Transition-Metal-Promoted Alkylations of Unsaturated Alcohols: The Selective Methylation of Homopropargyl Alcohols via Titanium Tetrachloride–Trimethylaluminum

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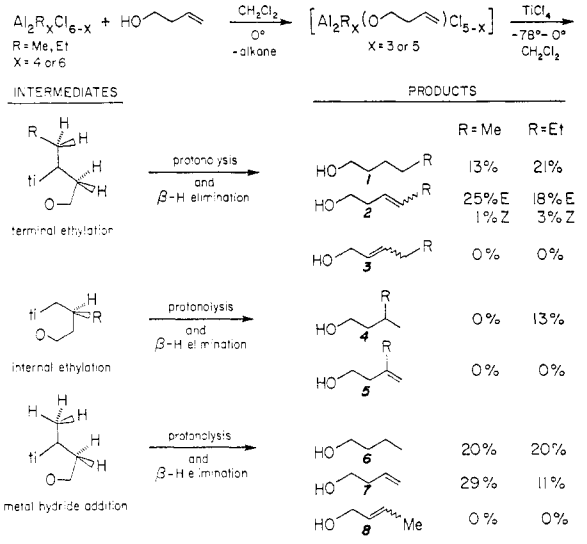
The reactions of homopropargyl alcohols with titanium tetrachloride–trimethylaluminum in methylene chloride under mild conditions selectively yield after hydrolysis alkenols of the type $HOCH(R)CH_2CH{=}C(R')CH_3$, R = H, Me, and Et and R′ = H, Me, Et, *n*-Pr, *i*-Pr, *n*-C_4H_9, *n*-C_5H_{11}, and Ph.

Ziegler–Natta polymerization catalysts are remarkably facile and repetitive carbometalating reagents toward alkene and alkyne functionalities. While Z–N reagents have been widely successful in the synthesis of stereoregular polyolefins since the 1950's, relatively little attention has been given to controlling their carbometalating properties in a manner that would extend their usefulness to non-macromolecular synthetic organic chemistry. As part of our continuing interest in synthetic applications of Z–N reagents,[1-4] we recently reported the reaction of 3-hexyn-1-ol with trimethylaluminum–titanium tetrachloride to give in good yield the single carbometalation derived product, (*Z*)-4-methyl-3-hexen-1-ol,[5] an alkenol used by Corey et al. in the synthesis of *d,l*-C_{18} *Cecropia* juvenile hormone[6] and by Baker et al. in the synthesis of the trial pheromone of the Pharaoh's ant.[7,8] In this paper we wish to report further studies on the selective methylation of homopropargyl alcohols with the titanium tetrachloride–trimethylaluminum reagent system.

Scheme I



Experimental Section

Materials. The alkynols were purchased from Farchan and used without further purification except for storage over 3-Å molecular sieves. Titanium tetrachloride and neat trimethylaluminum were obtained from Aldrich and the Ethyl Corp., respectively, and used without purification. Trimethylaluminum and titanium tetrachloride solutions were prepared in a nitrogen-filled Vacuum Atmospheres Dri-Lab. Methylene chloride was redistilled over P_2O_5 under nitrogen before use. All chemistry was performed under nitrogen or argon atmospheres by using syringe techniques to transfer reagents.

Procedure for Alkynol Methylations. In a typical reaction, 40 mmol of $Al(CH_3)_3$ was transferred by syringe into 75 mL of CH_2Cl_2 contained in a 250-mL three-necked round-bottom flask equipped with a gas inlet, rubber septa, and a magnetic stirring bar. Titanium tetrachloride (18 mmol) was transferred by syringe into 50 mL of CH_2Cl_2 contained in a 120-mL "pop-bottle", which was then fitted with an appropriate septum and crown capped. The above transfers were made in Vacuum Atmospheres Dri-Lab; subsequent chemistry was done at the bench under a nitrogen atmosphere.

