



Phosphorus, Sulfur, and Silicon and the Related Elements

Publication details, including instructions for authors and subscription information:

<http://www.tandfonline.com/loi/gpss20>

Synthesis and Conformational Studies of Tertiary Alcohols Derived from Tetrahydro-4H-pyran-4-one and Tetrahydrothiopyran-4-one

Kevin Tran ^a, K. Darrell Berlin ^a, Elizabeth M. Holt ^a, Randal Hallford ^b, Margaret A. Eastman ^c, Valentina K. Yu ^d & K. D. Praliev ^d

^a Department of Chemistry, Oklahoma State University, Stillwater, Oklahoma

^b Department of Chemistry, Oklahoma State University, Stillwater, Oklahoma
Department of Chemistry, Midwestern State University, Wichita Falls, Texas

^c Department of Chemistry, Oklahoma State University, Stillwater, Oklahoma

^d Institute of Chemical Sciences, Ministry of Science and Education, Kazakhstan

Published online: 01 Feb 2007.

To cite this article: Kevin Tran, K. Darrell Berlin, Elizabeth M. Holt, Randal Hallford, Margaret A. Eastman, Valentina K. Yu & K. D. Praliev (2005) Synthesis and Conformational Studies of Tertiary Alcohols Derived from Tetrahydro-4H-pyran-4-one and Tetrahydrothiopyran-4-one, *Phosphorus, Sulfur, and Silicon and the Related Elements*, 180:1, 53-66, DOI: [10.1080/104265090507641](https://doi.org/10.1080/104265090507641)

To link to this article: <http://dx.doi.org/10.1080/104265090507641>

PLEASE SCROLL DOWN FOR ARTICLE

Taylor & Francis makes every effort to ensure the accuracy of all the information (the "Content") contained in the publications on our platform. However, Taylor & Francis, our agents, and our licensors make no representations or warranties whatsoever as to the accuracy, completeness, or suitability for any purpose of the Content. Any opinions and views expressed in this publication are the opinions and views of the authors, and are not the views of or endorsed by Taylor & Francis. The accuracy of the Content should not be relied upon and should be independently verified with primary sources of information. Taylor and Francis shall not be liable for any losses, actions, claims, proceedings, demands, costs, expenses, damages, and other liabilities whatsoever or howsoever caused arising directly or indirectly in connection with, in relation to or arising out of the use of the Content.

This article may be used for research, teaching, and private study purposes. Any substantial or systematic reproduction, redistribution, reselling, loan, sub-licensing, systematic supply, or distribution in any form to anyone is expressly forbidden. Terms & Conditions of access and use can be found at <http://www.tandfonline.com/page/terms-and-conditions>

Synthesis and Conformational Studies of Tertiary Alcohols Derived from Tetrahydro-4H-pyran-4-one and Tetrahydrothiopyran-4-one

Kevin Tran

K. Darrell Berlin

Elizabeth M. Holt

Department of Chemistry, Oklahoma State University,
Stillwater, Oklahoma

Randal Hallford

Department of Chemistry, Oklahoma State University,
Stillwater, Oklahoma and Department of Chemistry,
Midwestern State University, Wichita Falls, Texas

Margaret A. Eastman

Department of Chemistry, Oklahoma State University,
Stillwater, Oklahoma

Valentina K. Yu

K. D. Praliev

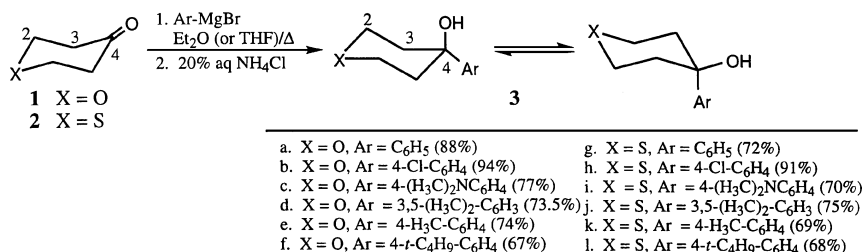
Institute of Chemical Sciences, Ministry of Science and
Education, Kazakhstan

A series of derivatives of tetrahydro-4H-pyran-4-one and tetrahydrothiopyran-4-one have been prepared by condensation with aryl Grignard reagents. IR spectra, ^1H and ^{13}C NMR spectral analyses, and elemental analyses support the structures. A single-crystal X-ray diffraction analysis of 4-(3,5-dimethylphenyl)tetrahydrothiopyran-4-ol [$a = 9.729(10)$, $b = 12.846(2)$, $c = 9.970(10)$ Å; space group $Pna2(1)$] confirmed the aryl group is located in a pseudo equatorial position, and the heterocyclic ring is slightly flattened near the sulfur end of the molecule.

Keywords 1,2-Addition; Grignard reagents; NMR analysis; pyranols; thiopyranols; X-ray data

Received April 18, 2004; accepted June 3, 2004.

