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Synthesis of (*E*,*Z*)-1-Alkoxy-3-acyloxy-2-methylpenta-1,3-dienes via Danishefsky-Type Dienes or *O*-Acylation of Enones

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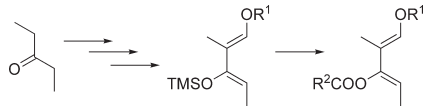

1-Alkoxy-2-methyl-3-acyloxy-(*E*,*E*)-penta-1,3-dienes have been prepared applying among others a modified Danishefsky's general method, including chiral, racemic, and achiral derivatives.

Danishefsky's dienes (1,3-dioxy-substituted 1,3-dienes) are extremely useful reagents for the construction of natural products and analogues of biological interest.[1,2] Especially interesting are (*E*,*Z*)-1-alkoxy-3-trialkylsilyloxy-2-methylpenta-1,3-dienes[3,4] used to prepare polypropionates[5] such as rifamycin S,[6] zincophorin,[7] 6-deoxyerythronolide B,[8] discodermolide,[9] epothilones,[10] migrastatin,[11] (+)-prelactone C and (+)-9-deoxygoniopyrone,[12] phorboxazoles,[13] and dictyostatin.[14] Their synthesis involves a hetero-Diels−Alder addition of aldehydes,[15,16] in contrast to the one of yohimbine congeners[17] applying hetero-Diels−Alder addition of imines.[18−20]

In 1997 our group uncovered a new C−C bond forming reaction cascade that condenses butadiene-1-yl ethers **1**, enoxysilanes **2**, and SO_2 to generate γ,δ-unsaturated silylsulfinates **3**. After desilylation, the corresponding sulfinic

(1) (a) Danishefsky, S.; Yan, C.-F.; Singh, R. K.; Gammill, R. B.; McCurry, P. M.; Fritsch, N.; Clardy, J. *J. Am. Chem. Soc.* **1979**, *101*, 7001–7008. (b) Danishefsky, S. *Acc. Chem. Res.* **1981**, *14*, 400–406. (c) Danishefsky, S.; Kerwin, J. F.; Kobayashi, S. *J. Am. Chem. Soc.* **1982**, *104*, 358–360. (d) Danishefsky, S.; Kerwin, J. F. *J. Org. Chem.* **1982**, *47*, 3183–3184. (e) Danishefsky, S.; Kitahara, T.; Schuda, P. F. *Org. Synth.* **1983**, *61*, 147–151. (f) Danishefsky, S.; Harvey, D. F.; Quallich, G.; Uang, B. J. *J. Org. Chem.* **1984**, *49*, 392–393.

(2) (a) Bednarski, M.; Danishefsky, S. *J. Am. Chem. Soc.* **1986**, *108*, 7060–7067. (b) Danishefsky, S. J.; Maring, C. J.; Barbachyn, M. R.; Segmuller, B. E. *J. Org. Chem.* **1984**, *49*, 4564–4565. (c) Danishefsky, S.; Uang, B. J.; Quallich, G. *J. Am. Chem. Soc.* **1985**, *107*, 1285–1293. (d) Danishefsky, S. J.; Simoneau, B. *J. Am. Chem. Soc.* **1989**, *111*, 2599–2604. (e) Danishefsky, S. J.; DeNinno, S. L.; Chen, S. H.; Boisvert, L.; Barbachyn, M. *J. Am. Chem. Soc.* **1989**, *111*, 5810–5818. (f) Dai, M.; Krauss, I. J.; Danishefsky, S. J. *J. Org. Chem.* **2008**, *73*, 9576–9583. (g) Angeles, A. R.; Waters, S. P.; Danishefsky, S., J. *J. Am. Chem. Soc.* **2008**, *130*, 13765–13770.

(3) (a) Danishefsky, S.; Kitahara, T. *J. Am. Chem. Soc.* **1974**, *96*, 7807–7808. (b) Danishefsky, S.; Bednarski, M.; Izawa, T.; Maring, C. *J. Org. Chem.* **1984**, *49*, 2290–2292.

(4) Myles, D. C.; Bigham, M. H. *Org. Synth.* **1992**, *70*, 231–239.

