

ACCOUNTS OF CHEMICAL RESEARCH

FEBRUARY, 1988

Registered in U.S. Patent and Trademark Office; Copyright 1988 by the American Chemical Society

Olefin Synthesis via Organometallic Coupling Reactions of Enol Triflates

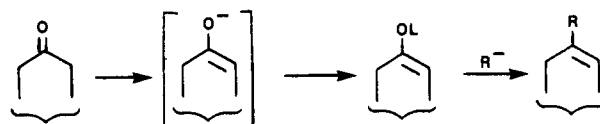
WILLIAM J. SCOTT*[†] and JOHN E. MCMURRY*[‡]

Department of Chemistry, The University of Iowa, Iowa City, Iowa 52242, and Department of Chemistry, Cornell University, Ithaca, New York 14853

Received August 26, 1987 (Revised Manuscript Received October 27, 1987)

The carbonyl group has been called the most versatile functionality available to the synthetic organic chemist. One major reason is the ability to convert a carbonyl compound into the corresponding olefin, a result normally achieved by addition of a nucleophile followed by dehydration of the intermediate alcohol. Neither of the two steps is necessarily straightforward, however. For example, sterically hindered ketones are often inert to nucleophilic addition. Similarly, sterically hindered nucleophiles either will not add to, or can act as reducing agents toward, ketones. Even more troublesome is the fact that dehydration of the intermediate alcohol is rarely regioselective. A mixture of olefin products often results from alcohol dehydration, lessening the value of the procedure for synthesis. Because of these problems, much research has been directed at the development of new methods for the regioselective synthesis of olefins from ketones.

An attractive alternative to the nucleophilic addition/dehydration route would be to take advantage of known methods¹ for regioselectively generating an enolate ion. Thus, formation and trapping of an enolate ion, followed by substitution of the enol derivative with a nucleophile, would lead to regiospecific formation of an olefin.



The key step, displacement of a leaving group from an enol derivative, requires a nucleophilic substitution reaction at an sp^2 center. Although similar substitution reactions at the sp^2 centers of vinylic halides have been known since 1968,² it was not until 1976 that Blaszcak demonstrated the replacement of an enolate oxygen by reaction of an enol diphenyl phosphate with lithium dibutylcopper.³ Unfortunately, use of the less reactive lithium dimethylcopper led to low product yields.

Since sulfonates are often used as leaving groups in nucleophilic substitution reactions, it occurred to us that trapping of an enolate ion as its enol sulfonate, followed by displacement, might constitute a general scheme for olefin synthesis. Enol *p*-toluenesulfonates (tosylates) are not easily prepared, but the corresponding enol trifluoromethanesulfonates (triflates) are well-known and have been much studied as a source of vinylic cations.⁴ Thus, the conversion of ketones into olefins via the corresponding enol triflates was investigated.

William J. Scott received a B.S. degree from the University of Rochester in 1973, an M.S. from Wright State University in 1978, and the Ph.D. (with John McMurry) from Cornell University in 1983. Following postdoctoral work with John Stille at Colorado State University, he joined the faculty at The University of Iowa, where he is presently Assistant Professor of Chemistry. His research interests include natural-products synthesis, the use of transition metals in synthetic methodology, and polymer synthesis.

A short biography of John E. McMurry appeared previously in *Acc. Chem. Res.* **1983**, *16*, 405.

* The University of Iowa.

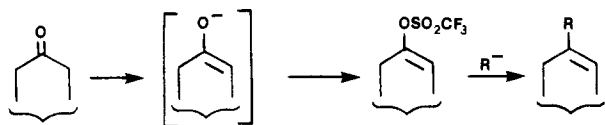
[‡] Cornell University.

(1) d'Angelo, J. *Tetrahedron* **1976**, *32*, 2979-2990.

(2) Corey, E. J.; Posner, G. H. *J. Am. Chem. Soc.* **1968**, *90*, 5615-5616.

(3) Blaszcak, L.; Winkler, J.; O'Kuhn, S. *Tetrahedron Lett.* **1976**, *17*, 4405-4408.

(4) Stang, P. J.; Rappoport, Z.; Hanack, M. C.; Subramanian, L. R. *Vinyl Cations*; Academic: New York, 1979.

