Regiospecific Synthesis of Homoallylic Alcohols from Tosylhydrazones

Michael F. Lipton and Robert H. Shapiro*

Department of Chemistry, University of Colorado, Boulder, Colorado 80309

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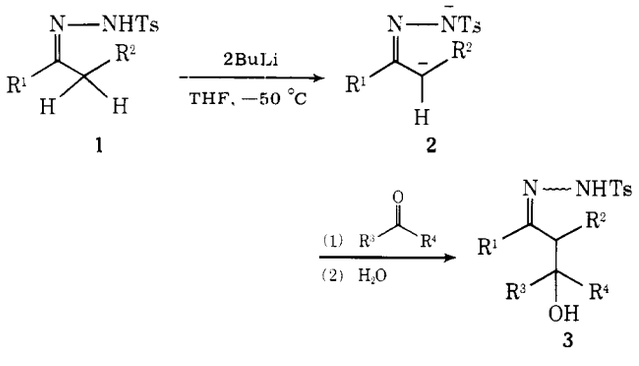
Regiospecifically generated tosylhydrazone dianions are trapped with aldehydes and ketones yielding β-hydroxytosylhydrazone dianions. Neutralization affords β-hydroxytosylhydrazones, which may be converted with or without isolation cleanly and in good yield to homoallylic alcohols upon treatment with alkyllithium reagents. A rationale is provided for the regiochemistry of this elimination. All attempts to obtain β-hydroxy ketones from the corresponding tosylhydrazone were unsuccessful.

The formation of alkenes from tosylhydrazones and alkyllithium reagents,[1] or lithium diisopropylamide,[2] has proved to be a useful reaction. In the alkyllithium reaction, alkene formation is known to proceed via a syn dianion,[3] through a vinyldiimide anion,[3] and to a vinyl anion,[3,4] with subsequent protonation to give the product. It is also known that proton abstraction from solvent may occur,[5] and in favorable cases under the influence of excess base an allyl anion may be generated. The high cis/trans ratios previously observed in acyclic systems[6] coupled with the fact that a primary deuterium isotope effect is observed for the abstraction of a syn α proton (7.5 ± 2.2 determined for pinacolone tosylhydrazone-α-*d* by mass spectrometry) point to an E1cB mechanism for the elimination reaction. We now wish to report that the syn dianion is readily trapped on carbon with aldehydes and ketones, yielding β-hydroxytosylhydrazones (**3**) after protonation (Scheme I).

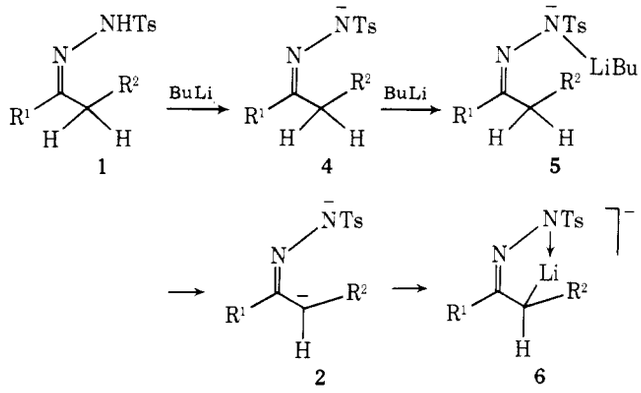
Our initial report concerning the regiochemistry of dianion formation[3] has been followed by much work in similar systems which also produce syn dianions upon treatment with alkyllithium reagents.[7-9] Tosylhydrazones lacking α protons undergo reductive alkylation,[10] as do aldehyde tosylhydrazones.[11] The enhanced acidity of the syn α protons in oximes[7,8] has been attributed to the chelation effect[12,13] and a 6π electron nonbonded through space interaction.[14] Since the observed regiochemistry of proton abstraction in both oximes and tosylhydrazones is a result of kinetic control, we feel that the intermediate nitrogen monoanion (**4**, Scheme II) is exerting a directional effect on the incoming second equivalent of alkyllithium reagent. It is well-known that heteroatoms, by virtue of their nonbonding electron pairs, may direct lithium bases to a nearby site via a transient coordinated species (**5**). The dianion is reluctant to invert configuration, which strongly suggests that it is present as the internally coordinated metallocycle (**6**). For instance, phenylacetone tosylhydrazone yields allylbenzene in the elimination reaction.[3] Internally coordinated metallocyclic intermediates have ample precedent,[7,8,13,15] and their formation has been proposed only in systems which bear a 1,4 relationship between heteroatom and the carbon bearing the incipient negative charge.

Scheme I



1 2 3

Scheme II



1 4 5 2 6

The regiochemistry of tosylhydrazone dianion formation toward the less hindered side of the imino carbon has been found to be a general phenomenon, and since a strong steric bias exists in the formation of tosylhydrazones from unsymmetrical ketones, the route ketone → tosylhydrazone → dianion represents a convenient method for the regiospecific generation of enolate equivalents. In order to further test the regioselectivity of dianion formation, a symmetrical system, dibenzyl ketone tosylhydrazone, was chosen for study. The 60-MHz ^{1}H NMR spectrum of this tosylhydrazone ($CDCl_3$) shows the methylene signals separated by 10 Hz. Conversion to dianion (>2 equiv of *n*-butyllithium, THF, 0 °C)[16] followed by quenching with D_2O affords the α-deuteriotosylhydrazone (>97% labeled by MS) in 83% yield. The 60-MHz ^{1}H NMR spectrum indicates that deuteration has occurred, within the limits of detection, only on the upfield methylene group. Similar results have been obtained at −78 °C with acetone tosylhydrazone. That the upfield signal in the ^{1}H NMR spectrum corresponds to the syn α protons may be inferred from the 60-MHz ^{1}H NMR spectra ($CDCl_3$) of the series of tosylhydrazones of acetone, 2-butanone, 3-methyl-2-butanone, and pinacolone, the methyl absorptions of which are displayed in Table I. The assignments of syn and anti (entries 2, 3, and 4) are in accord with the known isomer ratios for the corresponding oximes.[17]

Further support for the syn regiospecificity of dianion formation comes from the deuteration of a syn/anti mixture (83:17) of 2-butanone tosylhydrazone. Conversion to the dianion (>2 equiv of *n*-butyllithium, THF, −50 °C) followed by D_2O quenching yields a mixture of labeled tosylhydrazones. Mass spectral analysis indicates that the mixture is labeled 81% on methyl and 19% on methylene.

