rently investigating the chemical reactivity of these new enamine reagents derived from nitriles and their synthetic uses.

Registry No. 1, 56977-62-9; 2 (R = R′ = H), 78108-63-1; 2-(*E*) (R = CH_3; R′ = H), 78108-64-2; 2-(*Z*) (R = CH_3; R′ = H), 78108-65-3; 2-(*E*) (R = R′ = CH_3), 78108-66-4; 2-(*E*) (R = Ph; R′ = H), 78108-67-5; 2-(*Z*) (R = Ph; R′ = H), 78108-68-6; 2 (R = R′ = Ph), 78108-69-7; 2-(*E*) (R = 2-cyanophenyl; R′ = H), 78108-70-0; 2-(*Z*) (R = 2-cyanophenyl; R′ = H), 78108-71-1; 2-(*E*) (R = MeO; R′ = H), 78108-72-2; 2-(*Z*) (R = MeO; R′ = H), 78108-73-3; 2-(*E*) (R = COOEt; R′ = H), 78108-74-4; 2-(*E*) (R = 2-methyl-1,3-dioxolan-2-yl; R′ = Ph), 78108-75-5; 2-(*Z*) (R = 2-methyl-1,3-dioxolan-2-yl; R′ = Ph), 78108-76-6; 2-(*E*) (R = 6-(1,4-dioxaspiro[4.5]decyl)methyl; R′ = H), 78108-77-7; 2-(*Z*) (R = 6-(1,4-dioxaspiro[4.5]decyl)methyl; R′ = H), 78108-78-8; 3-(*E*), 78108-79-9; 3-(*Z*), 78108-80-2; 4, 78108-81-3; 5, 78108-82-4; acetonitrile, 75-05-8; propanenitrile, 107-12-0; 2-methylpropanenitrile, 78-82-0; benzeneacetonitrile, 140-29-4; α-phenylbenzeneacetonitrile, 86-29-3; hexanedinitrile, 111-69-3; 2-cyanobenzeneacetonitrile, 3759-28-2; methoxyacetonitrile, 1738-36-9; cyanoacetic acid, ethyl ester, 105-56-6; 2-methyl-α-phenyl-1,3-dioxolane-2-acetonitrile, 78108-83-5; 1,4-dioxaspiro[4.5]decane-6-propanenitrile, 78108-84-6; acetaldehyde, 75-07-0; propanal, 123-38-6; 2-methylpropanal, 78-84-2; benzeneacetaldehyde, 122-78-1; α-phenylbenzeneacetaldehyde, 947-91-1; 6-oxohexanenitrile, 3523-02-2; 3-oxopropanoic acid, ethyl ester, 34780-29-5; acetaldehyde 2,4-DNP, 1019-57-4; propanal 2,4-DNP, 725-00-8; 2-methylpropanal 2,4-DNP, 2057-82-1; benzeneacetaldehyde 2,4-DNP, 2074-04-6; α-phenylbenzeneacetaldehyde 2,4-DNP, 10479-11-5; 6-oxohexanenitrile 2,4-DNP, 13050-18-5; 3-oxopropanoic acid, ethyl ester 2,4-DNP, 2003-74-9.

Robert J. P. Corriu,* Joël J. E. Moreau
Magali Pataud-Sat
Laboratoire des Organométalliques
E.R.A. No. 554
Université des Sciences et Techniques du Languedoc
34060 Montpellier, France
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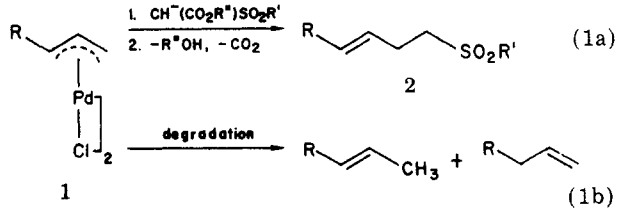
Regio- and Stereoselective Anti-Markovnikov Hydrosulfonylation of Conjugated Dienes via π-Allylpalladium Complex: Synthesis of (*Z*)-Δ³-Alkenyl Sulfones

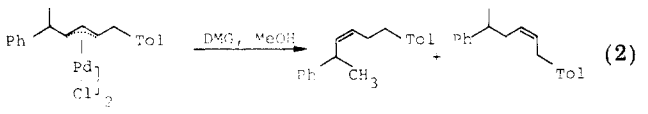
Summary: Butadienes of type 4 may be converted to products of type 7 by means of palladium chloride.