The $Al(CH_3)_3$ solution was cooled to 0 °C and 18 mmol of the alkynol was added slowly by syringe through a septum. The liberated methane was vented through the gas inlet and safety bubbler attached to a nitrogen manifold. Both solutions were cooled to the appropriate temperatures by using slush baths. With use of a 16-gauge stainless steel needle, the $TiCl_4$ solution was transferred in ca. 1 min under nitrogen pressure into the stirred organoaluminum solution. The reaction mixture was stirred after $TiCl_4$ addition for the set time and then quenched via syringe addition of 10 mL of methanol precooled to 0 °C. An aqueous 3 N HCl solution saturated with NaCl (60 mL) was then added. The reaction mixture was allowed to warm to room temperature and stirred for 30 min.

The product alkenols were isolated by separation of the organic layer from the reaction mixture followed by extraction of the aqueous layer with diethyl ether. The organic layers were then combined, dried over $MgSO_4$, and filtered, and the solvents were removed under reduced pressure. The product alkenols can be isolated by preparative GLC or simple distillation. The products were characterized readily by NMR spectroscopy as presented in Results and Discussion.

Gas Chromatography. Yields were determined by GLC (HP 5711A FID-HP3380S integrator) via the internal standard technique with a 3.0 m × 0.32 cm 10% Carbowax 20M column; the yields are corrected for response factors. Samples were isolated for characterization by preparative GLC (HP 5750 TCD) by using a 3.0 m × 0.64 cm 20% Carbowax 20M column. Products were also checked for isomeric purity with a 25 m × 0.31 mm Carbowax 20M capillary column (HP 5793 FID).

Spectra. ^1H and ^{13}C NMR spectra were obtained with a Varian FT80A spectrometer. Carbon spectra for all reported compounds

(1) Thompson, D. W.; Munsey, W. R. C.; Harris, T. V. *Inorg. Chem.* **1973**, *12*, 2190.
(2) Thompson, D. W.; Harris, T. V. "Abstracts of Papers", 167th National Meeting of the American Chemical Society, Los Angeles, CA, 1974, American Chemical Society: Washington, D.C.; INOR-30.
(3) (a) Coleman, R. A.; O'Doherty, C. M.; Tweedy, H. E.; Harris, T. V.; Thompson, D. W. *J. Organometal. Chem.* **1976**, *107*, C15. (b) Tweedy, H. E.; Coleman, R. A.; Thompson, D. W. *J. Organometal. Chem.* **1977**, *129*, 69.
(4) (a) Smedley, L. C.; Tweedy, H. E.; Coleman, R. A.; Thompson, D. W. *J. Org. Chem.* **1977**, *42*, 4147. (b) Brown, D. A.; Nichols, S. A.; Coleman, R. A.; Thompson, D. W. *J. Org. Chem.* **1979**, *44*, 3457.
(5) Schiavelli, M. D.; Plunkett, J. J.; Thompson, D. W. *J. Org. Chem.* **1981**, *46*, 807.
(6) Corey, E. J.; Katzenellenbogen, J. A.; Gilman, N. W.; Roman, S. A.; Erikson, B. W. *J. Am. Chem. Soc.* **1968**, *90*, 5618.
(7) Baker, R.; Billington, D. C.; Ekanayake, N. *J. Chem. Soc., Chem. Commun.* **1981**, 1234.
(8) Marfat, A.; McGuirk, P. R.; Helquist, P. *J. Org. Chem.* **1979**, *44*, 3888 and references therein.

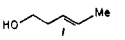
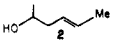
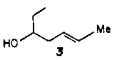
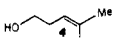
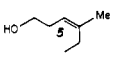
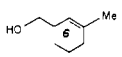
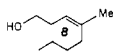
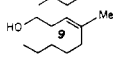
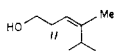
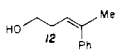
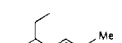
0022-3263/85/1950-2124$01.50/0

Table I. Methylation of 3-Butyn-1-ol with Titanium Tetrachloride-Trimethylaluminum[a]

reaction					
temp, °C	time, min	solvent	product	yield, %	3-butyn-1-ol recovered, %
−78	180	CH_2Cl_2	(*E*)-3-penten-1-ol	73	16
−45	180	CH_2Cl_2	(*E*)-3-penten-1-ol	37	10
−78	180	toluene	(*E*)-3-penten-1-ol	32	34
−45	180	toluene	(*E*)-3-penten-1-ol	47	11
−78	180	hexanes	(*E*)-3-penten-1-ol	24	16
−45	180	hexanes	(*E*)-3-penten-1-ol	9	6
−78	1	CH_2Cl_2	(*E*)-3-penten-1-ol	67	13
−45	1	CH_2Cl_2	(*E*)-3-penten-1-ol	72	7
−78 with added CH_3OH[b]	180	CH_2Cl_2	none	0	95

[a] All reactions were carried out with a stoichiometry of Ti:Al:ROH = 1.1:2.2:1.0. [b] Stoichiometry: Ti:Al:ROH:CH_3OH = 1.1:2.2:1.0:1.0.