(5) (a) Danishefsky, S.; Kato, N.; Askin, D.; Kerwin, J. F. *J. Am. Chem. Soc.* **1982**, *104*, 360–362. (b) Danishefsky, S.; Larson, E. R.; Askin, D. *J. Am. Chem. Soc.* **1982**, *104*, 6457–6458. (c) Danishefsky, S.; Larson, E.; Askin, D.; Kato, N. *J. Am. Chem. Soc.* **1985**, *107*, 1246–1255. (d) Danishefsky, S.; Harvey, D. F. *J. Am. Chem. Soc.* **1985**, *107*, 6647–6652.

(6) Danishefsky, S. J.; Myles, D. C.; Harvey, D. F. *J. Am. Chem. Soc.* **1987**, *109*, 862–867.

(7) Danishefsky, S. J.; Selnick, H. G.; Zelle, R. E.; DeNinno, M. P. *J. Am. Chem. Soc.* **1988**, *110*, 4368–4378.

(8) Myles, D. C.; Danishefsky, S. J.; Schulte, G. *J. Org. Chem.* **1990**, *55*, 1636–1648.

(9) (a) Yang, G.; Myles, D. C. *Tetrahedron Lett.* **1994**, *35*, 2503–2504. (b) Harried, S. S.; Lee, C. P.; Yang, G.; Lee, T. I. H.; Myles, D. C. *J. Org. Chem.* **2003**, *68*, 6646–6660.

(10) (a) Bertinato, P.; Sorensen, E. J.; Meng, D.; Danishefsky, S. J. *J. Org. Chem.* **1996**, *61*, 8000–8001. (b) Meng, D.; Bertinato, P.; Balog, A.; Su, D.-S.; Kamenecka, T.; Sorensen, E. J.; Danishefsky, S. J. *J. Am. Chem. Soc.* **1997**, *119*, 10073–10092. (c) Biswas, K.; Lin, H.; Njardarson, J. T.; Chappell, M. D.; Chou, T.-C.; Guan, Y.; Tong, W. P.; He, L.; Horwitz, S. B.; Danishefsky, S. J. *J. Am. Chem. Soc.* **2002**, *124*, 9825–9832.

(11) (a) Gaul, C.; Danishefsky, S. J. *Tetrahedron Lett.* **2002**, *43*, 9039–9042. (b) Gaul, C.; Njardarson, J. T.; Danishefsky, S. J. *J. Am. Chem. Soc.* **2003**, *125*, 6042–6043. (c) Gaul, C.; Njardarson, J. T.; Shan, D.; Dorn, D. C.; Wu, K.-D.; Tong, W. P.; Huang, X.-Y.; Moore, M. A. S.; Danishefsky, S. J. *J. Am. Chem. Soc.* **2004**, *126*, 11326–11337.

(12) Yamashita, Y.; Saito, S.; Ishitani, H.; Kobayashi, S. *J. Am. Chem. Soc.* **2003**, *125*, 3793–3798.

(13) Lucas, B. S.; Luther, L. M.; Burke, S. D. *J. Org. Chem.* **2005**, *70*, 3757–3760.

(14) Dilger, A. K.; Gopalsamuthiram, V.; Burke, S. D. *J. Am. Chem. Soc.* **2007**, *129*, 16273–16277.

(15) (a) Larson, E. R.; Danishefsky, S. *J. Am. Chem. Soc.* **1982**, *104*, 6458–6460. (b) Gaul, C.; Njardarson, J. T.; Danishefsky, S. J. *J. Am. Chem. Soc.* **2003**, *125*, 6042–6043. (c) Danishefsky, S. J.; Pearson, W. H.; Harvey, D. *J. Am. Chem. Soc.* **1984**, *106*, 2456–2458.

