Thallium in Organic Synthesis. 61. Intramolecular Capture of Radical Cations from Thallium(III) Trifluoroacetate Oxidation of Arylalkanoic Acids and Arylalkanols. New Routes to Oxygen Heterocycles[1-3]

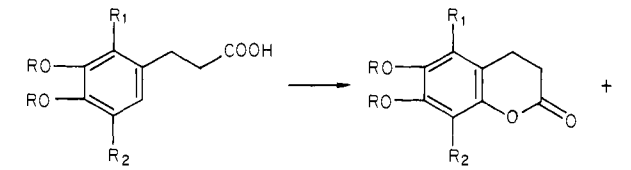
Edward C. Taylor,*,†,4 Juan G. Andrade,† Gerhardus J. H. Rall,† Ignatius J. Turchi,† Kosta Steliou,† G. Erik Jagdmann, Jr.,† and Alexander McKillop*,‡

Contribution from the Department of Chemistry, Princeton University, Princeton, New Jersey 08544, and the School of Chemical Sciences, University of East Anglia, Norwich NR4 7TJ, Norfolk, England. *Received February 4, 1981*

Abstract: Treatment of electron-rich arylpropionic acids with TTFA in TFA containing a small amount of BF_3·etherate results in the formation of dihydrocoumarins and spirocyclohexadienone lactones by initial formation of aromatic radical cations followed by intramolecular cyclization involving the side-chain carboxyl group. The scope and limitations of this reaction with respect to aromatic substitution and the length of the alkanoic acid side chain have been examined; the reaction has been extended with analogous results to 1-naphthalenylalkanoic acids. Oxidation of a series of homologous phenyl- and naphthalenyl-1-alkanols with TTFA under similar conditions results in intramolecular cyclization to give fused or pendant cyclic ethers. It is suggested that the observed propensity for intramolecular cyclization may be due to complexation of both the aryl group and the side-chain basic substituent (-COOH or -OH) with thallium(III).

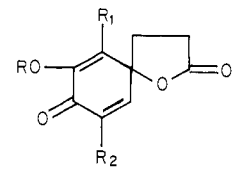
Thallium(III) trifluoroacetate (TTFA) has been shown to effect electrophilic thallation of a wide variety of aromatic substrates carrying a variety of substituent groups (moderately activating to moderately deactivating). The resulting arylthallium bis(trifluoroacetates) are exceptionally versatile intermediates for the regiospecific introduction of new substituents into the aromatic nucleus. Since the process of electrophilic thallation is reversible, it can in certain instances be carried out under conditions of thermodynamic rather than kinetic control; this leads to an unusual degree of orientation control in these aromatic substitution reactions.[5] With highly activated aromatic substrates, however, electrophilic thallation is not normally observed; instead, a 1-electron oxidation takes place to generate a radical cation whose subsequent fate is determined by the nature of the reaction medium and of the substrate itself. The ability of thallium(III) reagents to act as 1-electron oxidants of such highly activated aromatic substrates is now well documented[6-10] and has been exploited for the synthesis of biaryls,[11,12] including aporphine and homoaporphine alkaloids,[13,14] from nonphenolic precursors. These latter transformations represent capture (both inter- and intramolecular) of the initially generated aromatic radical cation by another aromatic compound acting as a nucleophile. We describe in the present paper the preparation of a variety of novel cyclization products arising from intramolecular capture of aromatic radical cations by suitably positioned side-chain carboxylic acids and alcohols.[15]

Since previous work had shown that 1,2-dimethoxybenzene undergoes aryl coupling rather than electrophilic thallation upon treatment with TTFA,[11] the substrate initially chosen for an examination of intramolecular capture of intermediate radical cations by side-chain carboxylic acid groups was 3-(3,4-dimethoxyphenyl)propionic acid (**1**). Reaction of this compound with 1 equiv of TTFA in trifluoroacetic acid (TFA) containing a small amount of BF_3·etherate[16] at -20 °C instantaneously produced a deep purple-green color, attributed to formation of a charge-transfer complex.[6] Oxidation was allowed to proceed for only a few seconds and was then stopped, with elimination of the deep color, by addition of *tert*-butyl alcohol.[17] Workup followed by chromatography on silica gel, using chloroform/methanol as eluent, gave methyl 3-(2-hydroxy-4,5-dimethoxyphenyl)propionate (**2**) in moderate yield (30%). Control experiments revealed that this compound was not a primary oxidation product, but was formed by acid-catalyzed ring opening by methanol of 6,7-dimethoxydihydrocoumarin (**3**). A second primary oxidation

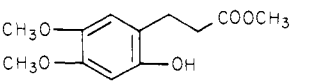


1, R = CH_3; R_1 = R_2 = H
5, R = C_2H_5; R_1 = R_2 = H
8, R = CH_3; R_1 = OCH_3; R_2 = H
10, R = $H_2C<$; R_1 = R_2 = H
12, R = CH_3; R_1 = H; R_2 = OCH_3

3, R = CH_3; R_1 = R_2 = H
6, R = C_2H_5; R_1 = R_2 = H
9, R = CH_3; R_1 = OCH_3; R_2 = H
11, R = $H_2C<$; R_1 = R_2 = H



4, R = CH_3; R_1 = R_2 = H
7, R = C_2H_5; R_1 = R_2 = H
13, R = CH_3; R_1 = H; R_2 = OCH_3



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(1) For the preceding paper in this series, see: Taylor, E. C.; Andrade, J. G.; Rall, G. J. H.; Steliou, K.; Jagdmann, G. E., Jr.; McKillop, A. *J. Org. Chem.* **1981**, *46*, 3078-3081.

(2) We are indebted for financial support of this work to the National Science Foundation (Grant Nos. CHE76 16506 and CHE 7918676 to Princeton University).

(3) Preliminary communication: Taylor, E. C.; Andrade, J. G.; Rall, G. J. H.; McKillop, A. *J. Org. Chem.* **1978**, *43*, 3632-3634.

(4) John Simon Guggenheim Memorial Fellow, 1979-1980.

(5) McKillop, A.; Taylor, E. C. *Chem. Br.* **1973**, *9*, 4-11.

(6) Elson, I. H.; Kochi, J. K. *J. Am. Chem. Soc.* **1973**, *95*, 5060-5062.

(7) Eloranta, J.; Sippula, A. *Finn. Chem. Lett.* **1975**, 170-173.

(8) Eloranta, J.; ljäs, M. *Finn. Chem. Lett.* **1975**, 174-178.

(9) Eloranta, J.; Kolehmainen, S. *Finn. Chem. Lett.* **1977**, 10-12.

(10) Sullivan, P. D.; Menger, E. M.; Reddoch, A. H.; Paskovich, D. H. *J. Phys. Chem.* **1978**, *82*, 1158-1160.

(11) McKillop, A.; Turrell, A. G.; Taylor, E. C. *J. Org. Chem.* **1977**, *42*, 764-765.

†Princeton University.
‡University of East Anglia.

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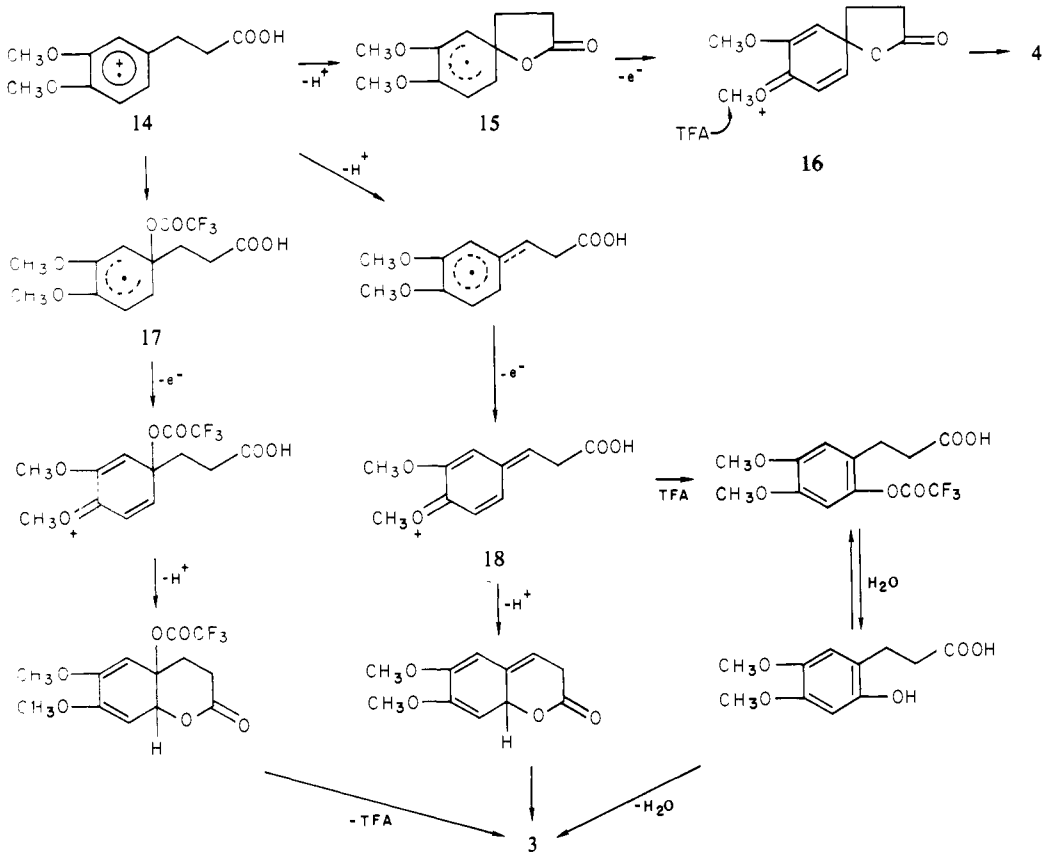
Scheme 1



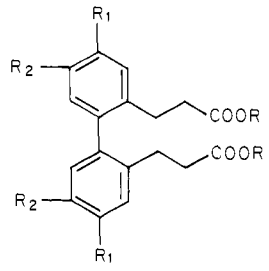
product isolated from this chromatography proved to be the spirocyclohexadienone lactone **4**. The ratio of **3**:**4** was 2:1 in a 57% combined yield. Addition of methanol rather than *tert*-butyl alcohol to the reaction mixture led directly to the methyl ester **2**, although in lower yield (20%). In analogous fashion, TTFA oxidation of 3-(3,4-diethoxyphenyl)propionic acid (**5**) gave the dihydrocoumarin **6** and the spirocyclohexadienone lactone **7** (ratio of 1:10).

