reactions can be defined, it should be possible to draw conclusions about the relative extent of overall charge development in the transition states.[13] We show below that overall charge development can be inferred from correlations of ρ_R^+ values with ^{13}C chemical shifts of stable carbocations.

The application of Taft's DSP equation to rate data for naphthalene protodetritiation[1] and for solvolysis[2,3] is shown in Table I. Detritiation data for the 3-, 6-, and 7-positions was available for only two substituents besides hydrogen, so the DSP equation could not be applied to those data. The $-\rho_R^+$ values are plotted vs. ^{13}C chemical shifts for the corresponding positions in the stable ions in Figure 1. The correlations of $-\rho_R^+$ with δ_C are excellent: for protodetritiation, slope = 0.091, intercept = -11.1, correlation coefficient = 0.997; for solvolysis, slope = 0.123, intercept = -15.0, correlation coefficient = 0.997. The correlations are supportive of the postulates that both ρ_R^+ and δ_C are charge-related properties, at least in the naphthalene system.[10]

Direct comparison of ρ_R^+ values from the two reactions for positions 4 and 5 (the only common positions) suggests that greater charge is developed at these two positions in protodetritiation than in solvolysis. However, these positions are also more deshielded in the stable naphthalenium ion than in the (1-naphthyl)ethyl cation, suggesting that inherently more charge is found at these positions in the naphthalenium ion, so that the larger ρ_R^+ values are not necessarily due to greater overall charge development. Figure 1 reveals that the solvolysis reaction has the steeper slope in the correlation of ρ_R^+ with δ_C. The δ_C values presumably reflect the charge distribution in the case of equal and complete charge development for both ions. Hence, it is the solvolysis reaction that has greater charge development at the transition state. The ratio of the slopes in Figure 1 is 1.35. Thus, we infer 1.35 times greater charge development at the solvolysis transition state than at the protodetritiation transition state.

Further evidence and assumptions are needed to estimate the actual extent of charge development. We have previously estimated about 35% charge development for protodetritiation from comparison of substituent effects on protodetritiation in bithienyl and on the rotational barrier in protonated bithienyl.[14] A similar estimate of 38% was obtained[14] by comparing substituent effects on the protodetritiation of substituted benzenes[15] to STO-3G calculations of the energies involved in full protonation.[16] Strictly speaking, these estimates of charge development are based on energy-energy relationships and rest on the assumption of a direct relation between changes in charge and changes in energy.[5,17] Combining these estimates with the factor of 1.35 leads to an estimate of 47-51% charge development at the solvolysis transition state.

Charge development of about 50% for solvolysis is low compared to 89% estimated if the slope observed by Arnett in the plot of free energies of activation for solvolysis vs. heats of ionization is equated to the degree of charge separation.[5] However, Arnett's observation was based on tertiary alkyl chlorides undergoing limiting solvolysis and on secondary systems corrected for the degree of nucleophilic solvent participation. Nucleophilic solvent participation is expected for the secondary 1-naphthylethyl chlorides[18] and would reduce the extent of charge developed at the transition state.[19]

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(18) The comparable 1-phenylethyl chloride shows evidence for nucleophilic solvent participation in the ratio $(k_{EW}/k_{CH_3COOH})_Y = 2.5$, from the solvolysis rate in aqueous ethanol having the same Y value as acetic acid: (a) Streitwieser, A., Jr. *Chem. Rev.* **1956**, *56*, 571-752. (b) Bentley, T. W.; Schleyer, P. v. R. *J. Am. Chem. Soc.* **1976**, *98*, 7658-7666.
(19) Note Added in Proof: A more apt comparison may be to the solvolysis of allylic chlorides uncorrected for solvent participation, for which 52% carbocation character at the transition state was estimated: Mayr, H.; Förner, W.; Schleyer, P. v. R. *J. Am. Chem. Soc.* **1979**, *101*, 6032-6040.

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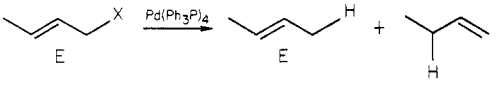
Regio- and Stereoselective Reductive Replacement of Allylic Oxygen, Sulfur, and Selenium Functional Groups by Hydride via Catalytic Activation by Palladium(0) Complexes

Summary: The combination of $Pd(Ph_3P)_4$ and $LiBHEt_3$ provides an effective system for reductive removal of allylic ethers, sulfides, sulfones, selenides, and *tert*-butyldimethylsilyl ethers.