Address correspondence to K. D. Berlin, Department of Chemistry, Oklahoma State University, Stillwater, Oklahoma 74078, USA. E-mail: kdb@okstate.edu



SCHEME 1

INTRODUCTION

A search of the literature revealed that tetrahydro-4*H*-pyranone (**1**) and tetrahydrothiopyranone (**2**) have not been extensively investigated in terms of 1,2-additions by organometallics. Ketone **1** has found use as a synthon in the generation of part of the vitamin D₃ ring A.¹ Relatively few tertiary alcohols **3** derived from ketones **1** and **2** have been recorded, with the exception of **3g**.² The preparation of 4-*t*-butylthiopyran-4-ol and 4-vinylthiopyran-4-ol have also been recently reported and appear to possess analgesic and muscle-relaxing activities in mice.³ Herein we report the general syntheses and conformational studies of alcohols derivatives of ketones **1** and **2**.

RESULTS AND DISCUSSION

Syntheses of alcohols **3** proceeded via condensation of ketone **1** and/or **2** with selected aryl Grignard reagents. The reactions occurred under mild conditions in anhydrous ether or in dry THF. Workup was minimal, yields of alcohols **3** were good to excellent, and purification was achieved by flash column chromatography over silica gel. Elemental analyses and ¹H and ¹³C NMR spectral data (Tables I and II) support the structures. Chemical shifts in the ¹H and ¹³C NMR spectra of compounds **3a–l** were assigned partially on the basis of electronegativity effects of the heteroatoms on the protons and carbons at the α positions. If a flattened chair is assumed for the heterocyclic ring, the aryl group would be expected to occupy a pseudo-equatorial position. The γ-shielding effects of groups larger than hydrogen, such as the axial O-H group in **3**, are known⁴ in six-member rings. Such steric effects can induce conformational changes in such systems as reflected in the NMR analysis.⁵ The configurations of the 4-pyranols were corroborated by the ¹³C chemical shifts data (Table II). It was noted that shielding at C4 only varied by slightly less than 2 ppm in the C-13

TABLE I ¹H Chemical Shifts of Alcohols 3a-l (δ, DCCl₃)

δ	3a	3b	3c	3d	3e	3f	3g	3h	3i	3j	3k	3l
H _{(3,5)a}	1.69–1.74 m	1.59–1.64 m	1.68–1.70 m	1.62–1.64 m	1.62–1.64 m	1.68–1.73 m	1.98–2.03 m	1.94–1.95 m	1.97–2.03 m	1.95–2.00 m	1.98–2.03 m	2.00–2.05m
H _{(3,5)e}	2.15–2.25 m	2.02–2.12 m	2.08–2.13 m	2.10–2.15 m	2.08–2.19 m	2.12–2.23 m	2.13–2.23 m	2.08–2.18 m	2.08–2.18 m	2.11–2.20 m	2.13–2.22 m	2.13–2.23 m
H _{(2,6)a}	3.86–3.91 m	3.76–3.82 m	3.80–3.82 m	3.81–3.84 m	3.80–3.86 m	3.84–3.89 m	2.43–2.48 m	2.42–2.47 m	2.42–2.46 m	2.42–2.46 m	2.46–2.49 m	2.45–2.49 m
H _{(2,6)e}	3.93–4.01 m	3.83–3.92 m	3.88–3.92 m	3.88–3.92 m	3.87–3.96 m	3.90–3.98 m	3.16–3.25 m	3.12–3.22 m	3.11–3.20 m	3.14–3.24 m	3.15–3.25 m	3.17–3.25 m
OH	2.00 s	2.40 s	1.90 s	2.05 s	1.86 s	1.65 s	1.63 s	1.75 s	1.62 s	1.61 s	1.53 s	1.52 s
CH ₃	x	x	2.32 s	2.32 s	2.34 s	1.33 s	x	x	2.93 s	2.32 s	2.34 s	1.32 s
H _(2,6')	7.30–7.35 m	7.30–7.33 m	6.72–6.73 d	7.08 s	7.35–7.36 d	7.25–7.26 d	7.46–7.49 m	7.30–7.33 m	6.70–6.73 d	7.07 s	7.34–7.37 d	7.36–7.42 m
H _(3,5')	7.40–7.45 m	7.38–7.41 m	7.33–7.35 d	x	7.16–7.19 d	7.41–7.42 d	7.27–7.29 m	7.38–7.41 m	7.30–7.33 d	x	7.16–7.19 d	(Ar-H)
H _{4'}	7.52–7.55 m	x	x	6.92 s	x	x	7.34–7.39 m	x	x	6.91 s	x	x

m = multiplet, s = singlet, x = not applicable. Protons on aromatic rings are indicated as numbers with (') sign.