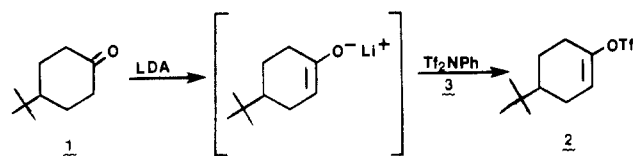


Synthesis of Enol Triflates

The first step of the projected transformation involves conversion of a ketone into its enol triflate, a reaction that has been accomplished in two general ways. The most common method is the reaction of a ketone with trifluoromethanesulfonic anhydride (triflic anhydride) in the presence of a mild nonnucleophilic base.⁵ The enol triflate is thought to be formed by initial reaction of triflic anhydride with the ketone, followed by loss of a proton, and the reaction normally leads to production of the more thermodynamically stable product. For example, treatment of 2-methylcyclohexanone (4) with triflic anhydride and base gives 2-methyl-1-cyclohexenyl triflate (5) as the major product.⁶

The second general method of enol triflate synthesis is by conversion of a ketone into its enolate ion followed by trapping. Although stable enolate ions derived from highly acidic ketones can be trapped with triflic anhydride in good yield,⁷ the more reactive enolates derived from monoketones tend to C-sulfonate, affording α -keto sulfone products.⁸

In order to find a more general method of enolate trapping, we initiated a comparative study of a number of potential sulfonating agents. Using as our test system the enolate ion prepared by deprotonation of 4-*tert*-butylcyclohexanone (1) with lithium diisopropylamide (LDA), we found that reaction with triflic anhydride failed to yield any of the desired product 2, but that reaction with (trifluoromethanesulfonyl)imidazole⁹ provided 2 in 48% yield and reaction with *N*-phenyltriflimide¹⁰ (3) gave 2 in 82% isolated yield.¹¹



One of the most important features of the enolate-trapping method is its ability to define the regiochemistry of the enol triflate, as exemplified by the selective conversion of 2-methylcyclohexanone (4) into either its thermodynamic (5) or kinetic (6) enol triflate by choice of reaction conditions. Treatment of 4 with LDA, followed by trapping, gives enol triflates 6 and 5 in a 19:1 ratio,¹¹ whereas treatment with bromomagnesium diisopropylamide¹² followed by trapping gives the two products in a 1:19 ratio.¹³ By contrast, treatment of

(5) Stang, P. J.; Hanack, M. C.; Subramanian, L. R. *Synthesis* 1982, 85-126.

(6) Collins, C. J.; Garcia-Martinez, A.; Martinez-Alvarez, R.; Arranz-Aguirre, J. *Chem. Ber.* 1984, 117, 2815-2824.

(7) Stang, P. J.; Treptow, W. L. *J. Med. Chem.* 1981, 24, 468-472.

(8) Subramanian, L. R.; Bentz, H.; Hanack, M. C. *Synthesis* 1973, 293-294.

(9) Effenberger, F.; Mack, K. E. *Tetrahedron Lett.* 1970, 11, 3947-3948.

(10) Hendrickson, J. B.; Bergeron, R. *Tetrahedron Lett.* 1973, 14, 4607-4610.

(11) McMurry, J. E.; Scott, W. J. *Tetrahedron Lett.* 1983, 24, 979-982.

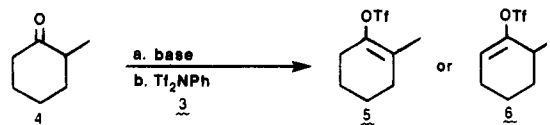
(12) Krafft, M. E.; Holton, R. E. *Tetrahedron Lett.* 1983, 24, 1345-1348.

(13) Scott, W. J.; Stille, J. K. *J. Am. Chem. Soc.* 1986, 108, 3033-3040.

Table I
Preparation of Enol Triflates from Ketones

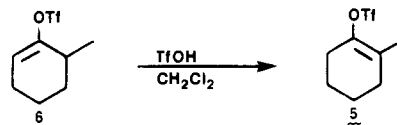
entry		yield, %	ref
1		80	11
2		65	11
3		97	11
4		65	11
5		65	11
6		65	11
7		93	14

4 with triflic anhydride and sodium carbonate gives 6 and 5 in a 1:3 ratio.⁶



N-Phenyltriflimide was also found to be effective for trapping a variety of enolates generated in a number of different ways (Table I).^{11,14} Enolate ions prepared by treatment of silyl enol ethers with methylolithium, by addition of diorganocuprate reagents to conjugated ketones, and by reduction of conjugated ketones with either sodium in liquid ammonia or with *L*-Selectride, can all be converted into the corresponding enol triflate by reaction with *N*-phenyltriflimide.

Finally, enol triflates can be equilibrated under anhydrous acidic conditions in a manner similar to that used for silyl enol ethers.^{15,16} Thus, treatment of 6-methyl-1-cyclohexenyl triflate (6) with a catalytic amount of anhydrous triflic acid yields the thermodynamically more stable 2-methyl-1-cyclohexenyl triflate (5).^{17,18}



Coupling Reactions of Enol Triflates with Diorganocuprates

With efficient methods for the regioselective preparation of enol triflates available, we turned our attention to reactions of the triflates with organometallic reagents. We found in short order that, although alkylolithiums effect sulfur-oxygen bond cleavage with enol triflates, diorganocuprates effect carbon-oxygen cleavage and

(14) Crisp, G. T.; Scott, W. J. *Synthesis* 1985, 335-337.