Table II. Methylation of Homoproparylic Alcohols with Titanium Tetrachloride-Trimethylaluminum

	reaction				
alkynol	temp, °C	time, min	product	yield, %	starting material recovered, %
	*a*				
	−78	120		80	9
	−45	1		63	0
	−78	120		46	46
	−45	30		61	15
	−45	5		58	26
	−78	120		75	16
	−78	120		81	11
	−78	240		66	20
	−23	1		85	5
	−45	1		75	14
	−45	1		72	21
	−45	30		63	34
	−45	120		61	29
	−45	180		47	22
	−23	5		67	25
	−23	1		66	24
	−70	240		23	72
	−45	240		76	19
	−23	240		12	32
	−78	240		41	49
	−45	240		66	18

[a] See Table I.

were recorded both fully decoupled and with off-resonance decoupling to confirm assignments.

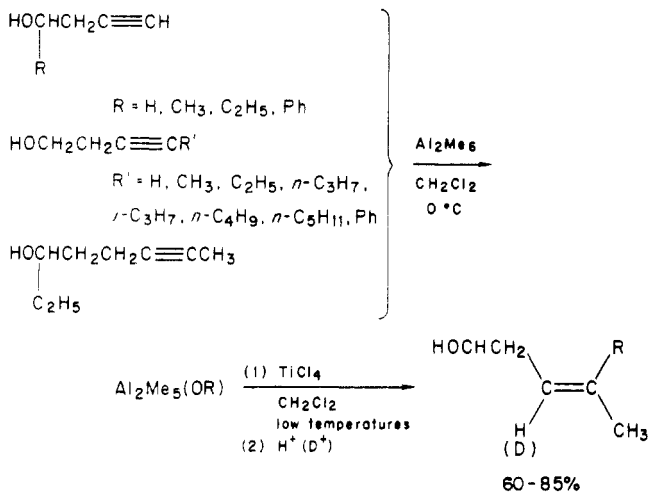
Results and Discussion

Our initial interest in the chemistry of Z–N catalyst systems was not centered in exploiting them for use in organic synthesis. Rather, we were committed to examining chemical systems which would serve as exemplars for single-growth and chain-termination steps in Z–N-catalyzed olefin polymerization. It was our hope that these model studies would lead to a fuller understanding of the catalyst chemistry. Toward this end we investigated the methyltitanation and ethyltitanation of the 3-buten-1-oxy group as a substrate probe in several typical catalyst systems such as $TiCl_4$–$Al_2Et_3Cl_2(OCH_2CH_2CH{=}CH_2)$ and $TiCl_4$–$Al_2Me_5(OCH_2CH_2CH{=}CH_2)$.[9,10] The results of these studies with the 3-buten-1-oxy ligand (see Scheme I) were of rather limited synthetic interest since in addition to the expected "hydroalkylated" end products (**1** and **4**), undesired side products were observed including olefinic alcohols (**2**) arising from β-hydride elimination after carbometalation and 1-butanol (**6**) arising from hydrometalation via in situ formation of metal hydride species (through presumably β-hydride elimination but possibly via α-elimination of titanium methyl groups[10]).