TABLE II ^{13}C Chemical Shifts of Alcohols 3a–h (ppm, DCCl_3)

ppm	3a	3b	3c	3d	3e	3f	3g	3h	3i	3j	3k	3l
$\text{C}_{(3,5)}^{\alpha}$	38.58	38.47	38.65	38.67	38.74	38.72	39.43	39.33	39.61	39.55	39.55	39.59
$\text{C}_{(2,6)}^{\beta}$	63.74	63.57	63.93	63.80	63.87	63.91	24.08	23.96	24.34	24.17	24.19	24.26
C_7^{γ}	70.38	70.05	69.81	70.31	70.38	70.44	71.80	71.61	71.19	71.75	71.64	71.64
C_4^{δ}	x	x	38.65	21.41	20.91	31.28	x	x	40.52	21.44	20.88	31.31
CH_3	x	x	x	x	x	34.41	x	x	x	x	x	34.42
$\text{C}_{1'}$	148.04	146.64	148.01	148.11	136.87	144.98	148.93	147.45	125.05	149.05	146.13	146.02
$\text{C}_{2',6'}$	127.10	128.40	125.21	122.18	124.32	125.37	127.02	128.40	125.98	121.98	124.11	125.35
$\text{C}_{3',5'}$	124.38	125.94	112.30	137.83	129.10	124.11	128.36	125.74	112.31	137.90	129.05	123.98
$\text{C}_{4'}$	128.36	132.78	149.63	128.69	145.12	150.18	124.15	132.77	149.54	128.64	136.70	150.03

x = not applicable, carbons on aromatic ring are indicated as numbers with apostrophes.

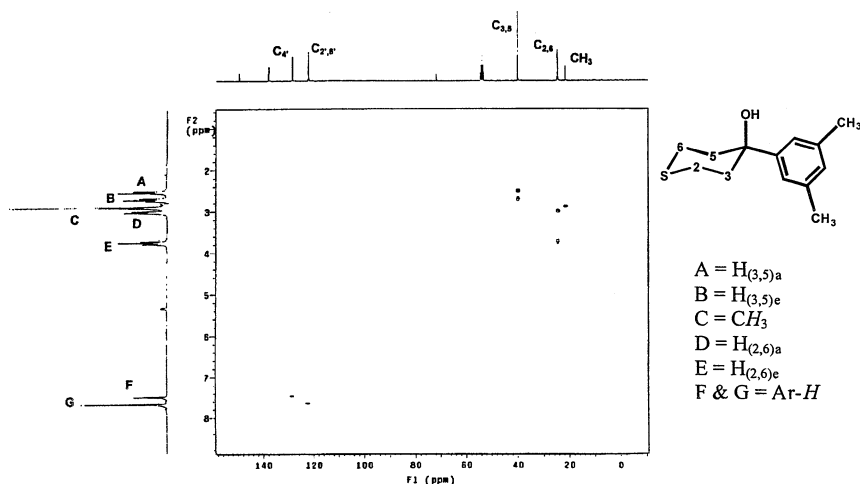


FIGURE 1 The gHMQC spectra of **3j**.

chemical shifts in **3**. The implication is that all of the C4 carbons are in the same environment. Similar carbons in epimeric alcohols vary ~ 5 ppm.⁴

Alcohol **3j** was selected for an in depth NMR analysis. A 2D Gradient Heteronuclear Quantum Correlation (gHMQC) spectrum was obtained for **3j** to determine if the correlations existed between the protons and carbons in the heterocyclic ring (Figure 1). Signal **A** shows a correlation between $C_{(3,5)}$ and $H_{(3,5)a}$, while **B** indicates a correlation of $C_{(3,5)}$ and $H_{(3,5)e}$. Signal **C** belongs to the CH_3 groups. Signal **D** represents a correlation between $C_{(2,6)e}$ and $H_{(2,6)e}$ while **E** exhibits a correlation of $C_{(2,6)}$ and $H_{(2,6)e}$. Both **F** and **G** are for carbons and the corresponding hydrogens at the ortho and para positions of the aromatic ring.

Although the 1H and ^{13}C analyses suggested a single conformer for each alcohol with some long-range couplings being visible in individual patterns, a variable low-temperature 1H NMR analysis of **3j** was performed. The 1H spectra of **3j** in CD_2Cl_2 were obtained at $28^\circ C$, $0^\circ C$, $-60^\circ C$, $-78^\circ C$, and $-88^\circ C$ at 399.90 MHz. The spectra (Figure 2) showed similar shifts and patterns at all temperatures with the exception that at -78 and $-88^\circ C$ the signal for the hydroxyl proton was shifted downfield from δ 1.45 to δ 2.62 and δ 3.82. It is well known that the chemical shift of the OH proton is concentration dependent.⁶ The possibility exists for the dimerization or trimerization of two or three alcohol molecules in the solution at -78 and $-88^\circ C$. It was recently reported⁷ that at low temperatures two or three molecules with NH and/or OH groups may form a low-barrier hydrogen bond (Figure 3)