(16) For catalyzed cycloadditions of a carbonyl compound with asymmetric induction, see, e.g.: (a) Bednarski, M.; Maring, C.; Danishefsky, S. *Tetrahedron Lett.* **1983**, *24*, 3451–3454. (b) Maruoka, K.; Itoh, T.; Shirasaka, T.; Yamamoto, H. *J. Am. Chem. Soc.* **1988**, *110*, 310–312. (c) Maruoka, K.; Yamamoto, H. *J. Am. Chem. Soc.* **1989**, *111*, 789–790. (d) Togni, A. *Organometallics* **1990**, *9*, 3106–3113. (e) Gao, Q.; Maruyama, T.; Mouri, M.; Yamamoto, H. *J. Org. Chem.* **1992**, *57*, 1951–1952. (f) Gao, Q.; Ishihara, K.; Maruyama, T.; Mouri, M.; Yamamoto, H. *Tetrahedron* **1994**, *50*, 979–988. (g) Motoyama, Y.; Mikami, K. *Chem. Commun.* **1994**, 1563–1564. (h) Yao, S.; Roberson, M.; Reichel, F.; Hazell, R. G.; Jorgensen, K. A. *J. Org. Chem.* **1999**, *64*, 6677–6687. (i) Simonsen, K. B.; Svenstrup, N.; Roberson, M.; Jørgensen, K. A. *Chem.—Eur. J.* **2000**, *6*, 123–128. (j) Yamashita, Y.; Saito, S.; Ishitani, H.; Kobayashi, S. *Org. Lett.* **2002**, *4*, 1221–1223. (k) Anada, M.; Washio, T.; Shimada, N.; Kitagaki, S.; Nakajima, M.; Shiro, M.; Hashimoto, S. *Angew. Chem., Int. Ed.* **2004**, *43*, 2665–2668. (l) Valenzuela, M.; Doyle, M. P.; Hedberg, C.; Hu, W.; Holmstrom, A. *Synlett* **2004**, 2425–2428. (m) Landa, A.; Richter, B.; Johansen, R. L.; Minkkila, A.; Jørgensen, K. A. *J. Org. Chem.* **2007**, *72*, 240–245. (n) Yu, Z.; Liu, X.; Dong, Z.; Xie, M.; Feng, X. *Angew. Chem., Int. Ed.* **2008**, *47*, 1308–1311. (o) Scettri, A.; Acocella, M. R.; Palombi, L.; Scalera, C.; Villano, R.; Massa, A. *Adv. Synth. Catal.* **2006**, *348*, 2229–2236.

(17) Danishefsky, S.; Langer, M. E.; Vogel, C. *Tetrahedron Lett.* **1985**, *26*, 5983–5986.

(18) (a) Danishefsky, S.; Kerwin, J. F. *J. Org. Chem.* **1982**, *47*, 3183–3184. (b) Kitazawa, T.; Maruyama, Y.; Mukaiyama, T. *Heterocycles* **2007**, *73*, 255–261. (c) Heintzelman, G. R.; Meigh, I. R.; Mahajan, Y. R.; Weinreb, S. M. *Org. React.* **2005**, 65.

(19) For catalyzed cycloadditions of imines with asymmetric induction, see, e.g.: (a) Yao, S.; Saaby, S.; Hazell, R. G.; Jørgensen, K. A. *Chem.—Eur. J.* **2000**, *6*, 2435–2448. (b) Andreassen, T.; Haaland, T.; Hansen, L. K.; Gautun, O. R. *Tetrahedron Lett.* **2007**, *48*, 8413–8415. (c) Yao, S.; Johannsen, M.; Hazell, R. G.; Jørgensen, K. A. *Angew. Chem., Int. Ed.* **1998**, *37*, 3121–3124.

(20) For other cycloadditions see, e.g.: (a) Garcia Ruano, J. L.; Fernandez-Ibanez, M. A.; Maestro, M. C. *J. Org. Chem.* **2006**, *71*, 7683–7689. (b) Seth, P. P.; Chen, D.; Wang, J.; Gao, X.; Totah, N. I. *Tetrahedron* **2000**, *56*, 10185–10195.

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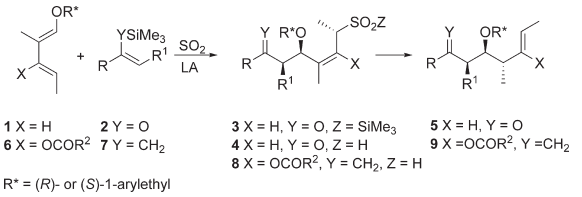
acids **4** undergo SO_2 elimination with formation of δ,ε-(*E*)-alkenes **5** with high selectivity.[21] The reaction cascade has been applied to several diene (**1**)/enoxysilane (**2**) pairs,[22−24] as well as to diene (**6**)/allylsilane (**7**) pairs[25] (Scheme 1), thus