(15) Stork, G.; Hudrik, P. F. *J. Am. Chem. Soc.* 1968, 90, 4262-4264.

(16) House, H. O.; Czuba, L. J.; Gall, M.; Olmstead, H. D. *J. Org. Chem.* 1969, 34, 2324-2336.

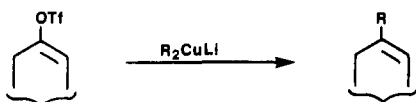
(17) Scott, W. J., unpublished results.

(18) Cacchi, S.; Morera, E.; Ortar, G. *Tetrahedron Lett.* 1980, 21, 4313-4316.

Table II
Coupling Reactions of Enol Triflates with Organocopper Reagents

entry	triflate	organocopper reagent	product	isolated yield, %	ref
1		Me ₂ CuLi		75	19
2		(CH ₂) ₂ CuMgBr		62	19
3		(C ₃ H ₅) ₂ CuMgBr		68	19
4		Ph ₂ CuLi		75	19
5		Me ₂ CuLi		95	19
6		Me ₂ CuLi		95	19
7		(CH ₂) ₂ CuMgBr		71	19

convert the triflate into the corresponding olefin.¹⁹ Thus, our initial hope of devising a regioselective olefin synthesis complementary to the standard nucleophilic addition/dehydration scheme had been realized.



As shown in Table II, yields of olefin products are high for a wide variety of diorganocuprates, including *n*-butyl, phenyl, vinyl, and cyclopropyl. Particularly noteworthy is the fact that yields remain high even when dimethylcuprate is used, in contrast to the result previously observed for reactions of enol diphenyl phosphates.³

The stereospecificity of the coupling reactions was demonstrated by treatment of pure (*Z*)-5-((trifluoromethanesulfonyloxy)-5-decene with lithium dimethylcopper to give (*E*)-5-methyl-5-decene of greater than 99% stereochemical purity (Table II, entry 5). Similarly, reaction of (*E*)-5-((trifluoromethanesulfonyloxy)-5-decene gave (*Z*)-5-methyl-5-decene of greater than 99% purity. Although a preliminary result suggested that a small amount of isomerization occurred during the coupling reaction, subsequent analysis has indicated this not to be the case.²⁰

Palladium-Catalyzed Coupling Reactions of Enol Triflates with Organostannanes

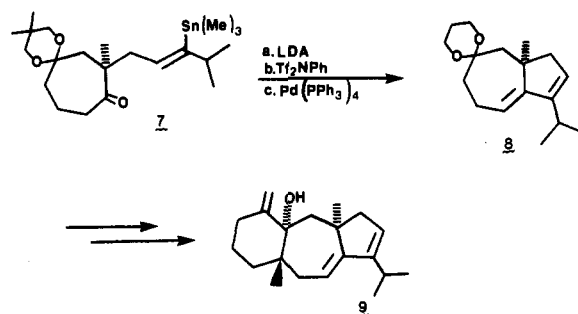
Transition metals have recently been found to catalyze the coupling reactions of a number of enol derivatives with carbon nucleophiles.²¹ For example, zero-

(19) McMurry, J. E.; Scott, W. J. *Tetrahedron Lett* 1980, 21, 4313-4316.

(20) Scott, W. J. Ph.D. Dissertation, Cornell University, Ithaca, NY, 1983.

(21) (a) Collman, J. P.; Hegedus, L. S.; Norton, J. R.; Finke, R. G. *Principles and Applications of Organotransition Metal Chemistry*; University Science Books: Mill Valley, CA, 1987. (b) Colquhoun, H. M.; Holton, J.; Thompson, D. J.; Twigg, M. V. *New Pathways for Organic Synthesis. Practical Applications of Transition Metals*; Plenum: New York, 1984. (c) Yamamoto, A. *Organotransition Metal Chemistry*; Wiley: New York, 1986. (d) Heck, R. F. *Palladium Reagents in Organic Synthesis*; Academic: London, 1985.

Scheme I
An Intramolecular Enol Triflate/Organostannane Coupling Route to Dolastane Sesquiterpenes



valent nickel complexes catalyze the coupling of Grignard reagents with methyl enol ethers^{22,23} and silyl enol ethers²⁴ to yield alkene products. Similarly, palladium complexes have been shown to catalyze the coupling of enol phosphates with alanes.²⁵

Enol triflates are also capable of undergoing transition-metal-catalyzed coupling with nucleophiles. Thus, treatment of 4-*tert*-butyl-1-cyclohexenyl triflate (3) with an organostannane²⁶ in the presence of 2 mol % of tetrakis(triphenylphosphine)palladium(0) and an excess of LiCl gives the coupled alkene product in high yields.^{13,27} The coupling can be carried out in most polar solvents except for chloroform. Even some water or air can be tolerated, but the reaction will not take place unless added salt is present. The reaction is general for a variety of organostannanes, including alkyl, vinyl, acetylenic, and allyl (Table III). Aryl- and benzylstannanes yield only traces of coupled products, however.