Likewise, 3-(2,3,4-trimethoxyphenyl)propionic acid (**8**) was smoothly converted to 5,6,7-trimethoxydihydrocoumarin (**9**) (53%), and 3-(3,4-(methylenedioxy)phenyl)propionic acid (**10**) underwent oxidative cyclization to give the dihydrocoumarin (**11**) (21%). By contrast, however, the only product isolated from the oxidation of 3-(3,4,5-trimethoxyphenyl)propionic acid (**12**) was the spirocyclohexadienone lactone **13**. The failure to observe dihydrocoumarin formation in this instance is presumably a reflection both of steric hindrance to ortho substitution and facile demethylation of the doubly flanked methoxy group; selective demethylation of the 2-methoxy group of 1,2,3-trimethoxyarenes has been observed previously both by acid[18,19] and by TTFA.[20]

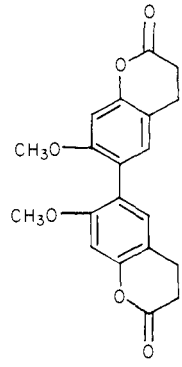
We suggest that these TTFA-mediated transformations occur by an initial 1-electron oxidation to a radical cation (e.g., **14**). Intramolecular capture of this radical cation by the side-chain carboxyl group to give **15**, a further 1-electron oxidation to the oxonium ion **16**, and demethylation by solvent (TFA) then leads to the spirocyclohexadienone lactone (e.g., **4**). We believe that the observed dihydrocoumarins arise by a competitive pathway involving intermolecular capture of the radical cation **14** by solvent (TFA). Oxidation of the resulting radical (**17**), intramolecular Michael addition by the carboxylic acid group, and aromatization then gives the dihydrocoumarin **3**. Alternatively, deprotonation of **14** could be followed by 1-electron oxidation to **18**, which could undergo intramolecular (or intermolecular) Michael addition ultimately to give **3**. Although we have made no effort to distinguish between these alternative pathways, we are convinced that the oxonium intermediate **16**, the penultimate precursor of **4**, is *not* a precursor of the dihydrocoumarin **3**. Thus, reaction of **4** with trimethyloxonium tetrafluoroborate was exceedingly slow; conversion to **3** (by O-methylation to **16**, followed by dienone–phenol rearrangement) was still incomplete after 20 min. By contrast, formation of **3** from **1** was instantaneous at 0 °C. In addition, the intermediacy of a spirocyclohexadienone lactone derivative analogous to **16** in the conversion of **8** to **9** is also ruled out, since the product of ring expansion (carbon, not oxygen, migration has been shown to take place in such systems)[21] would have been the isomeric 6,7,8-trimethoxydihydrocoumarin, no trace of which was found in the reaction mixture.

It is striking that electrochemical generation of the radical cation **14** leads only to the biaryl **19**.[22] It is not known at this time

(12) McKillop, A.; Turrell, A. G.; Young, D. W.; Taylor, E. C. *J. Am. Chem. Soc.*, **1980**, *102*, 6504–6512.
(13) Taylor, E. C.; Andrade, J. G.; McKillop, A. *J. Chem. Soc., Chem. Commun.* **1977**, 538–539.
(14) Taylor, E. C.; Andrade, J. G.; Rall, G. J. H.; McKillop, A. *J. Am. Chem. Soc.*, **1980**, *102*, 6513–6519.
(15) The synthetic potential of nucleophilic aromatic substitution via radical cation intermediates is a topic of significant current interest, see: Kurz, M. E.; Hage, G. W. *J. Org. Chem.* **1977**, *42*, 4080–4084 and references cited therein.
(16) Yields in this and subsequent TTFA-mediated oxidative cyclizations were routinely enhanced by addition of small amounts of BF_3·Et_2O, presumably as a result of promotion of the formation of charge-transfer complexes between the electrophilic Tl(III) reagent and the electron-rich aromatic ring (see ref 6), as well as by a lowering of the reduction potential of the Tl(III) reagent through the reaction $Tl(OCOCF_3)_3 + BF_3 \rightarrow [Tl(OCOCF_3)_2]^+ + (BF_3{\cdot}OCOCF_3)^-$.
(17) The role of *tert*-butyl alcohol in halting further oxidation by residual TTFA is probably due both to its Lewis basic properties and to conversion of TTFA into the much weaker oxidizing agent $(t\text{-BuO})Tl(OCOCF_3)_2$ [analogous to the well-known conversion of $Tl(OCOCH_3)_3$ to $CH_3OTl(OCOCH_3)_2$ with methanol: Criegee, R.; Kraft, L.; Rank, B. *Justus Liebigs Ann. Chem.* **1933**, *507*, 159–197].
(18) Brossi, A.; Van Burik, J.; Teitel, S. *Helv. Chim. Acta* **1968**, *51*, 1965–1979.
(19) Brossi, A.; Teitel, S. *Org. Prep. Proced.* **1969**, *1*, 171–172.
(20) Kende, A. S.; Rutledge, P. S. *Synth. Commun.* **1978**, *8*, 245–250.
(21) Davies, J. S.; Hassall, C. H.; Schofield, J. A. *J. Chem. Soc.* **1964**, 3126–3132.



19, R = H; $R_1 = R_2 = OCH_3$
21, R = R_2 = H; $R_1 = OCH_3$
25, R = CH_3; $R_1 = R_2 = OCH_3$



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whether these disparate results are due to the influence of the electrode in favoring biaryl formation, or to complexation of the aryl group *and* the carboxylic acid substituent by thallium(III), thus favoring intramolecular capture of the radical cation. The latter possibility suggests that thallium(III), in addition to serving as a 1-electron oxidant, may play a unique role in promoting intramolecular reactions. Experiments are in progress to clarify this intriguing point.

Further evidence in support of the above reaction mechanism for the conversion of **1** to **3** and **4**, and for the other TTFA-mediated intramolecular radical cation capture reactions cited above, comes from the following observations.

(1) Oxidation of 3-(3-methoxyphenyl)propionic acid (**20**) with TTFA gave only the biaryl **21** (56%). The absence of an alkoxy group para to the propionic acid side chain clearly prevents intramolecular capture, which would have led to products analogous to **3** and/or **4** (see Scheme I).

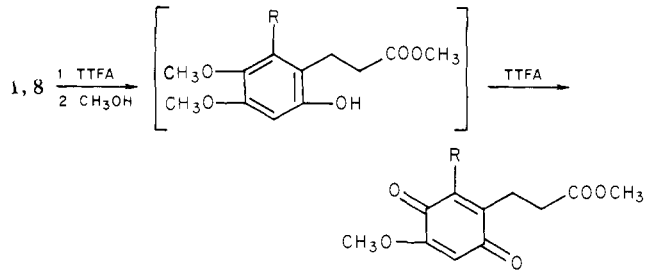
(2) TTFA oxidation of 3-(4-methoxyphenyl)propionic acid (**22**) again gave only one product in 36% yield, which is the result of both dihydrocoumarin formation and biaryl coupling (**23**). Here the inter- and intramolecular capture pathways appear to be competitive.

(3) Oxidation of the methyl ester of **1** (**24**) gave only the biaryl **25**. Intramolecular capture of the radical cation is clearly not possible in this instance, and biaryl formation becomes the exclusive reaction pathway.

3-(4-Acetoxyphenyl)propionic acid (**26a**) failed to react with TTFA under the above reaction conditions, undoubtedly as a result of its higher oxidation potential. By contrast, 3-(4-acetoxy-3-methoxyphenyl)propionic acid (**26b**) gave the spirocyclohexadienone lactone **4** in 40% yield as the only isolable reaction product. Only tar formation was observed upon treatment of 3-(3,4-dimethylphenyl)propionic acid (**27**) with TTFA, an unsurprising result in view of the many alternate pathways open to the intermediate radical cation.

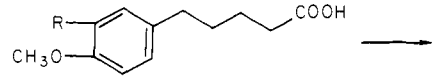
Since we have previously shown that 4-alkoxyphenols are smoothly oxidized to *p*-benzoquinones with TTFA,[23] it appeared that oxidation of 3-(3,4-dialkoxyphenyl)propionic acids, followed by addition of methanol, should result in direct formation of highly substituted *p*-benzoquinones provided that 2 equiv of TTFA were employed. These expectations were fully confirmed. Thus, treatment of **1** and **8** with 2 equiv of TTFA, followed by quenching of the reaction mixture with methanol, gave the *p*-benzoquinones **28** and **29** (31% and 40%, respectively).

The effect of lengthening the carbon chain separating the aromatic radical cation and the nucleophilic carboxylic acid substituent was then examined. No products were isolated from the reaction of 4-(4-methoxyphenyl)butyric acid or 4-(3,4-dimethoxyphenyl)butyric acid with TTFA, but the corresponding 5-arylvaleric acids **30** and **32** were converted in low yield into the δ lactones **31** and **33**, respectively. Base extraction of the latter

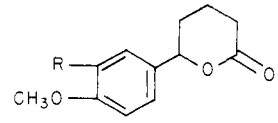


28, R = H
29, R = OCH_3

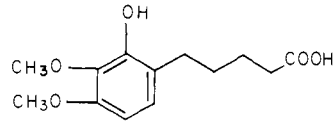
reaction mixture led to the isolation of substantial quantities (29.5%) of 5-(2-hydroxy-3,4-dimethoxyphenyl)valeric acid (**34**). Although this compound might have arisen by hydrolysis of an intermediate lactone, this seems improbable on mechanistic considerations (see Scheme I), and more likely is the result of capture of the intermediate radical cation by trifluoroacetic acid, followed by hydrolysis to the phenol during workup.