With the distinct lack of specificity in the alkylation of 3-buten-1-ol via $TiCl_4$-organoalane reagents, we did not expect that $TiCl_4$-promoted reactions of 3-butyn-1-ol and related substrates with organoaluminums would lead to selectively substituted olefinic alcohols. However, when the reaction of 3-butyn-1-ol with $TiCl_4$–$AlMe_3$ was eventually examined, we were pleasantly surprised to find a completely selective reaction giving good yields of the olefinic alcohol, (*E*)-3-penten-1-ol; subsequently, a variety of homopropargylic alcohols were selectively methylated to yield those homoallylic alcohols consistent with a syn-methyl metalation of the triple bond. The general reaction scheme and successfully methylated alkynols are shown in Scheme II. Yields and conditions of the methylation

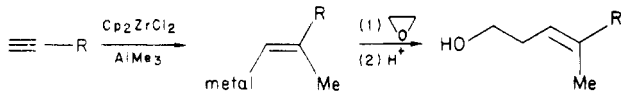
(9) Tweedy, H. E.; Hahn, P. E.; Smedley, L. C.; Youngblood, A. V.; Coleman, R. A.; Thompson, D. W. *J. Organometal. Chem.* **1978**, *146*, 221.
(10) Tebbe, F. N.; Parshall, G. W.; Reddy, G. S. *J. Am. Chem. Soc.* **1978**, *100*, 3611.

Scheme II

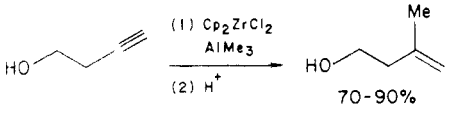


reactions are summarized in Tables I and II.

Since a wide variety of homopropargylic alcohols are readily available commercially and synthetically, our procedure is a straightforward route to the synthesis of (*Z*)-4-methyl-3-alken-1-ols (when R in Scheme I is other than H and CH_3). Within the group 4a-organoalane area, our efforts complement the work of Negishi and co-workers who have reported a Cp_2ZrCl_2–$AlMe_3$–alkyne route to (*E*)-4-methyl-3-alken-1-ols as shown:[11]

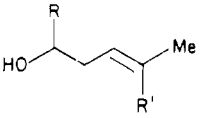


It has been also shown that the Cp_2ZrCl_2–$AlMe_3$–3-butyn-1-ol system leads to good yields of 3-methyl-3-buten-1-ol:[12]



Since 3-butyn-1-ol is the parent in the homopropargylic alcohol series, we chose to investigate its reaction with $TiCl_4$–$AlMe_3$ relative to the other alkynols under a greater variety of conditions. Results are summarized in Table I. Methylene chloride, toluene, and hexanes (and other saturated hydrocarbons) have been widely used in Z–N polymerization studies. Thus, we looked at the carbometalation of 3-butyn-1-ol in these three solvents under similar conditions. The best results were obtained in methylene chloride which gave at −78 °C a 73% yield (87% conversion) of the single product, (*E*)-3-penten-1-ol. While all of the reactions gave only (*E*)-3-penten-1-ol as the product, the yields and overall mass balance were distinctly lower in toluene and hexanes. As the temperature was increased from −78 to −45 °C for the 3 h reactions in the three solvents, the percentage of starting alkynol which could be accounted for as (*E*)-3-penten-1-ol and recovered starting material became less. While 3-butyn-1-ol is clearly being consumed significantly but without yielding a corresponding amount of monomethylated product, it is probable that some oligomerization is taking place. Since Z–N systems are remarkably facile carbometalating reagents, we thought that any further reaction (oligomerization) of monocarbometalated intermediates might be overcome by very short reaction times. Indeed, reactions of approximately 1 min in CH_2Cl_2 at −45 °C gave good yields of the singly methylated product and a much better mass balance. We further thought that the addition to Al_2Me_6 of an equimolar amount of a saturated alcohol with the 3-butyn-1-ol substrate might enhance the methylation; the results with methanol and 3-butyn-1-ol show complete inhibition of the methylation of the alkyne functionality. This observation is consistent with the fact that carbometalation of 3-butyn-1-ol with Al_2Me_6 in a 1 to 0.5 molar ratio gives essentially no alkenol product. Presumably formation of a stable dialkoxide-bridged $Al_2Me_4(OR)_2$ species inhibits carbometalation upon addition of $TiCl_4$.[13]

As seen from Table II a variety of terminal and internal homopropargylic alcohols can be selectively methylated to give alkenols of the type shown below. The only alkynol