SCHEME 1. Stereoselective Synthesis of Stereotriads via Hetero-Diels−Alder Addition of SO_2 to Danishefsky's Dienes

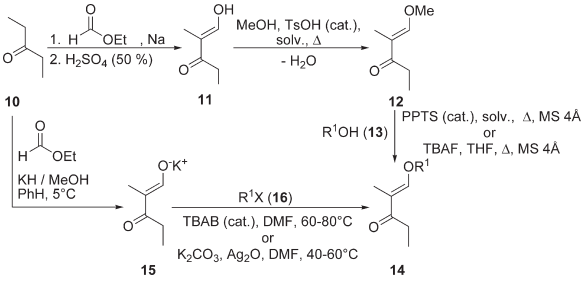


giving us the possibility to construct stereotriads in one-pot operations that can be used directly in the synthesis of long-chain polyketides and polypropionates.[22−24]

Nonracemic products were obtained starting with enantiomerically enriched dienes **1** and **6** derived from inexpensive (*R*)- or (*S*)-1-phenylethanol (R*OH).[26] As the 3-silyloxy analogues of **6** would undergo ene-reactions with SO_2 much faster than their hetero-Diels−Alder addition, a first requirement to promote the cross-coupling of the diene with enoxysilane (**2**) or allylsilane **7** was to use esters **6**, instead. We report here the synthesis of a number of diene derivatives **6** including achiral, racemic, and nonracemic analogues.

Preparation of 1-alkoxy-2-methyl-3-acyloxy-(*E*,*E*)-penta-1,3-dienes via Danishefsky-type dienes uses the general method for the preparation of 1-alkoxy-2-methyl-3-silyloxy-(*E*,*E*)-penta-1,3-dienes **17**, as developed by Danishefsky and co-workers, commencing from inexpensive 3-pentanone (**10**) and ethyl formate (Scheme 2). Their Claisen condensation

SCHEME 2. Methods for the Preparation of (*E*)-1-Alkoxy-2-methylpent-1-en-3-ones 14



and acidic workup produces enol-ketone **11**. Under acidic conditions, e.g. *p*-toluenesulfonic acid (*p*TsOH), enol-ketone **11** reacts with achiral alcohols like methanol to the corresponding ene-ethers **12** and H_2O, which is eliminated by azeotropic distillation with benzene, toluene, and $CHCl_3$, respectively. If the alcohol is an enantiomerically enriched 1-arylethanol derivative **13**, racemization of both alcohols **13** and ene-ethers **14** can occur due to acid-promoted S_N1 or E1/addition reactions. We circumvented this problem by using methyl enol ether **12** instead of enol-ketone **11**, as less acidic conditions, such as pyridinium *p*-toluenesulfonate (PPTS), catalyze the elimination of methanol.[27] The latter can be carried out through azeotropic distillation or, using neat reactants, under vacuum. If racemization cannot be avoided under the latter conditions, basic conditions should be applied. Thus, ene-ethers **14** can be generated from **12** by reaction with sensitive alcohols **13** (e.g.: Green's chiral

TABLE 1. Synthesis of Enones 14 with Alcohols 13

entry	R^1OH **13**	OR1 O **14** (yield %, ee %)
1	**13a**	**14a** (89, 97)
2	**13b** [a]	**14b** (80, 99)
3	**13c** [a]	**14c** (86, 99) [c]
4	**13d**	**14d** (72, 96)
5	**13e**	**14e** (87, 96)
6	**13f**	**14f** (68, 95)
7	**14g** [b]	**14g** (70, 95)
8	**13h**	**14h** (75, *rac*) [c]
9	**13i** [a]	**14i** (55, *rac*) [c]
10	**13j** [a]	**14j** (60, *rac*) [c]
11	**13k** [a]	**14k** (63, *rac*) [c]
12	**13l**	**14l** (82, *rac*) [c]
13	**13m** [30]	**14m** (70, *rac*) [c]

[a]For preparation see the Supporting Information. [b]Under basic conditions with TBAF. [c]Yield of crude product.