30, R = H
32, R = OCH_3



31, R = H
33, R = OCH_3



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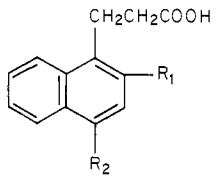
We then examined a series of naphthalenylalkanoic acids to see whether the above reactions observed with monocyclic substrates were capable of extension. Indeed, oxidation of 3-(4-methoxy-1-naphthalenyl)propionic acid (**35**) with TTFA under the above conditions (reaction time of a few seconds at −20 °C, followed by addition of *tert*-butyl alcohol) gave the benzo-fused cyclohexadienone lactone **36** in excellent yield (74%), presumably by the reaction pathway outlined in Scheme II. The same compound was obtained in considerably lower yield (36%) by oxidation of 3-(1-naphthalenyl)propionic acid (**38**) with 2 equiv of TTFA; the carbonyl oxygen in **36** presumably arises in this latter transformation from the TFA solvent. Treatment of **36** with acetic anhydride/sulfuric acid[21] gave 3-(2,4-diacetoxy-1-naphthalenyl)propionic acid (**37**) in 55% yield; the overall transformation from **35** thus represents a novel and potentially useful procedure for introduction of the elusive 1,3-dihydroxy functionality into the naphthalene nucleus.[24]

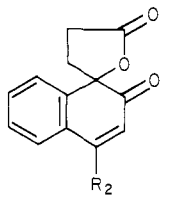
In analogous overall oxidations, 3-(2-methoxy-1-naphthalenyl)propionic acid (**39**) was converted to the lactone **40**,[25] and **41** was oxidized to **42**. In the latter transformation the ketone oxygen in the aromatic ring must arise, as in the conversion of **38** to **36**, by reaction of an intermediate radical cation or allyl carbenium ion with the trifluoroacetic acid solvent, followed by further oxidation.

These transformations were paralleled precisely with the homologous 4-(1-naphthalenyl)butyric acids **43** and **45**, which were

(22) Sainsbury, M.; Wyatt, J. *J. Chem. Soc., Perkin Trans. 1* **1979**, 108–114.
(23) McKillop, A.; Swann, B. P.; Taylor, E. C. *Tetrahedron* **1970**, *26*, 4031–4039.
(24) For previous methods of preparation of compounds of this type, see: (a) Soliman, G.; West, R. W. *J. Chem. Soc.* **1944**, 53–55. (b) Meyer, K.; Bloch, H. S. *Org. Synth. Collect.* **1955**, *3*, 637–641. (c) Iskander, G. M.; Sarrag, S. A.; Stansfield, F. *J. Chem. Soc. C* **1970**, 1701–1703. (d) Sammes, P. G.; Wallace, T. W. *J. Chem. Soc., Perkin Trans. 1* **1975**, 1377–1380. (e) Heck, R.; Winstein, S. *J. Am. Chem. Soc.* **1957**, 3105–3113, 3114–3118. (f) Loozen, H. J. J. *J. Org. Chem.* **1975**, *40*, 520–521.
(25) Berney, D.; Schuh, K. *Helv. Chim. Acta* **1980**, *61*, 918–923.

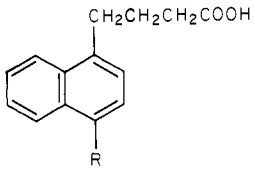


39, $R_1 = OCH_3$; $R_2 = H$
41, $R_1 = H$, $R_2 = CH_3$

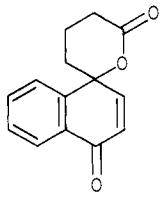


40, $R_2 = H$
42, $R_2 = CH_3$

converted with TTFA under the above reaction conditions to the spirolactones **44** (35%) and **46** (16.5%), respectively. However,



43, R = OCH_3
45, R = CH_3



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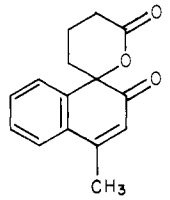

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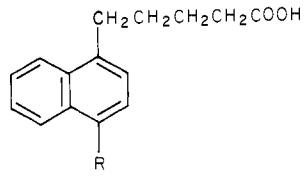
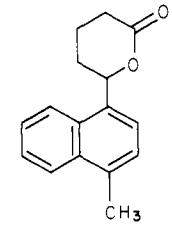
the next higher homologue, 5-(4-methyl-1-naphthalenyl)valeric acid (**47a**), underwent cyclization at the benzylic position to give the δ lactone **48** (53%). In this case, steric restrictions apparently inhibit formation of a spirolactone analogous to **42** or **46**, and the initially formed radical cation must undergo deprotonation and further 1-electron oxidation to a benzylic carbenium ion which then gives the observed δ-lactone by intramolecular capture. These results are thus analogous to the reported conversion of 4-phenylbutyric acid with various cobalt(III) salts to 4-phenyl-4-hydroxybutyric acid δ lactone, the formation of which has also been postulated to involve a 1-electron oxidation to give an aromatic radical cation, proton loss to the benzylic radical, further 1-electron oxidation to the benzyl carbenium ion, and intramolecular cyclization.[26,27]

The corresponding homologue of **43**, namely 5-(4-methoxy-1-naphthalenyl)valeric acid (**47b**), did not yield the expected δ lactone upon oxidation with TTFA. Instead, the product mixture contained a large amount of uncharacterizable tarry material together with a small amount of 1,4-naphthoquinone (9%). It is likely that the oxidation potential of **47b** is too low for the reagent and the reaction conditions employed; no suitable means was found to overcome this problem. Lower reaction temperatures (below −20 °C) could not be employed because of the insolubility of TTFA in the reaction medium, and available weaker Tl(III) oxidants were unreactive.



47a, R = CH_3
b, R = OCH_3



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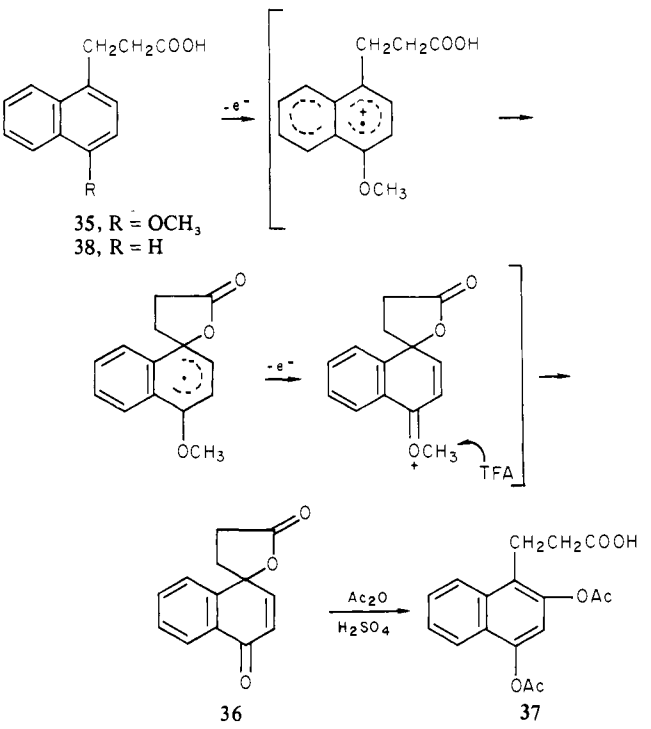
Reduction of esters of the above arylalkanoic acids with lithium aluminum hydride gave the corresponding alcohols which were subjected to TTFA oxidation. Particular attention is drawn (see Tables I and II) to the fused oxepins **54**, **65**, and **68** and the fused oxocin **58**, whose formation, albeit in low yield, may once again be a reflection of chelation involving the aromatic ring, the basic side chain, and thallium(III), with the consequence that the nucleophile (the terminal −OH group) and the electrophile (the aromatic radical cation) are held in close proximity. It would be interesting to know whether these products of intramolecular cyclization can be formed from radical cations generated electrochemically, and attempts to clarify this question are currently in progress.

The effect of an additional methoxy group can be seen in comparing the conversions **51** → **52**[28] with **53** → **54** and **55** → **56** with **57** → **58**. In both series, a single para-situated methoxy group directs intramolecular cyclization to the benzylic carbon atom, whereas the presence of the additional methoxyl group directs intramolecular cyclization to the aromatic ring (i.e., to a position para to the additional methoxy group). Oxidative cyclization of the naphthalenyl alcohols **59**, **61**, **63**, and **66** failed to give any trace of spiroethers corresponding to the spirolactones formed from the corresponding carboxylic acids. The reason for this divergence in reaction pathways is not clear.