One of the more important results shown in Table III is that palladium-catalyzed coupling of an enol triflate with hexamethyldistannane gives the corresponding vinylic stannane in good yield. Such regioselectively formed vinylic stannanes can then be further converted into vinylic iodides by reaction with I₂²⁸ or into vinylic lithium reagents by reaction with methyllithium.²⁹ Surprisingly, however, attempts to form vinylic stannanes by palladium-catalyzed coupling of enol triflates with hexabutyldistannane,^{13,29} or diethyl(trimethylstannyl)aluminum were unsuccessful.³⁰

Both the organocopper reaction and the palladium-catalyzed coupling of enol triflates with organostannanes are compatible with the presence of severe steric hindrance about both the electrophilic and the nucleophilic sites. Hindrance in the enol triflate affects

(22) Wenkert, E.; Michelotti, E. L.; Swindell, C. S. *J. Am. Chem. Soc.* 1979, 101, 2246-2247.

(23) Wenkert, E.; Michelotti, E. L.; Swindell, C. S.; Tingoli, M. *J. Org. Chem.* 1984, 49, 4894-4899.

(24) Hayashi, T.; Katsuro, Y.; Kumada, M. *Tetrahedron Lett.* 1980, 21, 3915-3918.

(25) Takai, K.; Sato, M.; Oshima, K.; Nozaki, M. *Bull. Chem. Soc. Jpn.* 1984, 57, 108-115.

(26) For a recent review of the palladium-catalyzed coupling reactions of electrophiles with organostannanes, see: Stille, J. K. *Angew. Chem., Int. Ed. Engl.* 1986, 25, 508-524.

(27) Scott, W. J.; Crisp, G. T.; Stille, J. K. *J. Am. Chem. Soc.* 1984, 106, 4630-4632.

(28) Kashin, A. N.; Beletskaya, I. P.; Malkasyan, A. T.; Reutov, O. A. *J. Org. Chem. USSR (Engl. Transl.)* 1974, 10, 2257-2261.

(29) Wulff, W. D.; Peterson, G. A.; Bauta, W. E.; Chan, K.-S.; Faron, K. L.; Gilbertson, S. R.; Kaesler, R. W.; Yang, D. C.; Murray, C. K. *J. Org. Chem.* 1986, 51, 277-279.

(30) Matsubara, S.; Hibino, J.; Morizawa, Y.; Oshima, K.; Nozaki, H. *J. Organomet. Chem.* 1985, 285, 163-172.

Table III
Palladium-Catalyzed Coupling of Enol Triflates with Organostannanes

entry	triflate	organostannane	product	isolated yield, %	ref
1		$\text{Bu}_3\text{Sn}-\text{CH}=\text{CH}_2$		91	13
2		$\text{Bu}_3\text{Sn}-\text{CH}=\text{CH}-\text{CH}=\text{CH}_2$		96	13
3		Bu_4Sn		80	13
4		$\text{Me}_3\text{SnSnMe}_3$		73	13
5		$\text{Bu}_3\text{Sn}-\text{CH}=\text{CH}-\text{CH}=\text{CH}_2$		80	13
6		$\text{Me}_3\text{Sn}-\text{CH}=\text{CH}-\text{SiMe}_3$		90	13
7		$\text{Me}_3\text{Sn}-\text{CH}=\text{CH}-\text{CH}=\text{CH}-\text{SnBu}_3$		75	13

Table IV
Palladium-Catalyzed Reduction of Enol Triflates

entry	triflate	hydride source	product	isolated yield, %	ref
1		Bu_3SnH		78	13
2		$-\text{[(Me)-HSiO]}_n-$		75	13
3		HCO_2H		79	35
4		DCO_2D		87	35

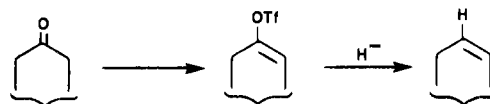
neither reaction rate nor yield.¹³ Thus, coupling of 4-*tert*-butyl-1-cyclohexenyl triflate with vinyltributyltin proceeds only 1.5 times as fast as the analogous reaction with 2,5,5-trimethyl-1-cyclopentenyl triflate. Hindrance in the organostannane appears to affect rate but not yield.

The reaction has already been put to good use in synthesis, most notably by Piers, who has used an intramolecular variant of the palladium-catalyzed coupling to synthesize five- and six-membered rings.³¹ This annulation served as the key step in a synthetic approach to the dolastane diterpenes (Scheme I).³² Surprisingly, LiCl was found to hinder, rather than help, the intramolecular reaction. The coupling has also been used in a stereospecific synthesis of peraplysin-1 (Table III, entry 7)¹³ and in an approach to vitamin D metabolites.³³

Palladium-Catalyzed Reduction of Enol Triflates

As previously mentioned, the conversion of a ketone into an enol triflate, followed by coupling with a carbon

nucleophile, is a regioselective alternative to the standard nucleophilic addition/dehydration scheme for olefin synthesis. In the same way, conversion of a ketone to an enol triflate, followed by reduction, would be a regioselective alternative to the standard reduction/dehydration scheme.



