49–50 °C (lit.[10b] $[\alpha]_D$ +93.5° (c 0.795, $CHCl_3$), mp 49–50 °C). ^1H and ^{13}C NMR spectra were in accordance with earlier reported NMR-data.[10b]

(2*R*,5*S*)-2-Methyl-5-hexanolide [(−)-5]. In the same manner as described above for compound (+)-5, (2*S*,5*R*)-7[20] (166 mg, 0.55 mmol) was converted to (−)-5 in 58% yield (93% cis). The product was recrystallized three times (hexane). $[\alpha]_D$: −92° (c 0.80, $CHCl_3$). Mp: 50 °C (lit.[10b] $[\alpha]_D$ −91° (c 0.730, $CHCl_3$), mp 49–50 °C). ^1H and ^{13}C NMR spectra were in accordance with earlier reported NMR data.[10b]

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Highly Selective Acylation of Di- and Polyhydroxyl Compounds by 3-Acylthiazolidine-2-thiones

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It is important in organic synthesis to distinguish among hydroxyl groups of various polyhydroxyl compounds. Selective etherification of primary hydroxyl groups has been accomplished by trityl chloride, and this method has been widely used in organic synthesis.[1] However, selective acylation of hydroxyl groups has not yet been achieved despite considerable effort.[2]

I have focused on 3-acylthiazolidine-2-thiones,[3] which have moderate reactivity and can easily react with a variety of nucleophiles to yield the corresponding carboxylic acid derivatives,[4] and has studied their potential usefulness for the selective acylation of diols and polyols.[5] In this paper, a general method for the highly selective acylation of primary hydroxyl groups of diols and polyols by 3-acylthiazolidine-2-thiones in the presence of NaH is described. This method may be one of the most selective so far reported.

The selective acylation of 1,4-pentanediol (4) using known 3-acetyl- (1)[6] and 3-benzoylthiazolidine-2-thione (3)[7] and newly prepared 3-pivaloylthiazolidine-2-thione (2)[8] as acylating reagents (Figure 1) was studied. The reaction of 1,4-pentanediol and 1.1 equiv of 1 in THF in the presence of 1.1 equiv of NaH at room temperature for 4 h gave a 75:1 mixture of 1-acetoxypentan-4-ol (**5a**) and 1,4-diacetoxypentane (**7a**) in 98% yield as shown in Table I. Moreover, 4-acetoxypentan-1-ol (**6a**) was not detectable. On the other hand, acetylation by acetyl chloride gave a 3:1.2:1 mixture of the primary and secondary alkyl esters and the diester. Other bases such as DMAP, t-BuOK, KH, and LiH were not as effective as NaH. Pivaloylation of 4 with 2 afforded the primary monoester **5b** with nearly 100% selectivity, while pivaloylation with pivaloyl chloride gave a 4.7:2.3:1 mixture of the primary and secondary alkyl ester and the diester as in the case of acetylation. Benzoylation was also performed using 3. As can be seen from these results, the regioselectivity of 3-acylthiazolidine-2-thiones with 4 is in the order of 3-pivaloyl- (2) > 3-acetyl- (1) > 3-benzoylthiazolidine-2-thione (3).

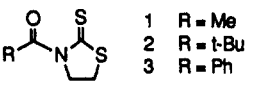
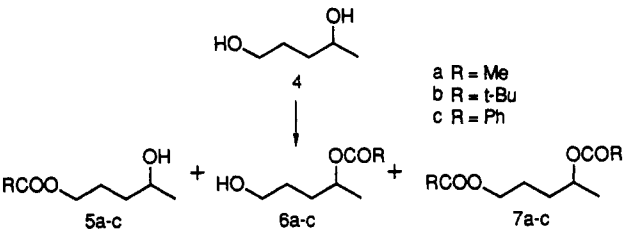


Figure 1.