Our preliminary report[3] indicated that tosylhydrazone dianions may be trapped with alkyl halides and that a large steric requirement accompanies dianion formation. Oxime dianions behave similarly.[7,8] In view of the fact that attempts to trap tosylhydrazone dianions with secondary alkyl halides were unsuccessful, a large steric requirement must also be present in the reaction of the electrophile with the dianion,

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Table I

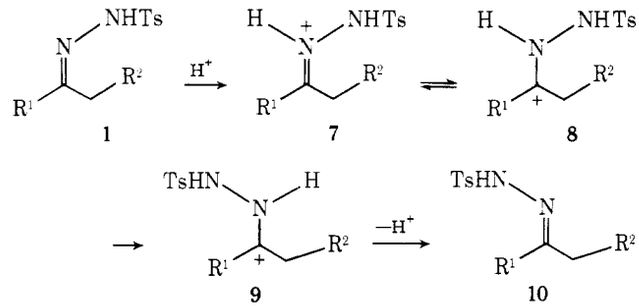
Tosylhydrazone of (syn/anti)	^{1}H NMR absorption, δ *syn*-α-Methyl	*anti*-α-Methyl
(1) Acetone (50:50)	1.80	1.92
(2) 2-Butanone (83:17)	1.80	1.92
(3) 3-Methyl-2-butanone (>92:<8)	1.80	1.92
(4) Pinacolone (100:0)	1.75	

and it is consistent with syn dianion formation. That the alkylated tosylhydrazone obtained upon treatment of cyclohexanone tosylhydrazone dianion with methyl iodide bears an anti relationship for tosylamido and methyl groups and is identical to the tosylhydrazone made from the treatment of 2-methylcyclohexanone with tosylhydrazine in hot acidic ethanol may be explained in terms of an acid-catalyzed isomerization during the isolation procedure (Scheme III.)

Acetone tosylhydrazone dianion yields an equilibrium mixture (syn/anti, 83:17) of 2-butanone tosylhydrazone in 67% yield when trapped with methyl iodide and subjected to neutral isolation. Also, dibenzyl ketone tosylhydrazone-*syn*-α-*d* quickly isomerizes upon treatment with dilute mineral acid to a mixture of syn- and anti-labeled material. Such isomerization has not been reported for oximes.

Tosylhydrazone dianions formed at −50 °C with *n*-butyllithium in THF when trapped with aldehydes and ketones afford β-hydroxytosylhydrazones in good to excellent yield as shown in Table II. We anticipated that based on the demonstrated regiospecificity of dianion formation (vida supra) such a reaction would provide a convenient modified crossed-aldol reaction since published procedures are available for the regeneration of ketones from tosylhydrazones.[18-20] Unfortunately, all attempts to generate β-hydroxy ketones from β-hydroxytosylhydrazones resulted in a retro-aldol reaction under acidic conditions or no reaction under basic conditions. Other routes to effect this seemingly facile conversion are currently under investigation.

Scheme III



However, treatment of β-hydroxytosylhydrazones with >3 equiv of alkyllithium reagent results in their smooth elimination at room temperature. For instance, acetophenone tosylhydrazone may be converted to the dianion at −50 °C and trapped with acetone to give 1-phenyl-3-hydroxy-3-methyl-1-butanone tosylhydrazone. Elimination of this β-hydroxytosylhydrazone with alkyllithium reagent leads to 1-phenyl-3-hydroxy-3-methyl-1-butene (cis and trans) in 76% yield.

The preferred regiochemistry of elimination in these systems, however, was found to be away from oxygen to form the homoallylic alcohol, as the data in Table III demonstrates. The uniformly good yields, regiospecificity, convenience, and ready availability of starting materials, as well as the apparent paucity of reliable methods for the generation of homoallylic alcohols,[21-24] prompted this report.

It appears that the steric factors which govern the regiochemistry of dianion formation, and hence elimination, in tosylhydrazones are not operative in β-hydroxytosylhydra-

Table II. β-Hydroxytosylhydrazones from Tosylhydrazones[a]

Tosylhydrazone of	Electrophile	Product (tosylhydrazone of)	Yield, %	Mp (dec), °C
Acetone	Acetone	2-Hydroxy-2-methyl-4-pentanone	57	134.0–135.5
	Propionaldehyde	4-Hydroxy-2-hexanone	78	131.5–132.0
2-Butanone	Acetone	2-Hydroxy-2-methyl-4-hexanone	61	130.5–132.5
	Propionaldehyde	5-Hydroxy-3-heptanone	74	132.0–133.0
Cyclohexanone	Acetone	2-(2-Hydroxy-2-propyl)cyclohexanone	79	153.5–155.0
	Propionaldehyde	2-Propyl(1-hydroxy)cyclohexanone	74	138.0–141.0
Phenylacetone	Acetone	1-Phenyl-4-hydroxy-4-methyl-2-pentanone[b]	80	128.0–130.0
	Propionaldehyde	1-Phenyl-4-hydroxy-2-hexanone	77	136.5–138.0
Acetophenone	Acetone	1-Phenyl-3-hydroxy-3-methyl-1-butanone	80	134.0–137.0

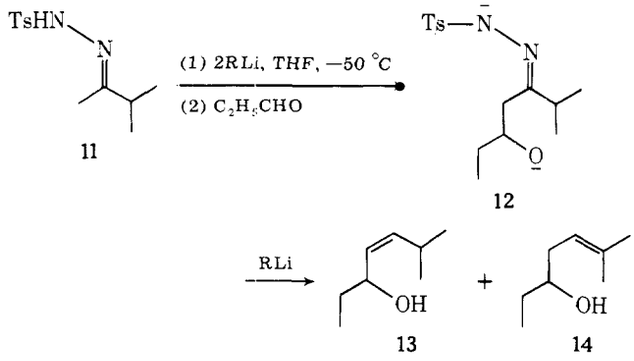
[a] All β-hydroxytosylhydrazones had spectral data consistent with the assigned structure (see Experimental Section). [b] This was the only compound obtained as a single isomer; all others were syn/anti mixtures by NMR.

