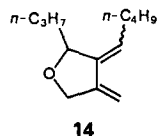


on C(2), while little effect has been observed with the minor isomer, in which the bulky endo siloxy group might prevent rotation of the phenyl group. The stereochemistry of other products, **6a**, **6b**, and **8b**, has been assigned by spectral comparison with **8a**.⁷ It should be mentioned here that the preference of the C(8)-exo isomer is the same as the stereoselection observed in the cobalt-promoted cyclization.²¹ⁿ Higher stereoselections have been attained with alkylacetylenes than with phenylacetylenes (**6a** versus **6b** and **8a** versus **8b**). The stereoselection did not depend on the solvent polarity (entries 3-5, 7, and 8). (5) A six-membered ring was also formed from a 1,7-enyne system (entry 11), tricyclic product (**12**) being formed as a single stereoisomer.⁸

tert-Butyl isocyanide could be used in place of 2,6-dimethylphenyl isocyanide. The primary products, cyclic imines, were directly hydrolyzed [CSA (1 equiv), THF/H₂O (5:1), room temperature, 17 h] to the corresponding ketones in approximately 40% overall yields, as shown in Scheme I. The stereoselectivities were similar to those observed with the aromatic isocyanide. Ketones **13** were also obtained by acidic hydrolysis of **6** under similar conditions in about 50% yield.

Although the mechanism has not yet been clarified, at least two possible mechanisms may be envisaged, as shown in Scheme II. One involves nickelacyclopentene intermediates (A)⁹ which undergo insertion of isocyanide,¹⁰ while the other proceeds through iminonickelacyclobutene intermediates (B)^{11,12} prior to the participation of the olefin part. The cyclization was completely inhibited by a bidentate ligand such as Ph₂P(CH₂)₂PPh₂ and also sensitive to the nickel-to-isocyanide ratios; no cyclization products were obtained in the presence of 3 equiv of isocyanide although the starting enynes were consumed. Cyclic 1,3-dienes anticipated from Trost's recent study⁴ were obtained as byproducts not from aromatic acetylenes but from aliphatic ones, e.g., **14** from **5b**,



14

especially in the absence of isocyanide. These observations might be pertinent to the elucidation of the mechanism, but we must wait for further studies to visualize the mechanism more clearly. The present reaction should be synthetically useful and may be added as a new member in a list of a variety of nickel-promoted carbon-carbon bond-forming reactions.¹³

Acknowledgment. We thank H. Fujita for measurements of 400-MHz NMR spectra.

Supplementary Material Available: A typical experimental procedure for the preparation of **6a** and spectral data for **2**, **4**, **6**, **8**, **10**, **12**, and **14** (4 pages). Ordering information is given on any current masthead page.

(7) In ¹H NMR spectra, the proton on C(8) appears at a higher field in exo isomers than in endo.

(8) The stereochemistry of **12** has not yet been determined, since the same stereoselection as other products may predict an α isomer at the newly formed bridgehead carbon and a boat form of the six-membered middle ring.

(9) Formation of nickelacyclopentanes²¹ and nickelacyclopentadienes from nickel(0) complexes with ethylene and acetylenes, respectively, has been reported. Eisch, J. J.; Damasevitz, G. A. *J. Organomet. Chem.* **1975**, *96*, C19.

(10) A closely related reaction is the formation of cyclic imines from bis(π-allyl)nickels and an isocyanide: Baker, R.; Cookson, R. C.; Vinson, J. R. *J. Chem. Soc., Chem. Commun.* **1974**, 515. Baker, R.; Copeland, A. H. *Tetrahedron Lett.* **1976**, 4535.

(11) Some bis(isocyanide)(acetylene)nickel(0) complexes have been isolated.^{3b} Dickson, R. S.; Ibers, J. A. *J. Organomet. Chem.* **1972**, *36*, 191. It has also been reported that the reaction of tetrakis(isocyanide)nickel(0) with diphenylacetylene affords diiminocyclobutenes: Suzuki, Y.; Takizawa, T. *J. Chem. Soc., Chem. Commun.* **1972**, 837.

(12) **Note Added in Proof.** Eisch and his co-workers reported several years ago nickel(0)-mediated reactions of diphenylacetylene with trimethylsilyl isocyanide and proposed an iminonickelacyclobutene intermediate: Eisch, J. J.; Aradi, A. A.; Han, K. I. *Tetrahedron Lett.* **1983**, *24*, 2073.

