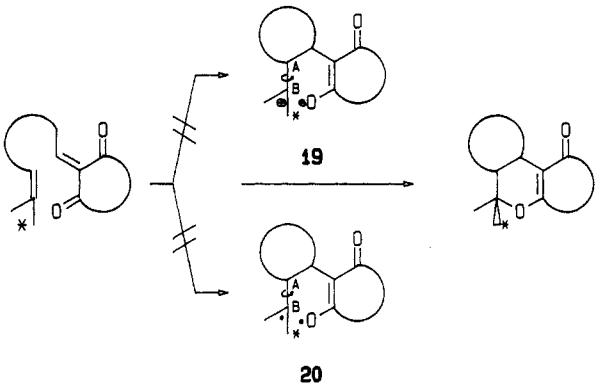
^{13}C NMR and ^{1}H NMR spectra has shown that during the synthesis of **10** some scrambling had occured. The distribution of the label was determined by integration[15] of the ^{13}C-satellites in the ^{1}H NMR spectrum for C-12 at δ 1.81 (J_{CH} = 126.5 Hz) and for C-13 at δ 1.75 (J_{CH} = 126.5 Hz) as 88.2:11.8. From the ^{13}C NMR spectrum of **10**, a ratio of 93.4:6.6 for C_{12}/C_{13} was found. The higher values determined from the ^{13}C spectra can be explained by different T_1 values of labeled and unlabeled methyl groups as pointed out by Benn.[16]

The aldehyde **10** was condensed with dimethylbarbituric acid (**11**), Meldrum's acid (**13**), the pyrazolone **15**, and the enantiomerically pure oxazepandione **17**, yielding the cycloadducts *rac*-**12**,[7a] *rac*-**14**,[7a] *rac*-**16**,[7b] and **18**[8] via the primarily formed 2-benzylidene-1,3-dicarbonyls, which were however not isolated except in the case of **17** (Table I). The percentage of the label in the equatorial methyl group at the dihydropyran ring in the cycloadducts was determined by comparison of the heights of the peaks for the equatorial and axial methyl groups in the ^{13}C NMR spectra as well as by integration of the appropriate ^{13}C-satellites in the ^{1}H NMR spectra. Generally the signals of the equatorial, predominately labeled methyl group appear at lower field in the ^{1}H and ^{13}C NMR spectra than the axial. The assignment has been confirmed by one- and two-dimensional NOE experiments of **12** and **16**. They clearly show that in **12** the β-methyl group (δ 1.60) is in close vicinity to H-6a. A NOE between the α-methyl group (δ 1.20) and H-6a could not be detected. However, in **16** the resonance of the two methyl groups is reversed, because of a different conformation of the pyranopyran system, since both methyl groups show NOE effects to H-5a. Also, a NOE is observed between H-11b and the high field methyl group at C-5, which carries the ^{13}C-label. This experiment therefore, demonstrates the cis relationship between the labeled methyl group and H-5a. There is no NOE between H-11b and the α-methyl group.

In all reactions the ratio of the labels in the two methyl groups has not been altered. Even high reaction temperatures and the use of Lewis acids[17] had no effect on the distribution of the label in the products (Table I). This shows clearly that the configuration of the dienophile is retained during the cycloaddition.

The observed stereospecificity is a characteristic of a truly concerted cycloaddition rather than an ionic or radical stepwise process. Also zwitterion **19** can be excluded as an intermediate, since the rates of the cycloadditons are similar in polar and nonpolar solvents. However, the occurrence of radical **20** is in agreement with the results if one assumes that the rotation about the single bond A-B in **20** is slow compared to the C-O bond formation.[18] Simulations[19] based on an estimated experimental error of ±0.5% in the distribution of the label in the products result in a $\Delta\Delta G^{\ddagger} \approx 3.0$ kcal/mol for the two reaction paths. By setting $\Delta G^{\ddagger} = 0$ for the C-O bond formation which would indicate a concerted mechanism, $\Delta G^{\ddagger} \approx 3.0$ kcal/mol would be found for the rotation about the C-C bond A-B in **20**. This value is higher than usually accepted for barriers to rotation of free tertiary radicals, for which a $\Delta G^{\ddagger} < 1.5$ kcal/mol was estimated.[20]



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Registry No. **7**, 91404-83-0; **8**, 107115-86-6; **9**, 90-02-8; **10**, 107115-85-5; **10-17** arylene-1,3-dicarbonyl product, 107115-87-7; **11**, 769-42-6; *rac*-**12**, 107115-88-8; **13**, 2033-24-1; *rac*-**14**, 107115-89-9; **15**, 89-25-8; *rac*-**16**, 107115-90-2; **17**, 67376-72-1; **18**, 107115-91-3; $(^{13}CH_3)_2CuLi$, 15681-48-8.