Sir: Stereocontrolled di- and trisubstituted olefin synthesis is still a problem of pressing concern in organic synthesis. Palladium chemistry has made a great contribution to this problem.[1] The reactions via π-allylpalladium intermediates, however, are generally limited to the syntheses of *E* olefins, reflecting the thermodynamically favored syn geometry.[2] Typical examples are illustrated in eq 1. The



1 2 (1a) (1b)

alkylation of 1 with sulfonylacetate anion provides (*E*)-Δ³-sulfone derivatives 2. Degradation with CH_3ONa–CH_3OH,[3] NaCN–CH_3OH,[4] or reducing agents ($NaBH_4$,[5] $LiAlH_4$,[6] HCO_2H–pyridine)[7] also gives rise to *E* olefins, but in these cases comparable amounts of mixtures of regioisomers are produced, predominately the more substituted ones. In sharp contrast to these, we have found that treatment of the π-allylpalladium complex (3) with 2 equiv of dimethylglyoxime (DMG; in CH_3OH in the presence of an appropriate amount of pyridine to dissolve 3 at ambient temperature overnight) provides *Z* olefins as a mixture of regioisomers [(*Z*)-1-*p*-tolyl-5-phenylhex-3-ene and (*Z*)-1-*p*-tolyl-5-phenylhex-2-ene in a ratio of 1:2 in virtually quantitative yield (eq 2)].[8] Interestingly, *this reaction is*



3 (2)

clearly accompanied by the inversion of configuration around the allylic moiety of 3.[9] We expected that the above stereoselectivity, coupled with the regioselectivity as observed in the anti-Markovnikov hydrosulfonylation of 1,3-dienes,[10] might be applied to the preparation of useful synthons, (*Z*)-Δ³-sulfones 7 (Scheme I). Indeed, this proved to be the case, and (*Z*)-Δ³-sulfones 7 were prepared in high regio- and stereoselectivities, independent of the configuration of the starting 1,3-dienes.[11] Results are summarized in Table I, which covers dienes with various structural features. The reaction consists of two steps: preparation of π-allylpalladium complexes 5 and 6 and degradation of these with DMG, as typified in the following example (entry 1). A mixture of 1,3-pentadiene (cis–trans mixture, 3 mmol), $PdCl_2$ (2 mmol), and sodium neophylsulfinate (4 mmol) in 20 mL of acetic acid was heated at 50 °C for 4 h with magnetic stirring. After the usual extractive workup with EtOAc ($NaHCO_3$–H_2O) and evaporation of the solvent, the yellow residue of **5a** and **6a** (R^1 = CH_3, R^2 = R^3 = H) was dissolved in CH_3OH[12] and treated with DMG (4 mmol). After the mixture was stirred overnight at ambient temperature and the CH_3OH evaporated, the yellow solid residue was washed several times with benzene–hexane. Purification of the extracts by column chromatography (silica gel, benzene–EtOAc

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(2) In some instances, *Z* olefins are prepared by kinetically controlled reactions using *Z*-allylic acetates as starting materials. Trost, B. M.; Verhoeven, T. R. *J. Org. Chem.* **1976**, *41*, 3215.

(3) (a) Faller, J. W.; Laffey, K. J. *Organomet. Chem. Synth.* **1972**, *1*, 471. (b) Christ, D.-C. H.; Hüttel, R. *Angew. Chem.* **1963**, *75*, 921. (c) Schenach, T. A.; Caserio, F. F., Jr. *J. Organomet. Chem.* **1969**, 17. (d) Hüttel, R.; Kochs, P. *Chem. Ber.* **1968**, *101*, 1043.

(4) Dunne, K.; McQuillin, F. J. *J. Chem. Soc. C* **1970**, 2196.

(5) (a) Bullpitt, M. L.; Kitching, W. *J. Organomet. Chem.* **1972**, *46*, 21. (b) Hutchins, R. O.; Learn, K.; Fulton, R. P. *Tetrahedron Lett.* **1980**, *21*, 27.

(6) Jones, D. N.; Knox, S. D. *J. Chem. Soc., Chem. Commun.* **1975**, 165.

(7) Tsuji, J.; Yamakawa, T. *Tetrahedron Lett.* **1979**, 613.

(8) Both isomers showed J = 11–12 Hz for of the olefinic protons in the ^1H NMR (100 MHz) and no =CH out of plane bending around 960 cm^{-1} in the IR (ascribable to trans-disubstituted olefins).

(9) The syn geometry of 3 (as a solution in $CDCl_3$ or CD_3OD) is apparent from the coupling pattern (triplet, J = 11.5 Hz) of the proton attached to the central carbon of allylic moiety. Robinson, S. D.; Shaw, B. L. *J. Chem. Soc.* **1963**, 4806.

