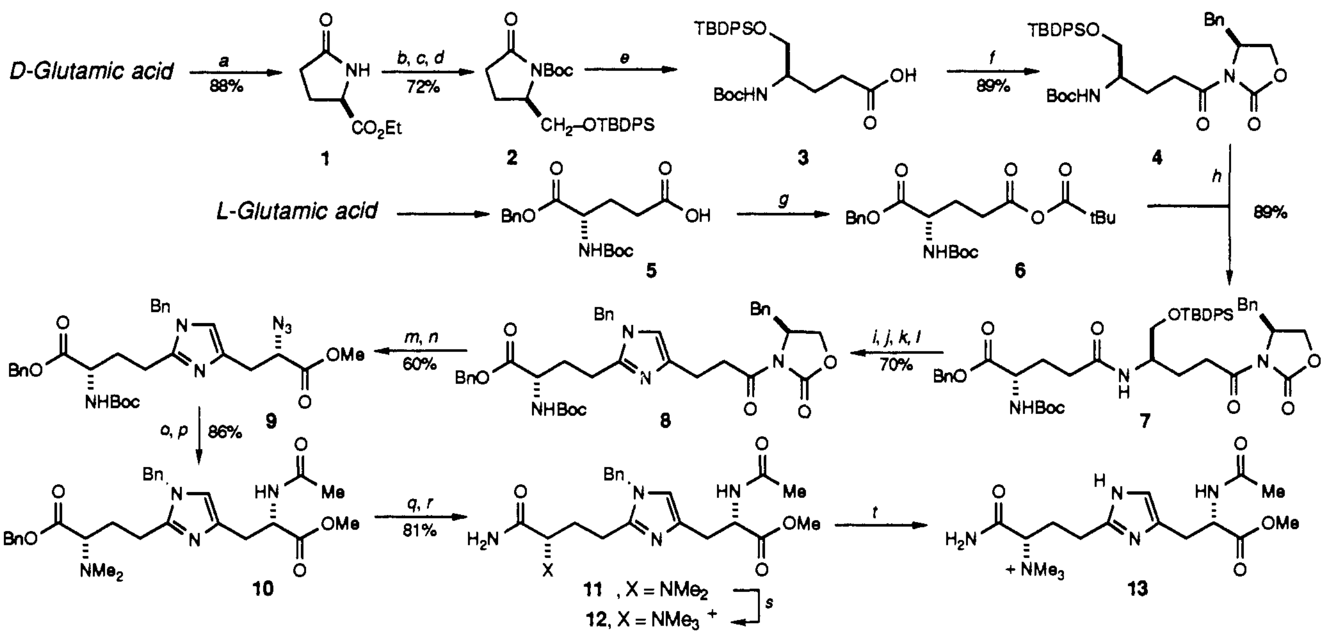
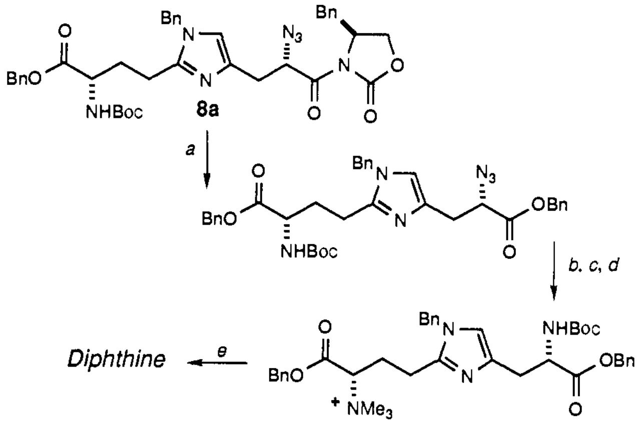
Scheme I[a]



[a]$SOCl_2$, EtOH; KOH; 150 °C. [b]$LiBH_4$. [c]TBDPSCl, Et_3N, DMAP. [d]BOC_2O, Et_3N, DMAP. [e]LiOOH. [f]t-BuCOCl, Et_3N; XpLi. [g]t-BuCOCl, Et_3N. [h]TFA; 6, Et_3N. [i]HF-Pyr. [j]Swern. [k]$BnNH_2$. [l]PPh_3, C_2Cl_6, Et_3N. [m]KHMDS; trisyl-N_3; HOAc. [n]MeOH. [o]AcSH. [p]TFA; CH_2O, $NaCNBH_3$. [q]H_2, Pd/C, EtOH/H_2O. [r]t-BuCOCl, Et_3N; NH_3. [s]MeI. [t]H_2 (50 psi), Pd black, HOAc/H_2O.

