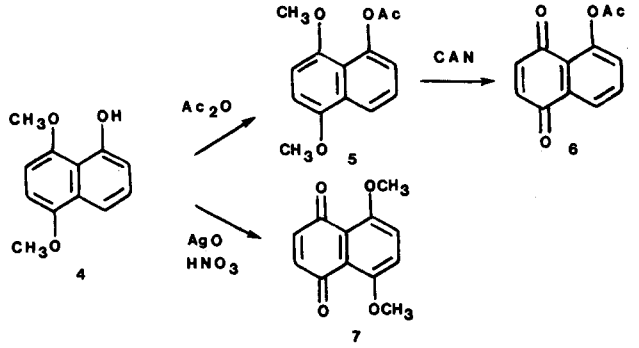
failure to detect this product from the cyclization attempt of the corresponding *N,N*-diethyl-*o*-crotylbenzamide suggests the operation of an even greater steric factor compared to that observed for the *o*-allyl analogue (entry 2). The *o*-allyl silane (entry 9), prepared in 72% yield by metalation–silylation of *N,N*-diethyl-*o*-allylbenzamide [(1) *sec*-BuLi/TMEDA/THF/−78 °C; (2) Me_3SiCl], was treated under the MeLi cyclization conditions described above to furnish the amide Peterson olefination product,[10] 1-(dimethylamino)naphthalene (entry 9).

Aside from its inherent value, the anionic cyclization also establishes a direct synthetic link between readily available benzamide derivatives and oxygenated naphthoquinones. Illustrative of this is the dual character of **4**, which by direct oxidation (AgO/HNO_3/acetone)[14] yields naphthoquinone **7**[15] in 31% yield and by initial conversion to its



acetate **5** (95%) followed by oxidation ($Ce(NH_4)_2(NO_3)_6$/MeCN–H_2O)[16] affords juglone acetate (**6**)[17] in 96% yield. These routes are highly competitive with previous synthetic methods devised for these valuable naphthoquinones.[18]

A tentative mechanistic rationalization (Scheme I) for the observed benzoannelation involves the initial formation of equilibrating anions whose energy minimum is best represented by the sickle-shaped species **8**.[19] Formation of naphthol **11** may occur via intermediate **12** by two pathways: (a) direct cyclization from the obligatory U-shaped anion **10** or (b) via the 2-vinylbenzocyclobutane carbinolamine alkoxide **9** followed by a [1,3]-sigmatropic rearrangement.[20,21] The formation of the 1-aminonaphthalene (entry 9) requires a cis alkoxide–Me_3Si relationship in **12**, R = Me_3Si to be consistent with the demonstrated stereochemical requirement for the Peterson olefination.[22] The rotational barrier between **8** and **10** (C_1–C_2 *E* to *Z* interconversion) appears to be prohibitive.[23] On the other hand, compelling evidence for the intermediacy of analogous 2-vinylbenzocyclobutanol alkoxide species in the reaction of benzyne with dienolates to form naphthalene derivatives has been provided by labeling and product analysis studies.[24] Complementary evidence for species **9** is currently being sought.

On the basis of these preliminary results, the anionic aromatic annelation process should be useful for regiospecific construction of naphthol and naphthoquinone derivatives. In addition, it may prove to be adaptable to the synthesis of naphthoquinone antibiotics.[25] Synthetic and mechanistic aspects of this reaction are under investigation.[26,27]

