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Robust and Efficient, Yet Uncatalyzed, Synthesis of Trialkylsilyl-Protected Cyanohydrins from Ketones

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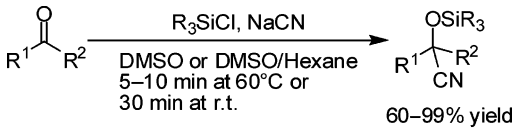

High-yielding cyanosilylation of ketones with NaCN and various chlorotrialkylsilanes in DMSO proceeds smoothly without catalysis to give silyl-protected ketone cyanohydrins. The unique role of DMSO consists in rendering naked cyanide anions that reversibly add to the C═O bond at the rate-determining step followed by fast trapping of the transient tertiary sodium cyanoalcoholates with chlorotrialkylsilanes or in situ generated cyanotrialkylsilanes. Preparatively, the reaction matches the best known catalytic cyanosilylation systems applying expensive Me_3SiCN and demonstrates unprecedented efficiency in the synthesis of sterically congested trialkylsilyl-protected cyanohydrins.

Introduction

For our study of enzyme-catalyzed enantioselective cyanohydrin syntheses,[1] we required a wide range of racemic ketone cyanohydrins, both as reference material and as starting material for enzymatic kinetic resolutions. The direct synthesis from ketones and HCN proved difficult owing to inherent thermodynamic instability of the ketone derivatives.[2] To circumvent this, cyanohydrins from ketones are generally prepared in *O*-protected form.[3] The cyanosilylation of ketones is particularly suitable since the silyl protecting groups can be removed under very mild reaction conditions. A fast, efficient, general, and cost-effective cyanosilylation of ketones is therefore required in order to develop the kinetic resolution of racemic cyanohydrins into a viable strategy.[1b,4] Careful examination of the existing literature procedures revealed that nearly all existing methods for both racemic[3a,5] and enantioselective[3b,6] cyanosilylation of ketones employ expensive and potentially hazardous Me_3SiCN, with Lewis acid or base catalysts being required.[7] Syntheses of ketone cyanohydrins containing silyl-protecting groups higher than trimethylsilyl are only scarcely described. Therefore, we aimed at developing a general and robust cyanosilylation method

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(1) (a) Sukumaran, J.; Hanefeld, U. *Chem. Soc. Rev.* **2005**, *34*, 530−542. (b) Holt, J.; Arends, I. W. C. E.; Minnaard, A. J.; Hanefeld, U. *Adv. Synth. Catal.* **2007**, *349*, 1341−1344. (c) Veum, L.; Hanefeld, U.; Pierre, A. *Tetrahedron* **2004**, *60*, 10419−10425. (d) Chmura, A.; van der Kraan, G. M.; Kielar, F.; van Langen, L. M.; van Rantwijk, F.; Sheldon, R. A. *Adv. Synth. Catal.* **2006**, *348*, 1655−1661. (e) Cabirol, F. L.; Hanefeld, U.; Sheldon, R. A. *Adv. Synth. Catal.* **2006**, *348*, 1645−1654.

(2) (a) Mowry, D. T. *Chem. Rev.* **1948**, *48*, 189−275. (b) von Langermann, J.; Mell, A.; Paetzold, E.; Daussmann, T.; Kragl, U. *Adv. Synth. Catal.* **2007**, *349*, 1418−1424.

(3) (a) Chen, F. X.; Feng, X. *Synlett* **2005**, 892−899. (b) Brunel, J. -M.; Holmes, I. P. *Angew. Chem., Int. Ed.* **2004**, *43*, 2752−2778 and references cited therein.

(4) (a) Rotčenkovs, G.; Kanerva, L. T. *J. Mol. Catal. B: Enzym.* **2000**, *11*, 37−43. (b) Kiljunen, E.; Kanerva, L. T. *Tetrahedron: Asymmetry* **1997**, *8*, 1551−1557. (c) Menéndez, E.; Brieva, R.; Rebolledo, F.; Gotor V. *J. Chem. Soc., Chem. Commun.* **1995**, 989−990.