Table III. Homoallylic Alcohols[a] from Tosylhydrazones[b]

Tosylhydrazone of	Electrophile	Product	Yield, %	Bp,[c] °C
Acetone	Acetone	2-Hydroxy-2-methyl-4-pentene	49	60 (15)
	Propionaldehye	4-Hydroxy-1-hexene	48	60 (12)
2-Butanone	Acetone	2-Hydroxy-2-methyl-4-hexene (cis and trans)	75	60 (7.0)
	Propionaldehyde	5-Hydroxy-2-heptene (cis and trans)	73	43 (5.0)
Cyclohexanone	Acetone	3-(2-Propyl-2-hydroxy)-1-cyclohexene	65	76–78 (4.5)
	Propionaldehyde	3-(1-Hydroxy-1-propyl)-1-cyclohexene	66	77–79 (3.5)
Phenylacetone	Acetone	1-Phenyl-4-hydroxy-4-methyl-1-pentene (cis/trans, 11:89)	59	95 (1.0)
	Propionaldehyde	1-Phenyl-4-hydroxy-1-hexene (cis/trans, 15:85)	43	87–89 (0.3)

[a] All homoallylic alcohols had spectral data consistent with the assigned structure (see Experimental Section). [b] The intermediate β-hydroxytosylhydrazones were not isolated. [c] Pressures are indicated in parentheses.

Scheme IV



zones. Although β-branching effects cannot be ruled out from the above series of β-hydroxytosylhydrazones, elimination of 2-methyl-5-hydroxy-3-heptanone tosylhydrazone dianion (**12**, Scheme IV) should produce allylic alcohol **13** in a sterically controlled reaction. In fact, elimination of this dianion (generated in situ by trapping 3-methyl-2-butanone tosylhydrazone dianion with aceteldehyde) with methyllithium leads to a 1.0:1.1 mixture of allylic alcohol **13** and homoallylic alcohol **14**. Since the tertiary side of both tosylhydrazones[3] and oximes[7,8] is reluctant to form a syn dianion, it appears that the elimination of β-hydroxytosylhydrazones may involve the abstraction of an anti α proton. Such an interpretation is not unreasonable in view of the fact that the negatively charged oxygen atom should by the inductive effect decrease the acidity of the syn α protons. Although an isomerization to form **16** under the reaction conditions has not been ruled out, it seems unlikely in view of the results obtained for elimination of **12** above, and those of Kofron.[7] The possible elimination pathways are depicted in Scheme V. Although a concerted elimination involving the generation of a trianion intermediate may be envisioned, no trianion has been trapped, and no evidence is presented for its formation.

We also wish to report that chloroformates make excellent traps for tosylhydrazone dianions. For example, cyclopentanone tosylhydrazone is converted via the dianion and trapping with ethyl chloroformate into the corresponding ethyl ester in 76% yield. Since lithium diisopropylamide is effective in tosylhydrazone eliminations in the presence of ester functions,[2] this method appears to be promising for the production of β,γ-unsaturated esters.

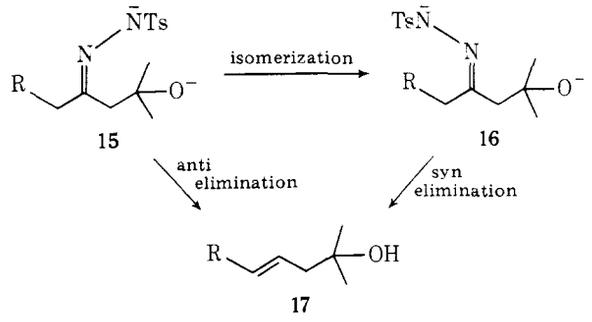
Experimental Section

Materials. Tosylhydrazine was conveniently prepared according to the procedure of Friedman.[25] Ketones were purchased from commercial suppliers and used without purification. *n*-Butyllithium was purchased as pentane solutions from Ventron and stored at −5 °C. Methyllithium was purchased from Ventron as ethereal solutions and stored at ambient temperature. Reagent grade tetrahydrofuran was purchased from Mallinckrodt and distilled from lithium aluminum hydride prior to use. D_2O was purchased from Merck. Acetone was distilled from $KMnO_4$ prior to use in the trapping experiments. Propionaldehyde was distilled prior to use. Reactions were carried out under a stream of dry nitrogen in glassware oven-dried at 140 °C overnight.

Instrumentation. All analytical gas chromatography analyses were done on a Varian Aerograph instrument (FID). Preparative gas chromatography work was done on a Varian 1600 instrument using a 6 ft × 0.25 in. 8% DC-550 column. Infrared spectra were recorded on a Perkin-Elmer Infracord spectrometer. ^1H NMR spectra were obtained with either a Varian A-60A instrument or a Varian T-60. Mass spectra were obtained on a Varian CH-5 mass spectrometer at 70-eV ionizing energy. Melting points were determined using a Thomas-Hoover capillary melting point apparatus and are uncorrected.

Procedures. Tosylhydrazones: General Procedure. In a 50-mL Erlenmeyer flask, tosylhydrazine (9.3 g, 50 mmol) is dissolved in 20 mL of ethanol containing 1 drop of concentrated HCl on a steam bath.

Scheme V



The flask is allowed to cool briefly, the ketone (50 mmol) is added, and the flask is swirled and heated for 1 min. After cooling to room temperature, the flask is cooled to −15 °C in the freezer, and the colorless crystals are isolated by suction filtration. Recrystallization from ethanol affords the tosylhydrazone in 78–95% yield.