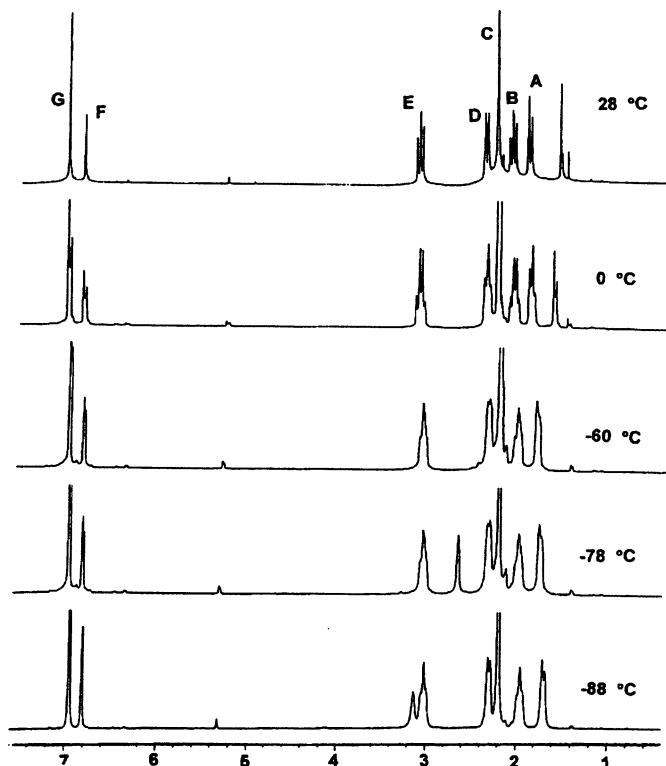


FIGURE 2 The ^1H NMR spectra of **3j** at various temperatures.

which likely affects the chemical shift of the proton on the OH group. At this time there does not appear to be another obvious argument that is tenable to explain our result with **3j**. Despite the ^1H NMR analyses suggesting a single conformer, it is not possible to eliminate a small but dynamic equilibrium involving more than one conformer of **3j** at room temperature. It is tentatively assumed that the major conformer

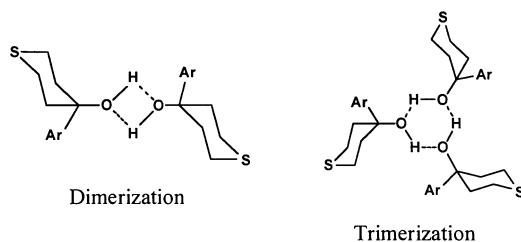


FIGURE 3 The possible dimer and trimer of **3j**.

is that with the aryl group in a pseudo-equatorial position in solution. In addition, to assure that a singlet at δ 1.45 belonged to the OH group, a D₂O-exchange experiment was conducted. The resulting spectrum (Figure 4) shows the disappearance of a singlet peak at δ 1.45 and the appearance of another singlet peak at δ 4.82. This proved that a singlet at δ 1.45 belonged to OH group of **3j**, and the new singlet at δ 4.82 was for HOD.

The shape of a ring system can also be estimated from analysis of vicinal ¹H NMR coupling constants. A potentially mobile ring system such as **3j** permits the measurement of two average coupling constants in a CH₂–CH₂ fragment, $J_{\text{trans}} = 0.5 (J_{\text{aa}} + J_{\text{ee}})$ and $J_{\text{cis}} = 0.5 (J_{\text{ae}} + J_{\text{ea}})$. The ratio $R = J_{\text{trans}}/J_{\text{cis}}$ ⁸ was utilized to assess the nature of the distortion present in the ring.⁹ In a distortion-free CH₂–CH₂ fragment⁴ of a ring, the ratio R of the average vicinal trans-coupling constant to the average vicinal cis coupling constant is in the range 1.9–2.2.^{8,9} A flattening of this fragment (eclipsing of the substituents,⁵) gives a lower R value while a puckered 6 increases R .^{8,9} The R value is related directly to the internal dihedral angle ψ by Equation 1.^{8,9} Thus, an undistorted R value of 1.9–2.2 corresponds to a torsional angle ψ of ≈ 56 – 58° . The flattened geometry ($R < 1.8$) corresponds to $\psi < 55^\circ$, and the puckered geometry ($R > 2.3$) corresponds to $\psi > 59^\circ$. The calculation of distortion angles of system **3j** using Equation 1 suggested that the sulfur-containing ring is flattened, $R (=1.07) < 1.8$ and $\psi = (46.3^\circ) < 55^\circ$.

$$\begin{aligned}
 J_{\text{trans}} &= J_{2a,3a} = J_{2e,3e} = 14.1 \text{ Hz} \\
 J_{\text{cis}} &= J_{2a,3e} = J_{2e,3a} = 13.2 \text{ Hz} \\
 R &= \frac{J_{\text{trans}}}{J_{\text{cis}}} = \frac{14.1 \text{ Hz}}{13.2 \text{ Hz}} = 1.07 \\
 \cos \psi &= \left(\frac{3}{2 + 4R} \right)^{1/2} = \left(\frac{3}{2 + 4(1.07)} \right)^{1/2} = 0.69
 \end{aligned}
 \tag{1}$$