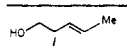
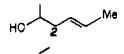
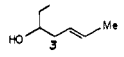
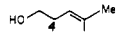
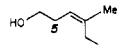
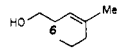
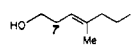
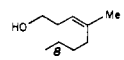
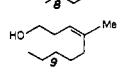
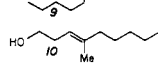
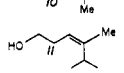
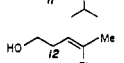
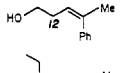


which did not lead to any isolable olefinic product was 1-phenyl-3-butyn-1-ol; the reason for this is unclear. In all cases the product alkenols are those consistent with a syn carbometalation; indeed, there are no documented examples of group 4a-organoalane systems adding to alkenes and alkynes giving anything but syn addition. The regioselective placement of the methyl group at the 4-carbon (relative to OH) is unaffected by substituents at either the 1- or 4-carbon atoms. It is interesting to observe that even alkynols with larger substituents at the 4-carbon such as isopropyl and *n*-pentyl give good yields with no loss of regioselectivity. Thus, these $TiCl_4$–$AlMe_3$–alkynol methylation reactions are highly regio- and stereoselective and rather insensitive to changes in alkyl substituents.

It seems certain that the oxygen atom of the alkynoxy group plays a crucial role in these successful monomethylation reactions. Simple alkynes such as 1-butyne are homopolymerized by Z–N catalysts,[14] and we have observed only 2% yields of monomethylated products from the reaction of the hydrocarbon 1-octyne with $TiCl_4$–$AlMe_3$; the 1-octyne is completely consumed forming significant quantities of dimers with some higher oligomeric species.[15] Likewise, Negishi and co-workers found significant dimer formation in the Cp_2TiCl_2–$AlMe_3$–1-octyne system.[16] We suggest that the methylation takes place via an intramolecular pathway as previously discussed.[1-5] In addition to the lack of oligomerization of the 3-butyn-1-oxy group, this intramolecular pathway is strongly supported by the lack of observation of β-hydride elimination products after carbometalation such as those observed to a large extent in the $TiCl_4$–$AlMe_3$–3-buten-1-ol system (Scheme I). In the cyclic intermediate (Scheme I) there are no β-hydrogen atoms which have orientations favorable for elimination. It has been observed that a trans metal–hydrogen arrangement is unfavorable for elimination[11] and that titanacyclic compounds do not eliminate endocyclic β-hydrogens readily.[18] Thus, the lack of formation

(11) Negishi, E.; Van Horn, D. E.; King, A. O.; Okukado, N. *Synthesis* **1979**, 501.
(12) Rand, C. L.; Van Horn, D. E.; Moore, M. W.; Negishi, E. *J. Org. Chem.* **1981**, *46*, 4093.
(13) Ashby, E. C.; Lacemnale, J.; Parris, G. E. *J. Organometal. Chem.* **1969**, *19*, P24.
(14) Boor, J. "Ziegler-Natta Catalysts and Polymerization", Academic Press: New York, 1979; pp 540–543.
(15) Maimon, J. D.; Thompson, D. W., unpublished results.
(16) Van Horn, D. E.; Valente, L. F.; Idacarage, M. J.; Negishi, E. *J. Organometal. Chem.* **1978**, *156*, C20.
(17) (a) Schwartz, J.; Hart, D. W.; McGiffert, B. *J. Am. Chem. Soc.* **1974**, *96*, 5613. (b) Schwartz, J.; Cannon, J. B. *Ibid.* **1974**, *96*, 2276.

Table III. Selected NMR Data for Homoallylic Alcohols Derived from Alkynol Methylations

	^{1}H NMR, δ olefinic CH_3	^{13}C NMR, δ olefinic CH_3	unsaturated carbons 3-C	unsaturated carbons 4-C
	1.68	18.0	127.4	128.3
	1.67	18.0	127.7	128.3
	1.66	17.8	127.2	128.9
	1.72	17.8 (trans H)	120.2	134.6
	1.64	25.8 (cis H)		
	1.70	23.0	120.0	140.1
	1.71	23.3	120.4	138.9
	1.60	16.0	119.9	138.8
	1.70	22.4-27.0	120.1	139.1
	1.70	22.6-27.8	120.1	139.3
	1.63	13.5	117.2	135.9
	1.64	18.0	118.9	144.3
	2.06	22.8	139.3	141.9
	1.73	17.8 (trans H)	120.1	134.9
	1.63	25.8 (cis H)		

of any 2,3-pentadien-1-ol via β-hydrogen elimination from the 2-carbon is quite consistent with a cyclic, chelated intermediate especially in light of the observation of Negishi et al. that the reaction of the hydrocarbon 5-decyne (no possibility of an intramolecular reaction) with Cp_2TiCl_2–$AlMe_3$ gave 92% of the β-hydrogen elimination product, 6-methyl-4,5-decadiene.[16]