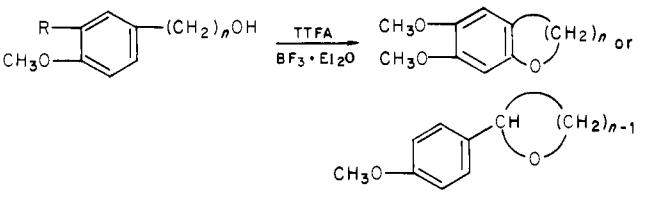
Scheme II



35, R = OCH_3
38, R = H

36 37

Table I. Oxidative Cyclization of *p*-Methoxyphenylalkanols with TTFA

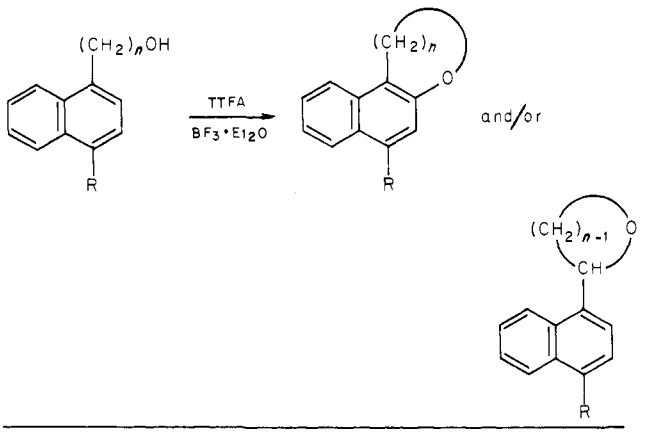


starting material			product (yield, %)	
compd	R	*n*		
49	CH_3O	3	50 (21)	
51	H	4		52 (5)
53	CH_3O	4	54 (13.5)	
55	H	5		56 (7)
57	CH_3O	5	58 (11)	

(26) Dessau, R. M.; Heiba, E. I. *J. Org. Chem.* **1975**, *40*, 3647–3649.
(27) Giordana, C.; Belli, A.; Citterio, A. *J. Org. Chem.* **1980**, *45*, 345–346.

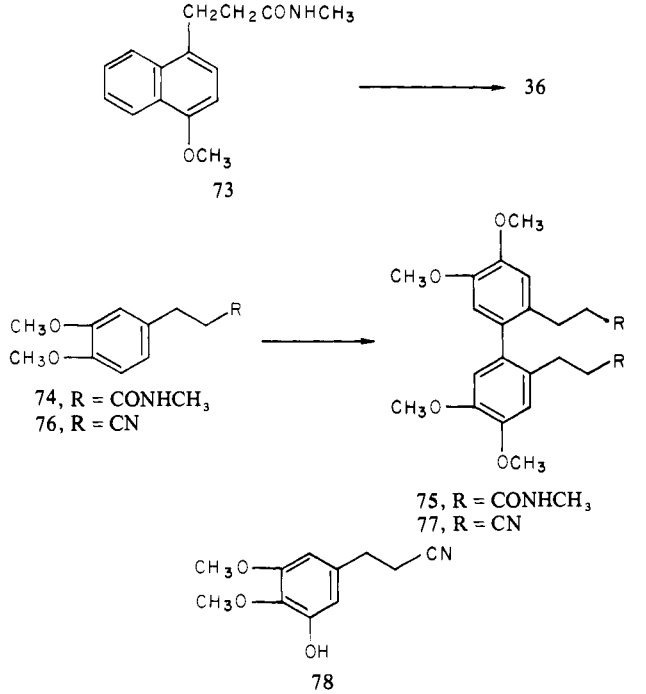
(28) Oxidation of 4-phenyl-1-butanol with ceric ammonium nitrate gives 2-phenyltetrahydrofuran (analogous to the conversion of **51** to **52**), but the postulated mechanism involves a 1,5-hydrogen transfer from an initially formed alkoxy radical, electron transfer to give a benzylic carbenium ion, and intramolecular cyclization: Doyle, M. P.; Zuidema, L. J.; Bade, T. R. *J. Org. Chem.* **1975**, *40*, 1454–1456.

Table II. Oxidative Cyclization of Naphthalenylalkanols with TTFA



starting material				
compd	R	n	product (yield, %)	
59	CH_3O	3	60 (29.5)	
61	CH_3	3	62 (19)	
63	CH_3O	4	65 (2.2)	64 (23)
66	CH_3	4	68 (4.6)	67 (17.5)
69	CH_3O	5		70 (28)
71	CH_3	5		72 (38)

Our initial efforts to involve other types of nucleophilic side chains in these intramolecular radical cation cyclizations have been unsuccessful. Reaction of the *N*-methylamide of 3-(4-methoxynaphthalenyl)propionic acid (**73**) with TTFA gave **36**, with oxygen rather than nitrogen participating as the nucleophile in the intramolecular cyclization. This reaction, which was not entirely unexpected, is thus directly analogous to the cyclization observed with the parent carboxylic acid itself. Only a small amount of the biaryl coupling product **75** was isolated from the reaction of the *N*-methylamide **74** with TTFA, while oxidation of the corresponding nitrile **76** gave a mixture of the biaryl **77** and the phenol **78**. The latter product is particularly interesting in that it must be formed via competitive capture of the intermediate radical cation by solvent. No trace of Ritter-type cyclization products could be found.



Despite the failure of other functional groups to undergo TTFA-induced cyclizations, the above results do demonstrate that aromatic radical cations can be trapped intramolecularly by suitably situated carboxyl or alcohol groups. Furthermore, a substantial degree of control is possible over the nature of the products obtained by variations in substrate structure, the amount of oxidant employed, and the actual isolation procedure. Our current efforts include TTFA oxidation of aromatic substrates carrying other nucleophilic side chains potentially capable of intramolecular cyclization with the intermediate radical cations, and a comparison of the radical cations generated electrochemically with those generated by thallium(III) in an attempt to elucidate the role of thallium in promoting intra- in contrast to intermolecular cyclization.

Experimental Section

General Procedure for TTFA Oxidative Cyclizations. Thallium(III) trifluoroacetate (TTFA, 1.1 equiv, 0.60 g/mmol of substrate) is dissolved in trifluoroacetic acid (TFA, 4–5 mL/mmol of substrate) and the solution diluted with methylene chloride (16–20 mL/mmol of substrate). BF_3·Et_2O (0.5 mL/mmol) is added, and the mixture is adjusted to −20 °C, under a stream of nitrogen, by means of a dry ice/carbon tetrachloride bath. A solution of the appropriate substrate (arylalkanoic acid or arylalkanol) in a minimum volume of methylene chloride and a little TFA, if needed for solubility, is added at once to the cooled and vigorously stirred mixture. After the specified period of time (see under the individual preparations listed below), the reaction mixture is rapidly quenched with *tert*-butyl alcohol (10 mL/mmol) and allowed to come to room temperature. The mixture is then washed with water (4 × 25 mL/mmol) followed by saturated aqueous base (25 mL/mmol of sodium carbonate with naphthalenylalkanoic acids; otherwise sodium bicarbonate). When arylalkanoic acids are used as substrates, unreacted starting material may often be recovered by acidification of these basic extracts; otherwise, they are discarded. The remaining organic solvent layer is dried over anhydrous Na_2SO_4 and evaporated and the residue chromatographed (silica gel, preparative TLC or column), or in some cases filtered and the product recrystallized. All reported products are isolated pure, as determined both by NMR and by TLC, unless otherwise noted.

6,7-Dimethoxy-3,4-dihydrocoumarin (3). 3-(3,4-Dimethoxyphenyl)-propionic acid was oxidized by the general procedure: 1 mmol scale, 5–10 s reaction time. The crude reaction product was separated by preparative TLC (5% acetone/chloroform): R_f 0.75; yield, 38%; mp (benzene/pentane) 84–86 °C; IR ($CHCl_3$) 1760 cm^{-1}; NMR ($CDCl_3$) δ 6.67 (s, 1 H), 6.62 (s, 1 H), 3.80 (s, 6 H), 2.65–3.05 (m, 4 H).

Anal. Calcd for $C_{11}H_{12}O_4$: C, 63.45; H, 5.81. Found: C, 63.37; H, 5.66.

7-Methoxy-1-oxaspiro[5.4]deca-6,9-diene-2,8-dione (4): isolated in 19% yield from the above preparative TLC; R_f 0.44; mp (benzene/pentane) 86–89 °C; IR ($CHCl_3$) 1792, 1781, 1688, 1652, 1626 cm^{-1}; NMR ($CDCl_3$) δ 6.87 (d d, 1 H, J = 3, 10 Hz), 6.24 (d, 1 H, J = 10 Hz), 5.78 (d, 1 H, J = 3 Hz), 3.71 (s, 3 H), 2.25–3.00 (m, 4 H).

Anal. Calcd for $C_{10}H_{10}O_4$: C, 61.85; H, 5.19. Found: C, 61.61; H, 5.32.

Compound **4** was also isolated (40% yield) by oxidation of 3-(4-acetoxy-3-methoxyphenyl)propionic acid (**26b**) at room temperature: 1 mmol scale, 15–20 s reaction time.

Methyl 3-(3,4-Dimethoxy-6-hydroxyphenyl)propionate (2). 3-(3,4-Dimethoxyphenyl)propionic acid was oxidized by the general procedure: 2 mmol scale, 0 °C, 20 s reaction time, water quench. The crude reaction product was separated by preparative TLC (10% methanol/chloroform) to give **4** (23%: least mobile), **3** (most mobile), and **2** (intermediate mobility). The most mobile fraction (**3**) was rechromatographed several times under the same conditions to ensure complete conversion into **2**: total yield 30%; R_f (5% acetone/chloroform) 0.62; IR ($CHCl_3$) 3150–3550 (br), 1735 cm^{-1}; NMR ($CDCl_3$) δ 6.60 (s, 1 H), 6.52 (s, 1 H), 3.80 (s, 6 H), 3.72 (s, 3 H), 2.70–2.90 (m, 4 H), m/e^+ calcd 240.09976, found 240.09950.

6,7-Diethoxy-3,4-dihydrocoumarin (6). 3-(3,4-Diethoxyphenyl)-propionic acid was oxidized by the general procedure: 7.5 mmol scale, 4–5 s reaction time. **6**: R_f (5% acetone/chloroform) 0.78; yield 5.3%; mp (benzene/pentane) 98–99 °C; IR ($CHCl_3$) 1760 cm^{-1}; NMR ($CDCl_3$) δ 6.70 (s, 1 H), 6.61 (s, 1 H), 4.06 (q, 4 H), 2.48–2.95 (m, 4 H), 1.43 (t, 6 H); m/e^+ calcd 236, found 236.