Registry No. **4**, 91963-30-3; **5**, 99618-32-3; **6**, 5196-28-1; **7**, 15013-16-8; *N,N*-diethyl-*o*-allylbenzamide, 88440-83-9; 6-methoxy-*N,N*-diethyl-2-allylbenzamide, 88440-84-0; 6-methoxy-*N,N*-dimethyl-2-allylbenzamide, 99618-27-6; 3-methoxy-*N,N*-diethyl-2-allylbenzamide, 88440-85-1; 4-methoxy-*N,N*-diethyl-2-allylbenzamide, 99618-28-7; 3,6-dimethoxy-*N,N*-diethyl-2-allylbenzamide, 88440-86-2; 4,6-dimethoxy-*N,N*-diethyl-2-allylbenzamide, 99618-29-8; *N,N*-dimethyl-*o*-crotylbenzamide, 99618-30-1; *N,N*-diethyl-o-(3-(trimethylsilyl)allyl)benzamide, 99618-31-2; 1-naphthol, 90-15-3; 8-methoxy-1-naphthol, 3588-75-8; 5-methoxy-1-naphthol, 3588-80-5; 6-methoxy-1-naphthol, 22604-07-5; 6,8-dimethoxy-1-naphthol, 51114-96-6; 2-methyl-1-naphthol, 7469-77-4; 1-(diethylamino)naphthalene, 84-95-7; *N,N*-dimethyl-*o*-bromobenzamide, 54616-47-6; crotyl bromide, 4784-77-4.

(14) Synder, C. D.; Rapoport, H. *J. Am. Chem. Soc.* **1972**, *94*, 227.
(15) Mp 152–155 °C (lit. mp 157 °C), cf.: Bruce, D. B.; Thomson, R. H. *J. Chem. Soc.* **1955**, 1089.
(16) (a) Hannan, R. L.; Barber, R. B., Rapoport, H. *J. Org. Chem.* **1979**, *44*, 2153. (b) Jacob, P., III; Callery, P. S.; Shulgin, A. T.; Castagnoli, N., Jr. *Ibid.* **1976**, *41*, 3627.
(17) Mp 150–151 °C (lit. mp 153–154 °C), cf.: Fieser, L. F.; Dunn, J. T. *J. Am. Chem. Soc.* **1937**, *59*, 1016.
(18) Muller, E., Ed. "Methoden der Organische Chemie (Houben-Weyl)"; Thieme Stuttgart, Vol. VII/3a, Part 1, pp 71, 78.
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(20) For alkoxy-accelerated [1,3]-sigmatropic shifts of 2-vinylcyclobutanols, see: Wilson, S. R.; Mao, D. T. *J. Chem. Soc., Chem. Commun.* **1978**, 479. Danheiser, R. L.; Martinez-Davila, C.; Sard, H. *Tetrahedron* **1981**, *37*, 3943. A concerted mechanism for the conversion of **9** into **12** may involve the trans or cis alkoxide–vinyl isomers of **9** by suprafacial-inversion and -retention pathways.
(21) For a potentially related thermal rearrangement of silyl cyanohydrins of vinylcyclobutanones, see: Byers, J. H.; Spencer, T. A. *Tetrahedron Lett.* **1985**, 713.
(22) Weber, W. P. "Silicon Reagents in Organic Synthesis"; Springer-Verlag: Berlin, 1983; p 58.
(23) The *Z* isomer of phenylallyllithium corresponding to **10** cannot be detected in THF solution at 5 °C.[19a] The carbamoyl substituent would be expected to increase the rotational barrier discouraging equilibration to **10**. However, coordination effects between the proximate carbamoyl and the allyllithium (σ- or π-bonded) groups and ultimate aromatization may constitute the overall driving force for the reaction.
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(26) All new compounds show analytical and spectral (IR, NMR, MS) data in full accord with the assigned structures.
(27) We are grateful to NSERC Canada and Merck Frosst for financial support of our synthetic programs. We are indebted to Professor John E. Baldwin for reference 20.

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Phase-Transfer-Catalyzed Conversion of Alkynes to Lactones Induced by Manganese Carbonyl Complexes

Summary: Alkynes react with methyl iodide, bromopentacarbonylmanganese (or dimanganese decacarbonyl), and carbon monoxide, under phase-transfer catalysis conditions, to give γ-butyrolactones; the reaction conditions are mild [35 °C (1 atm)], and the process is a regiospecific one.