β-Hydroxytosylhydrazones: General Procedure. The tosylhydrazone (10 mmol) is dissolved in 50 mL of THF in a 100-mL *two-neck round-bottom flask protected from moisture* and equipped with a rubber serum cap and magnetic stirrer. The solution is cooled to −50 °C by means of a dry ice/2-propanol bath and titrated to pale yellow with 10 mmol of *n*-butyllithium solution. An additional 10 mmol of *n*-butyllithium solution is added, the orange to deep red solution is allowed to stir for 1 min, and 11 mmol of acetone or propionaldehyde is added neat. The color bleaches immediately, and the pale yellow to colorless solution is allowed to warm with stirring to room temperature. It is then treated with 25 mL of 10% HCl and salted, the layers are separated, and the aqueous phase is extracted with 25 mL of THF. The combined organic extracts are dried ($MgSO_4$), and the solvent is removed on the rotory evaporator, leaving pale yellow crystals. The crude material is recrystallized from warm aqueous ethanol.

Homoallylic Alcohols: General Procedure. In a 100-mL two-neck round-bottom flask protected from moisture and equipped with a magnetic stirrer, reflux condenser, and rubber serum cap is placed 10 mmol of the tosylhydrazone and 50 mL of THF. The solution is cooled to −50 °C by means of a dry ice/2-propanol bath and is titrated to pale yellow with 10 mmol of *n*-butyllithium solution. An additional 10 mmol of *n*-butyllithium solution is added, the orange to deep red solution is allowed to stir for 1 min, and the mixture is then quenched with acetone or propionaldehyde. After warming to room temperature, 20 mmol of methyllithium solution is added, and the orange solution is allowed to stir for 6.0 h at room temperature. Hydrolysis is effected with dilute HCl at 0 °C, and the aqueous phase is saturated with salt and extracted with three 10-mL portions of THF. The combined organic phase is extracted with two 16-mL portions of 1 M NaOH, saturated with salt, washed with brine, and concentrated to ~5 mL by flash evaporation. The product is obtained by chromatography on alumina or by distillation.

Spectral data for the β-hydroxytosylhydrazones are as follows ("exchanges" refers to protons exchangeable with D_2O).

2-Hydroxy-2-methyl-4-pentanone tosylhydrazone: ^1H NMR ($CDCl_3$, Me_4Si) δ 1.11, 1.23 (6 H, pair of s), 1.87, 1.93 (3 H, pair of s), 2.33–2.53 (3 H, m, 1 exchanges), 2.42 (3 H, s), 7.20–8.00 (5 H, m, 1 exchanges); IR (film) 3325, 3000, 2840, 1600, 1565, 1310, 1145, 935, 810, 720 cm^{-1}; MS *m/e* (relative intensity) 284 (M^+, 1), 157 (7), 111 (8), 139 (9), 91 (23), 31 (28), 226 (36), 59 (59), 71 (100).

4-Hydroxy-2-hexanone tosylhydrazone: ^1H NMR ($CDCl_3$, Me_4Si) δ 0.89 (3 H, t, *J* = 7 Hz), 1.13–1.61 (2 H, m), 1.83, 1.91 (3 H, pair of s), 2.18–2.49 (2 H, m), 2.41 (3 H, s), 2.84 (1 H, s, exchanges), 3.50–3.93 (1 H, m), 7.15–7.96 (5 H, m, 1 exchanges); IR (film) 3340, 3000, 2800, 1660, 1570, 1325, 1155, 1075, 920, 840, 815, 700 cm^{-1}; MS *m/e* (relative intensity) 284 (M^+, 1), 92 (10), 157 (10), 111 (16), 41 (19), 46 (22), 91 (25), 226 (27), 45 (33), 43 (35), 59 (52), 31 (56), 71 (100).

2-Hydroxy-2-methyl-4-hexanone tosylhydrazone: ^1H NMR ($CDCl_3$, Me_4Si) δ 0.98 (3 H, t, *J* = 7.5 Hz), 1.15 (6 H, s), 2.13 (2 H, q, *J* = 7.5 Hz), 2.35 (3 H, s), 2.35 (2 H, s), 3.45 (1 H, s, exchanges), 7.27 (2 H, d, *J* = 8 Hz), 7.90 (2 H, d, *J* = 8 Hz), 7.92 (1 H, broad s, exchanges); IR (film) 3300, 2950, 2880, 1610, 1565, 1355, 1305, 1150, 940, 810, 755, 705 cm^{-1}; MS *m/e* (relative intensity) 298 (M^+, 2), 125 (4), 143 (6), 59 (7), 139 (8), 157 (9), 240 (23), 91 (28), 85 (100).

5-Hydroxy-3-heptanone tosylhydrazone: ^1H NMR ($CDCl_3$, Me_4Si) δ 0.89 (3 H, t, *J* = 7.5 Hz), 0.99 (3 H, t, *J* = 7 Hz), 1.43 (2 H, broad q, *J* = 7 Hz), 2.03–2.52 (4 H, m), 2.41 (3 H, s), 3.22 (1 H, s, exchanges), 3.74 (1 H, m), 7.20 (2 H, d, *J* = 8 Hz), 7.75 (2 H, d, *J* = 8 Hz),

7.78 (1 H, s, exchanges); IR (film) 3490, 3100, 2980, 1660, 1595, 1315, 1160, 910, 815, 700 cm^{-1}; MS *m/e* (relative intensity) 298 (M^+, <1), 157 (10), 226 (12), 92 (13), 39 (16), 59 (16), 65 (18), 67 (18), 70 (18), 41 (30), 42 (33), 91 (34), 43 (51), 71 (64), 111 (100).

2-(2-Hydroxy-2-propyl)cyclohexanone tosylhydrazone: ^1H NMR ($CDCl_3$, Me_4Si) δ 1.16, 1.31 (6 H, pair of s), 1.16–2.51 (8 H, m), 2.41 (3 H, s), 2.86 (1 H, t, J = 6 Hz), 3.04 (1 H, s, exchanges), 7.06–8.04 (5 H, m, 1 exchanges); IR (film) 3320, 2850, 1575, 1550, 1310, 1155, 1025, 955, 810, 700 cm^{-1}; MS *m/e* (relative intensity) 324 (M^+, <1), 112 (9), 266 (11), 81 (12), 41 (13), 67 (16), 91 (16), 43 (22), 31 (25), 151 (81), 111 (100).