Table I. Selective Acylation of 1,4-Pentanediol[a]



reagent	base	time, h	total yield,[b] %	product ratio[c] (5:6:7)
1	NaH	4	98	75:0:1
2	NaH	1	93	>100:0:1
3	NaH	2	95[d]	21:0:1
CH_3COCl	Et_3N	4	95	3:1.2:1
$(CH_3)_3CCOCl$	Py	2	92	6:2:1

[a] Conditions: see text. Acylations by 1–3 were conducted in THF and by acid chlorides were conducted in CH_2Cl_2. [b] GLC yield based on internal standard. Conversion of 4 was almost complete unless otherwise indicated. [c] Determined by GLC and/or 400 MHz ^1H NMR. [d] Isolated yield.

In order to explore the usefulness of this method, selective acylation of several diols was examined. The results are summarized in Table II. Acylation of 1,3-butanediol (**8a**), a cyclic diol **8b**, and 1,5-hexanediol (**8c**) was also achieved selectively in the same manner as with 4 to give primary alkyl esters in high yields. In general, the separation and purification of these primary and secondary alkyl esters are difficult because of the similarity of their physical properties. However, in this reaction the secondary monoesters are rarely generated and therefore the pure primary monoesters are obtained without difficulty. A limitation of this method was found in the acylation of 1,2-butanediol (**8d**). The lower selectivities are attributed to the ease of intramolecular 1,2-migration of the acyl groups under these reaction conditions. The present method was applicable not only to diols but also to polyols such as cholane-3α,7α,12α,24-tetrol (**12**)[8] (Scheme I). The monopivaloylation of the tetrol 12 by reagent 2 gave a

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(2) (a) Orazi, O. O.; Corral, R. A. *J. Am. Chem. Soc.* **1969**, *91*, 2162. (b) Nashed, M. A.; Anderson, L. *Tetrahedron Lett.* **1976**, 3503. (c) Havel, M.; Velek, J.; Pospisek, J.; Soucek, M. *Collect. Czech. Chem. Commun.* **1979**, *44*, 2443. (d) Mukaiyama, T.; Pai, F-C.; Onaka, M.; Narasaka, K. *Chem. Lett.* **1980**, 563. (e) Nagao, Y.; Fujita, E.; Kohno, T.; Yagi, M. *Chem. Pharm. Bull*, **1981**, *29*, 3202. (f) Sekine, M.; Kume, A.; Hata, T. *Tetrahedron Lett.* **1981**, *22*, 3617. (g) Posner, G. H.; Oda, M. *Tetrahedron Lett.* **1981**, *22*, 5003. (h) Rana, S. S.; Barlow, J. J.; Matta, K. L. *Tetrahedron Lett.* **1981**, *22*, 5007. (i) Tsuda, Y.; Haque, M. E.; Yoshimoto, K. *Chem. Pharm. Bull.* **1983**, *31*, 1612. (j) Kim, S.; Chang, H.; Kim, W. J. *J. Org. Chem.* **1985**, *50*, 1751. (k) Kunieda, T.; Mori, T.; Higuchi, T.; Hirobe, M. *Tetrahedron Lett.* **1985**, *26*, 1977. (l) Paradisi, M. P.; Zecchini, P.; Torrini, I. *Tetrahedron Lett.* **1986**, *27*, 5029.

(3) (a) Izawa, T.; Mukaiyama, T. *Chem. Lett.* **1977**, 1443. (b) Nagao, Y.; Kawabata, K.; Fujita, E. *J. Chem. Soc., Chem. Commun.* **1978**, 330.

(4) Fujita, E. *Pure Appl. Chem.* **1981**, *53*, 1141.

(5) Plusquellec and Backzko (*Tetrahedron Lett.* **1987**, *28*, 3809) reported that methyl α-D-glucoside was acylated by 3-acylthiazolidine-2-thiones to give methyl 6-*O*-acyl-α-D-glucosides in about 60–70% yields based on the acylating reagents. However, in this reaction 3 molar equiv of substrates were used in the presence of a catalytic amount of NaH and DMAP in dry pyridine. Only the long chain alkyl esters were synthesized and the isomer ratio was not reported.