(13) Tamao, K.; Kumada, M. In *The Chemistry of the Metal-Carbon Bond*; Hartley, F. R., Patai, S., Eds.; John Wiley: Chichester, 1987; Vol. 4, pp 819-887. Jolly, P. W. In *Comprehensive Organometallic Chemistry*; Wilkinson, G., Stone, F. G. A., Abel, E. W., Eds.; Pergamon Press: Oxford, 1982; Vol. 8, pp 613-797.

Regioselective Double Vicinal Carbon-Carbon Bond-Forming Reactions of Electron-Deficient Alkenes by Use of Allylic Stannanes and Organoiodo Compounds

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The introduction of two different carbon-functional groups into a carbon-carbon double bond of unsaturated molecules is of great value in organic synthesis. A number of approaches have been advanced to this problem for α,β-unsaturated ketone systems in recent years.¹ Most of these approaches involve the conjugated addition of a carbon nucleophile to the β-carbon of the enones, followed by trapping the enolate at the α-carbon with a carbon electrophile. However, such a three-component coupling reaction has been less well developed for the other unsaturated compounds.²⁻⁵ We now report a novel type of double vicinal C-C bond-forming reactions on electron-deficient alkenes by use of allylic stannanes and organoiodo compounds.^{6,7}

A benzene solution of 1,1-dicyano-2-phenylethene (**1a**, 1 mmol), allyltributylstannane (**2a**, 2 mmol), and methyl iodide (5 mmol) in the presence of azobis(isobutyronitrile) (AIBN, 0.2 mmol) was refluxed for 6 h under a nitrogen atmosphere⁸ (see Scheme I). Workup of the reaction mixture by partition between acetonitrile and hexane followed by column chromatography on silica gel gave 4,4-dicyano-5-phenyl-1-hexene (**3a**) as a sole product in 85% yield. In a similar manner, 1,1-dicyano-2-(*p*-substituted phenyl)ethenes were converted into the corresponding 5-aryl-4,4-dicyano-1-hexene derivatives in good yields.⁹ The electron-donating substituents on the phenyl ring of dicyanoethenes reduced the yields of products. The allyl function from allylstannane was regioselectively introduced into the α-carbon from the cyano group of the 1,1-dicyanoethenes and the methyl group from methyl iodide into the β-carbon.

Similarly a three component coupling reaction on 1,1-dicyano-2-phenylethene occurred by using a combination of allyl and 2-methyl-2-propenyltributylstannane¹⁰ with a variety of organoiodo compounds such as alkyl, allyl, and benzyl iodides as well as iodobenzene. The reactivity of alkyl iodides decreased in the following order: primary > secondary > tertiary. Allyl bromide and chloride could be utilized for this coupling reaction

(1) For general reviews of three component C-C coupling reactions, see: (a) Noyori, R.; Suzuki, M. *Angew. Chem., Int. Ed. Engl.* **1986**, *25*, 262. (b) Taylor, R. J. K. *Synthesis* **1985**, 364.

(2) Corey, E. J.; Katzenellenbogen, T. A. *J. Am. Chem. Soc.* **1969**, *91*, 1851.

(3) Celebuski, J.; Rosenblum, M. *Tetrahedron* **1985**, *41*, 5741.

(4) Zaitseva, N. T.; Grebenyuk, A. D. *Zh. Org. Khim.* **1969**, *5*, 904.

(5) For intramolecular three component coupling reactions, see: Moriya, O.; Kakihana, M.; Urata, Y.; Suguzaki, T.; Ueno, Y.; Endo, T. *J. Chem. Soc., Chem. Commun.* **1985**, 1401.

(6) For recent reviews of the chemistry of organotin compounds, see: (a) Pereyre, M.; Quintard, J.-P.; Rahm, A. *J. Organomet. Chem. Libr.* **1981**, *12*, 213-240. (b) Davies, A. G.; Smith, P. J. In *Comprehensive Organometallic Chemistry*; Wilkinson, G., Stone, F. G., Abel, E. W., Eds.; Pergamon: Oxford, England, 1982; Vol. 2, pp 519-627. (c) Giese, B. *Radicals in Organic Synthesis, Formation of Carbon-Carbon Bonds*; Pergamon: Oxford, England, 1986.