Sir: We recently reported that allylic esters are reductively reduced by $NaBH_3CN$ and $NaBH_4$ via catalytic activation by Pd(0) in THF.[1,2] However, with these relatively mild hydride transfer reagents, aliphatic systems suffer from considerable loss of both regio- and stereochemical control and mixtures of alkene products result.[1]

In this communication we describe the first successful hydride substitution of several other allylic functional groups that are normally inert toward displacement, including aryl[3] and aliphatic ethers, sulfides, sulfones,[4] selenides, and silyl ethers. Furthermore, use of the very potent (and bulky) hydride transfer reagent $LiBH(C_2H_5)_3$[5] leads to good to excellent maintanence of both the regio- and stereointegrity of the double bond (eq 1). Table I



(1)

presents results for a variety of allylic derivatives and demonstrates the scope of the process. Included for comparison are corresponding reductions with other reagents that display either inferior regio- and stereoselectivity (entries 2-6) or opposite regiospecificity (entries 7, 9, 14, 15). The use of the $LiBH(sec\text{-}Bu)_3$ did not improve the selectivity (entry 17). The utility of the reaction is augmented since the process may be employed to protect

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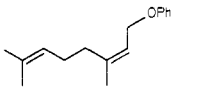
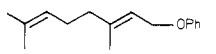
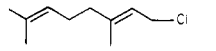
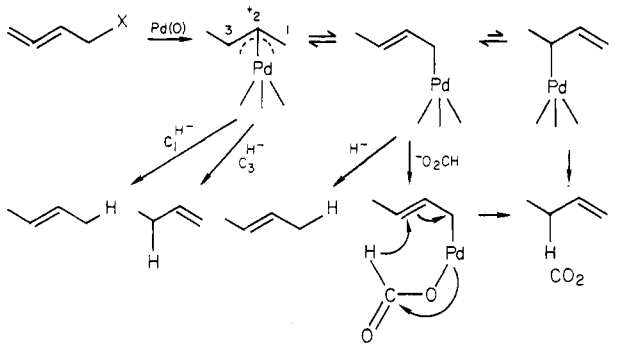
Table I. Reductive Removal of Allylic Functional Groups

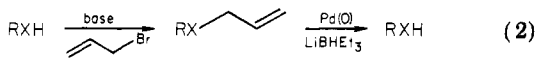
entry	derivative[a]	hydride[b]	temp, °C (time, h)	alkene isomers, %[c] (yield, %) E	Z	1-
1	(*E*)-$CH_3(CH_2)_6CH{=}CHCH_2OPh$	$LiBHEt_3$	66 (26)	97	3	Tr (100, 71[d])
2		$LiAlH_4$	66 (26)	89	8	3 (90)
3		$(i\text{-}Bu)_2AlH$	66 (26)	84	16	tr (99)
4		$NaBH_4$	66 (26)	40	5	55 (51)
5		$NaBH_3CN$	66 (26)	64	7	29 (84)
6		Ph_2SiH_2	66 (46)	49	6	45 (84)
7		NH_4O_2CH	66 (26)	10	2	88 (99)
8	(*E*)-$CH_3(CH_2)_6CH{=}CHCH_2OCH_3$	$LiBHEt_3$	66 (25)	94	3	3 (89)
9		NH_4O_2CH[e]	100 (14)[f]	6	16	78 (70)
10	(*E*)-$CH_3(CH_2)_6CH{=}CHCH_2SPh$	$LiBHEt_3$	66 (9)	94	5	1 (90)
11	(*E*)-$CH_3(CH_2)_6CH{=}CHCH_2SO_2Ph$	$LiBHEt_3$	66 (24)	86	13	1 (65)
12	(*E*)-$CH_3(CH_2)_6CH{=}CHCH_2SePh$	$LiBHEt_3$	66 (3)	81	18	1 (82)
13	(*E*)-$CH_3(CH_2)_6CH{=}CHCH_2OSiMe_2t\text{-}Bu$	$LiBHEt_3$	66 (72)	98	1	1 (80)
14		NH_4O_2CH[e]	100 (24)	23	9	68 (63)[d]
15		NH_4O_2CH	66 (24)	11	4	85 (91)[h]
16	(*Z*) 	$LiBHEt_3$[e]	100 (26)	2	97	1 (75)
17		$LiBH(sec\text{-}Bu)_3$[e]	100 (30)	2	94	4 (84)
18	(*E*) 	$LiBHEt_3$[e]	100 (39)	97	1	2 (74)
19	(*Z*) 	$LiBHEt_3$[g]	25 (3)	97	1	2 (96)
20	(*E*)-$C_6H_5CH{=}CHCH_2OPh$	$LiBHEt_3$	66 (14)	99	Tr	Tr (90)

[a] Reactions were 0.1 M in the allyl derivative, 0.07 M in Ph_3P, 0.02 M in $Pd(Ph_3P)_4$, and 0.2 M in the hydride reagent. [b] Specified otherwise. [c] The yields and ratio of isomers were determined by GLC, using internal standards unless noted. [d] Isolated yield. [e] Dioxane solvent. [f] Longer reaction times gave some double bond isomerization. [g] No Pd(0). [h] Product contained ca. 19% diene from elimination.