Anal. Calcd for $C_{13}H_{16}O_4$: C, 66.09; H, 6.83. Found: C, 65.87; H, 6.81.

7-Ethoxy-1-oxaspiro[5.4]deca-6,9-diene-2,8-dione (7): isolated in 49.4% yield from the above preparative TLC; R_f 0.48; mp (benzene/pentane) 99.5–100.5 °C; IR ($CHCl_3$) 1785, 1685, 1650, 1625 cm^{-1}; NMR ($CDCl_3$) δ 6.95 (d, 1 H), 6.23 (d, 1 H), 5.86 (d, 1 H), 3.89 (q, 2 H), 2.27–3.00 (m, 4 H), 1.38 (t, 3 H); m/e^+ calcd 208, found 208.

Anal. Calcd for $C_{11}H_{12}O_4$: C, 63.45; H, 5.81. Found: C, 63.51; H, 5.79.

5,6,7-Trimethoxy-3,4-dihydrocoumarin (9): from 3-(2,3,4-trimethoxyphenyl)propionic acid, 1 mmol scale, 5–10 s reaction time; R_f (5% acetone/chloroform) 0.66; yield, 53%; mp (benzene/pentane) 80–83 °C; IR ($CHCl_3$) 1772 cm^{-1}; NMR ($CDCl_3$) δ 6.43 (s, 1 H), 3.89 (s, 3 H), 3.80 (s, 6 H), 2.65–3.00 (m, 4 H).

Anal. Calcd for $C_{12}H_{14}O_5$: C, 60.50; H, 5.92. Found: C, 60.47; H, 6.08.

6,7-(Methylenedioxy)-3,4-dihydrocoumarin (11): from 3-(3,4-(methylenedioxy)phenyl)propionic acid, 1 mmol scale, 5–10 s reaction time; R_f (5% acetone/chloroform) 0.65; yield, 21%, mp (benzene/pentane) 83–85 °C; IR ($CHCl_3$) 1775, 1760 cm^{-1}; NMR ($CDCl_3$) δ 6.64 (s, 1 H), 6.61 (s, 1 H), 5.98 (s, 2 H), 2.65–3.00 (m, 4 H).

Anal. Calcd for $C_{10}H_8O_4$: C, 62.50; H, 4.20. Found: C, 62.35; H, 4.20.

7,9-Dimethoxy-1-oxaspiro[5.4]deca-6,9-diene-2,8-dione (13): from 3-(3,4,5-trimethoxyphenyl)propionic acid, 2.5 mmol scale, 20 s reaction time; R_f (5% acetone/chloroform) 0.35; yield, 37%; mp 136–138 °C dec; IR (KBr) 1770, 1685, 1655, 1625 cm^{-1}; NMR ($CDCl_3$) δ 5.79 (s, 2 H), 3.73 (s, 6 H), 2.83 (t, 2 H), 2.48 (t, 2 H); m/e^+ calcd 224, found 224.

2,2′-Bis(2-carboxyethyl)-4,4′-dimethoxybiphenyl (21): from 3-(3-methoxyphenyl)propionic acid, 1 mmol scale, 5–10 s reaction time; R_f (10% methanol/chloroform) 0.50; yield, 56%; mp (chloroform/hexane) 99–101 °C; NMR ($CDCl_3$) δ 7.66 (d, 2 H, J = 8.5 Hz), 6.83 (d, 2 H, J = 3 Hz), 6.54 (dd, 2 H, J = 8.5, 3 Hz), 3.75 (s, 3 H), 3.74 (s, 3 H), 2.50–3.15 (m, 8 H).

Anal. Calcd for $C_{20}H_{22}O_6$: C, 67.02; H, 6.19. Found: C, 66.84; H, 5.99.

6,6′-Bis(7-methoxy-3,4-dihydrocoumarin) (23): from 3-(4-methoxyphenyl)propionic acid, 1 mmol, 1 min reaction time at room temperature, 1.65 equiv of TTFA. The crude product was filtered through a short column of alumina (chloroform) and recrystallized from benzene/pentane: 36% yield; R_f (5% acetone/chloroform) 0.58; mp (benzene/pentane) 280–282 °C; IR ($CHCl_3$) 1762 cm^{-1}; NMR ($CDCl_3$) δ 7.02 (s, 2 H), 6.68 (s, 2 H), 3.75 (s, 6 H), 2.75–3.00 (m, 8 H); m/e^+ calcd 354, found 354.

Anal. Calcd for $C_{20}H_{18}O_6$: C, 67.79; H, 5.12. Found: C, 67.53; H, 5.43.

2,2′-Bis(2-carbomethoxyethyl)-4,4′,5,5′-tetramethoxybiphenyl (25): from methyl 3-(3,4-dimethoxyphenyl)propionate, 1 mmol scale, 5–10 s reaction time, 0.55 equiv of TTFA. The crude product was chromatographed on a silica gel column (chloroform): R_f (5% acetone/chloroform) 0.50; yield, 58%; mp (benzene/pentane) 70–73 °C; NMR ($CDCl_3$) δ 6.83 (s, 2 H), 6.67 (s, 2 H), 3.92 (s, 6 H), 3.85 (s, 6 H), 3.62 (s, 6 H), 2.56 (m, 8 H).

Anal. Calcd for $C_{24}H_{30}O_8$: C, 64.45; H, 6.77. Found: C, 64.72; H, 6.55.

2-Methoxy-5-(2-carbomethoxyethyl)-1,4-benzoquinone (28). Thallium(III) trifluoroacetate (1.2 g, 2.2 equiv) in 20 mL of TFA was cooled to 0 °C, and a solution of 210 mg (1 mmol) of 3-(3,4-dimethoxyphenyl)propionic acid in 5 mL of methylene chloride and 1 mL of $BF_3{\cdot}Et_2O$ added simultaneously. After 1 min 25 mL of methanol was added, the reaction mixture evaporated under reduced pressure, and the oily residue dissolved in chloroform, extracted with 2 × 20-mL portions of saturated aqueous sodium bicarbonate, washed with water, dried (Na_2SO_4), and chromatographed on a silica gel column. Elution with chloroform and recrystallization of the resulting crude product from carbon tetrachloride gave 73 mg (31%) of pure **28**: R_f (5% acetone/chloroform) 0.46; mp (carbon tetrachloride) 130–131 °C; IR ($CHCl_3$) 1740, 1683, 1657, 1611 cm^{-1}; NMR ($CDCl_3$) δ 6.48 (s, 1 H), 5.91 (s, 1 H), 3.80 (s, 3 H), 3.66 (s, 3 H), 2.55–2.85 (m, 4 H).

Anal. Calcd for $C_{11}H_{12}O_5$: C, 58.93; H, 5.39. Found: C, 59.18; H, 5.18.

2,6-Dimethoxy-5-(2-carbomethoxyethyl)-1,4-benzoquinone (29): from 3-(2,3,4-trimethoxyphenyl)propionic acid, 10 mmol scale, 30 s reaction time, by the procedure described above; R_f (5% acetone/chloroform) 0.45; yield, 40%; mp (carbon tetrachloride) 84–85 °C; IR ($CHCl_3$) 1737, 1690, 1650, 1607 cm^{-1}; NMR ($CDCl_3$) δ 5.82 (s, 1 H), 3.98 (s, 3 H), 3.78 (s, 3 H), 3.65 (s, 3 H), 2.40–2.90 (m, 4 H); m/e^+ calcd 254, found 254.

Anal. Calcd for $C_{12}H_{14}O_6$: C, 56.69; H, 5.55. Found: C, 56.59; H, 5.53.

5-Hydroxy-5-(4-methoxyphenyl)valeric Acid δ Lactone (31): from 5-(4-methoxyphenyl)valeric acid, 5 mmol scale, 20 s reaction time; R_f (5% acetone/chloroform) 0.40; yield, 6%; mp (ethanol) 60–61 °C (lit.[29] mp 143.5–144 °C);[30] IR ($CHCl_3$) 1730, 1615 cm^{-1}; NMR ($CDCl_3$) δ 7.25 (d, 2 H, J = 9 Hz), 6.87 (d, 2 H, J = 9 Hz), 5.27 (t, 1 H), 3.80 (s, 3 H), 2.50–2.75 (m, 2 H), 1.80–2.15 (m, 4 H).

Anal. Calcd for $C_{12}H_{14}O_3$: C, 69.89; H, 6.84. Found: C, 69.63; H, 6.62.

5-Hydroxy-5-(3,4-dimethoxyphenyl)valeric Acid δ Lactone (33): from 5-(3,4-dimethoxyphenyl)valeric acid, 5 mmol scale, 20 s reaction time; R_f (5% acetone/chloroform) 0.40; yield, 18%; mp (ethanol) 90–92 °C (lit.[31] mp 158–159 °C);[30] IR ($CHCl_3$) 1730, 1615 cm^{-1}; NMR ($CDCl_3$) δ 6.80–6.90 (m, 3 H), 5.25 (t, 1 H), 3.86 (s, 6 H), 2.50–2.70 (m, 2 H), 1.85–2.10 (m, 4 H).

Anal. Calcd for $C_{13}H_{16}O_4$: C, 66.09; H, 6.83. Found: C, 65.77; H, 6.84.

5-(3,4-Dimethoxy-2-hydroxyphenyl)valeric Acid (34). Acidification of the sodium bicarbonate washings from the above preparation (see the general procedure) yielded a crude acid which was purified by column chromatography (silica gel, 5% methanol/chloroform): yield, 375 mg (29.5%); R_f (5% methanol/chloroform) 0.40, as an oil; IR ($CHCl_3$) 3350 (br), 1705 (br), 1595 cm^{-1}; NMR ($CDCl_3$) δ 6.70 (d, 1 H, J = 12.5 Hz), 6.34 (dd, 1 H, J = 12.5, 1 Hz), 3.85 (s, 3 H), 3.83 (s, 3 H), 2.15–2.65 (m, 4 H), 1.40–1.80 (m, 4 H).