Thereby

$$\psi = \cos^{-1} 0.69 = 46.3^\circ$$

For conformational purposes, an X-ray diffraction analysis was also performed on a single crystal of **3j**. The X-ray data demonstrated that the aryl group was clearly attached to C4 at a pseudo-equatorial position (Figure 5). The torsion angles and crystal data of heterocyclic ring **3j** are given in Tables III and IV. The sum of the theoretical torsion angles for an alicyclic 6-member ring would be 360.0° if the ring were totally flat. The total observed torsion angles in **3j** is 350.1° , indicating a flattening

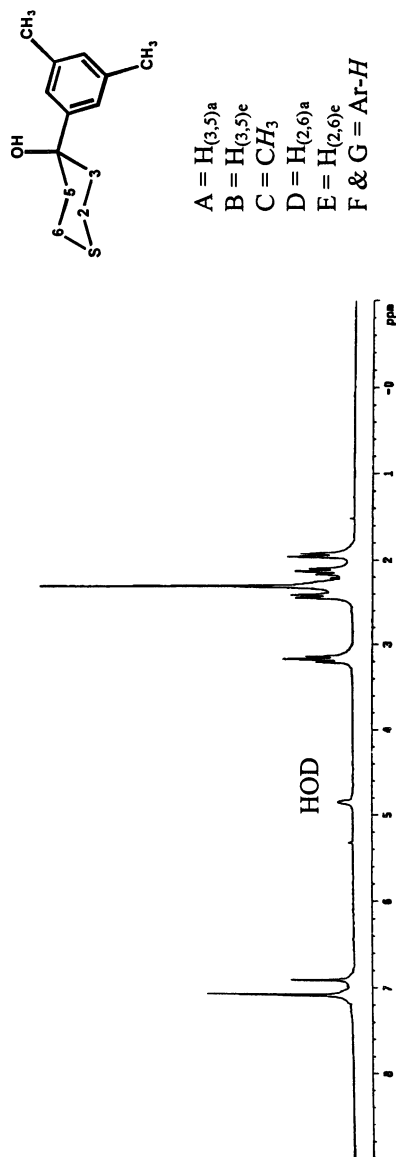
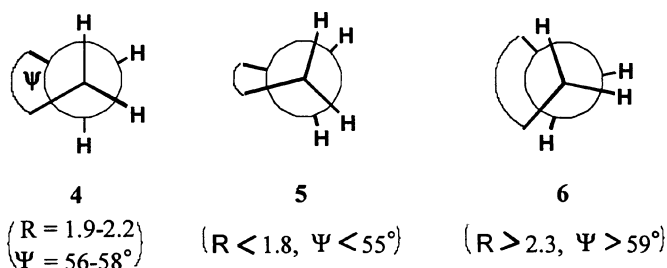


FIGURE 4 D₂O exchange ¹H NMR spectrum of **3j**.



$$\cos \psi = [3/(2 + 4R)]^{1/2}$$

near the sulfur end of the molecule. From another point of view, the plane of the base of the chair (C2-C3-C5-C6) subtends an angle of 51.8° with the S1-C2-C6 plane and an angle of 49.6° with the C3-C4-C6 plane. The interplanar angles would each be 60° if the chair had theoretical geometry. The angles are smaller, and thus the ends of the chair are each flattened by about 10° from ideal.

In summary, we have prepared a series of the title compounds in which the aryl group prefers a pseudo-equatorial position in the solid state. NMR data implies this type of conformation may also predominate in solution, perhaps due to intermolecular H-bonding involving two or more molecules in CD_2Cl_2 . The tertiary alcohols generated can serve as useful synthons for a variety of heterocyclic systems. Moreover, the physical and spectral properties of these alcohols can be important standards for related systems.

EXPERIMENTAL

General Methods

Grignard reagents were purchased either from Rieke Metals, Inc. (1001 Kingbird Road, Lincoln, NE 68521) or from Aldrich Chemical Company (P.O. Box 2060, Milwaukee, WI 53201). Melting points were taken on Thomas-Hoover capillary apparatus and were uncorrected. IR spectra

TABLE III Torsion Angles of 3j

S1-C2-C3-C4	-61.3°
C2-C3-C4-C5	-56.4°
C3-C4-C5-C6	56.6°
C4-C5-C6-S1	-61.4°
C5-C6-S1-C2	57.3°
C6-S1-C2-C3	-57.1°

Total: 350.1° ; Theoretical: 360.0° .

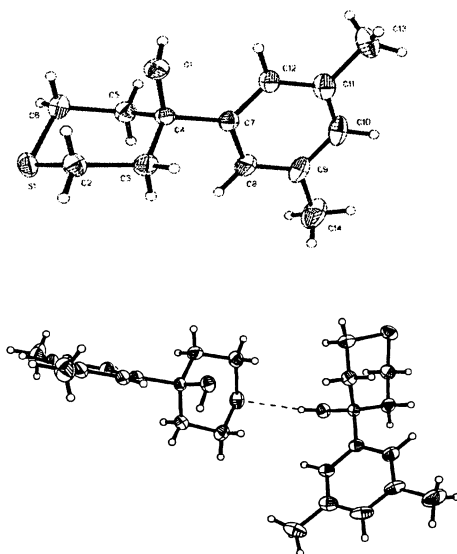


FIGURE 5 Perspective view of **3j**.

were recorded on a Perkin-Elmer 2000 FT-IR spectrometer as films. Both ^1H and ^{13}C NMR spectral data were obtained on Varian Gemini 2000 High-Resolution NMR operating at 300.09 MHz and 75.46 MHz and on a Varian Inova 400 NMR unit operating at 399.91 MHz and 100.01 MHz, respectively. The variable temperature NMR study and 2D work on **3j** were performed on the Inova 400 unit. Chemical shifts are reported as δ or ppm values. Elemental analyses were performed by Alantic Microlab, Inc., Norcross, Georgia.