In practice, reduction of enol triflates with standard hydride reducing agents such as LiAlH_4 or $(i\text{-Bu})_2\text{AlH}$ results only in sulfur-oxygen bond cleavage, regenerating the enolate ion.^{13,34} The desired reaction can be accomplished smoothly, however, when tributylstannane,^{13,27} various organosilanes, or formic acid³⁵ is used in the presence of a palladium catalyst (Table IV). The overall sequence represents an extremely mild method for preparing olefins and should find use in natural-products synthesis. Of particular importance is the fact that dienol triflates reduce smoothly to yield dienes, a conversion that is difficult or impossible to achieve cleanly by other methods.

Palladium-Catalyzed Olefination of Enol Triflates

In addition to their ability to undergo coupling reactions with organocuprates and organostannanes, enol triflates also react with olefins and alkynes in a palladium-catalyzed Heck olefination reaction (Table V).^{18,36} No added salt is necessary, and the reaction takes place in most common solvents, although dimethylformamide is normally chosen. The best yields are obtained when the olefin reactant is substituted by an electron-with-

(31) Piers, E.; Friesen, R. W.; Keay, B. A. *J. Chem. Soc., Chem. Commun.* 1985, 809-810.

(32) Piers, E.; Friesen, R. W. *J. Org. Chem.* 1986, 51, 3405-3406.

(33) Castedo, L.; Mourino, A.; Sarandeses, L. A. *Tetrahedron Lett.* 1986, 27, 1523-1526.

(34) Stang, P. J.; Mangum, M. G.; Fox, D. P.; Haak, P. *J. Am. Chem. Soc.* 1974, 96, 4562-4569.

(35) Cacci, S.; Morera, E.; Ortar, G. *Tetrahedron Lett.* 1984, 25, 4821-4824.

(36) Scott, W. J.; Pena, M. R.; Sward, K.; Stoessel, S. J.; Stille, J. K. *J. Org. Chem.* 1985, 50, 2302-2308.

Table V
Palladium-Catalyzed Olefination of Enol Triflates

entry	triflate	olefin	product	isolated yield, %	ref
1				89	36
2				86	36
3				95	36
4				89	36
5				92	36
6				77	18
7				60	18

Table VI
Palladium-Catalyzed Carbonylative Couplings of Enol Triflates

entry	triflate	organostannane	product	isolated yield, %	ref
1				76	37
2 ^a				95	37
3 ^a				73	37
4 ^a				93	37
5				95	37
6				77	37

^a One equivalent of ZnCl₂ added.

drawing group, as in a conjugated ketone or ester. Steric hindrance about the enol triflate has little effect on the reaction rate, and double-bond stereochemistry of the final product is normally the result of a palladium-catalyzed equilibration. Thus, only the more thermodynamically stable *E* product is formed when either methyl acrylate or methyl vinyl ketone is used.

Palladium-Catalyzed Carbonylations of Enol Triflates

Still another kind of coupling process occurs when enol triflates are allowed to undergo palladium-catalyzed reaction with vinylic or acetylenic stannanes in the presence of LiCl and 1 atm of carbon monoxide.³⁷

Although the reaction conditions must be carefully controlled, high yields of divinyl ketones can result from carbonylative coupling (Table VI). No reaction takes place at low temperatures, and direct noncarbonylative coupling can be competitive at high temperature. Optimal conditions vary with the organostannane, although most react best at a temperature just below the boiling point of the solvent. Vinylic stannanes appear to retain their stereochemical integrity during the carbonylative coupling process, but the cross-conjugated ketone products must be purified carefully to prevent acid-catalyzed equilibration of *Z*-enones to their more stable *E* isomers.

(37) Crisp, G. T.; Scott, W. J.; Stille, J. K. *J. Am. Chem. Soc.* 1984, 106, 7500-7506.

Table VII
Formation of Aldehydes, Esters, and Amides from Enol Triflates

entry	triflate	nucleophile	product	isolated yield, ^a %	ref
1		Bu ₃ SnH		53 (86)	38
2		Bu ₃ SnH		50 (96)	38
3		Et ₂ NH		74	39
4		<i>i</i> -PrOH		85	39
5 ^b		HCO ₂ H/Et ₃ N		87	39

^a Parentheses indicate crude yield as determined by GC. ^b The mixed anhydride is believed to be formed initially.