(5) (a) Wang, X.; Tian, S.-K. *Tetrahedron Lett.* **2007**, *48*, 6010−6013. (b) Song, J. J.; Gallou, F.; Reeves, J. T.; Tan, Z.; Yee, N. K.; Senanayake, C. H. *J. Org. Chem.* **2006**, *71*, 1273−1276. (c) Kano, T.; Sasaki, K.; Konishi, T.; Mii, H.; Maruoka, K. *Tetrahedron Lett.* **2006**, *47*, 4615−4618. (d) Wang, L.; Huang, X.; Jiang, J.; Liu, X.; Feng X. *Tetrahedron Lett.* **2006**, *47*, 1581−1584. (e) Kurono, N.; Yamaguchi, M.; Suzuki, K.; Ohkuma, T. *J. Org. Chem.* **2005**, *70*, 6530−6532. (f) Baeza, A.; Nájera, C.; de Gracia Retamosa, M.; Sansano, J. M. *Synthesis* **2005**, 2787−2797. (g) Fetterly, B. M.; Verkade, J. G. *Tetrahedron Lett.* **2005**, *46*, 8061−8066. (h) De, S. K.; Gibbs, R. A. *J. Mol. Catal. A: Chem.* **2005**, *232*, 123−125. (i) He, B.; Li, Y.; Feng, X.; Zhang, G. Synlett **2004**, 1776−1778. (j) Yadav, J. S.; Reddy, B. V. S.; Sridhar Reddy, M.; Prasad, A. R. *Tetrahedron Lett.* **2002**, *43*, 9703−9706. (k) Wilkinson, H. S.; Grover, P. T.; Vandenbossche, C. P.; Bakale, R. P.; Bhongle, N. N.; Wald, S. A.; Senanayake, C. H. *Org. Lett.* **2001**, *3*, 553−556. We thank one of the reviewers for identifying a few relevant references.

(6) (a) Takamura, M.; Yabu, K.; Nishi, T.; Yanagisawa, H.; Kanai, M.; Shibasaki, M. *Synlett* **2003**, 353−356. (b) He, B.; Chen, F.-X.; Li, Y.; Feng, X.; Zhang, G. *Eur. J. Org. Chem.* **2004**, *22*, 4657−4666. (c) Chen, F.-X.; Zhou, H.; Liu, X.; Qin, B.; Feng, X.; Zhang, G.; Jiang, Y. *Chem.−Eur. J.* **2004**, *10*, 4790−4797. (d) Masumoto, S.; Suzuki, M.; Kanai, M.; Shibasaki, M. *Tetrahedron* **2004**, *60*, 10497−10504. (e) Chen, F.-X.; Qin, B.; Feng, X.; Zhang, G.; Jiang, Y. *Tetrahedron* **2004**, *60*, 10449−10460. (f) Danet, M.; Normand-Bayle, M.; Mahuteau, J.; d'Angelo, J.; Morgant, G.; Desmaele, D. *Eur. J. Org. Chem.* **2004**, *9*, 1911−1922. (g) Shen, Y.; Feng, X.; Li, Y.; Zhang, G.; Jiang, Y. *Eur. J. Org. Chem.* **2004**, *1*, 129−137. (h) Choi, M. C. K.; Chan, S.-S.; Chan, M.-K.; Kim, J. C.; Iida, H.; Matsumoto, K. *Heterocycles* **2004**, *62*, 643−653. (i) Kitani, Y.; Kumamoto, T.; Isobe, T.; Fukuda, K.; Ishikawa, T. *Adv. Synth. Catal.* **2005**, *347*, 1653−1658. (j) Maki, K.; Motoki, R.; Fujii, K.; Kanai, M.; Kobayashi, T.; Tamura, S.; Shibasaki, M. *J. Am. Chem. Soc.* **2005**, *127*, 17111−17117. (k) Liu, X.; Qin, B.; Zhou, X.; He, B.; Feng, X. *J. Am. Chem. Soc.* **2005**, *127*, 12224−12225. (l) Hong, R.; Chen, Y.; Deng, L. *Angew. Chem., Int. Ed.* **2005**, *44*, 3478−3481. (m) Fuerst, D. E.; Jacobsen, E. N. *J. Am. Chem. Soc.* **2005**, *127*, 8964−8965. (n) Suzuki, M.; Kato, N.; Kanai, M.; Shibasaki, M. *Org. Lett.* **2005**, *7*, 2527−2530. (o) Ryu, D. H.; Corey, E. J. *J. Am. Chem. Soc.* **2005**, *127*, 5384−5387. (p) Silva, M. M. C.; Andrade, L. C. R.; Paixão, J. A.; Jose de Almeida, M.; Sá e Melo, M. L. *Steroids* **2005**, *70*, 145−151. (q) Kim, S. S.; Kwak, J. M. *Tetrahedron* **2006**, *62*, 49−53. (r) Tian, S.-K.; Deng, L. *Tetrahedron* **2006**, *62*, 11320−11330. (s) Belokon, Y. N.; Chusov, D.; Borkin, D. A.; Yashkina, L. V.; Dmitriev, A. V.; Katayev, D.; North, M. *Tetrahedron: Asymmetry* **2006**, *17*, 2328−2333. (t) Qin, Y.-C.; Liu, L.; Sabat, M.; Pu, L. *Tetrahedron* **2006**, *62*, 9335−9348. (u) Kim, S. S.; Lee, S. H.; Kwak, J. M. *Tetrahedron: Asymmetry* **2006**, *17*, 1165−1169. (v) Li, Q.; Liu, X.; Wang, J.; Shen, K.; Feng, X.; *Tetrahedron Lett.* **2006**, *47*, 4011−4014. (w) Xiong, Y.; Huang, X.; Gou, S.; Huang, J.; Wen, Y.; Feng, X. *Adv. Synth. Catal.* **2006**, *348*, 538−544. (x) Qin, B.; Liu, X.; Shi, J.; Zheng, K.; Zhao, H.; Feng, X. *J. Org. Chem.* **2007**, *72*, 2374−2378.