(21) (a) Deguin, B.; Roulet, J.-M.; Vogel, P. *Tetrahedron Lett*. **1997**, *38*, 6197–6200. (b) Roulet, J.-M.; Puhr, G.; Vogel, P. *Tetrahedron Lett*. **1997**, *38*, 6201–6204. (c) Vogel, P.; Turks, M.; Bouchez, L.; Markovic, D.; Varela-Alvarez, A.; Sordo, J. A. *Acc. Chem. Res*. **2007**, *40*, 931–942.

(22) Turks, M.; Murcia, M. C.; Scopelliti, R.; Vogel, P. *Org. Lett*. **2004**, *6*, 3031–3034.

(23) Turks, M.; Huang, X.; Vogel, P. *Chem.—Eur. J*. **2005**, *11*, 465–476.

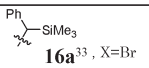
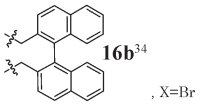
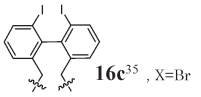
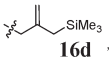
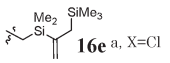
(24) Craita, C.; Didier, C.; Vogel, P. *Chem. Commun*. **2007**, 2411–2413.

(25) Turks, M.; Fonquerne, F.; Vogel, P. *Org. Lett*. **2004**, *6*, 1053–1056.

(26) For other enantiomerically enriched derivatives, see: (a) Bednarski, M.; Danishefsky, S. *J. Am. Chem. Soc*. **1983**, *105*, 6968–6969. (b) Danishefsky, S.; Bednarski, M.; Izawa, T.; Maring, C. *J. Org. Chem*. **1984**, *49*, 2290–2292. (c) Larsen, D. S.; Stoodley, R. J. *J. Chem. Soc., Perkin Trans. 1* **1989**, 1841–1852.

(27) Zadel, G.; Rieger, R.; Breitmaier, E. *Liebigs Ann. Chem*. **1991**, 1343–1346.

TABLE 2. Synthesis of Enones with Halides 16

entry	RX **16**	**14** (yield %)
1	 **16a**[33], X=Br	**14n** (82)[a]
2	 **16b**[34], X=Br	**14o** (87)[a]
3	 **16c**[35], X=Br	**14p** (75)[a]
4	 **16d**, X=Cl	**14q** (72)
5	 **16e** a, X=Cl	**14r** (73)

[a]Yield of crude product.

auxiliaries (**13b**),[28] or (*R*)-1-(4-methoxyphenyl)ethanol (**13g**)) in the presence of TBAF. Another alternative route to **14** is presented by the S_N2 displacement of halides RX (**16**: X = Cl, Br) with potassium enolate **15** in DMF and a catalytic amount of TBAB for X = Br or K_2CO_3/Ag_2O for X = Cl (Scheme 2).[29] The results are in Tables 1 and 2.

Treatment of enones **14** with Me_3SiOTf/Et_3N provides the corresponding Danishefsky-type dienes **17** in good yields (Scheme 3). Silyl/acyl exchange to furnish dienes **20** is carried out under Schlosser's conditions[31] by reaction of **17** with acyl fluorides **19** and a catalytic amount of TBAF (Scheme 3,

SCHEME 3. Synthesis of 3-Acyloxy-1-alkoxy-2-methyl-(*E*,*E*)-penta-1,3-dienes 20

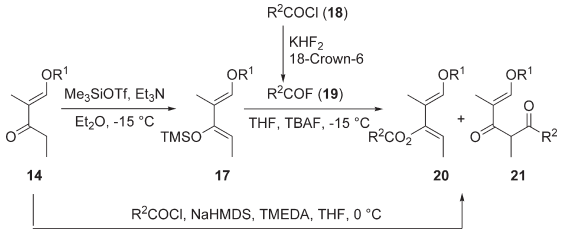
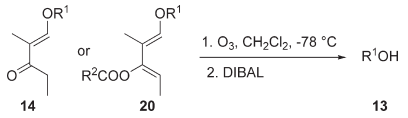


Table 3). Acyl fluorides **19** can be obtained, if not commercially available, by reaction of the corresponding acyl chlorides **18** with KHF_2/18-crown-6.