This material was further characterized as its acetylated derivative (88% yield; acetic anhydride/pyridine); R_f (10% acetone/chloroform) 0.60; IR ($CHCl_3$) 1755, 1710, 1605 cm^{-1}; NMR ($CDCl_3$) δ 6.70 (d, 1 H, J = 12.5 Hz), 6.55 (dd, 1 H, J = 12.5, 1 Hz), 3.85 (s, 3 H), 3.81 (s, 3 H), 1.90–2.65 (m, 4 H), 2.30 (s, 3 H), 1.35–1.80 (m, 4 H).

Calcd for $C_{15}H_{20}O_6$: m/e^+ 296.125978. Found: m/e^+ 296.125914.

6,7-Benzo-1-oxaspiro[5.4]deca-6,9-diene-2,8-dione (36): from 3-(4-methoxy-1-naphthalenyl)propionic acid,[32] 20 mmol scale, 20 s reaction time. The crude material was recrystallized from ethanol to give **36**: yield, 74%; R_f (5% methanol/chloroform) 0.60; mp (acetone/hexane) 127–128 °C; IR ($CHCl_3$) 1780, 1675 cm^{-1}; NMR ($CDCl_3$) δ 7.35–8.20 (m, 4 H), 7.05 (d, 1 H, J = 10 Hz), 6.35 (d, 1 H, J = 10 Hz), 2.30–3.15 (m, 4 H).

Anal. Calcd for $C_{13}H_{10}O_3$: C, 72.89; H, 4.70. Found: C, 72.68; H, 4.94.

The same compound was obtained in 12.5% yield, after a 10 min reaction time, from *N*-methyl-3-(4-methoxy-1-naphthalenyl)propionamide [mp (acetone) 106–107 °C; NMR ($CDCl_3$) δ 8.20–8.37 (m, 1 H), 7.82–8.05 (m, 1 H), 7.37–7.58 (m, 2 H), 7.17 (d, 1 H, J = 8 Hz), 6.64 (d, 1 H, J = 8 Hz), 5.73 (bs, 1 H), 3.92 (s, 3 H), 3.30 (t, 2 H), 2.68 (d, 3 H), 2.49 (t, 2 H); IR ($CHCl_3$) 3450, 2940, 1662, 1590 cm^{-1}].

3-(2,4-Diacetoxy-1-naphthalenyl)propionic Acid (37). The above spirolactone (428 mg) was stirred at room temperature for 48 h in a mixture of 20 mL of acetic anhydride and 4 drops of concentrated sulfuric acid, and the temperature was then raised to 60 °C for 6 h. The reaction mixture was cooled, diluted to 100 mL with ice water, and extracted with 3 × 100-mL portions of ether. The combined extracts were dried ($MgSO_4$) and evaporated under reduced pressure (with care taken to remove all traces of acetic acid), and the residual solid was filtered through a short silica gel column (eluted with 5% methanol/chloroform) and then recrystallized from acetone/hexane to give **37**: yield, 350 mg (55%); R_f (5% methanol/chloroform) 0.33; mp 141–143 °C; IR ($CHCl_3$) 1760 (br), 1710 cm^{-1}; NMR ($CDCl_3$) δ 10.70 (br s, 1 H), 7.90–8.10 (m, 2 H), 7.45–7.70 (m, 2 H), 7.13 (s, 1 H), 3.40 (t, 2 H), 2.70 (t, 2 H), 2.46 (s, 3 H), 2.40 (s, 3 H).

Anal. Calcd for $C_{17}H_{16}O_6$: C, 64.55; H, 5.10. Found: C, 64.84; H, 5.23.

6,7-Benzo-1-oxaspiro[5.4]deca-6,8-diene-2,10-dione (40): from 3-(2-methoxy-1-naphthalenyl)propionic acid,[33] 5 mmol scale, 40 s reaction time. The crude neutral material was purified by column chromatography (silica gel, 5% methanol/chloroform) and then recrystallized from aqueous ethanol (1:4): yield, 18%; R_f (10% acetone/chloroform) 0.52; mp (acetone/hexane) 134–135.5 °C (lit.[25] mp 138–139 °C); IR ($CHCl_3$) 1785, 1680 cm^{-1}; NMR ($CDCl_3$) δ 7.30–7.70 (m, 5 H), 6.15 (d, 1 H, J = 10 Hz), 2.40–3.00 (m, 4 H).

(29) van der Zanden, J. M. *Recl. Trav. Chim. Pays-Bas* **1942**, *61*, 365–372.

(30) We have repeated the alleged literature preparations of **31** (ref 29) and **33** (ref 31) [by reduction of 5-(4-methoxyphenyl)-5-oxovaleric acid and 5-(3,4-dimethoxyphenyl)-5-oxovaleric acid, respectively]. Acidification of the reduction mixtures to pH ≤1 with concentrated HCl, followed by extraction, yielded **31** and **33**, identical in every respect with the compounds prepared herein. By contrast, acidification of the above reduction mixtures to pH ~6, followed by extraction, yielded malodorous compounds which melted as previously claimed, but which did *not* exhibit a δ lactone IR carbonyl absorption band at 1730 cm^{-1}. We conclude that the previous claims for the synthesis of **31** and **33** are in error, and that the compounds actually formed were probably the uncyclized 5-aryl-5-hydroxyvaleric acids.

(31) Barltrop, J. A.; Johnson, A. J.; Meakins, G. D. *J. Chem. Soc.* **1951**, 181–185.

(32) Kindler, K.; Li, T. *Chem. Ber.* **1941**, *74*, 321–327.

(33) Koelsch, C. F.; Hood, H. E. *J. Org. Chem.* **1955**, *20*, 1282–1287.

Anal. Calcd for $C_{13}H_{10}O_3$: C, 72.89; H, 4.71. Found: C, 72.82; H, 4.69.

8-Methyl-6,7-benzo-1-oxaspiro[5.4]deca-6,8-diene-2,10-dione (42): from 3-(4-methyl-1-naphthalenyl)propionic acid,[34] 2 mmol scale, 45 s reaction time, 2.2 equiv of TTFA. The crude neutral product was passed through a short column of silica gel (eluted with 2% methanol/chloroform) to give, on evaporation of solvent, pure **42**: yield, 52%; R_f (5% methanol/chloroform) 0.63; mp (acetone/hexane) 125–126 °C; IR ($CHCl_3$) 1780, 1675, 1615 cm^{-1}; NMR (acetone-d^6) δ 7.25–7.75 (m, 4 H), 6.05 (q, 1 H), 2.40 (d, 3 H), 1.95–2.85 (m, 4 H).

Anal. Calcd for $C_{14}H_{12}O_3$: C, 73.67; H, 5.30. Found: C, 73.46; H, 5.44.

7,8-Benzo-1-oxaspiro[5.5]undeca-7,10-diene-2,9-dione (44): from 4-(4-methoxy-1-naphthalenyl)butyric acid,[35] 2 mmol scale, 20–30 s reaction time. The crude material was purified by column chromatography (silica gel, 5% acetone/chloroform): yield, 35%; R_f (5% acetone/chloroform) 0.36; mp (acetone/hexane) 159–160.5 °C; IR ($CHCl_3$) 1740, 1675, 1600 cm^{-1}; NMR ($CDCl_3$) δ 8.00–8.15 (m, 1 H), 7.40–7.70 (m, 3 H), 7.20 (d, 1 H, J = 10.5 Hz), 6.35 (d, 1 H, J = 10.5 Hz), 2.65–2.85 (m, 2 H), 2.00–2.15 (m, 4 H).

Anal. Calcd for $C_{14}H_{12}O_3$: C, 73.67; H, 5.30. Found: C, 73.83; H, 5.32.

9-Methyl-7,8-benzo-1-oxaspiro[5.5]undeca-7,9-diene-2,11-dione (46): from 4-(4-methyl-1-naphthalenyl)butyric acid,[36] 2 mmol scale, 45 s reaction time, 2.2 equiv of TTFA. The crude material was purified by column chromatography (silica gel, 5% acetone/chloroform): yield, 16.5%; R_f (5% acetone/chloroform) 0.47; mp (acetone/hexane) 120–121.5 °C; IR ($CHCl_3$) 1740, 1675 cm^{-1}; NMR ($CDCl_3$) δ 7.30–7.70 (m, 4 H), 6.07 (br s, 1 H), 2.55–2.95 (m, 2 H), 2.38 (br s, 3 H), 1.85–2.20 (m, 4 H).

Anal. Calcd for $C_{15}H_{14}O_3$: C, 74.36; H, 5.83. Found: C, 74.16; H, 5.74.

5-Hydroxy-5-(4-methyl-1-naphthalenyl)valeric Acid δ Lactone (48): from 5-(4-methyl-1-naphthalenyl)valeric acid (mp 134–136 °C, prepared from 1-methylnaphthalene and glutaric anhydride, followed by reduction), 2 mmol scale, 1 min reaction time. The base extraction step was omitted; purification by column chromatography (silica gel, 5% acetone/chloroform) gave pure **48**: R_f (5% acetone/chloroform) 0.48; yield, 53%; mp (ethanol) 111–113 °C; IR ($CHCl_3$) 1730 cm^{-1}; NMR ($CDCl_3$) δ 7.75–8.05 (m, 2 H), 7.33–7.55 (m, 3 H), 7.23 (br d), 6.00 (t, 1 H), 2.63 (s, 3 H), 2.50–2.75 (m, 2 H), 1.75–2.25 (m, 4 H).