We have also recently found that 5-yn-3-en-1-ols can be selectively methylated via $TiCl_4$–$AlMe_3$ to give (3*Z*)-4-methylalka-3,5-dien-1-ols in good yields.[19] Again, these reactions are selective giving products derived from syn carbometalation with the incoming methyl group exclusively at the 4-carbon.

For the disubstituted product alkenols (**1**–**3**) vinylic ^{1}H NMR resonances only in the δ 5.0–5.5 region establish the fact that the methyl group has added to the terminal carbon atom of the alkynol. The methyl resonances at ca. 18 ppm in the ^{13}C NMR spectra arise from the methyl group cis to a hydrogen.[20a] (NMR data are contained in Table III.)

As can be seen from Table III, the trisubstituted alkenols **5**, **6**, **8**, and **9** have olefinic methyl resonances centered about δ 1.70 (J_{H-CH} ~ 1–1.5 H) and thus have a cis H–CH_3 stereochemistry, i.e., (*Z*)-alkenols.[8,11] The ^{1}H NMR spectrum of 6-methyl-5-hepten-3-ol in the olefinic methyl and hydrogen regions is shown in Figure 1 and is a clear example of the shift and coupling differences between cis and trans H–CH_3 arrangements in trisubstituted olefins. That the incoming methyl group is at the 4-carbon in alkenols **5**, **6**, **8**, **9**, and **11** is unambiguously established through ^{13}C shift relationships as previously discussed.[5] The ^{13}C NMR methyl resonances in the δ 22–25 region are also consistent with the *Z* configurations.

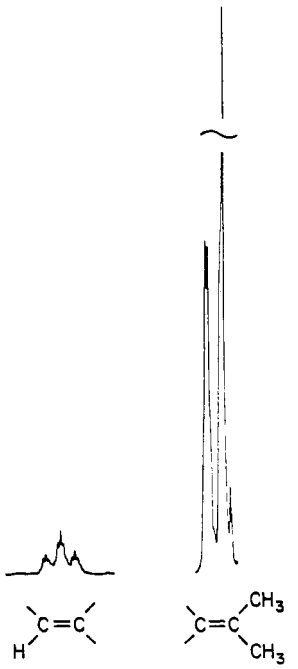


Figure 1. Selected regions of the ^{1}H NMR spectrum for 6-methyl-5-hepten-3-ol. (See Table III; —CH= center at 5.1 ppm.)

For product **11** with an isopropyl substituent at the 4-carbon, the ^{1}H NMR chemical shift of the lone olefinic proton is at δ 1.64. We feel that this is consistent with the expected *Z* configuration and simply reflects the inductive effect of a second α-methyl group; this effect is also seen in the upfield ^{13}C NMR shift of the 4-methyl group (δ 18.0).[20a] We cannot at this point characterize with certainty the structure of 4-phenyl-3-penten-1-ol; however, it seems reasonable to assume that it adopts the *Z* configuration as well.

To this point the group 4a-organoalanes do hold promise for the selective alkylation of homopropargylic alcohols yielding homoallylic alcohols. Since a wide variety of titanium and zirconium compounds function as components of Z–N catalysts, it is entirely reasonable that other systems may be uncovered to extend the range of utility. However, to this time it seems that the most generally useful carbometalation approach to the selective synthesis of homoallylic alcohols is that due to Helquist and coworkers who have refined the basic organocopper–alkyne carbometalation reaction into a versatile approach for *E* and *Z* alkenol synthesis.[8]

Acknowledgment. We thank the donors of the Petroleum Research Fund, administered by the American Chemical Society, for partial support of the work. We also thank the Jeffress Memorial Trust for research support, the Ethyl Corporation for gifts of organoalanes, and E. I. duPont de Nemours and Company and the National Science Foundation for funds with which to purchase gas chromatographs.