General Procedure to Obtain **3**

To a solution of the appropriate Grignard reagent in a system under N_2 was added dropwise ketone **1** (0.5–5.0 g, 0.005–0.05 mol) and/or **2** (0.05–5.0 g, 0.0043–0.043 mol) in anhydrous THF (35 mL) for **1a,b,e,f** and/or **2g,h,k,l**, respectively. The mmol ratio was 2:1 for the arylmagnesium bromide:monocyclic ketone. Ether was the solvent for reactions involving **1c,d** and **2i,j**. The suspension was gently boiled (1–3 h), was stirred overnight (RT), and was then decomposed *cautiously* with aqueous 20% NH_4Cl (ice bath). The mixture was extracted (ether, 3×100 mL), and the combined extracts were dried (K_2CO_3). Evaporation of the solvent gave good yields of the solids all of which were purified using “Baker” silica gel (40 μm) via flash column chromatography. The proton and ^{13}C NMR chemical shifts (DCCl_3) are given for each alcohol in Tables I and II (referenced to TMS).

TABLE IV Crystal Data for 3j

Mol. formula	C ₁₃ H ₁₈ OS	Crystal size	0.15 × 0.15 × 0.2 mm
MWT	222.33	Theta range for data collection	2.59 to 27.10 deg.
Temperature	293 (2) K	Index ranges	−1 ≤ h ≤ 12, −16 ≤ k < 1, −12 ≤ l ≤ 1
Wavelength	0.71073 Å	Reflections collected/unique	1955/1616 [R (int) = 0.0303]
Space group	Pna2(1)	Completeness to2theta = 27.10	99.7%
Crystal system	Orthorhombic	Absorption corection	Empirical
		Max. and min. transmission	0.992 and 0.827
Cell Dimensions		Refinement method	Full-matrix least-squares on F ²
a = 9.729 (10) Å	α = 90°	Data/restraints/parameters	1616/1/137
b = 12.846 (2) Å	β = 90°	Goodness-of-fit on F ²	0.929
c = 9.970 (10) Å	γ = 90°	Final R indices [I > 2sigma (I)]	R1 = 0.0539, wR2 = 0.1374
V	1246 (3) Å ³	R indices (all data)	R1 = 0.0915, wR2 = 0.1624
Z, D _{calc.}	4, 1.185 mg/m ³	Absolute structure parameter	−0.09 (19)
Ab. Coeff.	0.233 mm ^{−1}	Extinction coefficient	0.000 (3)
F (000)	480	Largest diff. peak and hole	0.203 and −0.185 e. Å ^{−3}

4-Phenyltetrahydropyran-4-ol (3a). [1 (5.0 g, 0.05 mol):PhMgBr (0.1 mol)]. Yield: 7.83 g (88%); mp 100–100.5°C. IR 3337 (O–H), 687 and 780 (mono) cm^{-1} . Eluant solvents: ether:hexanes (1:1). Anal. Calcd for $\text{C}_{11}\text{H}_{14}\text{O}_2$: C, 74.13; H, 7.92. Found: C, 73.89; H, 8.05.

4-(4-Chlorophenyl)tetrahydropyran-4-ol (3b). [1 (5.0 g, 0.05 mol):4-Cl- C_6H_4 -MgBr (0.1 mol)]. Yield: 9.96 g (94%); mp 77–78°C. IR 3393 (O–H), 828 (para) cm^{-1} . Eluant solvents: ether:hexanes (1:1). Anal. Calcd for $\text{C}_{11}\text{H}_{13}\text{ClO}_2$: C, 62.12; H, 6.16; Cl, 16.67. Found: C, 62.37; H, 6.14; Cl, 16.71.

4-(4-*N,N*-Dimethylaminophenyl)tetrahydropyran-4-ol (3c). [1 (5.0 g, 0.05 mol):4-Me₂N- C_6H_4 -MgBr (0.1 mol)]. Yield: 8.50 g (77%); mp 102–103°C. IR 3437 (O–H), 817 (para) cm^{-1} . Eluant solvents: ether:hexanes (1:1). Anal. Calcd for $\text{C}_{13}\text{H}_{19}\text{NO}_2$: C, 70.56; H, 8.65; N, 6.33. Found: C, 70.73; H, 8.66; N, 6.21.