Scheme II[a]



[a]BnOH, imidazole. [b]TFA; CH_2O, $NaCNBH_3$. [c]$SnCl_2$; BOC_2O, $NaHCO_3$. [d]MeI. [e]H_2 (50 psi), Pd black, HOAc/H_2O.

be selectively hydrogenolyzed (10% Pd/C, 9:1 EtOH/H_2O, 15 psi of H_2, 15 h) without concomitant removal of the imidazoyl benzyl moiety and that the derived acid could be transformed to the primary amide **11** in good yield via the derived mixed pivaloyl anhydride. In the next step, selective methylation of the dimethylamino nitrogen, in the presence of the imidazole ring, was achieved with excess methyl iodide (MeOH, 48 h, 25 °C). The final N-debenzylation of **12** was achieved with Pd black (4:1 HOAc/H_2O, 50 psi of H_2, 2-3 days).

In addition, (*S*,*S*)- and (*S*,*R*)-diphthine were prepared from the *S* azido imide **8a** and the enantiomeric (*R*) azido imide **8b**, respectively (Scheme II).[16] All of the diastereomers were distinguishable by NMR, suggesting that no epimerization had occurred in the synthesis of the amino acids. Bodley has demonstrated that the synthetic and natural diphthine coeluted during amino acid hydrolysis.[17]

Future publications will report the synthesis of other diphthamide diastereomers and the associated studies with diphtheria toxin.

Acknowledgment. Support has been provided by the National Institutes of Health. The NIH BRS Shared Instrument Grant Program (1-S10-RR04870) and the NSF (Grant CHE88-14019) are acknowledged for providing NMR facilities. We are grateful to Professors R. J. Collier (Harvard Medical School) and J. W. Bodley (University of Minnesota Medical School) for their involvement in this collaboration.

Supplementary Material Available: Complete experimental procedures as well as spectral and analytical data for all compounds (10 pages). Ordering information is given on any current masthead page.

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[16] For simplicity, only the *S*,*S* products are shown.

[17] Bodley, J. W.; Donovan, M., University of Minnesota, unpublished results.

Interception of a Thermally Generated Biradical by Intramolecular Hydrogen Atom Transfer

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Thermally generated, presumably singlet, biradicals are arguably among the most elusive of reactive intermediates. While triplet biradicals and certain classes of specially stabilized singlet biradicals can be directly detected[1] or trapped in bimolecular reactions,[2] it has hitherto been difficult to find reactions that could

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[1] Examples include the following: (a) Herman, M. S.; Goodman, J. L. *J. Am. Chem. Soc.* **1988**, *110*, 2681. (b) Adam, W.; Grabowski, S.; Wilson, R. M.; Hannemann, K.; Wirz, J. *J. Am. Chem. Soc.* **1987**, *109*, 7572. (c) Dowd, P.; Chang, W.; Paik, Y. H. *J. Am. Chem. Soc.* **1987**, *109*, 5284. (d) Zilm, K. W.; Merrill, R. A.; Greenberg, M. M.; Berson, J. A. *J. Am. Chem. Soc.* **1987**, *109*, 1567. (e) Kelley, D. F.; Mazur, M. R.; Rentzepis, P. M.; Berson, J. A. *J. Am. Chem. Soc.* **1982**, *104*, 3764. (f) Doubleday, C., Jr. *Chem. Phys. Lett.* **1982**, *85*, 65. (g) Closs, G. L.; Miller, R. J. *J. Am. Chem. Soc.* **1981**, *103*, 3586. (h) Kaupp, G.; Teufel, E.; Hopf, H. *Angew. Chem.* **1979**, *91*, 232. (i) Muller, J. F.; Muller, D.; Dewey, H. J.; Michl, J. *J. Am. Chem. Soc.* **1978**, *100*, 1629. (j) Closs, G. L.; Doubleday, C. E. *J. Am. Chem. Soc.* **1973**, *95*, 2735.