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Palladium-Catalyzed Denitro-Sulfonylation and Amination of β,γ-Epoxy Nitro Compounds

Summary: β-Alkyl-β,γ-epoxy nitro compounds undergo the weak base catalyzed conversion to γ-hydroxy-α-nitro olefins followed by isomerization of the resulting double bond and the subsequent Pd(0)-catalyzed allylic substitution of the hydroxy allylic nitro intermediates by $PhSO_2Na$ and piperidine in a single-pot to afford hydroxy sulfones and amines, respectively.

Sir: We have recently revealed a general synthetic method to prepare allylic nitro compounds by *N,N*-dimethylethylenediamine-catalyzed condensation of primary nitroalkanes with various ketones.[1] This procedure in combination with Pd(0)[2] or Lewis acid[3] mediated allylic substitution of allylic nitro compounds by nucleophiles offers a new synthetic route to take carbonyl compounds

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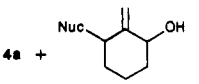
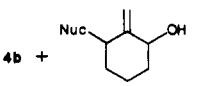
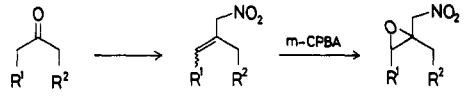
Table I. Pd(0)-Catalyzed Denitro-Sulfonylation and Amination of β,γ-Epoxy Nitro Compounds (eq 3 and 4)

entry	epoxy nitro compd	Nuc	time, h	product[a]	yield,[b] %
1	1 (n = 1)	$PhSO_2$	2	**4a**	60
2	1 (n = 1)	$C_5H_{10}N$	24	**4b**	83
3	1 (n = 2)	$PhSO_2$	2	 55:45	47
4	1 (n = 2)	$C_5H_{10}N$	24	 84:36	56
5	1 (n = 3)	$PhSO_2$	2	**4a**	83
6	1 (n = 3)	$C_5H_{10}N$	24	**4b**	77
7	1 (n = 4)	$PhSO_2$	2	**4a**	80
8	1 (n = 8)[c]	$PhSO_2$	2	**4a** (E/Z = 76/24)	71
9	**5** (R = Me)	$PhSO_2$	2	**8a**	71
10	**5** (R = Me)	$C_5H_{10}N$	2	**8b**	80
11	**5** (R = $(CH_2)_4Me$)	$PhSO_2$	2	**8a**	75
12	**5** (R = $(CH_2)_4Me$)	$C_5H_{10}N$	2	**8b**	73
13	**5** (R = CH_2CHMe_2)	$PhSO_2$	2	**8a**	72
14	**5** (R = $(CH_2)_2COOMe$)	$PhSO_2$	2	**8a**	70

[a] All new products were fully characterized by means of infrared and ^1H NMR spectra and elemental analyses. [b] Isolated yield. [c] Prepared from a 73:27 mixture of (E)- and (Z)-1-(nitromethyl)cyclododecenes.

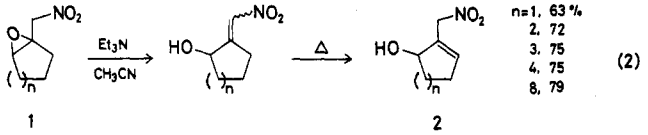
into the functionalized allylic systems. In order to obtain more functionalized and synthetically useful allylic systems from these readily available allylic nitro compounds, we attempted to introduce an allylic alcohol portion into the allylic nitro substrates. The epoxide was the functional group of choice for this purpose.[4] In this paper we report the regioselective Pd(0)-catalyzed denitro-sulfonylation and amination reactions of β,γ-epoxy nitro compounds to produce allylic sulfones and amines containing allylic hydroxy group.