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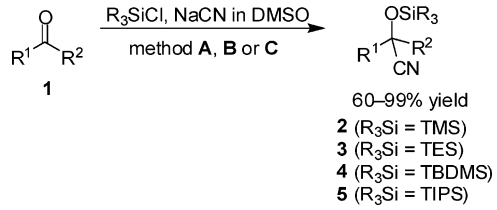
SCHEME 1. Synthesis of Trialkylsilyl-Protected Cyanohydrins in DMSO

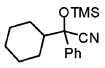
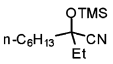
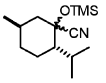
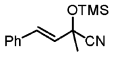
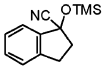
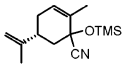


which would encompass a wide range of ketones and commercially available trialkylsilyl protecting groups.

Since chlorotrialkylsilanes are the most common and inexpensive trialkylsilyl protecting agents, we decided to use the respective chlorosilanes in combination with stable and inexpensive NaCN. However, the latter salt has negligible solubility in most aprotic solvents. For this reason, we turned our attention to DMSO which features the highest polarity among common dipolar aprotic solvents[8] combined with enhanced solvating ability toward hard metal cations. Conversely, anions in such media are poorly solvated and hence highly reactive. For this reason, inorganic salts with sodium or potassium cations soluble in DMSO are often referred to as "naked" anions[9] for their enhanced nucleophilicity. We first noticed that NaCN is appreciably soluble in DMSO especially at 60 °C (≥2 mmol/mL). Under these conditions, a cyanosilylation of the model substrate, acetophenone **1a** using TBDMSCl required only 5 min to attain conversions greater than 90% into the desired TBDMS-protected cyanohydrin **4a**.[10] Much to our satisfaction, high-yielding facile syntheses of a wide range of ketone cyanohydrins bearing various trialkysilyl protecting groups were possible (Scheme 1, Tables 1 and 2) under these conditions (method A, Experimental Section).