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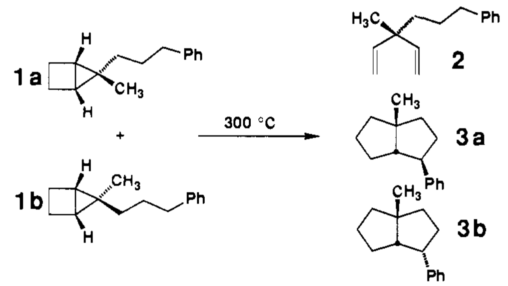
Scheme I

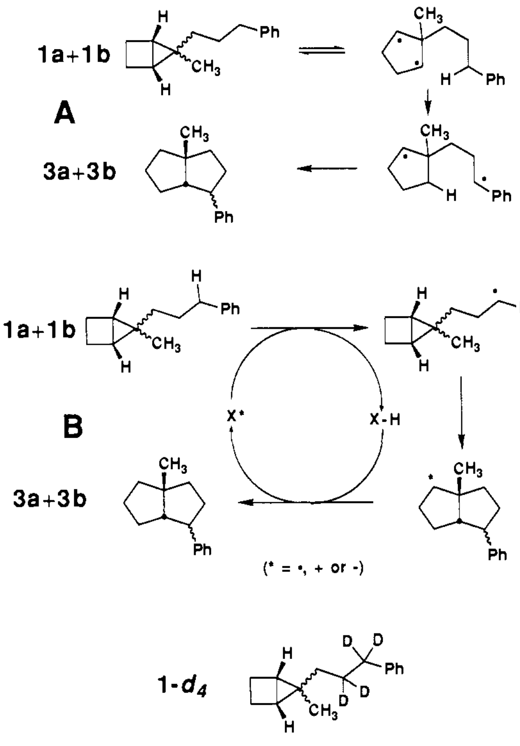


compete with the extremely rapid intramolecular bond formation of unstabilized singlet-state biradicals. This feature of their behavior has made the participation of singlet biradicals as true intermediates the subject of hot debate in many reactions[3] and, in reactions where they are generally agreed to be intermediates, has greatly hampered study of their properties. We have recently suggested that, at least in some cases, their behavior could be further obscured by the possibility that product ratios from singlet biradicals may not be correctly predicted by the traditional models of kinetics.[4]

In the particular case of cyclopentane-1,3-diyls, recent work has shown that those stabilized by allylic or cyclopropylcarbinyl interactions are interceptible intermediates, but there remains the question of whether unstabilized singlet cyclopentane-1,3-diyl could be only a transition state for interconversion of bicyclo[2.1.0]pentane epimers.[5]

In this communication we show that an unstabilized, thermally generated cyclopentane-1,3-diyl can apparently be intercepted by intramolecular hydrogen atom transfer, in a manner somewhat akin to the photochemical Norrish type II reaction.[6,7] Given that a transition state must have only one negative eigenvalue to its force constant matrix, and therefore cannot give more than one product,[8] this result suggests that the present unstabilized cyclopentane-1,3-diyl derivative is *not* just a transition state.

Scheme II. Two Possible Mechanisms for the Pyrolysis Reactions and the Deuterium Distribution in the Reactant Used To Distinguish between Them[a]



[a] X* represents any catalytically active radical, cation, or anion.

Pyrolysis of a mixture of bicyclopentanes **1a** and **1b** in the gas phase at temperatures between 280 and 300 °C resulted in the formation of diene **2** and bicyclooctanes **3a** and **3b** (Scheme I) in ratios between 3.0:3.4:1 and 4.2:2.9:1, respectively, as determined by gas chromatography. Compounds **1a** and **1b** were prepared in a near 1:1 mixture and were not separated because they interconverted rapidly under the conditions of the pyrolysis. The products were shown to be stable to the reaction conditions.

Suppression of Lewis and/or Brønsted acid-catalyzed ring-opening reactions proved unusually difficult during the pyrolysis. Standard techniques such as dimethyldichlorosilane treatment of the glass surfaces or pyrolysis in the presence of 2,6-lutidine were ineffective. In Pyrex tubes, suppression of the undesired reactions could be achieved only by pyrolysis of the hydrocarbons in the presence of potassium *tert*-butoxide. Alternatively the use of lead-glass tubes was found to prevent most side reactions.[9]