(7) For C-C coupling reaction by use of allylic stannanes, see: (a) Keck, G. E.; Enholm, E. J.; Yates, J. B.; Wiley, M. R. *Tetrahedron* **1985**, *41*, 4079. (b) Kosugi, M.; Kurino, K.; Takayama, K.; Migita, T. *Ibid.* **1973**, *56*, C11. Webb, R. R.; Danishefsky, S. *Tetrahedron Lett.* **1983**, *24*, 1357. Russell, G. A.; Herold, L. L. *J. Org. Chem.* **1985**, *50*, 1037. (c) Borg, R. M.; Mariano, P. S. *Tetrahedron Lett.* **1986**, *27*, 2821. Maruyama, K.; Imahori, H.; Osuka, A.; Takuwa, A.; Tagawa, H. *Chem. Lett.* **1986**, 1719. Mizuno, K.; Toda, S.; Otsuji, Y. *Chem. Lett.* **1987**, 203. *Nippon Kagaku Kaishi* **1987**, 1183.

(8) Benzoyl peroxide could also be utilized as a radical initiator, but it was less effective.

(9) All the new compounds obtained in this study showed satisfactory spectral data (¹H NMR, ¹³C NMR, IR, and mass) and elemental analyses.

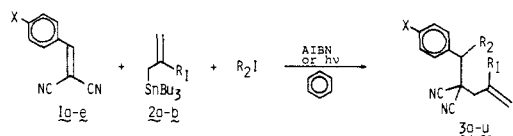
(10) When 3-methyl-2-butenyltributylstannane and benzyltributylstannane were used, no coupling products were obtained; cf. ref 7a.

Table I. Double Vicinal C-C Bond-Forming Reactions on Electron-Deficient Alkenes by Allylic Stannanes and Organoiodo Compounds

electron-deficient alkene	allylic stannane	organoiodo compd	method ^a	reactn time, ^f h	product		yield, ^{b,i} %
					R ₁	R ₂	
1a , X = H	2a , R ₁ = H	MeI	A; B	6; 12	3a	H Me	85; 65
1b , X = CN	2a	MeI	A; B	6; 6	3b	H Me	88; 60
1c , X = Cl	2a	MeI	A; B	6; 12	3c	H Me	90; 66
1d , X = Me	2a	MeI	A	12	3d	H Me	66
1e , X = OMe	2a	MeI	A	24	3e	H Me	29
1a	2a	<i>n</i> -C ₃ H ₇ I	A; B	12; 12	3f	H <i>n</i> -C ₃ H ₇	51; 50
1a	2a	<i>n</i> -C ₄ H ₉ I	A; B	11	3g	H <i>n</i> -C ₄ H ₉	67; 92
1a	2a	<i>n</i> -C ₇ H ₁₅ I	A	15	3h	H <i>n</i> -C ₇ H ₁₅	76
1a	2a	<i>i</i> -C ₃ H ₇ I	A; B	12; 12	3i	H <i>i</i> -C ₃ H ₇	65; 75
1a	2a	<i>c</i> -C ₆ H ₁₁ I ^c	A	12	3j	H <i>c</i> -C ₆ H ₁₁	47
1a	2a	<i>t</i> -C ₄ H ₉ I	A; B	24; 38	3k	H <i>t</i> -C ₄ H ₉	25; 46 ^d
1a	2a	CH ₂ =CHCH ₂ I ^e	A	10	3l	H CH ₂ =CHCH ₂	73
1a	2a	PhCH ₂ I	A	6	3m^f	H PhCH ₂	82
1a	2a	PhI	A	48	3n	H Ph	13
1a	2a	ClCH ₂ (CH ₂) ₂ CH ₂ I	B	18	3o	H ClCH ₂ (CH ₂) ₃	75
1a	2a	Br-CH ₂ (CH ₂) ₂ CH ₂ I	B	20	3p	H Br-CH ₂ (CH ₂) ₃	91
1a	2a	HOCH ₂ (CH ₂) ₂ CH ₂ I	B	12	3q	H HOCH ₂ (CH ₂) ₃	40
1a	2a	CH ₃ COCH ₂ CH ₂ I	A	12	3r	H CH ₃ COCH ₂ CH ₂	55
1a	2a		A; B		3s^h	H	60; 54
1a	2b , R ₁ = Me	MeI	A	12	3t	Me Me	87
1a	2b	CH ₂ =CMeCH ₂ I	A	12	3u	Me CH ₂ =CMeCH ₂	65
4a , Y = H	2a	MeI	A	60	5a	H Me	38
4b , Y = CN	2a	MeI	A	60	5b	H Me	39
6a , R ₃ = Et	2a	MeI	A	12	7a	H Me	60
6b , R ₃ = Bu	2a	MeI	A	12	7b	H Me	61