(18) (a) McDermott, J. X.; Whitesides, G. M. *J. Am. Chem. Soc.* **1974**, *96*, 947. (b) McDermott, J. X.; White, J. F.;; Whitesides, G. M. *Ibid.* **1973**, *95*, 4451. (c) Whitesides, G. M.; Gaasch, J. F.; Stedronsky, E. R. *Ibid.* **1972**, *94*, 5258.

(19) Zitzelberger, T. J.; Schiavelli, M. D.; Thompson, D. W. *J. Org. Chem.* **1983**, *48*, 4781.

(20) (a) Breitmaier, E.; Hass, G.; Voelter, W. "Atlas of Carbon-13 NMR data"; Heyden: London, 1979. (b) Couperus, P. A.; Clague, A. D. H.; van Dongen, J. P. C. M. *Org. Magn. Reson.* **1976**, *8*, 426. (c) DeHaan, J. W.; van de Ven, L. J. M. *Org. Magn. Reson.* **1973**, *5*, 147.

(21) (a) Trost, B. M. *Acc. Chem. Res.* **1970**, *3*, 120. (b) Faulkner, D. J. *Synthesis* **1971**, 175. (c) Bowlus, S. B.; Katzenellenbogen, J. A. *J. Org. Chem.* **1973**, *38*, 2733. (d) Reference 8.

Registry No. 1, 764-37-4; 2, 54560-70-2; 3, 64884-87-3; 4, 763-89-3; 5, 21019-60-3; 6, 13679-01-1; 7, 13679-00-0; 8, 96308-69-9; 9, 96308-70-2; 10, 75476-47-0; 11, 96308-71-3; 12, 20047-26-1; 13, 96206-33-6; $HO(CH_2)_2C{\equiv}CH$, 927-74-2; $HOCH(CH_3)CH_2C{\equiv}CH$, 2117-11-5; $HOCH(C_2H_5)CH_2C{\equiv}CH$, 19780-84-8; $HO(CH_2)_2C{\equiv}CCH_3$, 10229-10-4; $HO(CH_2)_2C{\equiv}CC_2H_5$, 1002-28-4; $HO(CH_2)_2C{\equiv}CC_3H_7$-*n*, 14916-79-1; $HO(CH_2)_2C{\equiv}CC_4H_9$-*n*, 14916-80-4; $HO(CH_2)_2C{\equiv}CC_5H_{11}$-*n*, 31333-13-8; $HO(CH_2)_2C{\equiv}CC_3H_7$-*i*, 96308-72-4; $HO(CH_2)_2C{\equiv}CPh$, 10229-11-5; $HOCH(C_2H_5)CH_2C{\equiv}CCH_3$, 19781-82-9.

Substituent Effects on Hydrogenation of Aromatic Rings: Hydrogenation vs. Hydrogenolysis in Cyclic Analogues of Benzyl Ethers

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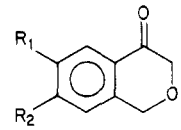
Carbalkoxy substituents are shown to retard the hydrogenation of aromatic rings over Rh/C catalyst. Hydrogenolysis predominates with acyclic (benzyloxy)acetates over this catalyst, but both hydrogenation and hydrogenolysis become sluggish with 2-isochroman-4-ones (1). However, phthalides may be cleanly hydrogenated in moderate to excellent yields without significant hydrogenolysis. Placing a benzyl ether in a ring system appears to greatly retard hydrogenolysis relative to the acyclic analogues.

As part of a plan to investigate heteroatom effects on conformational equilibria and on rate phenomena in 6- and 7-carbomethoxy-*trans*-2-heteradecalins,[1,2] we needed to prepare the 2-oxadecalin analogues. Utilization of the route previously developed[1] for the 1-oxadecalins would involve synthesis of the appropriately substituted 2-isochroman-4-ones (1) followed by reduction of the aromatic ring.