Scheme I



allylic OH, SH, SO_2H, and SeH functionalities via allyl derivatives and subsequent deprotection by Pd(0)/hydride reduction as depicted in eq 2.



(2)

X = O, S, SO_2, Se

The dependence of regio- and stereoselectivity on the hydride reagent may reflect mechanistic differences in which both σ-bonded organopalladium and (π-allyl)palladium complexes are involved (Scheme I).[6] Thus, very potent nucleophilic hydride sources ($LiBHEt_3$, $LiAlH_4$) may rapidly attack intermediate π-allyl complexes at the less hindered terminal site to give the observed 2-alkenes before significant double bond isomerization. Likewise, reduction of σ complexes either by nucleophilic displacement or via hydride transfer from a palladium hydride species should favor 2-alkene formation since the less congested terminal σ complex is favored. Results with less effective hydride transfer reagents (i.e., $NaBH_3CN$, $NaBH_4$) may stem from increased attack of π-allyl systems at the site best able to accommodate positive charge (C_3), leading to increased amounts of 1-alkenes. Reduction by formate appears to be a special case since hydride is transfered regioselectively to afford terminal alkenes. This suggests either SN_i transfer of hydride from formate complexed to the preferred terminal σ-Pd species[7b] (Scheme I) or hydride transfer preferentially to the more electropositive carbon of π-allylic Pd complexes. In any case, the relative role of (σ-allyl)- and (π-allyl)palladium complexes in nucleophilic displacements requires further investigation.

The experimental procedure employed is straightforward and illustrated for the reduction of *trans*-2-decenyl phenyl ether. To a solution of the ether (1.16 g, 5 mmol), Pd-$[(C_6H_5)_3P]_4$[9] (580 mg, 0.5 mmol), and triphenylphosphine (920 mg, 3.5 mmol) in 50 mL of dry THF was added $LiBHEt_3$ (10 mmol, 10 mL of 1 M solution). The mixture was refluxed under Ar with stirring for 6 h and then quenched with 10% aqueous NaOH. The resulting solution was diluted with brine and extracted with three 50-mL portions of pentane. The pentane solution was washed with 10% aqueous NaOH, dried ($MgSO_4$), concentrated, and distilled at reduced pressure (Kugelrohr apparatus) to yield 0.50 g (71%) of a clear liquid. Analysis by GLC

(6) Reductions of σ-bonded organopalladium complexes with retention of stereochemistry have been demonstrated (ref 7) and appear to implicate palladium hydride intermediates. Likewise, (π-allyl)palladium species are attacked by several nucleophiles, and the regiochemistry depends on the type and bulk of the nucleophile with hindered examples preferring the less substituted site and attack from the side opposite palladium (ref 2a). Furthermore, interconversion of (π-allyl)- and (σ-allyl)palladium species has been demonstrated (ref 8).

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(Carbowax 20M column) indicated the composition listed in Table I (entry 1).

In summary, the processes described may be employed synthetically to reductively displace several allylic functional groups[10] that are otherwise difficult to remove (OR, SR, SO_2R, SeR, OSi-*t*-$BuMe_2$) and demonstrate that these groups should also be displaceable by other nucleophiles (i.e., carbonions). This possibility is being explored.

Acknowledgment. We thank the National Science Foundation for support of our programs on hydride chemistry (CHE-7909167).

Registry No. (*E*)-$CH_3(CH_2)_6CH{=}CHCH_2OPh$, 83026-82-8; (*E*)-$CH_3(CH_2)_6CH{=}CHCH_2OCH_3$, 57648-47-2; (*E*)-$CH_3(CH_2)_6CH{=}CHCH_2SPh$, 83026-83-9; (*E*)-$CH_3(CH_2)_6CH{=}CHCH_2SO_2Ph$, 83026-84-0; (*E*)-$CH_3(CH_2)_6CH{=}CHCH_2SePh$, 83026-85-1; (*E*)-$CH_3(CH_2)_6CH{=}CHCH_2OSiMe_2$-*t*-Bu, 83026-86-2; (*Z*)-$CH_3C(CH_3){=}CH(CH_2)_2C(CH_3){=}CHCH_2OPh$, 41515-57-5; (*E*)-$CH_3C(CH_3){=}CH(CH_2)_2C(CH_3){=}CHCH_2OPh$, 35266-82-1; (*E*)-$CH_3C(CH_3){=}CH(CH_2)_2C(CH_3){=}CHCH_2Cl$, 5389-87-7; (*E*)-$C_6H_5CH{=}CHCH_2OPh$, 37464-41-8; $LiBHEt_3$, 22560-16-3; $Pd(Ph_3P)_4$, 14221-01-3; (*E*)-$CH_3(CH_2)_6CH{=}CHCH_3$, 20063-97-2; $CH_3(CH_2)_7CH{=}CH_2$, 872-05-9; (*Z*)-$CH_3(CH_2)_6CH{=}CHCH_3$, 20348-51-0; (*Z*)-$CH_3C(CH_3){=}CH(CH_2)_2C(CH_3){=}CHCH_3$, 2492-22-0; (*E*)-$CH_3C(CH_3){=}CH(CH_2)_2C(CH_3){=}CHCH_3$, 2609-23-6; (*E*)-$C_6H_5CH{=}CHCH_3$, 873-66-5.