^aMethod A: A mixture of 1, 2, organoiodo compound, and AIBN (1:2:5:0.5 ratio) in benzene was refluxed under a nitrogen atmosphere. Method B: A benzene solution of 1, 2, and organoiodo compound (1:2:5 ratio) was irradiated through a Pyrex filter under a nitrogen atmosphere. ^bIsolated yield based on 1-aryl-2,2-dicyanoethene. ^cCyclohexyl iodide. ^d1,1-Dicyano-3,3-dimethyl-2-phenylbutane was also obtained as a minor product. ^eWhen allyl chloride or allyl bromide was used in the place of allyl iodide, the yield of 3l appreciably decreased: method A, trace for allyl chloride and 15% for allyl bromide; method B, 12% for allyl chloride and 46% for allyl bromide. ^fMp 94–94.5 °C. ^gGonzalez, F. B.; Bartlett, P. A. *Org. Synth.* **1985**, *64*, 175. ^hMp 162–163 °C. ⁱThe number preceding the semicolon is the number that goes with method A; the number following the semicolon is the number that goes with method B.

Scheme I

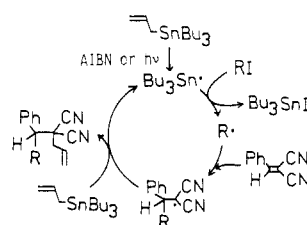


in place of allylic iodides, but the reaction with these halides occurred less efficiently. No coupling reaction occurred with alkyl bromides and chlorides. The results are summarized in Table I.

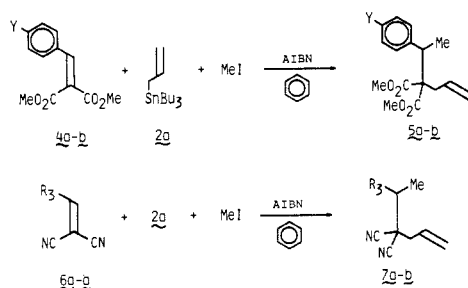
Irradiation of the dicyanoethene–allylic stannane–alkyl iodide systems in benzene with a Pyrex filtered light (>280 nm) without added AIBN afforded the same products in good yields.

A possible mechanism for the three component coupling reaction is shown in Scheme II. The primary process is the AIBN-initiated or photolytic formation of a tributylstannyl radical.^{6a,7a} The stannyl radical abstracts an iodine atom from an organoiodo compound (R₂I) to give a free radical (R₂•), which adds to an electron-deficient alkene.^{11,12} The radical intermediate thus produced attacks an allylic stannane and regenerates the stannyl radical.¹³

Scheme II



Scheme III



(11) The formation of tributyltin iodide was confirmed by comparison with the spectral properties of the authentic specimen: Jones, W. J.; Evans, D. P.; Gulwell, T.; Griffiths, D. C. *J. Chem. Soc.* **1935**, 39.

(12) A similar mechanism would operate for the formation of 5a,b and 7a,b.

The coupling reaction could be extended to the other electron-deficient alkenes. Thus, 1-aryl-2,2-bis(methoxycarbonyl)-

ethenes (**4a,b**) and 1,1-dicyano-1-alkenes (**6a,b**) underwent the three component coupling reactions with allylic stannanes and methyl iodide, giving the corresponding products **5a,b** and **7a,b**^{14,15} (see Scheme III).

An important feature of the above reactions is that the coupling reactions occur efficiently under neutral, mild conditions in a highly regioselective manner. The functional group compatibility in these reactions is also wide. For example, this reaction tolerates the presence of some functional groups and can be applied to the compounds with carbonyl and lactone functionalities (Table I).

The detailed mechanism and synthetic applications of the above three component coupling reaction are now under investigation.

Acknowledgment. This work was partially supported by a Grant-in-Aid for Special Project Research from the Ministry of Education, Science, and Culture of Japan (no. 61225024 and 62215032).

Supplementary Material Available: NMR data given for **3a-u**, **5a,b**, and **7a,b** (9 pages). Ordering information is given on any current masthead page.

