction of 1 with $PhSO_2Na\cdot 2H_2O$ under various conditions (entries 1-4). No meaningful change of the product distribution was observed when solvent, reaction time and temperature were altered, giving 4 predominantly, while 4 was obtained exclusively when the reaction was carried out in the presence of $NaNO_2$ (1.0 equiv to 4). Similarly, 6 was the sole product from 2 by the addition of $NaNO_2$ (entry 6). Moreover, even when the deacetoxy-sulfonylation reaction of 3 with $PhSO_2Na\cdot 2H_2O$ was run in the presence of $NaNO_2$, the major product was not 9, but 8 (entry 8).

These results indicate that $Pd(PPh_3)_4$ is deactivated by $NaNO_2$ to generate a new palladium species which can be subjected to the oxidative addition of an allylic nitro compound and an allylic acetate, but is inert to an allylic sulfone. Thus palladium(0)-catalyzed isomerization of 4 and 6 to thermody-

Table. Palladium-catalyzed Denitro-sulfonylation and Deacetoxy-sulfonylation[a]

entry	substrate	catalyst[b]	solvent	time	temp. (°c)	isolated yield, %	product[c]	 :  (E/Z)[d]
1	**1**	A	DMF	1 h	70	82	**4** + **5**	77 : 23 (76/24)
2	**1**	A	DMF	7 days	25	64	**4** + **5**	82 : 18 (70/30)
3	**1**	A	THF-MeOH	7 days	25	71	**4** + **5**	75 : 25 (72/28)
4	**1**	B	DMF	21 h	25	79	**4**	100 : 0
5	**2**	A	DMF	1 h	70	91	**6** + **7**	72 : 28 (67/33)
6	**2**	B	DMF	21 h	25	83	**6**	100 : 0
7	**3**	A	DMF	3 h	70	76	**9**	0 : 100 (74/26)
8	**3**	B	DMF	3 h	70	72	**8** + **9**	80 : 20 (75/25)

a) Reactions were performed on 1.0mmol scale using 5 mol% of palladium catalyst and 1.1 equiv of $PhSO_2Na \cdot 2H_2O$. b) A: $Pd(PPh_3)_4$. B: $Pd(PPh_3)_4$ + $NaNO_2$(1.0mmol). c) Satisfactory infrared, ^1H and ^{13}C NMR spectra, and elemental analyses were obtained for all products. d) The E/Z ratio was determined by GLPC.

namically stable **5** and **7** was completely suppressed by adding $NaNO_2$, respectively (entries 4 and 6), while the isomerization occurred upon the treatment of **4** or **6** with 5 mol% of $Pd(PPh_3)_4$[13a]. The results shown in entries 1 and 5 are interpreted in terms of the deactivation of $Pd(PPh_3)_4$ by NO_2^- eliminated from **1** and **2** to result in the formation of the new palladium species in the course of the reaction, and the minor products **5** and **7** are considered to be produced from **4** and **6** by the $Pd(PPh_3)_4$-catalyzed isomerization, respectively, before $Pd(PPh_3)_4$ is completely deactivated.

Since some allylic nitro compounds are directly available from the condensation of cyclic ketones and nitromethane or from the conjugate addition of α-nitro olefins to α,β-unsaturated carbonyl compounds, denitro-sulfonylation describrd here would be a useful procedure for the synthesis of allylic sulfones similarly to other methods such as palladium-catalyzed deacetoxy-sulfonylation of allylic acetates[13] and simple sulfonylation of allylic halides. The application of this method to the regio-controlled synthesis of various allylic sulfones is in progress in connection with the exploitation of a new synthetic method for allylic nitro compounds.

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11) All products were fully characterized by means of infrared, ^1H and ^{13}C NMR spectra, and elemental analyses, The isomeric ratio of endo to exo products was determined by ^1H NMR (300 MHz) and GLPC.
12) The structure of E and Z isomers was determined by a NOE measurement (^1H NMR), which exhibited that the irradiation at vinylmethyl protons resulted in a clean increment of integration of olefin proton signal (19 %, 7) for Z isomer and none for E isomer, after both isomers were separated from each other by flash column chromatography (silica gel, 4:1 hexane/ethyl acetate).
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