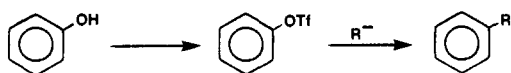
Alkyl-, aryl-, and allylstannanes can also be induced to undergo carbonylative coupling with enol triflates in good yield if a stoichiometric amount of ZnCl₂ is added to the reaction mixture.³⁸ It is thought that the organostannane undergoes transmetalation to the corresponding organozinc reagent, providing a more reactive nucleophile.

Simple variants of the carbonylative coupling reaction allow one to synthesize unsaturated aldehydes,³⁸ esters,³⁹ or amides³⁹ instead of ketones. Thus, reaction of an enol triflate with carbon monoxide and tributyltin hydride in place of a tetraorganostannane leads to production of an aldehyde. Similar use of alcohols or amines in place of the tetraorganostannane leads to esters or amides (Table VII). The aldehyde synthesis is sensitive both to steric hindrance in the triflate and to CO pressure. Unhindered enol triflates require higher pressures (3 atm) to suppress direct reduction, whereas more hindered substrates require lower pressures (1 atm).

As with other triflate reactions, carbonylative coupling has already found use in natural-products synthesis. Thus, Δ⁹⁽¹²⁾-capnellene has been prepared by an efficient route utilizing carbonylative couplings at two points (Scheme II).³⁷

Coupling Reactions of Aryl Triflates

If aryl triflates were to behave analogously to enol triflates in the various reactions just discussed, the result would be a series of new and useful methods for converting phenols into substituted aromatic compounds.

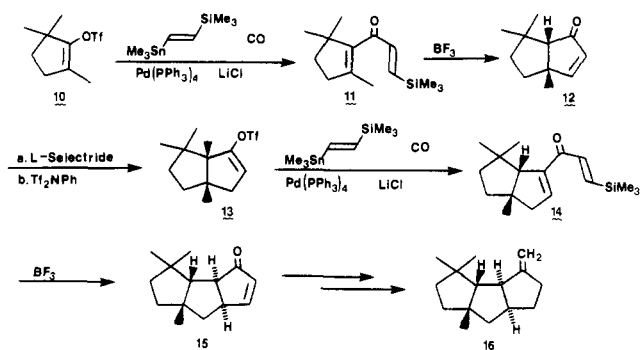


Though readily prepared by reaction of the corresponding phenols with triflic anhydride, aryl triflates are less reactive than their vinylic counterparts, and

(38) Baillargeon, V. P.; Stille, J. K. *J. Am. Chem. Soc.* 1986, 108, 452-461.

(39) Cacchi, S.; Morera, E.; Ortar, G. *Tetrahedron Lett.* 1985, 26, 1109-1112.

Scheme II Synthesis of Δ⁹⁽¹²⁾-Capnellene



treatment of aryl triflates with lithium diorganocuprates yields no coupled products.⁴⁰ When more reactive higher order mixed cuprates are used, however, coupling takes place cleanly to give the corresponding arenes in moderate yield.⁴¹ Substitution on the ring appears to have little effect on the reaction, which is compatible with the presence of both electron-withdrawing and electron-donating groups.

Aryl triflates also mimic their vinylic counterparts in other reactions. Thus, aryl triflates can be reduced to yield arenes on catalytic hydrogenation over a 10% palladium-on-carbon catalyst, a net removal of the OH group from a phenol.⁴² Similarly, aryl triflates undergo the palladium-catalyzed Heck olefination reaction to yield the corresponding styrenes,⁴³ undergo carbonylation in the presence of an amine to yield a benzamide,⁴⁴ and undergo reduction with formic acid to yield an arene.⁴⁵ Some of these different aryl triflate reactions are shown in Table VIII.

(40) McMurry, J. E.; Scott, W. J., unpublished results.

(41) McMurry, J. E.; Mohanraj, S. *Tetrahedron Lett.* 1983, 24, 2723-2736.

(42) Subramanian, L. R.; Garcia-Martinez, A.; Herrera-Fernandez, A.; Martinez-Alvarez, R. *Synthesis* 1984, 481-485.

(43) Chen, Q. Y.; Yang, Z. Y. *Tetrahedron Lett.* 1986, 27, 1171-1174.

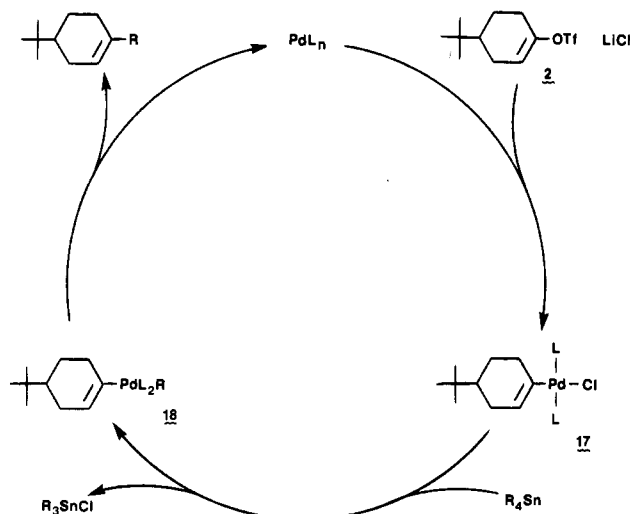
(44) Cacchi, S.; Ciattini, P. G.; Morera, E.; Ortar, G. *Tetrahedron Lett.* 1986, 27, 3931-3934.