The unusual conditions required to effect the clean conversion of **1a** + **1b** to **3a** + **3b** mandated consideration of an alternative mechanism for the reaction. Instead of the presumed intramolecular hydrogen transfer[10] to a reversibly formed biradical, as shown in mechanism A of Scheme II, the reaction could occur by a catalyzed process, as shown in B. The two mechanisms can be distinguished by a double-labeling crossover experiment. This experiment was conducted by preparing the reactants with four deuterium labels (**1**-d_4, shown in Scheme II). The use of four deuterium labels rather than just two was simply a matter of synthetic convenience. A 1:1 mixture of d_0 and d_4 bicyclopentanes gave **3a** and **3b** containing d_1 and d_3 products that could imply up to 30% crossover (exact amounts could not be determined because of hydrogen atom loss from the products in the mass spectrometer) when the potassium *tert*-butoxide method was used, but with <7% crossover when lead-glass tubes were used. This result suggests that in lead-glass tubes mechanism B is not operating to a significant extent and that intramolecular hydrogen transfer to a biradical has apparently been achieved.[7] If so, the

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(2) Examples from the last five years include the following: (a) Hall, H. K., Jr.; Padias, A. B.; Li, Y.; Clever, H. A.; Wang, G. *J. Chem. Soc., Chem. Commun.* **1991**, 1279. (b) Roth, W. R.; Ruhkamp, J.; Lennartz, H. W. *Chem. Ber.* **1991**, *124*, 2047. (c) Hastings, D. J.; Weedon, A. C. *Tetrahedron Lett.* **1991**, *32*, 4107. (d) Hwang, J. S.; Siddiqui, M. N.; Bukhari, A. M. *Tetrahedron Lett.* **1991**, *32*, 3711. (e) Adam, W.; Bottle, S. E. *Tetrahedron Lett.* **1991**, *32*, 1405. (f) Scaiano, J. C.; Wintgens, V.; Haider, K.; Berson, J. A. *J. Am. Chem. Soc.* **1989**, *111*, 8732. (g) Adam, W.; Platsch, W.; Wirz, J. *J. Am. Chem. Soc.* **1989**, *111*, 6896. (h) Stone, K. J.; Greenberg, M. M.; Blackstock, S. C.; Berson, J. A. *J. Am. Chem. Soc.* **1989**, *111*, 3659. (i) Roth, W. R.; Bauer, F.; Braun, K.; Offerhaus, R. *Angew. Chem., Int. Ed. Engl.* **1989**, *28*, 1056. (j) Burnett, M. N.; Boothe, R.; Clark, E.; Gisin, M.; Hassaneen, H. M.; Pagni, R. M.; Persy, G.; Smith, R. J.; Wirz, J. *J. Am. Chem. Soc.* **1988**, *110*, 2527.

(3) (a) Baldwin, J. E.; Ghatlia, N. D. *J. Am. Chem. Soc.* **1991**, *113*, 6273. (b) Houk, K. N.; Lin, Y.-T.; Brown, F. K. *J. Am. Chem. Soc.* **1986**, *108*, 554. (c) Dewar, M. J. S. *J. Am. Chem. Soc.* **1984**, *106*, 209. (d) Dewar, M. J. S.; Pierini, A. B. *J. Am. Chem. Soc.* **1984**, *106*, 203. (e) Gajewski, J. J.; Conrad, N. D. *J. Am. Chem. Soc.* **1978**, *100*, 6268. (f) Frey, H. M.; Pottinger, R. *J. Chem. Soc., Faraday Trans. 1* **1978**, *74*, 1827. (g) Baldwin, J. E.; Andrews, G. D. *J. Am. Chem. Soc.* **1976**, *98*, 6705. (h) Stephenson, L. M.; Gemmer, R. V.; Current, S. *J. Am. Chem. Soc.* **1975**, *97*, 5909. (i) Berson, J. A.; Malherbe, R. *J. Am. Chem. Soc.* **1975**, *97*, 5910. (j) Lehr, R. E.; Marchand, A. P. In *Pericyclic Reactions*; Marchand, A. P., Lehr, R. E., Eds.; Academic Press: New York, 1977; Vol. 1. (k) Goldstein, M. J.; Benzon, M. S. *J. Am. Chem. Soc.* **1972**, *94*, 7147. (l) Doering, W. von E.; Franck-Neumann, M.; Hasselman, D.; Kaye, R. L. *J. Am. Chem. Soc.* **1972**, *94*, 3833. (m) Doering, W. von E.; Toscano, V. G.; Beasley, G. H. *Tetrahedron* **1971**, *27*, 5299.