(6) Chung-shi, L.; Yuen-hwa, Y.; Yao, L.; Yong-jun, L.; Ai-hsueh, L.; Chi-yi, H. *Tetrahedron Lett.* **1981**, *22*, 3467.

(7) Izawa, T.; Mukaiyama, T. *Bull. Chem. Soc. Jpn.* **1979**, *53*, 555.

(8) Kuramoto, T.; Kihara, K.; Matsumoto, N.; Hoshita, T. *Chem. Pharm. Bull.* **1981**, *29*, 1136.

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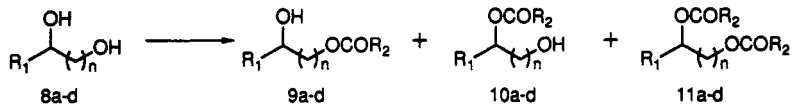
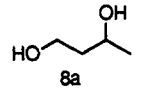
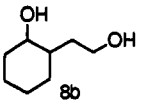
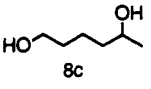
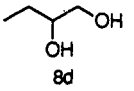
Table II. Selective Acylation of Several Diols

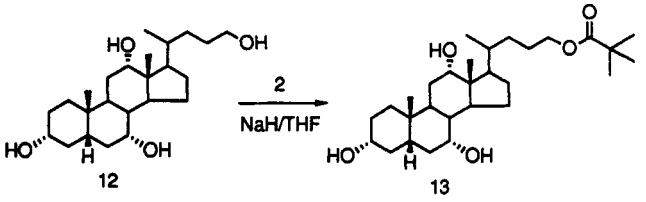


8a-d 9a-d 10a-d 11a-d

diol	reagent	base	solvent	time, h	total yield,[a] %	product ratio[b] (9:10:11)
 8a	1	NaH	THF	4	93	19:0:1
	2	NaH	THF	1.5	88	>100:0:1
	$(CH_3)_3COCl$	Py	CH_2Cl_2	2	92	4.7:2.3:1
 8b	1	NaH	THF	1	97	91:0:1
	2	NaH	THF	1	93	>100:0:1
 8c	1	NaH	THF	1	96	83:0:1
	$(CH_3)_3COCl$	Py	CH_2Cl_2	3	91	5:0.8:1
 8d	1	NaH	THF	3	98	3.8:1.2:1
	2	NaH	THF	2	96	4:0.7:1

[a] GLC yield based on internal standard. [b] Determined by GLC and/or 400-MHz ^1H NMR.

Scheme I



12 13

primary monoester **13** in 87% isolated yield, which is not readily available by the other methods.

It is thought that these high selectivities arise from a difference in the reactivity of the hydroxyl groups toward the reagents owing to steric factors and the good leaving ability[4] of the thiazolidine-2-thione group. In addition, since the alkoxides of the primary hydroxyl groups of the diols are more preferentially generated than the secondary ones because of their acidities,[9] the primary hydroxyl groups seemed to react with the reagents faster than the secondary ones.

The present method should thus be applicable to a variety of diols and polyols. Studies of extensions of this method are in progress and will be reported.

Experimental Section

General. Melting point determinations are uncorrected. TLC was carried out on a Merck Kiesel gel 60-PF_{254}. GLC was carried out using a 5% SE-30 or 10% DC-550 column (2 m × 3 mm). IR spectra were obtained as neat films between salt plates or as KBr pellets. ^1H and ^{13}C NMR spectra were recorded at 400 MHz using $CDCl_3$ as solvent ($SiMe_4$ as internal standard). High- and low-resolution mass spectra were recorded at an ionizing voltage of 70 eV by electron impact.