(10) Tamaru, Y.; Kagotani, M.; Yoshida, Z. *J. Chem. Soc., Chem. Commun.* **1978**, 367.

(11) *E* and *Z* mixtures of dienes were used without separation.

(12) It is crucial to dissolve 5 (and/or 6) completely before addition of DMG, otherwise the reaction loses its selectivity to give intractable mixtures, which mainly consist of 7 and/or 8 and their regio isomers, dienyl neophyl sulfones, and starting dienes. In cases where 5 showed very poor solubility in CH_3OH, a sufficient amount of pyridine (2–5 equiv to 5) or CH_2Cl_2 was added to dissolve the 5.

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Scheme I

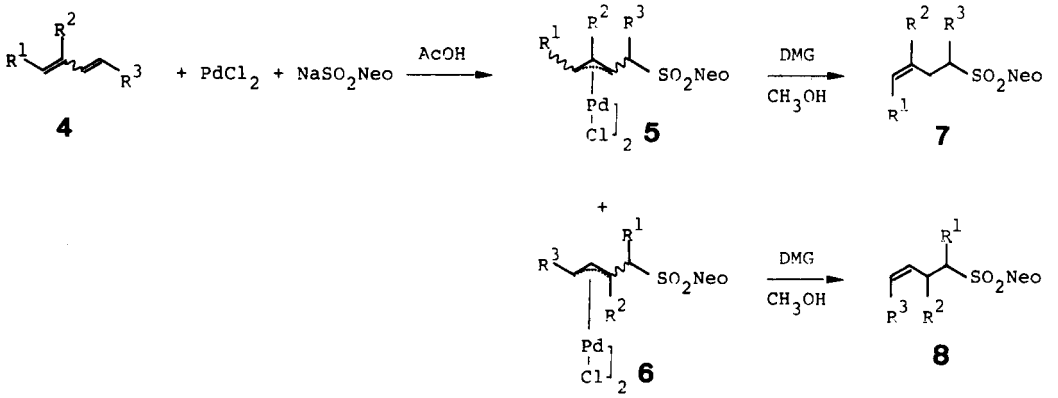
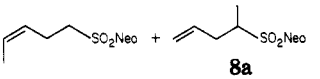
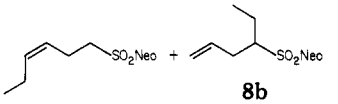
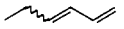
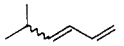
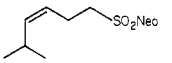
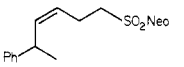
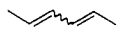
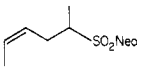
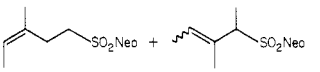


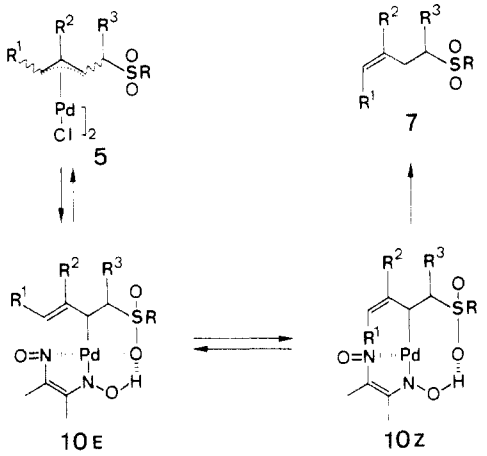
Table I. Regio- and Stereoselective Hydrosulfonylation of Conjugated Dienes

entry	diene[a]	reaction conditions[b] [sulfonylpalladation[c]/degradation]	% isolated yield of sulfone[d]
			 7a 8a
1	 4a	AcOH, 50 °C, 4 h/MeOH, room temp, 20 h	43 (55:45 7a/8a)
2		AcOH-H_2O, 40 °C, 4 h/MeOH-CH_2Cl_2, room temp, 20 h	50–60 (73:27 7a/8a)
			 7b 8b
3	 4b	AcOH, 75 °C, 2 h/MeOH, room temp, 20 h	82 (88:12 7b/8b)
4		AcOH-H_2O, 75 °C, 4 h/MeOH-CH_2Cl_2, room temp, 40 h	70 (91:9 7b/8b)
5	 4c	AcOH-H_2O, 70 °C, 4 h/MeOH, room temp, 20 h	 7c (55)
6	 4d	AcOH, 70 °C, 4 h/MeOH, room temp, 20 h	 7d (70)[e]
7	 4e	AcOH-H_2O, 70 °C, 4 h/MeOH, room temp, 20 h	 7e (64)
			 7f 9
8		AcOH, 80 °C, 1.5 h/MeOH-Py, room temp, 20 h	73 (87:13 7f/9)
9	4f	AcOH-H_2O, 90 °C, 2.5 h/MeOH-Py, room temp, 20 h	71 (98:2 7f/9)
10		AcOH-H_2O, 90 °C, 2.5 h/AcOH, room temp, 20 h	85 (97:3 7f/9)