2-Propyl(1-hydroxy)cyclohexanone tosylhydrazone: ^1H NMR ($CDCl_3$, Me_4Si) δ 0.90, 1.00 (3 H, pair of t, J = 7 Hz), 1.10–2.65 (10 H, m), 2.43 (3 H, s), 2.82 (1 H, broad t), 3.02 (1 H, s, exchanges), 3.67 (1 H, m), 7.12–8.14 (5 H, m, 1 exchanges); IR (film) 3400, 2900, 2810, 1650, 1575, 1325, 1160, 1030, 815, 705 cm^{-1}; MS *m/e* (relative intensity) 324 (M^+, <1), 112 (9), 139 (11), 67 (15), 41 (16), 266 (16), 81 (18), 91 (19), 151 (20), 154 (29), 31 (34), 111 (100).

1-Phenyl-4-hydroxy-4-methyl-2-pentanone tosylhydrazone: ^1H NMR ($CDCl_3$, Me_4Si) δ 1.14 (6 H, s), 2.31 (2 H, s), 2.43 (3 H, s), 3.06 (1 H, s, exchanges), 3.47 (2 H, s), 6.95–7.97 (10 H, m, 1 exchanges); IR (film) 3300, 2870, 2750, 1700, 1570, 1300, 1145, 1040, 810, 740, 695 cm^{-1}; MS *m/e* (relative intensity) 360 (M^+, 2), 31 (13), 115 (13), 92 (15), 65 (17), 187 (17), 43 (18), 117 (24), 118 (29), 130 (31), 302 (37), 59 (76), 91 (87), 147 (100).

1-Phenyl-4-hydroxy-2-hexanone tosylhydrazone: ^1H NMR ($CDCl_3$, Me_4Si) δ 0.90 (3 H, broad t, J = 7 Hz), 1.45 (2 H, broad q, J = 7 Hz), 2.37 (3 H, s), 2.81 (2 H, broad s), 2.90 (2 H, d, J = 6.5 Hz), 3.18 (1 H, s, exchanges), 3.82 (1 H, broad t, J = 6.5 Hz), 7.20–8.06 (10 H, m, 1 exchanges); IR (film) 3320, 2950, 2850, 1560, 1540, 1310, 1150, 1065, 930, 810, 750, 690 cm^{-1}; MS *m/e* (relative intensity) 360 (M^+, 4), 191 (13), 59 (14), 53 (15), 172 (15), 39 (17), 41 (17), 129 (19), 131 (20), 115 (22), 105 (29), 92 (30), 67 (34), 61 (35), 176 (38), 104 (39), 79 (46), 103 (64), 173 (75), 91 (90), 133 (100).

1-Phenyl-3-hydroxy-3-methyl-1-butanone tosylhydrazone: ^1H NMR ($CDCl_3$, Me_4Si) δ 1.20 (6 H, s), 2.42 (3 H, s), 2.93 (2 H, s), 3.03 (1 H, s, exchanges), 7.17–8.06 (9 H, m, 1 exchanges); IR (film) 3450, 3100, 3000, 1600, 1340, 1170, 1090, 910, 820, 805, 760, 695 cm^{-1}; MS *m/e* (relative intensity) 346 (M^+, 3), 152 (10), 105 (11), 132 (11), 78 (12), 134 (14), 173 (22), 65 (24), 77 (25), 288 (26), 92 (39), 59 (47), 91 (47), 103 (50), 104 (50), 43 (54), 133 (100).

Spectral data for the homoallylic alcohols are as follows.

4-Hydroxy-4-methyl-1-pentene: ^1H NMR (CCl_4, Me_4Si) δ 1.17 (6 H, s) 2.12 (1 H, s, exchanges), 2.18 (2 H, broad d, J = 7 Hz), 4.92 (1 H, m), 5.18 (1 H, m), 5.50–6.27 (1 H, m); MS *m/e* (relative intensity) 100 (M^+, <1), 41 (6), 71 (10), 57 (14), 43 (20), 44 (39), 42 (83), 59 (100).

4-Hydroxy-1-hexene: ^1H NMR (CCl_4, Me_4Si) δ 0.91 (3 H, t, J = 7 Hz), 1.12–1.71 (2 H, m), 2.18 (2 H, broad t), 3.33 (1 H, s, exchanges), 3.50 (1 H, m), 4.73–5.23 (2 H, m), 5.50–6.21 (1 H, m); IR (film) 3200, 2950, 2800, 1710, 1430, 1100, 955, 910, 775 cm^{-1}; MS *m/e* (relative intensity) 100 (M^+, <1), 58 (4), 60 (4), 28 (6), 42 (9), 57 (10), 71 (10), 39 (11), 27 (12), 29 (12), 43 (14), 41 (31), 31 (46), 59 (100).

5-Hydroxy-5-methyl-2-hexene (cis and trans): ^1H NMR (CCl_4, Me_4Si) δ 1.13, 1.17 (6 H, pair of s), 1.25 (2 H, s), 1.62 (3 H, d, J = 6 Hz), 2.04–2.30 (2 H, m), 3.30 (1 H, s, exchanges), 5.37–5.68 (2 H, m); IR (film) 3300, 2900, 1640, 1450, 1365, 1145, 1080, 1050, 965, 905, 780 cm^{-1}; MS *m/e* (relative intensity) 114 (M^+, <1), 79 (5), 42 (7), 60 (8), 99 (8), 53 (9), 96 (10), 55 (17), 39 (18), 56 (21), 81 (23), 41 (32), 43 (65), 59 (100).