(45) Cacchi, S.; Ciattini, P. C.; Morera, E.; Ortar, G. *Tetrahedron Lett.* 1986, 27, 5541-5544.

Table VIII
Some Coupling Reactions of Aryl Triflates

entry	triflate	nucleophile	product	isolated yield, %	ref
1		$\text{Bu}_2\text{Cu}(\text{CN})\text{Li}_2$		70	41
2		$\text{H}-\text{C}\equiv\text{C}-\text{SiMe}_3$		87	43
3				59	44
4		MeOH/CO		77	44
5		$\text{HCO}_2\text{H}/\text{Et}_3\text{N}$		81	45

Scheme III
Proposed Mechanism for the Palladium-Catalyzed Coupling of Enol Triflates with Organostannanes



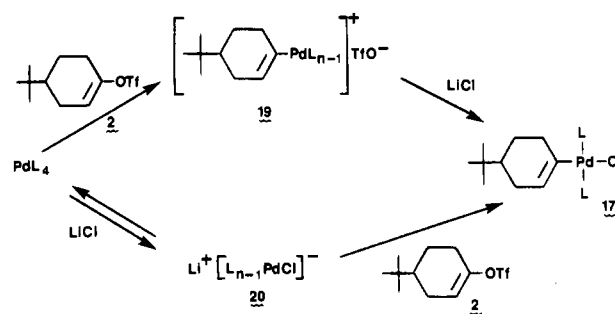
Mechanism of Palladium-Catalyzed Coupling Reactions of Enol Triflates

The details are not yet clear, but a plausible working mechanism for the palladium-catalyzed coupling of enol triflates with nucleophiles involves the initial oxidative addition of the triflate to the palladium(0) catalyst to afford an organopalladium(II) complex 17. Transmetalation with the organostannane then generates the bis(organopalladium(II)) complex 18, which rapidly undergoes reductive elimination to form coupled product and regenerate the palladium(0) catalyst (Scheme III).^{22,27}

Evidence for this mechanism comes from the observation that reaction of enol triflate 2 with $\text{Pd}(\text{PPh}_3)_4$ in the presence of LiCl forms the isolable *trans*-organopalladium(II) chloride complex 17.¹³ This complex was found to be an active catalyst for the coupling of 2 with vinyltributyltin to afford coupled product.

The reaction of $\text{Pd}(\text{PPh}_3)_4$ with LiCl and enol triflate 2 to give 17 might take place by either of two mechanisms (Scheme IV). Oxidative addition to give the corresponding organopalladium(II) triflate complex,

Scheme IV
Possible Mechanisms for the Formation of Complex 17



followed by ligand exchange with chloride ion, would give 17, or alternatively LiCl could complex with the palladium prior to oxidative addition.

In support of the latter mechanism, treatment of $\text{Pd}(\text{PPh}_3)_4$ with LiCl gave a new intermediate that could be detected by ^{31}P NMR.¹³ Addition of an excess of 2 to this species caused immediate consumption of the intermediate and production of 17. It has also been found, however, that $\text{Pt}(\text{PPh}_3)_4$ reacts directly with enol triflates to give an intermediate capable of further reaction with halide sources.⁴⁶ Thus, the sequence of events leading to formation of 17 is still in doubt.

Conclusion

The idea of using enol triflates as intermediates in the conversion of ketones into olefins has proven to be outstandingly successful. Regioselectively formed enolate ions can be trapped as their enol triflates, which can then be converted into a wide variety of olefins by reaction with organocopper reagents or other nucleophiles in the presence of palladium catalysts.

Among the different types of products that can be formed are dienes, enynes, conjugated enones, cross-conjugated enones, unsaturated aldehydes, and unsaturated esters. In addition, reduction of the enol triflate yields an alkene and conversion to the vinylstannane allows formation of vinylic halides and vinylic lithium reagents. Analogous reactions with aryl triflates allow the conversion of phenols into arenes, into substituted

styrenes, and into substituted benzamides.

Though the methodology described in this Account is barely 5 years old, a number of triflate-based transformations have already appeared in the context of

several natural-product syntheses. Enol triflates are proving to be extremely versatile reagents for the synthetic organic chemist, and we look forward to their ever-increasing use.

Flash Photolysis Electron Spin Resonance

K. A. McLAUHLAN* and D. G. STEVENS

Physical Chemistry Laboratory, South Parks Road, Oxford OX1 3QZ, U.K.