[a] Stereoisomeric mixture of diene was used. [b] Reaction conditions are given in the following order: solvent, temperature, and reaction time for the formation of π-allylpalladium complexes 5 and 6/solvent, temperature, and reaction time for treatment with DMG. For the experimental details, see the text. DMG, MeOH, AcOH, Py, and Neo refer to dimethylglyoxime, methanol, acetic acid, pyridine, and the neophyl group, respectively. [c] The isolated yields (after column chromatography on silica gel, benzene-EtOAc gradient) of compounds 5 are as follows: 5a ($R^1 = CH_3$, $R^2 = R^3 = H$), 74%; 5b ($R^1 = C_2H_5$, $R^2 = R^3 = H$), 91%; 5c ($R^1 = CH(CH_3)_2$, $R^2 = R^3 = H$), 57%; 5d ($R^1 = CH(Ph)CH_3$, $R^2 = R^3 = H$), 45%; 5e ($R^1 = R^3 = CH_3$, $R^2 = H$), 34%; 5f ($R^1 = R^2 = CH_3$, $R^3 = H$), 79%. [d] Overall yield for the isolated sulfone(s) (not optimized, after column chromatography on silica gel) based on $PdCl_2$. All reactions, except for entry 6, were carried out without isolation of 5 and/or 6. Separation of mixture of sulfones 7–9 was carried out by HPLC (μ-Porasil; hexane-EtOAc, 95:5). [e] Isolated yield of 7d based on isolated 5d.

gradient) provided a mixture of *cis*-3-pentenyl neophyl sulfone (**7a**) and 1-penten-4-yl neophyl sulfone (**8a**) in a ratio of 55:45 in 43% overall yield based on $PdCl_2$. When the R^1 group in the dienes is sterically small, two types of

Scheme II



complexes **5** and **6** are produced in comparable amounts (entries 1, 3, and 8). But formation of **6** could be minimized by conducting the sulfonylpalladation in CH_3CO_2H–H_2O (4–5:1 v/v, entries 2, 4, 9, and 10). Furthermore, complex **6** could be eliminated partially by passing a mixture of **5** and **6** through a silica gel column, probably due to decomposition of the latter as observed in the change of ratio of **7b** and **8b** (96:4; cf. entry 3).

The regio- and stereoselectivity of degradation of **5** with DMG is as high as 95%, and the structures of **7** are ascertained unequivocally by comparison of their spectral data (^1H NMR, IR) and VPC and/or HPLC retention times with those of authentic samples prepared by a relevant method.[13]

Although we have previously failed in the sulfonylpalladation of 2,4-hexadiene,[10] addition of water (CH_3CO_2H–H_2O, 5:1 v/v) effected the reaction (**5e**, R^1 = R^3 = CH_3, R^2 = H; 34% isolated yield), and **7e** was obtained as a single product in 64% overall yield.[14] Among the cases in Table I, especially rewarding is the formation of trisubstituted *Z* olefin **7f**. The *E* isomer was not detectable.[15] The structures of **7f** and its *E* isomer were determined on the basis of the nuclear Overhauser effect.[16] Irradiation of the allylic methylene protons of *E* isomer, prepared by alkylation of neophylsulfonyl methyllithium with (*E*)-2-methyl-2-butenyl bromide, enhanced the area intensity of the olefinic proton by 15%, whereas in **7f** irradiation of the analogous protons showed no effect on the intensity of the olefinic proton signal.

As expected, partial hydrogenation of **5b** (1 atm of H_2 for 10 min at ambient temperature in CH_3OH in the presence of 3 equiv of pyridine)[17] furnished a 1:1 mixture of (*E*)-2- and (*E*)-3-hexenyl neophyl sulfones in 63% yield. An attempted reduction of **5b** with $NaBH_4$ (0.33 molar equiv at 0 °C in CH_3OH) failed and gave 1,3-hexadienyl neophyl sulfone in 64% yield.