Sir: Although much work has been done on the application of phase-transfer catalysis to organometallic chemistry,[2] little has involved the utilization of manganese complexes. The binuclear manganese complex $Mn_2(CO)_9Br^-$ is formed

(1) John Simon Guggenheim Fellow, 1985–1986.
(2) Alper, H. *Fundam. Res. Homogeneous Catal.* **1984**, *4*, 79; *Adv. Organomet. Chem.* **1981**, *19*, 183.

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Table I. Phase-Transfer-Catalyzed Reaction of Alkynes with CH_3I, CO, and Manganese Complexes

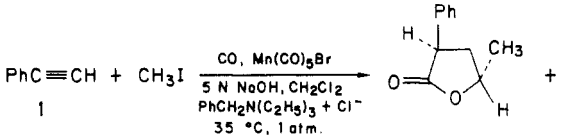
substrate	manganese complex	phase-transfer catalyst[a]	lactone,[b] (%)
PhC≡CH	$Mn(CO)_5Br$	A	4-methyl-2-phenyl-γ-butyrolactone (78)
	$Mn(CO)_5Br$		4-methyl-2-phenyl-γ-butyrolactone (17)
	$Mn(CO)_5Br$	B	4-methyl-2-phenyl-γ-butyrolactone (73)
	$Mn_2(CO)_{10}$	A	4-methyl-2-phenyl-γ-butyrolactone (65)
	$Mn_2(CO)_{10}$	B	4-methyl-2-phenyl-γ-butyrolactone (64)
$PhCH_2CH_2C{\equiv}CH$	$Mn(CO)_5Br$	A	4-methyl-2-(2-phenylethyl)-γ-butyrolactone (36)
n-$C_4H_9C{\equiv}CH$	$Mn(CO)_5Br$	A	4-methyl-2-n-butyl-γ-butyrolactone (35)
	$Mn(CO)_5Br$	B	4-methyl-2-n-butyl-γ-butyrolactone (42)
n-$C_6H_{13}C{\equiv}CH$	$Mn(CO)_5Br$	A	4-methyl-2-n-hexyl-γ-butyrolactone (44)
	$Mn_2(CO)_{10}$	A	4-methyl-2-n-hexyl-γ-butyrolactone (56)
p-$CH_3C_6H_4C{\equiv}CH$	$Mn(CO)_5Br$	A	4-methyl-2-p-tolyl-γ-butyrolactone (75)

[a] A = $PhCH_2N(C_2H_5)_3{}^+Cl^-$; B = PEG-400. [b] Products were identified on the basis of spectral (IR, NMR, MS) data, compared with authentic materials and/or the literature results.

by treatment of bromopentacarbonylmanganese with aqueous sodium hydroxide, methylene chloride, and a quaternary ammonium salt as the phase-transfer agent.[3,4] A novel perthiocarbonate complex was obtained on reaction of $Mn_2(CO)_9Br^-$ with sulfur.[5]

Carbonylation reactions are amongst the most useful phase-transfer-mediated process.[2] The reactions of unsaturated substrates (e.g., alkynes, dienes, allenes) with carbon monoxide, methyl iodide, and cobalt carbonyl are noteworthy in this context, with acylcobalt tetracarbonyl the probable key intermediate. It seemed conceivable to us that the use of bromopentacarbonylmanganese in phase-transfer-catalyzed carbonylation reactions of alkynes and methyl iodide might result in a novel route to heterocyclic systems. We now wish to report that manganese carbonyl complexes can indeed induce the regiospecific and stereoselective conversion of alkynes to saturated lactones (i.e., γ-butyrolactones) under very mild conditions.