(13) The nucleophilic alkyl radical first attacks 1,1-dicyanoethenes rather than allylic stannanes; however, the new radical so produced has an electrophilic nature and attacks allylic stannanes in a manner shown in Scheme II: Fleming, I. *Frontier Orbitals and Organic Chemical Reactions*; John Wiley & Sons: London, 1976; Chapter 5.

(14) The reactivity of the electron-deficient alkenes decreased in the order: **1a** > **6a** > **4a**.

(15) (*E*)-1-Nitro-2-phenylethene, (*E*)-1-cyano-2-phenylethene, 1,1-dicyano-2-phenyl-1-propene, and cyclohexylenepropanedinitrile were unreactive under similar conditions.

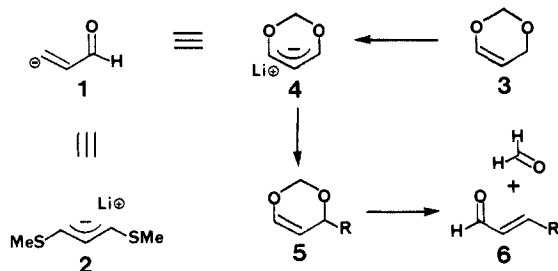
Metalation and Alkylation of 4*H*-1,3-Dioxin: A New β -Acyl Vinyl Anion Equivalent

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Synthetic equivalents of the β -acyl vinyl anion **1** have been extensively pursued² since the first report by Corey³ that 1,3-bis(methylthio)allyllithium (**2**) functions in this capacity. All of



these methods require at least one reagent-mediated step to unravel

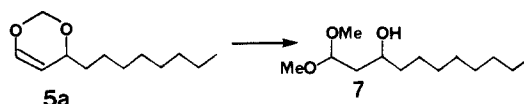
(1) Fellow of the Alfred P. Sloan Foundation, 1985-1987. Address correspondence to Department of Chemistry, 152 Davey Laboratory, The Pennsylvania State University, University Park, PA 16802.

(2) (a) Reich, H. J.; Clark, M. C.; Willis, W. W., Jr. *J. Org. Chem.* **1982**, *47*, 1618. (b) Oshima, K.; Yamamoto, H.; Nozaki, H. *Bull. Chem. Soc. Jpn.* **1975**, *48*, 1567. (c) Wada, M.; Nakamura, H.; Taguchi, T.; Takei, H. *Chem. Lett.* **1977**, 345. (d) Cohen, T.; Bennett, D. A.; Mura, A. J., Jr. *J. Org. Chem.* **1976**, *41*, 2506. (e) Otera, J.; Mandai, T.; Moriyama, T.; Nakayama, Y.; Sugino, K.; Kawada, M. *Tetrahedron Lett.* **1984**, *25*, 5913. (f) Ogura, K.; Iihama, T.; Takahashi, K.; Iida, H. *Tetrahedron Lett.* **1984**, *25*, 2671. (g) Clinet, J.-C.; Linstrumelle, G. *Ibid.* **1980**, *21*, 3987. (h) Bakuzis, P.; Bakuzis, M. L. F.; Weingarten, T. F. *Ibid.* **1978**, 2371. (i) Lansbury, P. T.; Britt, R. W. *J. Am. Chem. Soc.* **1976**, *98*, 4577. (j) Corbel, B.; Paugam, J.-P.; Dreux, M.; Savignac, P. *Tetrahedron Lett.* **1976**, 835. (k) Carlson, R. M.; Jones, R. W.; Hatcher, A. S. *Ibid.* **1975**, 1741. (l) Kondo, K.; Tunemoto, D. *Ibid.* **1975**, 1007. (m) Nakai, T.; Shiono, H.; Okawara, M. *Ibid.* **1974**, 3625. (n) Leroux, Y.; Roman, C. *Ibid.* **1973**, 2585. (o) Leroux, Y.; Mantione, R. *Ibid.* **1971**, 591, 593. (p) Leroux, Y.; Mantione, R. *J. Organomet. Chem.* **1971**, *30*, 295.

(3) Corey, E. J.; Erickson, B. W.; Noyori, R. *J. Am. Chem. Soc.* **1971**, *93*, 1724.