(4) (a) Carpenter, B. K. *J. Am. Chem. Soc.* **1985**, *107*, 5730. (b) Newman-Evans, R. H.; Simon, R. J.; Carpenter, B. K. *J. Org. Chem.* **1990**, *55*, 695. (c) Lyons, B. A.; Pfeifer, J.; Carpenter, B. K. *J. Am. Chem. Soc.* **1991**, *113*, 9006. (d) Peterson, T. H.; Carpenter, B. K. *J. Am. Chem. Soc.*, in press.

(5) Roth, W. R.; Bauer, F.; Breuckmann, R. *Chem. Ber.* **1991**, *124*, 2041.

(6) Turro, N. J. *Modern Molecular Photochemistry*; Benjamin/Cummins: Menlo Park, 1978; pp 364–367.

(7) There exists the formal possibility that the reaction described here proceeds by concerted cycloaddition of the C1–C4 bond of the bicyclopentane to a benzylic C–H bond, but we know of no precedent for such a reaction.

(8) Stanton, R. E.; McIver, J. W., Jr. *J. Am. Chem. Soc.* **1975**, *97*, 3632.

(9) (a) Getty, S. J.; Berson, J. A. *J. Am. Chem. Soc.* **1991**, *113*, 4607. (b) Doering, W. von E.; Beasley, G. H. *Tetrahedron* **1973**, *29*, 2231.

(10) The intramolecular transfer of hydrogen to a monoradical is predicted to be most favorable when it occurs 1–5, as here (Hunag, X. L.; Dannenberg, J. J. *J. Org. Chem.* **1991**, *56*, 5421).

biradical cannot be just the transition state for epimerization of the bicyclo[2.1.0]pentanes.

Acknowledgment. We thank Professor Jerome A. Berson, Mr. Michael Wendt, and Mr. Blair Wood for helpful suggestions on experimental procedure.

Nickel(0)-Catalyzed Alternating Copolymerization of Carbon Dioxide with Diynes to Poly(2-pyrones)

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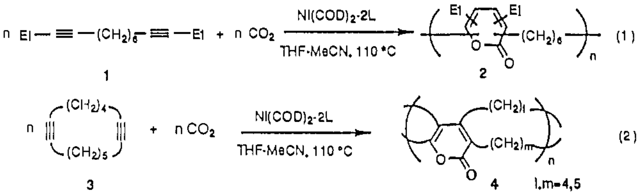
Received October 15, 1991

Use of CO_2 as a comonomer for polymer synthesis is an attractive approach to chemical utilization of CO_2, which is of great concern at the present time in relation to carbon resources and environmental problems, but there are few reports of CO_2 copolymerization which satisfy both alternating copolymerization and degree of polymerization. To our knowledge, alternating copolymerization of CO_2 with epoxides involving C–O bond formation is the only example to be cited.[1]

Recently we reported that diynes such as 1,6-heptadiyne, 1,7-octadiyne, and substituted diynes act as reactive substrates in nickel(0)-catalyzed CO_2 fixation into unsaturated hydrocarbons to afford bicyclic 2-pyrones fused with five- and six-membered carbocycles by intramolecular cyclization of diynes involving CO_2.[2] Here we report efficient alternating copolymerization of CO_2 with acyclic and cyclic diynes, which do not readily undergo intramolecular cyclization, to produce a new class of polymer, poly(2-pyrones), by nickel(0)-catalyzed intermolecular cyclization of diynes involving CO_2 (eqs 1 and 2). These are the first examples of alternating copolymerization of CO_2 with an unsaturated hydrocarbon and also one involving C–C bond formation.



When 3,11-tetradecadiyne (**1**) was treated with CO_2 under pressure in a mixed solvent of THF–MeCN[3] at 110 °C in the presence of a Ni(0) catalyst (10 mol %) generated from $Ni(COD)_2$ and 2 equiv of a tertiary phosphine ligand, a copolymer **2** was obtained by concentration of the reaction mixture under vacuum followed by precipitation with ether (eq 1, Table I).

Copolymers are pale yellow to brown solids. They are soluble in methylene chloride and chloroform, but are insoluble in ether, benzene, and hexane. Copolymers show IR and ^1H NMR absorptions assignable to a 2-pyrone ring. The most useful diagnosis of the 2-pyrone ring is by ^{13}C NMR spectroscopy.[4] The copolymers prepared in THF-MeCN exhibit five groups of ^{13}C NMR C=C and C=O absorptions characteristic of the 2-pyrone ring (Figure 1d).