It seems worthwhile to consider some mechanistic aspects of the somewhat unusual regio- and stereoselectivities of the present reaction. The stereocontrol might be rationalized in terms of protonation of the *Z*-allylic anion generated kinetically through intermediate (*Z*)-**10**[18] (due to either steric repulsion between R^1 and Pd or inherent stability of the *Z*-allylic anion as compared with the *E* counterpart;[19] Scheme II). In partial support of an intermediacy of allylic anion, it was observed that upon treatment of [1-[(neophylsulfonyl)methyl]-1,2-dimethyl-π-allyl]palladium chloride with DMG in CH_3OD selective monodeuteration took place at the 2-position of 2,3-dimethyl-3-butenyl neophyl sulfone. Taking into consideration the lack of regiocontrols in eq 2 and for other π-allylpalladium complexes,[20] the high regiocontrol in Scheme I might be a result of some kind of participation of the sulfonyl group, which involves a coordination of the sulfonyl oxygen to palladium(II) and also might involve a hydrogen bonding between the sulfonyl oxygen and the hydroxyl group of DMG to form a tricyclic intermediate as depicted in (*E*)-**10** and (*Z*)-**10**. Studies are in progress which are focussed on an elucidation of mechanism, an extension to reactions with electrophiles other than proton, and the stereoselective synthesis of trisubstituted olefins functionalized by groups other than a sulfonyl group.

Acknowledgment. Partial support from the Ministry of Education, the Japanese Government (Grant-in-Aid for Scientific Research No. 575559 and 443020 (A)), is gratefully acknowledged.

Registry No. 3, 77944-68-4; (*E*)-**4a**, 2004-70-8; (*Z*)-**4a**, 1574-41-0; (*E*)-**4b**, 20237-34-7; (*Z*)-**4b**, 14596-92-0; (*E*)-**4c**, 32763-70-5; (*Z*)-**4c**, 66597-11-3; (*E*)-**4d**, 64234-49-7; (*Z*)-**4d**, 77983-47-2; (*E,E*)-**4e**, 5194-51-4; (*Z,Z*)-**4e**, 6108-61-8; (*E*)-**4f**, 2787-43-1; (*Z*)-**4f**, 2787-45-3; **5a**, 77944-69-5; **5b**, 77944-70-8; **5c**, 77944-71-9; **5d**, 77944-72-0; **5e**, 77944-73-1; **5f**, 77944-74-2; **6a**, 77944-75-3; **6b**, 77944-76-4; **7a**, 77944-24-2; **7b**, 77944-25-3; **7c**, 77944-26-4; **7d**, 77944-27-5; **7e**, 77944-28-6; **7f**, 77944-29-7; **8a**, 77944-30-0; **8b**, 77944-31-1; **9**, 77944-32-2; (*Z*)-1-*p*-tolyl-5-phenylhex-3-ene, 77944-33-3; (*Z*)-1-*p*-tolyl-5-phenylhex-2-ene, 77944-34-4; (*E*)-2-hexenyl neophyl sulfone, 77944-35-5; (*E*)-3-hexenyl neophyl sulfone, 77944-36-6.

(13) All new compounds have been fully characterized by spectral means and elemental compositions.
(14) The large discrepancy between the yields of **5e** and **7e** may be due to decomposition of **5e** during column purification.
(15) The retention times of **9** and **7f** and its *E* isomer on VPC (SiDC550, 240 °C, He gas) are 6.5, 8.2, and 9.0 min, respectively.
(16) Gaudemer, A. In "Stereochemistry"; Kagan, H. B., Ed.; Georg Thieme Verlag: Stuttgart, 1977; Vol. 1.
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(20) Lawrence, R. V.; Ruff, J. K. *J. Chem. Soc., Chem. Commun.* **1976**, 9.

Yoshinao Tamaru, Masahiro Kagotani
Ryoshu Suzuki, Zen-ichi Yoshida*
Department of Synthetic Chemistry
Kyoto University
Yoshida, Kyoto 606, Japan
Received April 24, 1981

A Novel Synthesis of the Tricyclic Nucleus of Verrucarol

Summary: A substance possessing the ABC rings of verrucarol has been prepared, using a photochemical cycloaddition of acetylene and a cyclobutenyl carbinol → cyclopentenol rearrangement as key constructions for the C ring.

Sir: The biologically potent verrucarins and roridins, exemplified by verrucarin A (**1**), are macrocycles based on verrucarol (**2**) or a closely related nucleus of the trichothecane group.[1] A number of approaches to the synthesis

(1) Tamm, Ch.; *Fortschr. Chem. Org. Naturst.* **1974**, *31*, 63.

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