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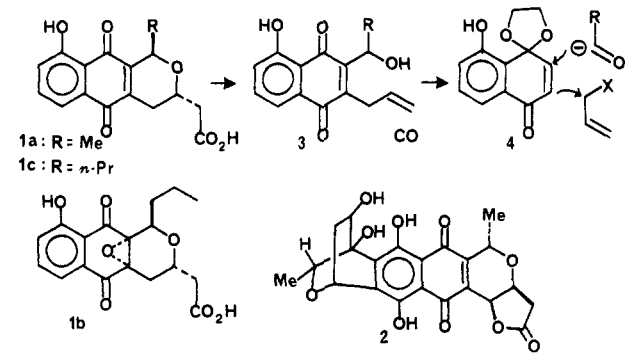
Synthesis of Naphthoquinone Antibiotics: Conjugate Addition/Electrophile Trapping with Acylnickel Carbonylate Anions

Summary: Conjugate addition of nickel acylate complexes followed by quenching with allyl iodide provide key intermediates for the synthesis of nanaomycin A and frenolicin.

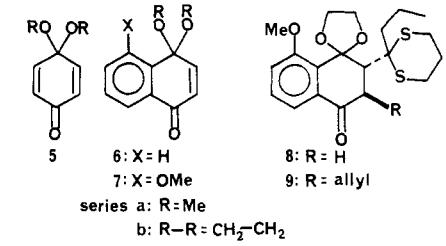
Sir: Nanaomycin A (**1a**),[3-4] frenolicin (**1b**),[5] and deoxyfrenolicin (**1c**)[4a,5b] are examples of a growing class of naphthoquinone derivatives with significant antibiotic activity. The presence of the 2,3-fused pyran ring opens the possibility that members of the class may serve as "bio-reductive alkylating agents",[6] and this feature is consistent with the significant antineoplastic activity of **1a**. As part of a general development of new approaches to naphthoquinones of this type with the goal of efficient preparation of the more complex analogue granaticin (**2**),[7,8] we have completed a short efficient synthesis of **1a** and **1c** following the strategy outlined in Scheme I.

Scheme I. Strategy



Related work has demonstrated that palladium(II)-promoted intramolecular alkoxycarbonylation (e.g., conversion of **3** to **1a** and **1c**) can be an efficient, stereoselective reaction in related cases.[9] An intermediate such as **3** might be obtained by conjugate addition of a carbonyl anion equivalent to a quinone monoketal (e.g., **4**) and reaction of the resulting enolate with allyl halide. Naphthoquinone monoketals are readily available[10] and useful intermediates[11] known to undergo conjugate addition to heteroatom[12] and highly stabilized carbanion nucleophiles.[13] However, conjugate addition of reactive carbanions with quinone monoketals has not been successful; dialkylcuprates have been observed to initiate reductive cleavage of benzoquinone monoketal rather than addition.[14] In the early stages of this work, we investigated the use of HMPA to promote 1,4-addition of more reactive nucleophiles,[15] as well as the addition of cuprates.

The use of HMPA, TMEDA, or Dabco in reaction of *n*-butyllithium with quinone monoketals **5**–**7** was not



(1) Visiting Scholar from Department of Chemistry, Florida International University, Miami, FL.

(2) Recipient of a National Research Service Award from the National Cancer Institute, NIH, for 1981–1982.

(3) (a) Omura, S.; Tanaka, H.; Koyama, Y.; Oiwa, R.; Katagiri, M. *J. Antibiot.* **1974**, *27*, 363–365. (b) Tanaka, H.; Koyama, K.; Marumo, H.; Oiwa, R.; Kagatiri, M.; Nagai, T.; Omura, S. *Ibid.* **1975**, *28*, 860–867. (c) Tanaka, H.; Murumo, H.; Nagai, T.; Okada, M.; Taniguchi, T.; Omura, S. *Ibid.* **1975**, *28*, 925–930.

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