When $Mn_2(CO)_9Br^-$ generated from bromopentacarbonylmanganese as previously described, was treated with methyl iodide, carbon monoxide, and then phenylacetylene (1), 2,4-disubstituted five-membered ring lactones were isolated in 78% yield, with 47% being *trans*-



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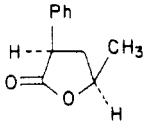

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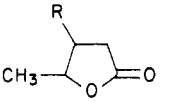
4-methyl-2-phenyl-γ-butyrolactone (2) and the cis isomer, 3, was obtained in 31% yield. The spectral data (infrared, nuclear magnetic resonance, mass)[6] of the products support the structural assignments for 2 and 3, and the results are in accord with published data for these compounds.[7]

An equimolar amount of alkyne and manganese complex was used in the reaction. Numerous products were formed when the reaction was repeated using a catalytic quantity of the complex. The lactones were produced in very low yield when nitrogen atmosphere was used instead of carbon monoxide, with two unidentified compounds as the major products. The conversion of the alkyne to 2 and 3 is an authentic phase-transfer process since, in the absence of the quaternary ammonium salt, only 17% of lactones were formed, the trans/cis ratio being 7.5/1.0. The stereoselectivity of the cyclocarbonylation reaction is also sensitive to the reaction time and to the phase-transfer agent. The above reactions were effected at 35 °C and 1 atm for 36 h. After 24 h the total lactone yield was 44% (32% trans; 12% cis). Recently, polyethylene glycols (PEG's) have become more widely used as phase-transfer catalysts.[8-10] When PEG-400 was employed as the phase-transfer agent, the yield of lactones (73%) was nearly as high as in the case of benzyltriethylammonium chloride, with the selectivity for the trans isomer (2) being greater for PEG (2/3, 59/14].

Phase-transfer-catalyzed reaction of a series of terminal alkynes with bromopentacarbonylmanganese, methyl iodide, and carbon monoxide affords lactones in reasonable yields (See Table I for data—yields were not optimized). It is noteworthy that this is a regiospecific process with none of the isomeric 3,4-disubstituted γ-butyrolactone 4 detected in any of these reactions. One can also use



4

dimanganese decacarbonyl [$Mn_2(CO)_{10}$] as the manganese reagent. For example, 4-methyl-2-phenyl-γ-butyrolactone was isolated in 65% yield when phenylacetylene was employed as the reactant with $Mn_2(CO)_{10}$.

The mechanism of the reaction is not known at present. By analogy with the generation of acylcobalt tetracarbonyl from the phase-transfer-catalyzed reaction of dicobalt octacarbonyl with methyl iodide and carbon monoxide, one can propose the formation of an acylmanganese complex from organomanganese precursors. However, the cobalt

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(4) Gibson, D. H.; Hsu, W.-L.; Ahmed, F. U. *J. Organomet. Chem.* **1981**, *215*, 379.

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(6) 2: IR ($CHCl_3$) ν_{CO} 1770 cm^{-1}; NMR ($CDCl_3$) δ 1.41 (d, 3 H, J = 6.0 Hz, CH_3), 2.30 (m, 1 H, $J_{2,3\beta}$ = 9.0 Hz, $J_{3\beta,4}$ = 6.8 Hz, $J_{3\alpha,3\beta}$ = 13.0 Hz, H-3β), 2.49 (m, 1 H, $J_{2,3\alpha}$ = 7.0 Hz, $J_{3\alpha,4}$ = 6.6 Hz, $J_{3\alpha,3\beta}$ = 13.0 Hz, H-3α), 3.88 (q, 1 H, $J_{2,3\alpha}$ = 7.0 Hz, $J_{2,3\beta}$ = 9.0 Hz, H-2), 4.72 (m, 1 H, $J_{3\alpha,4}$ = 6.6 Hz, $J_{3\beta,4}$ = 6.8 Hz), 7.25 (m, 5 H, Ph); MS, m/e 176 ([M]$^+$), 132 ([M − CO_2]$^+$). 3: IR ($CHCl_3$) ν_{CO} 1768 cm^{-1}; NMR ($CDCl_3$) δ 1.44 (d, 3 H, J = 6 Hz, CH_3), 1.96 (m, 1 H, $J_{2,3\beta}$ = 13.0 Hz, $J_{3\beta,4}$ = 10.8 Hz, $J_{3\alpha,3\beta}$ = 13.0 Hz, H-3β), 2.72 (m, 1 H, $J_{2,3\alpha}$ = 8.7 Hz, $J_{3\alpha,4}$ = 5.6 Hz, $J_{3\alpha,3\beta}$ = 13.0 Hz, H-3α), 3.83 (q, 1 H, $J_{2,3\alpha}$ = 8.7 Hz, $J_{2,3\beta}$ = 13.0 Hz, H-2), 4.56 (m, 1 H, $J_{3\alpha,4}$ = 5.6 Hz, $J_{3\beta,4}$ = 10.8 Hz, H-4), 7.24 (m, 5 H, Ph); MS, m/e 176 ([M]$^+$), 132 ([M − CO_2]$^+$). Various techniques including homonuclear correlation (2-D) were used to confirm the proton assignments in the NMR spectrum.