Synthesis of 3-Pivaloylthiazolidine-2-thione (2). To a solution of thiazolidine-2-thione (12.0 g, 0.1 mol) and triethylamine (13.0 g, 0.13 mol) in dry CH_2Cl_2 (50 mL) at 0 °C was added dropwise a solution of pivaloyl chloride (14.0 g, 0.11 mol) in CH_2Cl_2 (20 mL). The solution was stirred for 10 h at room temperature. The reaction mixture was washed with water, and the organic layer was dried over $MgSO_4$. Evaporation of the solvent gave a crude crystalline product, which was then recrystallized from ether–hexane to yield a pure specimen of **2** (15.8 g, 78%): mp 58.0–59.5 °C; IR (KBr) 1726 (C = O), 1388, 1280, 1245, 1209, 1149, 1045, 1003, 873 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.41 (s, 9 H), 3.48 (t, J = 7.25 Hz, 2 H), 4.19 (t, J = 7.25 Hz, 2 H); ^{13}C NMR ($CDCl_3$) δ 200.6, 187.8, 57.3, 44.5, 31.6, 27.7; MS m/z 203 (M^+, 17.3), 119 (8.6), 85 (15.6), 72 (16.0), 57 (100). Anal. Calcd for $C_8H_{11}NOS_2$: C, 47.26; H, 6.44; N, 6.89. Found: C, 46.98; H 6.57; N, 6.88.

General Procedure for the Monoacylation of Diols. To a solution of a diol (0.5 mmol) and the acylating reagent **1**–**3** (0.55 mmol) in dry THF (5 mL) was added sodium hydride (60% in oil, 0.5 mmol) at room temperature. The solution was stirred for 1–4 h under a nitrogen atmosphere. Saturated ammonium chloride solution (0.5 mL) was added to the reaction mixture, and the solution was extracted with $CHCl_3$. The organic layer was dried over $MgSO_4$ and concentrated to yield a crude product which was analyzed by GLC or by ^1H NMR after purification by preparative TLC.

Monopivaloylation of Cholane-3α,7α,24-tetrol (12). To a solution of **12** (90 mg, 0.23 mmol) and reagent **2** (70 mg, 0.35 mmol) in dry THF (8 mL) was added sodium hydride (60% in oil, 18 mg, 0.45 mmol) at room temperature under a nitrogen atmosphere. The solution was stirred for 10 h. The reaction mixture was washed with saturated ammonium chloride solution and then extracted with $CHCl_3$. The organic layer was dried over $MgSO_4$ and concentrated. The crude oily product was purified by preparative TLC eluting with $CHCl_3$–MeOH (10:1) to give pure primary monoester **13** (95 mg, 87%) as an oil: IR (KBr) 3410 (OH), 1730 (C = O), 1465, 1287, 1161, 1078 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.68 (s, 3 H), 0.89 (s 3 H), 1.20 (s, 3 H), 3.48 (m, 1 H), 3.85 (s, 1 H), 3.98 (s, 1 H), 4.03 (m, 2 H).

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Registry No. **1**, 76397-53-0; **2**, 138459-91-3; **3**, 70326-37-3; **4**, 626-95-9; **5a**, 18381-22-1; **5b**, 138459-92-4; **5c**, 128733-39-1; **7b**, 138459-93-5; **8a**, 107-88-0; **8b**, 7768-28-7; **8c**, 928-40-5; **8d**, 584-03-2; **9a** (R_2 = Me), 1851-86-1; **9a** (R_2 = ±-Bu), 138459-94-6; **9b** (R_2 = Me), 138459-95-7; **9b** (R_2 = ±-Bu), 138488-63-8; **9c** (R_2 = ±-Bu), 138488-64-9; **9c** (R_2 = ±-Bu), 138488-64-9; **9d** (R_2 = Me), 24469-20-3; **9d** (R_2 = ±-Bu), 138459-96-8; **11b** (R_2 = Me), 134979-03-6; **11b** (R_2 = ±-Bu), 138459-97-9; **11c** (R_2 = ±-Bu), 138459-98-0; **12**, 3758-71-2; **13**, 138459-99-1; $(CH_3)_3CCOCl$, 3282-30-2; thiazolidine-2-thione, 96-53-7.

Supplementary Material Available: Spectral data (IR, ^1H NMR, and MS) of the new products reported (2 pages). Ordering information is given on any current masthead page.

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