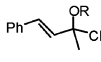
NaCN also acted as a base[9b] leading to partial α-C epimerization of the ketone **1f** (entry 6, Table 1) or conversion of the ketone **1i** to the corresponding silyl enol ether (entry 9, Table 1). The formation of the latter side product could be minimized using a two-phase hexane−DMSO system (method B, Experimental Section). Under these conditions, the yield of **2a** improved significantly (entry 1, Table 1). However, with this protocol 1,4 addition of the cyanide ion to carvone **1j** was observed (entry 10, Table 1).[11] When the reaction was performed at room temperature and greater dilution (method C, Experimental section), the addition of the cyanide anion to conjugated enones proceeded in favor of the 1,2-cyanosilylation product with limited undesirable 1,4-addition to **1j** or polymerization (Table 1). The TMS derivatives **2** were isolated in at least 98% purity (GC) by nonaqueous extraction of the products from

TABLE 1. Isolated Yields (%) for the Preparation of TMS Derivatives 2

Entry	Substrate	Product		Isolated Yield (Method)[a]
1	Acetophenone, **1a**		**2a**	83 (**A**), 99 (**B**), 93 (**C**)
2	3,3-Dimethyl-butan-2-one, **1b**		**2b**	96 (**A**)
3	Cyclohexyl-phenyl ketone, **1c**		**2c**	96 (**A**)
4	Nonan-3-one, **1d**		**2d**	>99 (**A**)
5	*Rac*-2-methylcyclo-hexanone, **1e**		**2e**	97 (**A**) *[79:21]*[b]
6	(*L*)-Menthone[c], **1f**		**2f**	95 (**A**) *[5:81:2:12]*[b, d, e] >99 (**C**) *[38:59:0:3]*[b,d]
7	(*E*)-4-Phenylbut-3-en-2-one, **1g**		**2g**	71 (**B**), 79 (**C**)
8	(*E*)-Pent-3-en-2-one, **1h**		**2h**	84 (**B**), 94 (**C**)
9	1-Indanone, **1i**		**2i**	84[f] (**B**), 68[g] (**C**)
10	(*R*)-Carvone, **1j**		**2j**	>99[h] (**B**) *[79:21]*[b], 97[i] (**C**) *[81:19]*[b]

[a] Experimental procedure as given in the Experimental Section. [b] Distribution of diastereoisomers [%:%]. [c] Contains at least 3% of another diastereoisomer according to GC. [d] The ratio of peaks as they appear on GC. [e] Formation of another pair of diastereoisomers is presumably due to partial epimerization of the starting ketone **1f** at 60 °C. [f] Contains 8% TMS-enol. [g] Contains **4**% TMS-enol. [h] Contains **14**% of 1−4 addition product. [i] Contains 5% of 1−4 addition product.

TABLE 2. Isolated Yields (%) for the Preparation of Trilakylsilyl Derivatives 3−5[a]

Structure	R=TES		R=TBDMS		R=TIPS	
	**3a**	83 (**A**), 92 (**B**)	**4a**	85 (**A**), 82 (**B**)	**5a**	82 (**A**)
	**3e**	>99 (**A**) *[88:12]*[b]	**4e**	82 (**A**) *[71:29]*[b]	**5e**	94 (**A**) *[81:19]*[b]
	**3g**	94 (**C**)	**4g**	60 (**C**)	**5g**	72 (**C**)[c]

[a] Experimental procedure as given in the Experimental Section. [b] Distribution of diastereoisomers [%:%]. [c] Reaction performed on 1 mmol scale and purified by semipreparative HPLC.

(7) In one notable exception, a combination of KCN and TMSCl in DMF has been used: (a) Rasmussen, J. K.; Heilmann, S. M. *Synthesis* **1978**, 219−221. However, application of DMF in industrial chemistry is undesirable due to its toxicity. Improvements of this method were later reported: (b) Duboudin, F.; Cazeau, P.; Moulines, F.; Laporte, O. *Synthesis* **1982**, 212−214. (c) Yoneda, R.; Santo, K.; Harusawa, S.; Kurihara, T. *Synthesis* **1986**, 1054−1055. (d) Sukata, K. *Bull. Chem. Soc. Jpn.* **1987**, *60*, 3820−3822. In all cases, relatively long reaction times were required for unreactive carbonyl compounds.

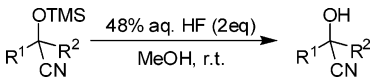
(8) Dielectric constants, $\epsilon = 47.2$ (DMSO); 38.8 (DMA); 38.2 (DMF); 36.6 (MeCN); 32.6 (NMP). See: Lide, D. R. In *CRC Handbook of Chemistry and Physics*, 81st ed.; CRC Press LLC: Boca Raton, 2000−2001; 6−149.