4-(3,5-Dimethylphenyl)tetrahydropyran-4-ol (3d). [1 (5.0 g, 0.05 mol): 3,5-(Me)₂- C_6H_3 -MgBr (0.1 mol)]. Yield: 7.56 g (73.5%); mp 102–103°C. IR 3387 (O–H) cm^{-1} . Eluant solvents: ether:hexanes (1:1). Anal. Calcd for $\text{C}_{13}\text{H}_{18}\text{O}_2$: C, 75.69; H, 8.80. Found: C, 75.69; H, 8.80.

4-*p*-Tolyltetrahydropyran-4-ol (3e). [1 (0.5 g, 0.005 mol):4-Me- C_6H_4 -MgBr (0.01 mol)]. Yield: 0.712 g (74%); mp 105–105.5°C. IR 3378 (O–H) 833 (para) cm^{-1} . Recrystallization of the white solid was from ether and petroleum ether (1:1). Anal. Calcd for $\text{C}_{13}\text{H}_{18}\text{O}_2$: C, 74.97; H, 8.39. Found: C, 74.95; H, 8.42.

4-(4-*t*-Butylphenyl)tetrahydropyran-4-ol (3f). [1 (0.5 g, 0.005 mol):4-*t*-Bu- C_6H_4 -MgBr (0.01 mol)]. Yield: 0.737 g (67%); mp 285.5–286°C. IR 3372 (O–H), 823 (para) cm^{-1} . Recrystallization of the white solid was from ether and petroleum ether (1:1). Anal. Calcd for $\text{C}_{15}\text{H}_{22}\text{O}_2$: C, 76.88; H, 9.46. Found: C, 76.90; H, 9.67.

4-Phenyltetrahydrothiopyran-4-ol (3g). [2 (5.0 g, 0.043 mol): Ph-MgBr (0.086 mol)]. Yield: 6.04 g (72%) (Lit^{2,10} 58%); mp 76–77°C (Lit^{2,10} 76–78°C). IR 3337 (O–H), 701 and 762 (mono) cm^{-1} . The compound had been recorded, but no IR and NMR data were reported.^{2,10} Eluant solvents: ether:hexanes (1:1).

4-(4-Chlorophenyl)tetrahydrothiopyran-4-ol (3h). [2 (5.0 g, 0.043 mol):4-Cl- C_6H_4 MgBr (0.086 mol)]. Yield: 8.89 g (91%); mp 86–87°C. IR 3409 (O–H), 862 (para) cm^{-1} . Eluant solvents: ethyl acetate:hexanes (1:1). Anal. Calcd for $\text{C}_{11}\text{H}_{13}\text{ClOS}$: C, 74.13; H, 7.92. Found: C, 73.89; H, 8.05.

4-(4-*N,N*-Dimethylaminophenyl)tetrahydrothiopyran-4-ol (3i). [2 (5.0 g, 0.043 mol): 4-Me₂N-C₆H₄-MgBr (0.086 mol)]. Yield: 7.13 g (70%); mp 110.5–112°C. IR 3402 (O–H), 813 (para) cm^{−1}. Eluant solvents: ethyl acetate:hexanes (3:1). Anal. Calcd for C₁₃H₁₉NOS: C, 65.78; H, 8.07; N, 5.90. Found: C, 65.86; H, 8.09; N, 5.82.

4-(3,5-Dimethylphenyl)tetrahydrothiopyran-4-ol (3j). [2 (5.0 g, 0.043 mol): 3,5-(Me)₂-C₆H₃-MgBr (0.086 mol)]. Yield: 7.16 g (75%); mp 76–77.5°C. IR 3402 (O–H) cm^{−1}. Eluant solvents: ethyl acetate:hexanes (1:1). Anal. Calcd for C₁₃H₁₈OS: C, 70.22; H, 8.16. Found: C, 70.19; H, 8.22.

4-*p*-Tolyltetrahydrothiopyran-4-ol (3k). [2 (0.5 g, 0.0043 mol): 4-Me-C₆H₄-MgBr (0.0086 mol)]. Yield: 0.618 g (69%); mp 74.0–74.5°C. IR 3413 (O–H), 817 (para) cm^{−1}. Anal. Calcd for C₁₂H₁₆OS: C, 69.19; H, 7.74. Found: C, 69.20; H, 7.93.

4-(4-*t*-Butylphenyl)tetrahydrothiopyran-4-ol (3l). [2 (0.5 g, 0.0043 mol): 4-*t*-Bu-C₆H₄-MgBr (0.0086 mol)]. Yield: 0.673 g (68%); mp 143–143.5°C. IR 3413 (O–H), 823 (para) cm^{−1}. Recrystallization of the white solid was from ether and petroleum ether (1:1). Anal. Calcd for C₁₅H₂₂OS: C, 71.95; H, 8.86. Found: C, 71.89; H, 8.93.