Received June 18, 1987 (Revised Manuscript Received October 23, 1987)

Of the techniques used to detect free radicals in solution only electron spin resonance (ESR) spectroscopy has the resolution to identify them positively. When placed in an external magnetic field the unpaired electron in the radical adopts one of two spin orientations, either parallel or antiparallel to the field, of different energy. In the ESR experiment transitions are caused between them by applying radiation of frequency ν to satisfy the condition

$$h\nu = g\mu_B B$$

where h is Planck's constant, g is a characteristic parameter of each radical, μ_B is the Bohr magneton, and B is the applied field strength. Typically B is 3400 G and ν is ca. 9.6 GHz, and resonance is approached by sweeping the field while keeping the frequency constant.

Rather than the single line expected from this description the ESR spectrum exhibits a hyperfine structure of several lines characteristic of the radical. It arises from the electron coupling to nearby magnetic nuclei in the radical and is analogous to spin-spin coupling in nuclear magnetic resonance spectroscopy. A methyl radical, for example, exhibits an ESR spectrum due to the electron coupling to three equivalent protons and which consequently consists of a quartet of equally spaced lines of relative intensities 1:3:3:1.

The hyperfine structure of an organic radical may extend over 1-200 G, a significant part of the applied field, and is normally displayed by applying an electric current to sweep coils mounted on the magnet. The

inductance of these coils prevents the field from being swept rapidly enough to study the transient radicals produced in flash photolysis experiments, and new methods have been developed to overcome this problem.^{1,2} The radicals are produced not once, in a single flash, but repetitively in a series of flashes that occur at different magnetic field values. Following each flash the signal is sampled either continuously, as in two-dimensional (2D) transient spectroscopy, or for some chosen period, as in time integration spectroscopy (TIS) and boxcar and spin-echo methods. The spectrum at the chosen period is subsequently reconstructed from the data obtained at each field value. The methods can be used within 20 ns of the photolysis flash.

In conventional ESR spectroscopy the transitions are observed in absorption with intensities controlled by the Boltzmann populations of the states at thermal equilibrium. However, when observed within a few microseconds of their creation, transient radicals usually exhibit spectra remarkable for their intensities and phases. They may appear in enhanced absorption, in emission, or with some hyperfine components in one phase and some in the other. This phenomenon is known as chemically induced dynamic electron polarization (CIDEP; see below). It reflects a departure from the equilibrium populations of the states of the radicals which arises at their formation, in the triplet mechanism (TM), or early in their existence, in the radical pair mechanism (RPM), and disappears subsequently by relaxation. CIDEP was first observed in a conventional experiment in 1963.³ Its magnitude is measured by the polarization, P , defined as the difference in the populations of the states connected by the ESR transition divided by their sum. In typical experiments $[P] \sim (10-100)P_{eq}$, where P_{eq} is the value at thermal equilibrium, facilitating radical detection at low concentrations. However, the greatest value of CIDEP is that the phases of the signals disclose the multiplicity of the precursor molecule whose reaction led to radical production directly without further experimentation.⁴

This aspect of CIDEP is covered only briefly here, for it has been the subject of recent articles.^{4,5} We

Keith McLauchlan was born in Bristol, U.K., on January 8, 1936. He graduated from Bristol University in 1956 with 1st Class Honours in Chemistry and in 1959 with his Ph.D., which was based on gas-phase radical studies. His postdoctoral period was spent working on radiation chemistry at the National Research Council of Canada. He returned to the U.K. in 1960 to work on nuclear magnetic resonance spectroscopy at the National Physical Laboratory, doing early work on double-resonance, double-quantum, and oriented-molecule experiments. In 1965 he became a lecturer at Oxford University, where he was awarded his M.A., and a Fellow of Hertford College. After extending his NMR interests, he became one of the pioneers of flash photolysis electron spin resonance and electron spin polarization (CIDEP), on which he has lectured worldwide in recent years. He also works on the effects of magnetic and microwave fields on chemical and biochemical reactions.

David Stevens was born in Poole, U.K., on July 9, 1962, and graduated with 1st Class Honours in Chemistry at Oxford in 1984. He joined British Petroleum as a Research Scientist after submission of his doctoral thesis in the summer of 1987. His research has been concerned mostly with the development of two-dimensional ESR techniques, with the extension of the Oxford time integration spectroscopy method, and with the analysis of CIDEP spectra.

(1) Atkins, P. W.; McLauchlan, K. A.; Simpson, A. F. *Nature (London)* 1968, 219, 927.

(2) Smaller, B.; Remko, J. R.; Avery, E. C. *J. Chem. Phys.* 1968, 48, 5174.

(3) Fessenden, R. W.; Schuler, R. H. *J. Chem. Phys.* 1963, 39, 2147.

(4) Buckley, C. D.; McLauchlan, K. A. *Mol. Phys.* 1985, 54, 1.