Table I. Nickel(0)-Catalyzed Alternating Copolymerization of Diyne with CO_2 to Poly(2-pyrone)[a]

diyne, mmol	ligand (L)	solvent	poly(2-pyrone)		
			yield,[b] %	M_n[c]	M_w/M_n
1					
1	PEt_3	THF	50	3300	4.4
		THF–MeCN	42	8400	2.3
			59	6500 (5600)[d]	2.4
			55[g]	8200	2.9
2			86	13300	2.3
1	$P(n\text{-}C_8H_{17})_3$	THF	34	9300	3.5
		THF–MeCN	58	11400	2.4
			63	8600 (8100)[d]	3.0
2			72	17900	3.2
1			61[e]	8100	2.7
	$P(c\text{-}C_6H_{11})_3$		0		
3					
1	PEt_3	THF	27	2900	2.1
		THF–MeCN	33	4600 (4200)[d]	3.9
			49[e]	3800	3.0
	$P(n\text{-}C_8H_{17})_3$	THF	11	2100	1.7
		THF–MeCN	30	3700	3.6
2			30[f]	5300	2.9
1			53[e]	5200 (4200)[d]	3.1
	$P(c\text{-}C_6H_{11})_3$		~0		

[a] Ni/diyne = 0.10; L/Ni = 2; CO_2, 50 kg/cm^2 (initial pressure at room temperature); solvent, 5 mL THF/MeCN = 1–2 (v/v); temperature, 110 °C; time, 20 h. [b] Based on the formation of a 1:1 alternating copolymer of diyne with CO_2. [c] Determined by GPC with polystyrene standards in chloroform. [d] Determined by VPO in chloroform. [e] L/Ni = 3. [f] Time, 40 h. [g] Temperature, 90 °C.

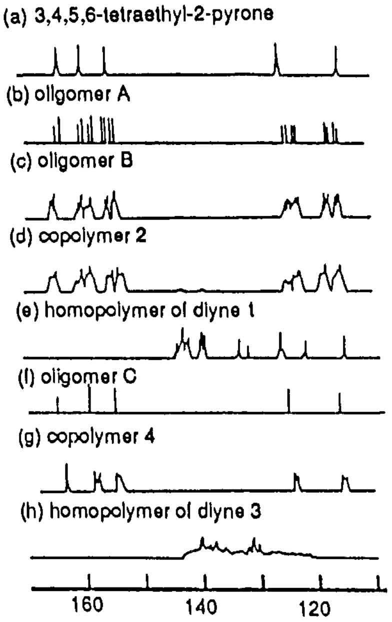


Figure 1. ^{13}C NMR spectra of copolymers and related compounds (δ, ppm).

To define a copolymer structure, preparation of co-oligomers and homopolymers of **1** were carried out. Ether-soluble co-oligomers A (15%) and B (10%) along with ether-insoluble copolymers (11%) were obtained by shortening the reaction time to 20 min. Spectroscopic data and elemental analyses demonstrate

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(1) (a) Inoue, S. *Organic and Bio-organic Chemistry of Carbon Dioxide*; Kodansha: Tokyo, 1981; p 153. (b) Aida, T.; Ishikawa, M.; Inoue, S. *Macromolecules* **1986**, *19*, 8.

(2) (a) Tsuda, T.; Sumiya, R.; Saegusa, T. *Synth. Commun.* **1987**, *17*, 147. (b) Tsuda, T.; Morikawa, S.; Sumiya, R.; Saegusa, T. *J. Org. Chem.* **1988**, *53*, 3140. (c) Tsuda, T.; Morikawa, S.; Saegusa, T. *J. Chem. Soc., Chem. Commun.* **1989**, 9. (d) Tsuda, T.; Morikawa, S.; Hasegawa, N.; Saegusa, T. *J. Org. Chem.* **1990**, *55*, 2978.

(3) (a) Walther, D.; Schønberg, H.; Dinjus, E.; Sieler, J. *J. Organomet. Chem.* **1987**, *334*, 377. (b) Behr, A.; He, R.; Juszak, K.-D.; Krüger, C.; Tsay, Y.-H. *Chem. Ber.* **1986**, *119*, 991.

(4) Staunton, J. *Comprehensive Organic Chemistry*; Pergamon: Oxford, UK, 1979; Vol. 4, p 629.

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