1a, $R_1 = R_2 = H$
b, $R_1 = CO_2Et$; $R_2 = H$
c, $R_1 = H$; $R_2 = CO_2Et$

Since the 2-isochromane system contains a benzyl ether function, reduction of the aromatic ring must compete effectively with hydrogenolysis of the benzyl ether C–O bond[3,4] in order for this synthesis to be feasible. Moreover, the presence of the electron-withdrawing ester groups in **1b** and **1c** might deactivate the ring toward hydrogenation,[4] thus favoring the hydrogenolysis. Increasing the amount of catalyst should increase the rate of hydrogenation, possibly overcoming the deactivating effect of the substituents.[3,4] Stocker[5] has reported the successful reductions of methyl benzyl ether and dibenzyl ether to their perhydro derivatives by using 5% Rh on charcoal at 3–4 atm of hydrogenation pressure, suggesting that this problem of hydrogenolysis may not be insurmountable.

Since literature preparations[6,7] of 2-isochroman-4-ones were somewhat lengthy, it was decided to first use simpler systems to investigate the extent to which ester substituents deactivate hydrogenation of an aromatic ring. The series of compounds **2–5** was selected because of their availability either commercially or as part of some other synthetic scheme. A methyl group and a second ester substituent were used to mimic the isochroman-4-one aromatic ring substitution pattern. Ethyl benzoate (**2**) is commercially available, while ethyl 2-methylbenzoate (**3**) was prepared in 90% yield from *o*-toluic acid. The route to diethyl 4-methylisophthalate (**4**) starts with 2,4-dichlorotoluene. The literature preparation[8] of 4-methylisophthalonitrile (**6**) presented problems until *N*-methylpyrrolidone was substituted[9] for pyridine as the solvent. Attempts to convert dinitrile **6** directly to diester **4** using 95% ethanol/concentrated H_2SO_4[10] or absolute ethanol/gaseous HCl[11] resulted in conversion only of the nitrile para to the methyl group, in line with Heppolette hypothesis[12] that the methyl groups would inhibit imido ester formation at the ortho position because the imido ester could not be coplanar with the ring as required for effective conjugation. A similar route from 2,5-dichlorotoluene produced diethyl 2-methylterephthalate (**5**).

Table I. Reduction of the Aromatic Ring of Alkyl Benzoates

no.	catalyst:substrate ratio[b]	time,[a,c] h	% yield
2	0.30	1	96
3	0.30	2.5	94
4	0.30	3	90
5	0.30	6	90

[a] Reduction carried out at room temperature. [b] 5% Rh on charcoal, purchased from Matthey Bishop Inc. (MBI). [c] Reaction stopped when calculated amount of H_2 was absorbed.

Hydrogenations of esters **2–5** were performed at room temperature over 5% Rh on charcoal. Reaction was

(1) Hirsch, J. A.; Schwartzkopf, G. *J. Org. Chem.* **1974**, *39*, 2040, 2044.
(2) Hirsch, J. A.; Kosley, R. W., Jr.; Morin, R. P.; Schwartzkopf, G.; Brown, R. D. *J. Heterocycl. Chem.* **1975**, *12*, 785.
(3) Augustine, R. L. "Catalytic Hydrogenation"; Marcel Dekker: New York, 1965.
(4) Hirsch, J. A.; Schwartzkopf, G. *J. Org. Chem.* **1973**, *38*, 3534.
(5) Stocker, J. H. *J. Org. Chem.* **1962**, *27*, 2288.
(6) Normant-Chefnay, C. *Bull. Soc. Chim. Fr.* **1971**, *4*, 1351.
(7) Thibault, J. *Ann. Chim.* **1971**, *6*, 263.
(8) Friedman, L.; Schechter, H. *J. Org. Chem.* **1961**, *26*, 2522.
(9) Newman, M. S.; Phillips, D. K. *J. Am. Chem. Soc.* **1959**, *81*, 3667.
(10) Pinner, A.; Klein, F. *Chem. Ber.* **1877**, *10*, 1889.
(11) Bose, A. K.; Greer, F.; Gots, J. S.; Price, C. C. *J. Org. Chem.* **1959**, *24*, 1309.
(12) Bayliss, S. N.; Heppolette, R. L.; Little, L. H.; Miller, J. *J. Am. Chem. Soc.* **1956**, *78*, 1978.

0022-3263/85/1950-2128$01.50/0