Anal. Calcd for $C_{16}H_{16}O_2$: C, 79.97; H, 6.71. Found: C, 79.83; H, 6.78.

6,7-Dimethoxy-3,4-dihydro-2*H*-1-benzopyran (50): from 3-(3,4-dimethoxyphenyl)propan-1-ol,[37] 5 mmol scale, 20 min reaction time. The crude product was purified by column chromatography (silica gel, chloroform): R_f 0.60 (chloroform); yield, 20.7%; mp 51.5–52 °C; NMR ($CDCl_3$) δ 6.55 (s, 1 H), 6.38 (s, 1 H), 4.15 (t, 2 H), 3.85 (s, 6 H), 2.72 (t, 2 H), 1.80–2.20 (m, 2 H).

Anal. Calcd for $C_{11}H_{14}O_3$: m/e^+ 194.094288. Found: m/e^+ 194.094254.

2-(4-Methoxyphenyl)tetrahydrofuran (52): from 4-(4-methoxyphenyl)butan-1-ol, 6 mmol scale, 5 s reaction time; R_f (chloroform) 0.40, oil; yield, 4.7%; NMR ($CDCl_3$) δ 7.25 (d, 2 H, J = 10 Hz), 6.85 (d, 2 H, J = 10 Hz), 4.82 (t, 1 H), 3.90–4.20 (m, 2 H), 3.80 (s, 3 H), 1.60–2.40 (m, 4 H).

Anal. Calcd for $C_{11}H_{14}O_2$: m/e^+ 178.099373. Found: m/e^+ 178.099252.

7,8-Dimethoxy-2,3,4,5-tetrahydro-1-benzoxepin (54): from 4-(3,4-dimethoxyphenyl)butan-1-ol,[24e] 5 mmol scale, 1–2 s reaction time; R_f (chloroform) 0.35; yield, 13.5%; mp 44–45 °C; NMR ($CDCl_3$) δ 6.66 (s, 1 H), 6.63 (s, 1 H), 4.00 (t, 2 H), 3.88 (s, 6 H), 2.78 (t, 2 H), 1.50–2.10 (m, 4 H).

Anal. Calcd for $C_{12}H_{16}O_3$: m/e^+ 208.109937. Found: m/e^+ 208.109853.

2-(4-Methoxyphenyl)tetrahydropyran (56): from 5-(4-methoxyphenyl)pentan-1-ol,[38] 5 mmol scale, 5 s reaction time; R_f (chloroform) 0.50; 6.7% yield; mp 43.5–45 °C; NMR ($CDCl_3$) δ 7.25 (d, 2 H, J = 9 Hz), 6.83 (d, 2 H, J = 9 Hz), 4.00–4.35 (m, 3 H), 3.77 (s, 3 H), 1.40–2.11 (m, 6 H).

Anal. Calcd for $C_{12}H_{16}O_2$: m/e^+ 192.115023. Found: m/e^+ 192.114871.

8,9-Dimethoxy-3,4,5,6-tetrahydro-2*H*-1-benzoxocin (58): from 5-(3,4-dimethoxyphenyl)pentan-1-ol,[24e] 5 mmol scale, 10 s reaction time; R_f (chloroform) 0.50; yield, 10.8%, oil; NMR ($CDCl_3$) δ 6.55 (s, 2 H), 4.00 (t, 2 H), 3.80 (s, 6 H), 2.65 (br t, 2 H), 1.40–1.60 (m, 6 H).

Anal. Calcd for $C_{13}H_{18}O_3$: m/e^+ 222.125586. Found: m/e^+ 222.125435.

6-Methoxy-2,3-dihydro-1*H*-naphtho[2,1-*b*]pyran (60): from 3-(4-methoxy-1-naphthalenyl)propan-1-ol (mp 45–46 °C; NMR ($CDCl_3$) δ 8.20–8.40 (m, 2 H), 7.85–8.05 (m, 2 H), 7.17 (d, 1 H, J = 8 Hz), 6.67 (d, 1 H, J = 8 Hz), 3.92 (s, 3 H), 3.78 (t, 2 H), 3.05 (t, 2 H), 1.80–2.10 (m, 2 H), 1.82 (s, 1 H); IR ($CHCl_3$) 3600, 3450 (br), 2930, 1590 cm^{-1}), 2 mmol scale, 2 min reaction time; R_f (carbon tetrachloride) 0.29; yield, 29.5%, oil; NMR ($CDCl_3$) δ 8.00–8.20 (m, 2 H), 7.30–7.55 (m, 2 H), 6.32 (s, 1 H), 4.20 (t, 2 H), 3.83 (s, 3 H), 2.72 (t, 2 H), 2.00 (m, 2 H).

Anal. Calcd for $C_{14}H_{14}O_2$: m/e^+ 214.099373. Found: m/e^+ 214.099370.

6-Methyl-2,3-dihydro-1*H*-naphtho[2,1-*b*]pyran (62): from 3-(4-methyl-1-naphthalenyl)propan-1-ol (mp 44–45 °C; NMR ($CDCl_3$) δ 7.85–8.20 (m, 2 H), 7.35–7.60 (m, 2 H), 7.22 (s, 2 H), 3.72 (t, 2 H), 3.13 (t, 2 H), 2.67 (s, 3 H), 1.80–2.20 (m, 2 H), 1.64 (s, 1 H); IR ($CHCl_3$) 3600, 3450 (br), 2930, 1600 cm^{-1}), 2 mmol scale, 5 min reaction time; R_f (carbon tetrachloride) 0.50; yield, 19%, oil; NMR ($CDCl_3$) δ 8.10–8.25 (m, 1 H), 7.70–7.95 (m, 1 H), 7.35–7.55 (m, 2 H), 6.92 (s, 1 H), 4.30 (t, 2 H), 2.80 (t, 2 H), 2.55 (s, 3 H), 1.85–2.20 (m, 2 H).

Anal. Calcd for $C_{14}H_{14}O$: m/e^+ 198.104459. Found: m/e^+ 198.104343.

2-(4-Methoxy-1-naphthalenyl)tetrahydrofuran (64): from 4-(4-methoxy-1-naphthalenyl)butan-1-ol (NMR ($CDCl_3$) δ 8.20–8.40 (m, 1 H), 7.80–8.00 (m, 1 H), 7.35–7.55 (m, 2 H), 7.13 (d, 1 H, J = 8 Hz), 6.62 (d, 1 H, J = 8 Hz), 3.89 (s, 3 H), 3.56 (t, 2 H), 2.95 (br t, 2 H), 2.00–2.35 (br s, 1 H), 1.40–1.90 (m, 4 H); IR (neat) 3100–3500 (br), 2925, 1585 cm^{-1}), 4 mmol scale, 15 s reaction time; R_f (methylene chloride) 0.44; yield, 23%; NMR ($CDCl_3$) δ 8.18–8.35 (m, 1 H), 7.75–7.95 (m, 1 H), 7.30–7.52 (m, 3 H), 6.65 (d, 1 H, J = 8 Hz), 5.42 (t, 1 H), 3.80–4.30 (m, 2 H), 3.85 (s, 3 H), 1.68–2.50 (m, 4 H).

Anal. Calcd for $C_{15}H_{16}O_2$: m/e^+ 228.115023. Found: m/e^+ 228.114825.

7-Methoxy-1,2,3,4-tetrahydronaphth[2,1-*b*]oxepin (65) was obtained from the above preparation: R_f 0.70; yield, 2.2%, oil; NMR ($CDCl_3$) δ 8.00–8.30 (m, 2 H), 7.20–7.60 (m, 2 H), 6.55 (s, 1 H), 4.05 (t, 2 H), 3.95 (s, 3 H), 2.80–3.00 (m, 2 H), 1.40–2.20 (m, 4 H).

Anal. Calcd for $C_{15}H_{16}O_2$: m/e^+ 228.115023. Found: m/e^+ 228.114598.

2-(4-Methyl-1-naphthalenyl)tetrahydrofuran (67): from 4-(4-methyl-1-naphthalenyl)butan-1-ol (NMR ($CDCl_3$) δ 7.80–8.10 (m, 2 H), 7.30–7.53 (m, 2 H), 7.12 (s, 2 H), 3.52 (t, 2 H), 2.99 (br t, 2 H), 2.60 (s, 3 H), 2.32 (s, 1 H), 1.40–2.00 (m, 4 H); IR (neat) 3150–3500 (br), 2930, 1600 (weak) cm^{-1}), 5 mmol scale, 30 s reaction time; R_f (methylene chloride) 0.65; yield, 17.5%; NMR ($CDCl_3$) δ 7.80–8.10 (m, 2 H), 7.35–7.60 (m, 3 H), 7.25 (d, 1 H, J = 8 Hz), 5.58 (t, 1 H), 3.80–4.32 (m, 2 H), 2.65 (s, 3 H), 1.50–2.60 (m, 4 H).

Anal. Calcd for $C_{15}H_{16}O$: m/e^+ 212.120109. Found: m/e^+ 212.119700.

7-Methyl-1,2,3,4-tetrahydronaphth[2,1-*b*]oxepin (68) was obtained from the above preparation: R_f (carbon tetrachloride) 0.32; yield, 4.6%, oil; NMR ($CDCl_3$) δ 8.15–8.35 (m, 1 H), 7.75–8.10 (m, 1 H), 7.30–7.60 (m, 2 H), 7.18 (s, 1 H), 4.10 (t, 2 H), 3.00 (t, 2 H), 2.60 (s, 3 H), 1.40–2.20 (m, 4 H).

Anal. Calcd for $C_{15}H_{16}O$: m/e^+ 212.120109. Found: m/e^+ 212.119907.