(9) (a) Carey, F. A.; Sundberg, R. J. *Advanced Organic Chemistry. Part A: Structure and Mechanisms*, 4th ed.; Springer Science+Business Media: New York, 2006; pp 240−241. The nucleophilicity of small and soft cyanide anions is particularly augmented in DMSO; see: (b) Landini, D.; Maia, A.; Montanari, F. *J. Am. Chem. Soc*. **1978**, *100*, 2796−2801. (c) Parker, A. J. *Chem. Rev*. **1969**, *69*, 1−32.

(10) Compound **4a** could be isolated in 86% yield after 3 h at r. t. using 1.2 eq of TBDMSCN in CH_2Cl_2 and a catalytic amount of ZnI_2 according to: Golinski, M.; Brock, C. P.; Watt D. S. *J. Org. Chem*. **1993**, *58*, 159−164. The synthesis of this compound in 99% yield could be achieved in 1 h at 0°C in THF upon the catalysis with a nonionic strong base (7 mol%).[5g]

(11) Samson, M.; Vandewalle, M. *Synth. Commun*. **1978**, *8*, 231−239.

SCHEME 2. Ketone Cyanohydrins by Deprotection of the TMS Derivatives 2



DMSO with hexane followed by filtration through a short pad of silica gel. The trialkylsilyl derivatives **3**−**5** were further purified by column chromatography or distillation to obtain this grade of purity.

The parent ketone cyanohydrins are smoothly liberated from the TMS derivatives **2** using aqueous HF in MeOH (Scheme 2).

DMSO proved to be crucial for activating our Lewis acid/base free cyanosilylation system. The reaction was extremely slow when performed in another dipolar aprotic solvent, DMF.[12] To account for the unique role of DMSO and shed light on the reaction mechanism, we carried out a comparative kinetic study on the conversion of acetophenone **1a** into the TBDMS derivative **4a**.

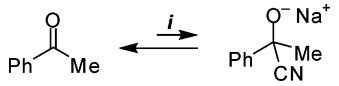
When TBDMSCN was used as a sole cyanide source (no NaCN added) no reaction could be observed, even in combination with TBDMSCl. This result demonstrates the crucial importance of free cyanide in inducing the observed cyanosilylation in DMSO.[13] TBDMSCl is found to react with NaCN to form TBDMSCN, the reaction rate being comparable with that of the cyanosilylation of the ketone **1a**. Parallel formation of TBDMSCN effectively reduces the concentration of free cyanide anions in the reaction medium. For this reason, a significant decrease in the reaction rate was observed when NaCN was used in equimolar amount with reference to TBDMSCl (1.2:1.2 ratio) when compared to the original ratio of TBDMSCl to NaCN of 1.2:2. The pivotal role of the free CN^- was further substantiated by the fact that the reaction rate increased when TBDMSCN was used as the trapping agent for the putative cyanoalcoholate (TBDMSCN to NaCN ratio of 1.2:2). Indeed, upon silylation with TBDMSCN, the concentration of free cyanide is maintained throughout the course of the reaction.

Thus, to account for the above observations, we suggest a two-step reaction pathway including addition of highly nucleophilic CN^- in DMSO across the C═O bond of the ketone at a rate-determining step followed by silylation of the intermediate tertiary sodium cyanoalcoholate with chlorotrialkylsilane or in situ formed cyanotrialkylsilane.

Despite the above kinetic evidence, we were unable to detect the putative tetrahedral intermediate, the cyanoalcoholate anion, in the mixture of acetophenone and NaCN by NMR in DMSO-d_6 at 60 °C (Scheme 3, see also Figure 1 in Supporting Information).

This result confirms that despite significantly enhanced nucleophilicity of naked cyanide in DMSO, the equilibrium between ketones and the tertiary cyanoalcoholates anions remains essentially unaltered. It lies to such an extent on the side of the starting material (Scheme 3) that the intermediate cannot be detected by standard NMR techniques. However, although thermodynamically only minute quantities of alcoholate are formed, the kinetics of the uncatalyzed equilibrium are such that they do not limit the synthesis of the protected cyanohydrins.