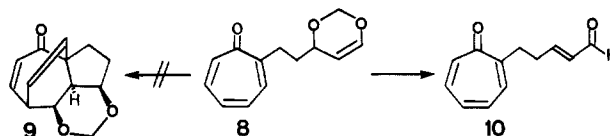
the α,β -unsaturated aldehyde **6** from the alkylated synthetic equivalent. For example, the Corey method requires a hydrolytic step with use of mercuric chloride in warm, aqueous acetonitrile.³ In some situations, it may become necessary to generate the α,β -unsaturated aldehyde by using even milder conditions. We describe herein a possible solution to this problem. In particular, we show that a new β -acyl vinyl anion equivalent, allyl anion **4**, affords alkylation products which then are simply heated in order to promote a facile bis-hetero retro-Diels-Alder reaction (**5** \rightarrow **6**) and unmask the α,β -unsaturated aldehyde.

We have found that 4*H*-1,3-dioxin (**3**)⁴ undergoes rapid metalation upon treatment with *sec*-butyllithium in THF at -78°C to provide only the allylic anion **4**.⁵ The various electrophiles employed in alkylation reactions with allyl anion **4** are shown in Table I. Typically, the alkylating agent was added to a solution of anion **4** (1.5 equiv, THF, -78°C) and allowed to warm to room temperature before quenching the reaction mixture with aqueous NaHCO_3 . The resulting 4-substituted 4*H*-1,3-dioxins **5** were then



isolated in good yields by using silica gel chromatography. It is worthwhile to note that none of the compounds **5** showed any tendency to decompose on silica gel. In fact, octyldioxin (**5a**) is stable to pyridinium tosylate (0.1 equiv) in refluxing MeOH (12 h). However, treatment of **5a** under more acidic conditions (HCl, MeOH, 0°C ; 1 h) did provide the β -hydroxy acetal **7** (90%).

Although liberation of the desired α,β -unsaturated aldehydes **6** could be accomplished by using aqueous acid, a much more convenient and milder procedure was discovered serendipitously. Thus, an attempted intramolecular Diels-Alder cycloaddition reaction of 2-[2-(dioxinyl)ethyl]tropone⁸ (**8**) in refluxing toluene



gave none of the desired cycloadduct **9** but, instead, furnished aldehyde **10** and "white material" that collected on the condenser. Evidently, a bis-hetero retrocycloaddition⁹ reaction had intervened. It might be argued that this result should have been anticipated based on a report that benzyldenemalonaldhyde¹⁰ equilibrates with the Diels-Alder cycloadduct dimer at room temperature and that acrolein and hexafluoroacetone produce a [4 + 2] cycloadduct.¹¹ Nonetheless, the susceptibility of substituted 4*H*-1,3-dioxins to [4 + 2] retrocycloaddition has not been previously documented,¹² despite numerous preparations of these com-

(4) Anteunis, M.; Camerlynck, R. *Tetrahedron* **1975**, *31*, 1837.

(5) This result is contrasted with the work of Gould⁶ who reported that deprotonation of *cis*-1,3-dibutoxypropene under similar conditions afforded only the α -vinyl anion. To rationalize this regioselectivity, Gould and Rossi⁷ employed ab initio calculations which suggested that the α -vinyl C-H bond of *cis*-1,3-dibutoxypropene is weakened and attributed this effect to a hyperconjugative interaction between the sp^2 lone pair on the vinyl oxygen and the adjacent C-H σ^* orbital. Overlap of this type (antiperiplanar) is geometrically precluded for dioxin **3**, and, therefore, the kinetic acidity of the α -vinyl C-H bond in **3** may be diminished.

(6) Gould, S. J.; Remillard, B. D. *Tetrahedron Lett.* **1978**, 4353.

(7) Rossi, A. R.; Gould, S. J.; Remillard, B. D. *Tetrahedron Lett.* **1978**, 4357.

(8) (a) Funk, R. L.; Bolton, G. L. *J. Am. Chem. Soc.* **1986**, *108*, 4655. (b) Funk, R. L.; Bolton, G. L. *J. Org. Chem.* **1987**, *52*, 3173.

(9) (a) Ripoll, J.-L.; Rouessac, A.; Rouessac, F. *Tetrahedron* **1978**, *34*, 19. (b) Lasne, M.-C.; Ripoll, J. L. *Nouv. J. Chim.* **1982**, 6.

(10) (a) Reichardt, C.; Yun, K.-Y. *Tetrahedron Lett.* **1982**, *23*, 3163. (b) Reichardt, C.; Yun, K.-Y.; Massa, W.; Schmidt, R. E. *Liebigs Ann. Chem.* **1985**, 1987.

(11) Fokin, A. V.; Kolomiets, A. F.; Krolevets, A. A. *Izv. Akad. Nauk SSSR* **1978**, 849.