Furthermore, dienes **20** are directly derived from enones **14** via *O*-acylation with NaHMDS/TMEDA and the corresponding acyl chlorides (Scheme 3, Table 4).[32] This pathway offers several advantages: acyl chlorides are cheaper than fluorides and a bigger variety of them are commercially available, there is no need to prepare acyl fluorides, which are often unstable, and one synthetic step is eliminated. It is noteworthy that this method gives best results only with aliphatic acyl chlorides as for aromatic acyl chlorides we observed also *C*-acylation to enone **21** as a side reaction (Table 4, entries 3−5). But tuning the reaction conditions, i.e. reaction temperature or concentration, can prevent this.

The enantiomeric purities of enones **14** and dienes **20** derived from chiral alcohols **13** were determined by chiral HPLC or by Mosher's ester analysis[36] of 1-arylethanols, which were obtained by ozonolysis and reductive workup (Scheme 4).

SCHEME 4. Cleavage of Enones 14 and Dienes 20 to Alcohols 13 for Determination of the Enantiomeric Excess



This study disclosed the preparation of a large variety of 1-alkoxy-3-acyloxy-2-methyl-(*E*,*E*)-penta-1,3-dienes, including enantiomerically enriched analogues that should find useful applications in the total, asymmetric synthesis of natural products and analogues of biological interest, applying Diels−Alder and hetero-Diels−Alder additions, as well as C−C cross-coupling reactions with enoxysilanes or allylsilanes via SO_2−Umpolung.

Experimental Section

General Method for the Silyl/Acyl Exchange of 17. To the solution of the silyl derivative **17** (0.14 mol, 1 equiv) in THF (160 mL) was added acyl fluoride **19** (0.14 mol, 1.01 equiv) at −15 °C, followed by a 1 M THF solution of TBAF (2.8 mL, 2.8 mmol, 0.02 equiv). The mixture was stirred at this temperature for 30 min (^{1}H NMR control). The solvent was evaporated and the residue was purified by FC to provide pure **20**.

General Method for *O*-Acylation of Enones 14. To a solution of NaHMDS (0.65 mL, 0.65 mmol, 2 equiv, 1 M in THF) and TMEDA (0.097 mL, 0.65 mmol, 2 equiv) in 0.6 mL of THF at 0 °C was added a solution of ketone **14** (0.33 mmol) in 0.6 mL of THF. The reaction mixture was stirred at 0 °C for 30 min. The resulting red solution was cannulated into a flask containing acyl chloride **18** (0.67 mmol, 2 equiv) in THF (0.36 mL) at 0 °C. The mixture was stirred for a further 30 min and poured into aq NH_4Cl solution, extracted with Et_2O (3 × 5 mL), and dried ($MgSO_4$). After evaporation of solvent the crude mixture was purified by FC to yield **20**.

(28) (a) Delair, P.; Kanazawa, A. M.; de Azevedo, M. B. M.; Greene, A. E. *Tetrahedron: Asymmetry* **1996**, *7*, 2707–2710. (b) Kanazawa, A.; Delair, P.; Pourashraf, M.; Greene, A. E. *J. Chem. Soc., Perkin Trans. 1* **1997**, 1911–1912. (c) Kanazawa, A.; Gillet, S.; Delair, P.; Greene, A. E. *J. Org. Chem.* **1998**, *63*, 4660–4663.

(29) (a) Mikami, K.; Matsumi, S.; Okubo, Y.; Ito, O.; Fukuzumi, S. *J. Am. Chem. Soc.* **2000**, *122*, 2236. (b) Ando, R.; Sugawara, T. *Kuwajima* **1983**, 1514–1515.

(30) Degl'Innocenti, A.; Mordini, A.; Pagliai, L.; Ricci, A. *Synlett* **1991**, 155–156.

(31) (a) Limat, D.; Schlosser, M. *Tetrahedron* **1995**, *51*, 5799–5806. (b) Narkevitch, V.; Megevand, S.; Schenk, K.; Vogel, P. *J. Org. Chem.* **2001**, *66*, 5080–5093.

(32) (a) Harwood, L. M.; Houminer, Y.; Manage, A.; Seeman, J. I. *Tetrahedron Lett.* **1994**, *35*, 8027–8030. (b) House, H. O.; Auerbach, R. A.; Gall, M.; Peet, N. P. *J. Org. Chem.* **1973**, *38*, 514–522. (c) De Cusati, P. F.; Olofson, R. A. *Tetrahedron Lett.* **1990**, *31*, 1405–1408.