5-Hydroxy-2-heptene (cis and trans): ^1H NMR (CCl_4, Me_4Si) δ 1.08 (3 H, t, J = 7 Hz), 1.23 (2 H, m), 1.54–1.78 (3 H, m), 2.13 (2 H, q, J = 7 Hz), 3.42 (1 H, s, exchanges), 3.25–3.71 (1 H, m), 5.35–5.67 (2 H, m); IR (film) 3350, 2900, 1650, 1460, 1360, 1045, 1025, 960, 900, 780, 680 cm^{-1}; MS *m/e* (relative intensity) 114 (M^+, <1), 39 (5), 51 (5), 54 (5), 41 (6), 45 (6), 81 (6), 58 (8), 87 (8), 53 (10), 67 (12), 38 (20), 69 (22), 85 (23), 55 (27), 57 (35), 43 (37), 56 (80), 40 (87), 59 (100).

3-(2-Propyl-2-hydroxy)-1-cyclohexene: ^1H NMR (CCl_4, Me_4Si) δ 1.10, 1.15 (6 H, pair of s), 1.18–2.35 (6 H, m), 3.13 (1 H, s, exchanges), 3.23–3.79 (1 H, m), 5.75 (2 H, m); IR (film) 3250, 2830, 1620, 1420, 1360, 1140, 1040, 950, 910, 890, 825, 765, 720 cm^{-1}; MS *m/e* (relative intensity) 140 (M^+, 1), 53 (5), 81 (5), 107 (5), 122 (5), 31 (6), 82 (6), 54 (7), 41 (9), 79 (10), 67 (13), 59 (100).

3-(1-Hydroxy-1-propyl)-1-cyclohexene: ^1H NMR (CCl_4, Me_4Si) δ 0.94 (3 H, t, J = 7 Hz), 1.11–2.40 (8 H, m), 3.13 (1 H, s, exchanges), 3.02–3.93 (2 H, m), 5.77 (2 H, m); IR (film) 3250, 2830, 1630, 1440, 1110, 965, 930, 875, 780, 720 cm^{-1}; MS *m/e* (relative intensity) 140 (M^+, <1), 66 (5), 83 (5), 93 (5), 122 (5), 65 (6), 68 (6), 80 (7), 44 (8), 51 (8), 57 (11), 77 (11), 55 (13), 79 (17), 81 (17), 53 (19), 54 (49), 59 (63), 52 (82), 67 (100).

1-Phenyl-4-hydroxy-4-methyl-1-pentene (cis and trans): ^1H NMR (CCl_4, Me_4Si) δ 1.17 (6 H, s), 2.45 (2 H, dd, J = 7, 2 Hz), 3.05 (1 H, exchanges), 5.57–6.67 (2 H, m), 7.23 (5 H, s); IR (film) 3300, 2900, 1625, 1580, 1555, 1480, 1365, 1130, 1070, 1020, 945, 910, 760, 695 cm^{-1}; MS *m/e* (relative intensity) 176 (M^+, <1), 119 (6), 129 (7), 116 (8), 39 (9), 128 (9), 158 (10), 41 (13), 91 (15), 115 (18), 143 (19), 117 (29), 43 (33), 118 (59), 59 (100).

1-Phenyl-4-hydroxy-1-hexene (cis and trans): ^1H NMR (CCl_4, Me_4Si) δ 0.78 (3 H, t, J = 7 Hz), 1.30 (2 H, m), 2.19 (2 H, broad q), 3.19 (1 H, s, exchanges), 3.35 (1 H, m), 6.17 (2 H, m), 7.05 (5 H, m); IR (film) 3400, 2950, 2750, 1625, 1560, 1300, 1140, 1000, 935, 900, 810, 760, 700 cm^{-1}; MS *m/e* (relative intensity) 78 (5), 43 (5), 129 (6), 106 (6), 51 (7), 57 (8), 105 (10), 77 (10), 41 (10), 119 (11), 116 (11), 176 (M^+, 12), 31 (15), 115 (18), 91 (20), 59 (33), 117 (53), 118 (100).

Cyclopentanone Tosylhydrazone. In a 50-mL Erlenmeyer flask, tosylhydrazine (9.3 g, 50 mmol) was dissolved in 20 mL of ethanol containing 1 drop of concentrated HCl on a steam bath. The flask was allowed to cool briefly, and 4.2 g (50 mmol) of cyclopentanone was added and the flask swirled. Vigorous boiling occured, and on cooling to room temperature a colorless precipitate formed. Further cooling in the freezer followed by suction filtration afforded 12.7 g (94%) of cyclopentanone tosylhydrazone, mp 180–184 °C dec; ^1H NMR ($CDCl_3$, Me_4Si) δ 1.75 (4 H, m), 2.22 (4 H, m), 2.45 (3 H, s), 7.33 (2 H, d, J = 8 Hz), 7.75 (1 H, broad s), 7.92 (2 H, d, J = 7 Hz); MS *m/e* (relative intensity) 140 (10), 157 (10), 53 (14), 252 (M^+, 16), 80 (17), 65 (18), 68 (21), 91 (32), 96 (34), 41 (38), 67 (56), 97 (100).

2-Carboethoxycyclopentanone Tosylhydrazone. Cyclopentanone tosylhydrazone (1.26 g, 5.0 mmol) was dissolved in 25 mL of THF in a 50-mL two-neck round-bottom flask protected from moisture and equipped with a reflux condenser, rubber serum cap, and magnetic stirrer. The solution was cooled to −50 °C by means of a dry ice/2-propanol bath, and 5.0 mL (10 mmol) of a 2.0 M solution of *n*-butyllithium in pentane was added slowly with a syringe. After ~1 min of stirring, the red solution was treated with 0.55 g (5 mmol) of freshly distilled ethyl chloroformate, the cold bath removed, and the yellow solution allowed to stir for 30 min. Neutralization with dilute HCl, salting, and separation of the layers were followed by extraction of the aqueous phase with THF (3 × 10 mL). Drying ($MgSO_4$) and removal of the solvent on the rotoevaporator afforded a yellow oil which on recrystallization from ethanol/water yielded 1.22 g (76%) of 2-carboethoxycyclopentanone tosylhydrazone (syn/anti mixture) as pale yellow crystals, mp 134–135 °C dec. Major isomer [minor isomer]: ^1H NMR ($CDCl_3$, Me_4Si) δ 1.23 [1.17], (3 H, t, J = 7 Hz), 1.50–2.83 (7 H, m), 2.45 (3 H, s), 4.12 [4.09] (2 H, d, J = 7 Hz), 6.80–8.24 symmetrical complex (4 H, m), 8.45 (1 H, broad s); MS *m/e* (relative intensity) 251 (5), 140 (6), 122 (7), 139 (8), 141 (9), 124 (10), 155 (11), 43 (12), 121 (12), 168 (13), 80 (16), 65 (17), 324 (M^+, 20), 95 (25), 41 (26), 91 (28), 67 (79), 123 (99), 169 (100).