The requisite β,γ-epoxy nitro compounds were obtained in 80–90% yield by epoxidation of the corresponding allylic nitro compounds with m-CPBA (eq 1). First, we examined



(1)

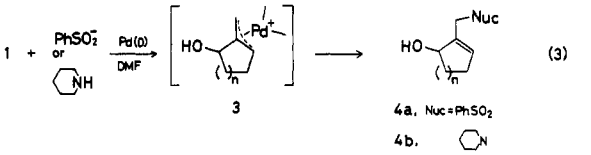
whether or not the base-catalyzed conversion of the epoxy nitro compounds to γ-hydroxy-α-nitro olefins and subsequent isomerization of the resulting double bond were feasible in such a way as to give the expected allylic nitro and alcohol systems. In the case of 1-(nitromethyl)-1,2-epoxycycloalkanes **1**, this is the case: treatment of the epoxy nitro compound **1** with a catalytic amount (0.1 equiv) of Et_3N immediately led to the formation of γ-hydroxy-α-nitro olefins and the subsequent heating resulted in the isomerization of the double bond to produce the desired hydroxy allylic nitro compounds **2** (eq 2). This transformation stems from (i) the high acidity of the nitromethylene protons and (ii) the thermodynamic stability of the endocyclic olefin.



(2)

1 2

Keeping this result in mind, we attempted the Pd(0)-catalyzed reaction of **1** with soft nucleophiles. When the epoxy nitro compounds **1** were allowed to react with $PhSO_2Na{\cdot}2H_2O$ (1.5 equiv) or piperidine (2.0 equiv) in DMF at 70 °C in the presence of 3 mol % of $Pd(PPh_3)_4$ and $Ph_2PCH_2CH_2PPh_2$ (dppe), the hydroxy allylic sulfones or amines **4** were obtained, respectively (eq 3). The results



(3)

are summarized in Table I. Sulfonylation proceeds smoothly without amine base, suggesting that the Pd(0) catalyst or the phosphine ligand is a sufficient base to induce both the ring opening and the isomerization.[5] In the absence of dppe, the yield of **4** decreases by the range of 5–10%. In amination piperidine must act as the base as well as the nucleophile. Since allylic substitutions do not occur without Pd(0) catalyst, these reactions should involve the nucleophilic attack on the (π-allyl)palladium complex intermediates **3**.[2,6] Regioselective attack of the nucleophiles at the exocyclic carbon atom of the (π-allyl)palladium complex occurs, except for the six-membered substrate (entries 3 and 4).

Noteworthy is the case of 1-nitro-2-methyl-2,3-epoxyalkanes **5**, where although treatment of **5** with 0.1 equiv of Et_3N only resulted in the formation of the γ-hydroxy-α-nitro olefins **6**, Pd(0)-catalyzed denitro-sulfonylation and amination of **5** proceeded smoothly to produce the desired allylic products **8** as presented in eq 4 and Table I. Apparently, equilibrium between **6** and the allylic isomer **7**, which lies heavily on the side of **6** under usual basic conditions, shifts to **7** as the Pd(0)-catalyzed reaction proceeds.[7]

(4) The isomerization of epoxide to allylic alcohol is a general and useful functional group interchange. For reviews, see: (a) Crandall, J. K.; Apparu, M. *Org. React. (N.Y.)* **1983**, *29*, 345–443. (b) Rao, A. S.; Paknikar, S. K.; Kirtane, J. G. *Tetrahedron* **1983**, *39*, 2323–2367. (c) Smith, J. G. *Synthesis* **1984**, 629–656.

(5) Ph_3P is capable of catalyzing the Michael addition of α-nitro ketones to the activated olefins. (a) Kostova, K.; Riatsch, A. L.; Nakashita, Y.; Hesse, M. *Helv. Chim. Acta* **1982**, *65*, 249–251. (b) Cookson, R. C.; Ray, P. S. *Tetrahedron Lett.* **1982**, *23*, 3521–3524. (c) Ono, N.; Miyake, H.; Kaji, A. *J. Chem. Soc., Chem. Commun.* **1983**, 875–876.