SCHEME 3. Equilibrium between the Parent Carbonyl Compound and the Tetrahedral Cyanoalcoholate in the Presence of NaCN in DMSO-d_6



i: NaCN, 60°C, in DMSO-d_6

In conclusion, the cyanosilylation protocol described herein enables the most general synthesis of racemic silyl protected cyanohydrins known to date, applicable to a wide range of ketones and trialkylsilyl protecting groups. The method is simple, robust, cost-effective, and safe since it requires neither catalysis nor expensive and potentially hazardous silyl cyanides.

Experimental Section

General Method A. To a solution of sodium cyanide (20 mmol) in dry DMSO (10 mL) at 60 °C under inert atmosphere was added the carbonyl compound (10 mmol). The mixture was stirred for 5 min at this temperature, and the trialkylsilyl chloride (12 mmol) was added dropwise at 60 °C. The reaction mixture was then stirred at 60 °C under inert atmosphere for 5 min (TMS, TES, and TBDMS derivatives) or 10 min (TIPS derivatives). The DMSO phase was extracted with hexane (3 × 15 mL), and the combined hexane phases were cooled in an ice bath to separate residual DMSO. After evaporation of the solvent the residue was filtered through a short pad of silica using hexane as eluent. The solvent was then removed under reduced pressure to give the TMS derivatives in good purity (>98%). Other derivatives were further purified by column chromatography or distillation.

General Method B. To a solution of sodium cyanide (20 mmol) in dry DMSO (10 mL) at 60 °C under inert atmosphere was added dry hexane (10 mL). An initial amount of trialkylsilyl chloride (3 mmol) was added to the stirred mixture at 60 °C under inert atmosphere followed immediately by dropwise addition of a solution of the carbonyl compound (10 mmol) and trialkylsilyl chloride (12 mmol) in hexane (5 mL). The reaction was allowed to proceed for 5 min at this temperature. The reaction mixture was then treated as described in general method A.

General Method C. A solution of sodium cyanide (30 mmol) in dry DMSO (15 mL) under inert atmosphere was heated gently with a heat gun to ensure saturation and the mixture was allowed to cool to rt. The respective trialkylsilyl chloride (20 mmol) was added to the thick mixture at rt, and stirring was continued for 1 min (TMS and TES derivatives) or 15 min (TBDMS and TIPS derivatives). The carbonyl compound (10 mmol) was then added slowly at rt under inert atmosphere and the mixture was stirred for 30 min under these conditions. The reaction mixture was then treated as described in general method A.

General Method for the Deprotection of TMS Derivatives 2. To a solution of TMS-protected cyanohydrin in methanol (1 mmol/mL) was added commercial 48% aqueous solution of HF (2 equiv) and the reaction was stirred at ambient temperature. Toward the end of the reaction (NMR monitoring), the mixture was diluted with water and extracted with CH_2Cl_2. The combined organic layers were dried over $MgSO_4$, and the solvent was removed under reduced pressure to give the corresponding cyanohydrin. TMS-acetophenone cyanohydrin **2a** was deprotected according to this

(12) The reaction did not gain appreciable acceleration when DMSO was used as an additive in DMF/DMSO 9:1 mixture.

(13) It rules out an alternative mechanism that would involve nucleophilic catalysis by DMSO. The activation of a silyl group or a cyanoformate by coordination with the DMSO−oxygen was indeed suggested for the silylation of alcohols, and the cyanocarboxylation of aldehydes in DMSO respectively, see: (a) Watahiki, T.; Matsuzaki, M.; Oriyama, T. *Green Chem.* **2003**, *5*, 82−84. (b) Watahiki, T.; Ohba, S.; Oriyama, T. *Org. Lett.* **2003**, *5*, 2679−2681. (c) Iwanami, K.; Hinakubo, Y.; Oriyama, T. *Tetrahedron Lett.* **2005**, *46*, 5881−5883. However, *O*-nucleophilic tertiary amine *N*-oxides are well-known to catalyze addition of TMSCN to both aldehydes and ketones.[3a]

procedure within 2 h, and acetophenone cyanohydrin was obtained in 99% yield and excellent purity (NMR) without further purification.

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Supporting Information Available: Experimental details for all protected cyanohydrins prepared according to methods A, B, or C including spectral data, experimental procedure of the kinetic study, and ^{1}H NMR spectra to illustrate the purity of the products obtained. This material is available free of charge via the Internet at http://pubs.acs.org.

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