(33) (a) Andringa, H.; Heux-Kloos, Y. A.; Brandsma, L. *J. Organomet. Chem.* **1987**, *336*, C41–C43. (b) Fry, A. J.; Touster, J. *J. Org. Chem.* **1989**, *54*, 4829–4832.

(34) Hayashi, T.; Hayashizaki, K.; Koyoi, T.; Ito, Y. *J. Am. Chem. Soc.* **1988**, *110*, 8153–8156.

(35) Pugin, B.; Steiner, I; Aufdenblatten, R. N.; Togni, A. *Eur. Pat. Appl.* **2000**, 30 pp.; *Chem. Abstr.* **2000**, *133*, 351206.

(36) Dale, J. A.; Mosher, H. S. *J. Am. Chem. Soc.* **1973**, *95*, 512–519.

TABLE 3. Preparation of Dienes 20 via Danishefsky's Dienes 17 and Acyl Fluorides 19

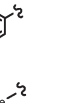
	 14	17	 19	20		 14	 17	 19	 20
entry	R^1 =	(yield %)	R^2 =	(yield %, ee %)	entry	R^1 =	(yield %)	R^2 =	(yield %, ee %)
1	 **14a**	**17a** (97)		**20a** (90, 97)	14	 **14i**	**17i** (96)		**20n** (83, *rac*)
2	 **14a**	**17a** (97)		**20b** (87, 97)	15	 **14j**	**17j** (93)		**20o** (78, *rac*)
3	 **14a**	**17a** (97)		**20c** (92, 96)	16	 **14k**	**17k** (97)		**20p** (79, *rac*)
4	 **14a**	**17a** (97)		**20d** (60, 97)	17	 **14l**	**17l** (89)		**20q** (87, *rac*)
5	 **14a**	**17a** (97)		**20e** (50, 97)	18	 **14m**	**17m** (94)		**20r** (83, *rac*)
6	 **14b**	**17b** (92)		**20f** (92, 99)	19	 **14n**	**17n** (93)		**20s** (49, *rac*)
7	 **14b**	**17b** (92)		**20g** (92, *rac*)	20	 **14o**	**17o** (95)		**20t** (64, -)
8	 **14c**	**17c** (90)		**20h** (75, 96)	21	 **14o**	**17o** (95)		**20u** (59, -)
9	**14d**	**17d** (95)		**20i** (67, 96)	22	**14p**	**17p** (91)		**20v** (58, -)
10	**14e**	**17e** (89)		**20j** (71, 96)	23	**14q**	**17q** (94)		**20w** (80, -)
11	**14f**	**17f** (98)		**20k** (76, 93)	24	**14r**	**17r** (95)		**20x** (75, -)
12	**14g**	**17g** (100)		**20l** (54, 95)	25	**14r**	**17r** (95)		**20y** (81, -)
13	**14h**	**17h** (95)		**20m** (80, *rac*)					

TABLE 4. Preparation of Dienes 20 via Direct *O*-Acylation with NaHMDS and Acyl Chlorides 18

	14	18	20 21		14	18	20 21
entry	R^1 =	R^2 =	(ratio **20**:**21**, yield %, ee %)	entry	R^1 =	R^2 =	(ratio **20**:**21**, yield %, ee %)
1	**14a**		**20b** (-, 97, 97)	6	**14d**		**20ac** (-, 62, 95)
2	**14a**		**20z** (-, 96, 97)	7	**14e**		**20ad** (-, 85, 95)
3	**14a**		**20c** + **21a** (1:1, 27, n.d.)	8	**14f**		**20ae** (-, 80, 95)
4	**14a**		**20aa** + **21b** (87:13, 49, n.d.)[a]	9	**14g**		**20af** (-, 56, 94)
5	**14a**		**20ab** + **21c** (1:1, 14, n.d.)				

[a]Transmetalation with 1 equiv of $ZnCl_2$ in DME prior to quench.

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Supporting Information Available: Further experimental procedures, compound characterization data, and ^1H and ^{13}C NMR spectra. This material is available free of charge via the Internet at http://pubs.acs.org.