2-(4-Methoxy-1-naphthalenyl)tetrahydropyran (70): from 5-(4-methoxy-1-naphthalenyl)pentan-1-ol (NMR ($CDCl_3$) δ 8.20–8.40 (m, 1 H), 7.85–8.05 (m, 1 H), 7.35–7.70 (m, 2 H), 7.17 (d, 1 H, J = 8 Hz), 6.67 (d, 1 H, J = 8 Hz), 3.93 (s, 3 H), 3.60 (t, 2 H), 3.00 (br t, 2 H), 1.30–2.00 (m, 7 H); IR (neat) 3150–3500 (br), 2930, 1590 cm^{-1}), 4 mmol scale, 15 s reaction time; R_f (methylene chloride) 0.60; yield, 28%, oil; NMR ($CDCl_3$) δ 8.20–8.40 (m, 1 H), 7.90–8.10 (m, 1 H), 7.30–7.60 (m, 3 H), 6.73 (d, 1 H, J = 8 Hz), 4.80–5.00 (m, 1 H), 4.00–4.30 (m, 2 H), 3.92 (s, 3 H), 1.50–2.10 (m, 6 H).

Anal. Calcd for $C_{16}H_{18}O_2$: m/e^+ 242.130607. Found: m/e^+ 242.130672.

2-(4-Methyl-1-naphthalenyl)tetrahydropyran (72): from 5-(4-methyl-1-naphthalenyl)pentan-1-ol (NMR ($CDCl_3$) δ 7.84–8.10 (m, 2 H), 7.30–7.55 (m, 2 H), 7.14 (s, 2 H), 3.52 (br t, 2 H), 3.00 (br t, 2 H), 2.61 (s, 3 H), 2.25 (br s, 1 H), 1.20–1.90 (m, 6 H); IR (neat) 3150–3500 (br), 2930, 1600 (weak) cm^{-1}), 4 mmol scale, 30 s reaction tme; R_f (methylene chloride) 0.73; yield, 38%, oil; NMR ($CDCl_3$) δ 7.80–8.10 (m, 2 H), 6.95–7.60 (m, 4 H), 4.80–5.00 (br s, 1 H), 4.00–4.30 (m, 1

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H), 3.50–3.80 (m, 1 H), 2.58 (s, 3 H), 1.40–2.10 (m, 6 H).

Anal. Calcd for $C_{16}H_{18}O$: m/e^+ 226.135758. Found: m/e^+ 226.135719.

2,2′-Bis(2-((methylamino)carbonyl)ethyl)-4,4′,5,5′-tetramethoxybiphenyl (75): from *N*-methyl-3-(3,4-dimethoxyphenyl)propionamide (mp (acetone) 68–70 °C; NMR ($CDCl_3$) δ 6.73 (s, 3 H), 6.27 (br s, 1 H), 3.82 (s, 6 H), 2.91 (t, 2 H), 2.75 (d, 3 H), 2.47 (t, 2 H); IR ($CHCl_3$) 3450, 2935, 1662, 1595 (weak) cm^{-1}), 3 mmol scale, 1–2 s reaction time; R_f (5% methanol/chloroform) 0.27; yield, 6%; mp (acetone) 216–217 °C; IR ($CHCl_3$) 3450, 1650 cm^{-1}; NMR ($CDCl_3$) δ 6.80 (s, 2 H), 6.60 (s, 2 H), 5.80–6.10 (br s, 2 H), 3.90 (s, 6 H), 3.82 (s, 6 H), 2.76 (s, 3 H), 2.73 (t, 4 H), 2.70 (s, 3 H), 2.30 (t, 4 H).

Anal. Calcd for $C_{24}H_{32}N_2O_6$: C, 64.85; H, 7.26; N, 6.30. Found: C, 64.69; H, 7.14; N, 6.12.

2,2′-Bis(2-cyanoethyl)-4,4′,5,5′-tetramethoxybiphenyl (77): from 3-(3,4-dimethoxyphenyl)propionitrile (oil, prepared from the corresponding acrylonitrile by Mg/methanol reduction; NMR ($CDCl_3$) δ 6.73–6.85 (m, 3 H), 3.88 (s, 3 H), 3.85 (s, 3 H), 2.88 (t, 2 H), 2.58 (t, 2 H); IR (neat) 2250, 1595, 1517 cm^{-1}), 10 mmol scale, 20 s reaction time. The crude material was passed through a silica gel filtration column ($CHCl_3$) and then chromatographed (silica gel, 5% acetone/chloroform) to give the biaryl **77**: R_f (5% acetone/chloroform) 0.46; yield, 34%; mp (acetone/hexane) 169–171 °C; IR ($CHCl_3$) 2935, 2250, 1607 cm^{-1}; NMR ($CDCl_3$) δ 6.87 (s, 2 H), 6.72 (s, 2 H), 3.93 (s, 6 H), 3.85 (s, 6 H), 2.30–2.95 (m, 8 H).

Anal. Calcd for $C_{22}H_{24}N_2O_4$: C, 69.46; H, 6.36; N, 7.36. Found: C, 69.24; H, 6.54; N, 7.21.

3-(3,4-Dimethoxy-5-hydroxyphenyl)propionitrile (78) was obtained from the above preparation: R_f 0.38; mp (carbon tetrachloride) 116–118 °C dec; yield, 49%; IR ($CHCl_3$) 3515, 2935, 2250, 1600 cm^{-1}; NMR ($CDCl_3$) δ 6.43 (d, 1 H, J = 2 Hz), 6.34 (d, 1 H, J = 2 Hz), 6.10 (br s, 1 H), 3.86 (s, 6 H), 2.45–2.95 (m, 4 H).

Anal. Calcd for $C_{11}H_{13}O_3N$: m/e^+ 207.089537. Found: m/e^+ 207.089492.

Interaction of Nickel(0) Complexes with Allyl Carboxylates, Allyl Ethers, Allylic Alcohols, and Vinyl Acetate. π-Complex Formation and Oxidative Addition to Nickel Involving Cleavage of the Alkenyl–Oxygen Bond

Takakazu Yamamoto,* Junichi Ishizu, and Akio Yamamoto

Contribution from the Research Laboratory of Resources Utilization, Tokyo Institute of Technology, 4259 Nagatsuta, Midori-ku, Yokohama 227, Japan. *Received April 15, 1981*

Abstract: Interaction of various allylic compounds with bis(1,5-cyclooctadiene)nickel, $Ni(cod)_2$, in the absence and presence of tertiary phosphines, causes cleavage of allyl—oxygen bonds. Allyl acetate reacts with $Ni(cod)_2$ to afford a mixture of $Ni(\eta^3\text{-}C_3H_5)_2$ and $Ni(OCOCH_3)_2$ presumably through an intermediate, allylnickel acetate, followed by its disproportionation. Similar reactions in the presence of tertiary phosphine ligands, PR_3 (triphenylphosphine (PPh_3), ethyldiphenylphosphine ($PEtPh_2$), tricyclohexylphosphine (P-c-Hx_3)), give $Ni(\eta^3\text{-}C_3H_5)(OCOCH_3)(PR_3)$ (**1–3**). Allyl formate can be catalytically converted into propylene and CO_2 at 25 °C by a $Ni(cod)_2$–PPh_3 mixture. A reaction of allyl phenyl ether with a mixture of $Ni(cod)_2$ and PPh_3 at 30 °C also leads to cleavage of the C—O bond to yield $Ni(\eta^3\text{-}C_3H_5)(OC_6H_5)(PPh_3)$ (**4**). Complexes **1–4** react with morpholine to produce *N*-allylmorpholine in 65–82% yields. On the other hand, similar reactions of diallyl ether with mixtures of $Ni(cod)_2$ and phosphine ligands do not cause C—O bond cleavage under mild conditions and yield complexes formulated as Ni(π-diallyl ether)(PR_3) (PR_3 = PPh_3, P-c-Hx_3) (**5** and **6**). Allylic alcohols $RCH{=}CHCH_2OH$ (R = H, CH_3, C_6H_5) are dismutated into $RCH{=}CHCH_3$, $RCH{=}CHCHO$, and H_2O on interaction with mixtures of $Ni(cod)_2$ and phosphines at 30–50 °C. The mixture of $Ni(cod)_2$ and PPh_3 serves as a catalyst for the allylation of morpholine by allyl alcohol. The C—O bond in vinyl acetate is also cleaved on interaction with $Ni(cod)_2$ alone or mixtures of $Ni(cod)_2$ and phosphines. Complexes **1–6** are characterized by elemental analysis and spectroscopy (IR and NMR). As for the mechanism of the C—O bond-cleavage reaction of allyl–oxygen compounds, one involving coordination of the allylic compound to Ni through the C=C double bond followed by a bond rearrangement involving C—O bond cleavage is proposed.

Oxidative addition of a substrate to a transition metal often constitutes a key elementary step in various catalytic reactions, and extensive studies were made on the oxidative addition of compounds such as alkyl halides and acyl halides to transition metals.[1]

In comparison with oxidative addition reactions involving carbon–halogen bond cleavage those involving C–O bond cleavage of esters and ethers were much less explored.[2] In previous papers we examined the C–O bond cleavage of aryl esters involving acyl–O scission promoted by Ni(0) complexes under mild conditions.[3a,b]

$$RCO\text{–}OR' + NiL_n \rightarrow RCO\text{–}NiL_n\text{–}OR'$$

We now report on other types of oxidative addition involving the allyl–O and vinyl–O bond cleavages of allyl carboxylates, vinyl acetate, allyl aryl ethers, and allylic alcohols.

$$RCOO\text{–}R' + NiL_n \rightarrow RCOO\text{–}NiL_n\text{–}R'$$

$$R''O\text{–}R' + NiL_n \rightarrow R''O\text{–}NiL_n\text{–}R'$$

R = alkyl or H, R′ = allyl or vinyl group, R″ = aryl or H

The oxidative additions involving the allyl–carboxylate bond cleavage were recognized and utilized for organic synthesis[1b,c,2b,h] and polymerization.[2a] There are, however, very few examples

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