Registry No.—Acetone tosylhydrazone, 3900-79-6, (*E*)-2-butanone tosylhydrazone, 62460-90-6; (*Z*)-2-butanone tosylhydrazone, 62460-91-7; (*E*)-3-methyl-2-butanone tosylhydrazone, 64884-92-0; (*Z*)-3-methyl-2-butanone tosylhydrazone, 64884-93-1; (*Z*)-pinacolone tosylhydrazone, 64884-94-2; 2-butanone tosylhydrazone, 4031-16-7; cyclohexanone tosylhydrazone, 4545-18-0; phenylacetone tosylhydrazone, 14195-24-5; acetophenone tosylhydrazone, 4545-21-5; propionaldehyde, 123-38-6; (*E*)-2-hydroxy-2-methyl-4-pentanone tosylhydrazone, 64884-95-3; (*Z*)-2-hydroxy-2-methyl-4-pentanone tosylhydrazone, 64884-96-4; (*E*)-4-hydroxy-2-hexanone tosylhydrazone, 64884-97-5; (*Z*)-4-hydroxy-2-hexanone tosylhydrazone, 64884-98-6; (*E*)-2-hydroxy-2-methyl-4-hexanone tosylhydrazone, 64884-99-7; (*Z*)-2-hydroxy-2-methy-4-hexanone tosylhydrazone, 64885-00-3; (*E*)-5-hydroxy-3-heptanone tosylhydrazone, 64885-01-4; (*Z*)-5-hydroxy-3-heptanone tosylhydrazone, 64885-02-5; (*E*)-2-(2-hydroxy-2-propyl)cyclohexanone tosylhydrazone, 64885-03-6; (*Z*)-2-(2-hydroxy-2-propyl)cyclohexanone tosylhydrazone, 64885-04-7; 2-propyl(1-hydroxy)cyclohexanone tosylhydrazone, 64885-05-8; 1-phenyl-4-hydroxy-4-methyl-2-pentanone tosylhydrazone, 64885-06-9; (*E*)-1-phenyl-4-hydroxy-2-hexanone tosylhydrazone, 64885-07-0; (*Z*)-1-phenyl-4-hydroxy-2-hexanone tosylhydrazone, 64885-08-1; (*E*)-1-phenyl-3-hydroxy-3-methyl-1-butanone tosylhydrazone, 64885-09-2; (*Z*)-1-phenyl-3-hydroxy-3-methyl-1-butanone tosylhydrazone, 64884-85-1; 2-hydroxy-2-methyl-4-pentene, 624-97-5; 4-hydroxy-1-hexene, 688-99-3; (*Z*)-2-hydroxy-2-methyl-4-hexene, 19639-96-4; (*E*)-2-hydroxy-2-methyl-4-hexene, 19639-97-5; (*Z*)-5-hydroxy-2-heptene, 64884-86-2; (*E*)-5-hydroxy-2-heptene, 64884-87-3; 3-(2-propyl-2-hydroxy)-1-cyclohexene, 5723-91-1; 3-(1-hydroxy-1-propyl)-1-cyclohexene, 64884-88-4; (*Z*)-1-phenyl-4-hydroxy-4-methyl-1-pentene, 64884-89-5; (*E*)-1-phenyl-4-hydroxy-4-methyl-1-pentene, 55552-38-0; (*Z*)-1-phenyl-4-hydroxy-1-hex-

ene, 54985-30-7; (*E*)-1-phenyl-4-hydroxy-1-hexene, 54985-35-2; tosylhydrazine, 1576-35-8; 3-methyl-2-butanone, 563-80-4; pinacolone, 75-97-8; acetone, 67-64-1; 2-butanone, 78-93-3; cyclohexanone, 108-94-1; phenylacetone, 103-79-7; acetophenone, 98-86-2; cyclopentanone, 120-92-3; cyclopentanone tosylhydrazone, 17529-98-5; ethyl chloroformate, 541-41-3; (*Z*)-2-carboethoxycyclopentanone tosylhydrazone, 64884-90-8; (*E*)-2-carboethoxycyclopentanone tosylhydrazone, 64884-91-9.