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and manganese acyl complexes, if formed, react differently with alkynes; i.e., hydroxy-substituted unsaturated lactones are obtained by using cobalt,[11] while saturated lactones lacking a hydroxyl substituent are formed with manganese carbonyl complexes.

The following general procedure was used: To 2.0 mmol of $Mn(CO)_5Br$ in CH_2Cl_2 (35 mL) was added 5 N NaOH (35 mL) containing benzyltriethylammonium chloride. The reaction mixture was stirred under nitrogen for 3 h at 35–40 °C. The gas was switched from nitrogen to carbon monoxide, a methylene chloride (2 mL) solution of methyl iodide (0.82 mL, 5.0 mmol) was added, and the mixture was stirred at room temperature for 15 min. The alkyne (2.0 mmol) in CH_2Cl_2 (2 mL) was added, and the solution was stirred at 35 °C for 36 h. The layers were separated, the aqueous phase was washed with ether (3 × 15 mL), neutralized to pH 7 with HCl, and then extracted with ether (3 × 20 mL), dried ($MgSO_4$), and concentrated. Pure lactone (confirmed by gas chromatography and analysis) was obtained by thin-layer chromatography (silica gel) using hexane–ether (3:1) as the developing solvent.

In conclusion, phase-transfer-catalyzed reaction of manganese carbonyl complexes with methyl iodide, carbon monoxide, and alkynes constitutes a simple and novel approach to the synthesis of γ-butyrolactones.

Acknowledgment. We are indebted to the Natural Sciences and Engineering Research Council of Canada for support of this research. Dr. S. C. Shim is thanked for carrying out several initial experiments.

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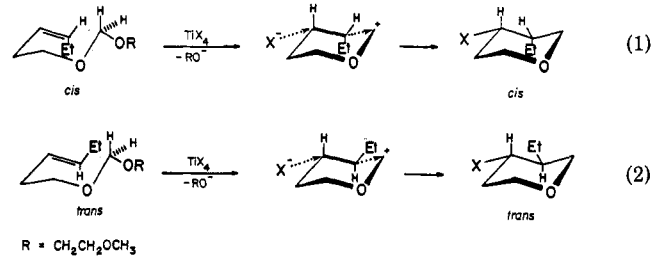
A Selective Synthesis of 3-Alkyl-4-halotetrahydropyrans via the Titanium Tetrahalide Promoted Cyclization of Unsaturated Acetals

Summary: A stereospecific, high-yield approach to the synthesis of *cis*- and *trans*-3-ethyl-4-chloro(bromo)tetrahydropyrans and *all-cis*- and *all-trans*-2-methyl-3-ethyl-4-chloro(bromo)tetrahydropyrans via the Lewis acid promoted carbon–carbon bond-forming cyclization of acetals derived from *cis*- and *trans*-3-hexen-1-ol is described.