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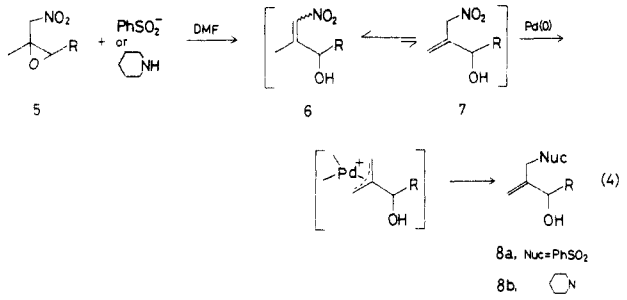
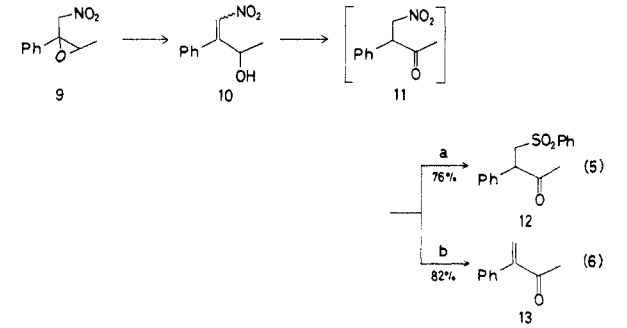


A typical experimental procedure for denito-sulfonylation follows: A mixture of 1-nitro-2-methyl-2,3-epoxybutane (5) (262 mg, 2.0 mmol), $PhSO_2Na{\cdot}2H_2O$ (600 mg, 3.0 mmol), $Pd(PPh_3)_4$ (69 mg, 0.06 mmol), and dppe (24 mg, 0.06 mmol) in DMF (4 mL) was stirred at 70 °C for 2 h. The reaction mixture was partitioned between ether and water, and the aqueous phase was extracted with ether (3 × 30 mL). The ether extracts were washed with brine (3 × 30 mL) and water (30 mL), dried over $MgSO_4$, and concentrated in vacuo. Purification of the crude product by column chromatography (1:1 hexane–ethyl acetate) gave 320 mg (71%) of 2-[(phenylsulfonyl)methyl]-3-hydroxy-1-butene (**8a**) as a pale yellow oil.

Thus, the presence of an alkyl group at the epoxy carbon β to the nitro group in the epoxy nitro compound to permit equilibration with an allylic nitro isomer is a mandatory requirement for these Pd(0)-catalyzed allylic substitutions to occur. In the case of 1-nitro-2-phenyl-2,3-epoxybutane (**9**) bearing a phenyl group at the β carbon atom, irrespective of the presence of Pd(0) catalyst, $PhSO_2^-$ reacted with **9** to give 3-phenyl-4-(phenylsulfonyl)-2-butanone (**12**) (eq 5). Moreover, treatment of **9** with excess Et_3N afforded the conjugated enone **13** (eq 6). These facts indicate that in the reaction of eq 5, $PhSO_2^-$ acts as a base to convert **9** to **13** via **10** and **11** and the concomitantly generated $PhSO_2H$ adds to **13** to produce **12**.



(a) 1.5 equiv of $PhSO_2Na{\cdot}2H_2O$, DMF, 70 °C, 3 h; (b) excess Et_3N, DMF, 70 °C, 24 h

The products 4 and 8 as well as **2** are believed to be useful synthetic intermediates owing to their possession of two allylic functional groups within a molecule. For example, hydroxy allylic sulfones **8a** are of interest in view of the recent studies on [3 + 2]-cycloaddition reactions.[8] Namely, the sulfones **8a** are the key intermediates for the Pd(0)-catalyzed cycloaddition with the activated olefins.[9]

Results described here attest to the ease of availability, the high reactivity, and the synthetic utility of β,γ-epoxy nitro compounds. Particularly, β-alkyl-β,γ-epoxy nitro compounds have been proven to serve as reactive substrates for Pd(0)-mediated denitro-sulfonylation and amination reactions. Further studies on this chemistry are in progress.

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Diels–Alder Cycloadditions Using Electrophilic Sulfonylpyridones

Summary: Examples are presented of 5–7-kbar [2 + 4]-cycloadditions of electrophilic 1,3-disulfonyl-2-pyridones with vinyl ethers leading regioselectively and stereoselectively to unsaturated, bridged, bicyclic lactams and, ultimately, to polyfunctionalized cyclohexanes.

Sir: We recently reported the first examples of Diels–Alder cycloadditions using an electrophilic 3-sulfinyl-2-pyrone[1] and an even more electrophilic 3-sulfonyl-2-pyrone,[2] with an application to a total synthesis of (−)-methyl triacetyl-4-epi-shikimate.[3] 2-Pyridones[4] have more aromatic character than 2-pyrones,[5] and consequently 2-pyridones generally do not enter effectively into [2 + 4]-cycloadditions.[6] It seemed appropriate, therefore, to determine

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