References and Notes

(1) For a review, see R. H. Shapiro, *Org. React.*, **23**, 405 (1976).
(2) (a) K. J. Kolonko and R. H. Shapiro, *J. Org. Chem.*, companion paper, this issue; (b) C. A. Bunnell and P. L. Fuchs, *J. Am. Chem. Soc.*, in press; (c) P. L. Fuchs, *J. Org. Chem.*, **41**, 2937 (1976); (d) S. D. Yound and W. T. Burden, *Tetrahedron Lett.*, 4019 (1976).
(3) R. H. Shapiro, M. F. Lipton, K. J.Kolonko, R. A. Buswell, and L. A. Capuano, *Tetrahedron Lett.*, 1811 (1975).
(4) J. E. Stemke and F. T. Bond, *Tetrahedron Lett.*, 1815 (1975).
(5) R. H. Shapiro and M. J. Heath, *J. Am. Chem. Soc.*, **89**, 5734 (1967).
(6) R. H. Shapiro, *Tetrahedron Lett.*, 345 (1968).
(7) W. G. Kofron and M. K. Yeh, *J. Org. Chem.*, **41**, 439 (1976).
(8) M. E. Jung, P. A. Blair, and J. A. Lowe, *Tetrahedron Lett.*, 1439 (1976).
(9) R. M. Sandifer, S. E. Davis, and C. F. Beam, *Synth. Commun.*, **6**, 339 (1976).
(10) R. H. Shapiro and T. Gadek, *J. Org. Chem.*, **39**, 3418 (1974).
(11) E. Vedejs and W. T. Stolle, *Tetrahedron Lett.*, 135 (1977).
(12) F. E. Henoch, K. G. Hampton, and C. R. Hauser, *J. Am. Chem. Soc.*, **91**, 676 (1969).
(13) F. N. Jones and C. R. Hauser, *J. Org. Chem.*, **27**, 701 (1962).
(14) N. D. Epiotis, *J. Am. Chem. Soc.*, **95**, 3087 (1973).
(15) W. C. Still and T. L. Mcdonald, *J. Am. Chem. Soc.*, **96**, 5561 (1974).
(16) Due to solubility problems, the reaction was run at the elevated temperature.
(17) G. J. Karabatsos and R. A. Taller, *Tetrahedron*, **24**, 3347 (1968).
(18) T. Ho and C. M. Wong, *J. Org. Chem.*, **39**, 3453 (1974).
(19) G. Rosini, *J. Org. Chem.*, **39**, 3504 (1974).
(20) A. Bahati, *Chem. Commun.*, 476 (1965).
(21) M. P. Dryfuss, *J. Org. Chem.*, **28**, 3269 (1963), and references cited therein.
(22) E. J. Corey and M. F. Semmelhack, *J. Am. Chem. Soc.*, **89**, 2755 (1967).
(23) J. A. Katzenellenbogen and R. S. Lenox, *J. Org. Chem.*, **38**, 326 (1973).
(24) M. Naruse, K. Utimoto, and H. Nozaki, *Tetrahedron Lett.*, 2741 (1973).
(25) L. Friedman, R. L. Little, and W. R. Reichle, *Org. Synth.*, **40**, 93 (1960).

Studies on Selective Preparation of Aromatic Compounds. 15. The Lewis Acid Catalyzed Transalkylation of Some *tert*-Butyldiphenylmethanes and -ethanes in Aromatic Solvents[1]

Masashi Tashiro,* Takehiko Yamato, and Gouki Fukata

Research Institute of Industrial Science, Kyushu University 86, Hakozaki, Higashi-ku, Fukuoka 812, Japan

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The Lewis acid catalyzed transalkylation of *tert*-butyl derivatives of diphenylmethanes (**2a–f**) and -ethanes (**25a–g**) in benzene or toluene was carried out under various conditions. It was found in the transalkylation of **2** that the $AlCl_3$–CH_3NO_2 catalyzed transbenzylation with trans-*tert*-butylation was observed and the $TiCl_4$ transbenzylation of electron-rich *tert*-butyldiphenylmethanes having highly steric crowdedness such as 2,2′,6,6′-tetramethyl- (**2d**) and 2,2′,3,3′-tetramethyldiphenylmethane (**2f**) took place without trans-*tert*-butylation. However, no $AlCl_3$–CH_3NO_2 catalyzed transalkylation of **25** was observed and only trans-*tert*-butylation in benzene took place to afford the desired 2,2′-dimethyl-(**27b**), 2,2′-diethyl-(**27c**), 2,2′-dimethoxy-(**27d**), 2,2′,3,3′-tetramethyl-(**27e**), and 2,2′,6,6′-tetramethyldiphenylethane (**27f**). Based on the above result it could be concluded that *tert*-butyl group can be used as a positional protective group for the preparation of some diphenylethanes but not diphenylmethanes.

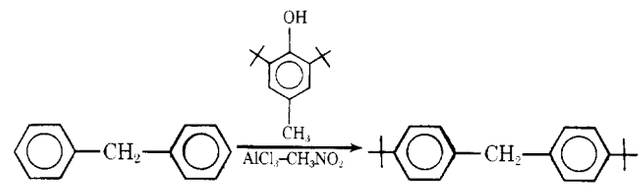
Although $AlCl_3$–CH_3NO_2 does not catalyze the transbenzylation and isomerization of diphenylmethanes,[2-8] it catalyzes transbenzylation of some 4,4′-dihydroxydiphenylmethane derivatives in toluene as was recently reported.[9]

We undertook the present study to obtain more detailed information about factors influencing the above novel transbenzylation of diphenylmethanes and in general to gain a better understanding of the mechanism of transalkylation.

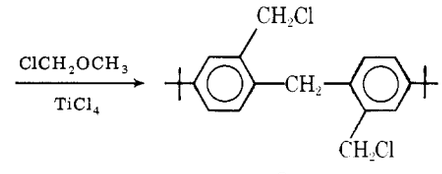
Results and Discussion

Preparation of Some *tert*-Butyldiphenylmethanes. The $AlCl_3$–CH_3NO_2 catalyzed *tert*-butylation of diphenylmethane (**1**) with 2,6-di-*tert*-butyl-*p*-cresol[10] afforded 4,4′-di-*tert*-butyldiphenylmethane (**2a**) in good yield. 4,4′-Di-*tert*-butyl-2,2′-dimethyldiphenylmethane (**2b**) was prepared from **2a** via **3.** The chloromethylation of 4-*tert*-butyltoluene (**4a**) and 5-*tert*-butyl-1,3-dimethyl- (**4b**) and 4-*tert*-butyl-1,2-dimethylbenzene (**4c**) afforded the corresponding 5-*tert*-butyl-2-methyl- (**5a**), 4-*tert*-butyl-2,6-dimethyl- (**5b**), and 5-*tert*-butyl-2,3-dimethylbenzyl chloride (**5c**), respectively, in good yields.

In the $TiCl_4$ catalyzed benzylation of **4a, 4b,** and **4c** with the chlorides, 5,5′-di-*tert*-butyl-2,2′-dimethyl- (**2c**), 4,4′-di-*tert*-butyl-2,2′,6,6′-tetramethyl- (**2d**), 4,5′-di-*tert*-butyl-



1 **2a**



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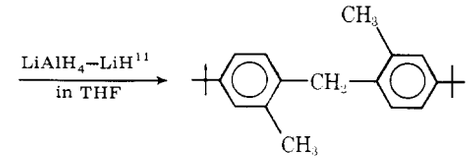

2b

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