Sir: In 1969 Stapp[1] reported the synthesis of six 4-halo-3-alkyltetrahydropyrans from the direct reaction of 1-alkenes, paraformaldehyde, and hydrogen halides. While the yields of the tetrahydropyrans were satisfactory, the stereoselectivity was limited with the author stating that "throughout this work 3-alkyl-4-halotetrahydropyrans are cis/trans isomer mixtures" (60–85% trans).[1] The isolation of 3-buten-1-ol from a reaction of propylene, paraformaldehyde, and hydrogen chloride suggested a pathway involving homoallylic alcohols. Indeed, earlier Hanschke[2a] and Colonge and Boisde[2b] had shown that the terminal homoallylic alcohols 3-buten-1-ol and 4-penten-2-ol react with simple aldehydes in the presence of hydrogen halide to give 4-halotetrahydropyrans in yields of 40–65%. No stereochemical characterization was reported.

With the increasing interest in tetrahydropyran nuclei within the natural products area, we wish to report a stereospecific, high-yield approach, related to the above-mentioned chemistry, to the synthesis of *cis*- and *trans*-3-alkyl-4-halotetrahydropyrans. Specifically, we describe the selective synthesis of *cis*- and *trans*-3-ethyl-4-chloro(bromo)tetrahydropyrans and *all-cis*- and *all-trans*-2-methyl-3-ethyl-4-chloro(bromo)tetrahydropyrans via the Lewis acid promoted carbon–carbon bond-forming cyclization of acetals derived from *cis*- and *trans*-3-hexen-1-ol.

The acetal cyclization reactions we examined are summarized in Table I. The MEM chloride and ethyl vinyl ether based acetals of *cis*- and *trans*-3-hexen-1-ol are readily prepared in high yield by well-established procedures.[3,4] These acetals are clearly similar to the α-halo ethers proposed by Stapp as intermediates in his hydropyran synthesis. The acetals are rapidly cyclized in the presence of titanium tetrachloride or tetrabromide under mild conditions, and the yields of tetrahydropyran products are excellent.[5] However, more striking is the excellent selectivity. The cis and trans MEM chloride acetals give predominately *cis*- and *trans*-3-ethyl-4-halotetrahydropyrans, respectively, with a ca. 9:1 selectivity ratio.[6] This cis to cis, trans to trans reaction pattern can be rationalized by a pathway involving trans addition of an oxocarbocation and X^- to the unsaturation as illustrated in eq 1 and 2.



(1)

(2)

R = $CH_2CH_2OCH_3$

Trans addition predominates in cationic polyene cyclizations reported by Johnson et al.[10] In view of stereochemical studies of product formation from conformationally locked 4-*tert*-butylcyclohexenyl cations, it does not appear that a free carbocation at the 4-carbon is involved since this should lead to substantial axial attack of the incoming halogen.[11]

The ethyl vinyl ether acetals cyclize with almost complete selectivity to one of four diastereomers. The *trans*-acetal gives *all-trans*-2-methyl-3-ethyl-4-halotetrahydropyrans while the *cis*-acetal gives *all-cis*-tetrahydropyran products.[12] The conformations of the all-trans products are clearly 2,3,4-equatorial. For the all-cis products, the predominant conformation must be equatorial methyl, axial ethyl, equatorial halogen since conformational energies are ca. 2.9 (2-Me), 1.4 (3-Et), and 0.3 kcal/mol (halogen). The all-trans and all-cis isomers are the products which one would expect on the basis of the observed preference for trans addition in tetrahydropyran formation seen above in the 3-ethyl-4-halo analogues and

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(4) Greene, T. W. "Protective Groups in Organic Synthesis"; Wiley-Interscience: New York, 1981; Chapter 2.
(5) For a typical cyclization reaction 15 mmol of an unsaturated acetal dissolved in ca. 100 mL of dry CH_2Cl_2 was treated with 20 mmol of $TiCl_4$ at −45 °C. The reaction mixture was stirred for 30 min after which 5 mL of CH_3OH followed by 35 mL of 3 N HCl saturated with NaCl was added. The products were extracted with diethyl ether and isolated for spectral analysis by preparative GLC.

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