Crystallographic Experimental Data for 3j^a

A single crystal [orthorhombic, Pna2 (1)] of **3j** (from ether:hexanes, 1:1) with dimensions 0.15 × 0.15 × 0.2 mm was mounted on a Bruker-Siemens-Nicolet P4 diffractometer equipped with a molybdenum source (graphite monochromator, MoK α radiation, λ = 0.71703 Å) and a θ –2 θ data collection method (variable scan rate between 10 and 30 seconds per degree, based upon the intensity observed per scan).^a The unit cell was determined by least squares refinement of the best angular positions for 48 independent reflections. Data (1955 points) were collected at 301 K (Table IV) and corrected for Lorentz, polarization, and background effects.¹¹ The intensities of three standard reflections were monitored after every 97 reflections. Crystal decomposition was found to be insignificant. After removal of redundant and space group forbidden data, atomic positions were determined with SHELXS,¹² and 1150 observed data ($I > 3.0 \cdot (I)$) were refined using full matrix least squares [function minimized, $\sum_w (F_o^2 - F_c^2)^2$] until convergence (SHELXL¹³). Hydrogen positions were calculated and included in the final cycles of refinement in constrained positions with fixed isotropic thermal parameters and with a C–H distance of 0.97 Å. Absorption corrections were

^aTables of all X-ray data have been deposited with the Cambridge Crystallographic Data Centre (CCDC), United Kingdom. CCDC 242498.

made using a semi-empirical method based on psi-scans. Extinction was refined but was minimal. Molecular graphics were prepared using the program, XP.¹⁴ The final cycle of refinement led to an agreement factor of $R = 5.39\%$ and $R_w = 9.15\%$ with 137 parameters refined. The other crystal data are in Table IV.

ACKNOWLEDGMENTS

We (KDB) thank the College of Arts and Sciences of the Oklahoma State University for partial support of this work. We (VKY and KDB) gratefully acknowledge and thank the U.S. Civilian R&D Foundation (CRDF) for the Independent States of the Former Soviet Union for partial support of this research (grant KC2-2288). We also thank the National Science Foundation (BIR-9512269), the Oklahoma State Regents for Higher Education, the W. M. Keck Foundation, and Conoco, Inc. for funds to purchase the 300, 400, and 600 MHz NMR spectrometers. We dedicate this work to the memory of Dr. Elizabeth M. Holt.

REFERENCES

- [1] M. M. Kabat, M. Lange, P. M. Wovkulich, and M. R. Uskokovic, *Tetrahedron Lett.*, **33**, 7701 (1992).
- [2] (a) G. M. Bennett and W. D. Waddington, *J. Chem. Soc.*, 2829 (1929); (b) R. L. Crumbie, D. D. Ridley, and P. J. Steel, *Aust. J. Chem.*, **38**, 119 (1985).
- [3] C. S. Sunder and K. Klessing (William Schwabe G.m.b.h. and Company), German; DE 19954569 (5/17/2001) and WO 2001035938 (5/25/2001). *Chem. Abstr.*, **134**, 353255 (2001).
- [4] J. D. Robert, F. J. Weigert, J. I. Kroschwite, and H. Reich., *J. Am. Chem. Soc.*, **92**, 1338 (1970).
- [5] D. K. Dalling and D. M. Grant, *J. Am. Chem. Soc.*, **89**, 6612 (1967).
- [6] (a) M. Rappon and R. M. Johns, *J. Mol. Liq.*, **40**, 155 (1989). (b) J. L. Kirsch and D. R. Coffin, *J. Phys. Chem.*, **80**, 2448 (1976). (c) L. Kimtys, P. Mikulskis, N. N. Shapet'ko, *Org. Magn. Res.*, **5**, 361 (1973).
- [7] (a) M. Rospenk, L. Sobczyk, P. Schah-Mohammedi, H. Limbach, N. S. Golubev, and S. M. Melikova, *Magn. Reson. Chem.*, **39**, S81 (2001). (b) E. M. B. Janke, A. Dunger, H. Limbach, and K. Weisz, *Magn. Reson. Chem.*, **39**, S177 (2001). (c) S. N. Smirnov, H. Benedict, N. S. Golubev, G. S. Demisov, M. M. Kreevoy, R. L. Schowen, and H. Limbach, *Can. J. Chem.*, **77**, 943 (1999).
- [8] J. B. Lambert, *J. Am. Chem. Soc.*, **89**, 1836 (1967).
- [9] J. B. Lambert, *Account Chem. Res.*, **4**, 87 (1971).
- [10] M. J. Cook, H. Dorn, and A. R. Katritzky, *J. Chem. Soc. B*, **12**, 1467 (1968).
- [11] Siemens (1991). XSCANS Users Manual, Siemens Analytical X-ray Instruments, Inc., Madison, Wisconsin, USA.
- [12] G. M. Sheldrick, *Acta. Cryst.*, **A46**, 467 (1990).
- [13] G. M. Sheldrick, SHELXL97. Program for the Refinement of Crystal Structures, 1997, University of Gottingen, Germany.
- [14] Siemens (1990). XP. Interactive Molecular Graphics Program. Version 4.1. Siemens Analytical X-ray Instruments, Inc., Madison, Wisconsin, USA.