Procedure for Recycling the KF/Basic Alumina. The used KF/basic alumina was recycled by first washing with distilled water and then adding 4 g of the washed alumina to a solution of 1.7 g of $KF \cdot 2H_2O$ in 20 mL of distilled water. Removal of water and activation of the KF/basic alumina as described above yielded a fresh sample of the solid base. This recycled base was then used to effect a Michael reaction between 3 mL (33 mmol) of 1-nitropropane and 1 mL (9.2 mmol) of ethyl acrylate in 2 h at 25 °C, yielding 1.6 g (93%) of ethyl 4-nitrohexanoate after removal of solvent and excess 1-nitropropane as described above.

Acknowledgment. The support by the donors of the Petroleum Research Fund, administered by the American Chemical Society, and the Robert A. Welch Foundation is gratefully acknowledged.

Registry No. CH_3NO_2, 75-52-5; $CH_3CH_2NO_2$, 29-24-3; $CH_3(CH_2)_2NO_2$, 108-03-2; $(CH_3)_2CHNO_2$, 79-46-9; CH_2=CHC(O)OEt, 140-88-5; PhCH=CHC(O)Ph, 94-41-7; CH_2=CHC(O)OBu, 141-32-2; $(CH_3)_2C$=CHC(O)CH_3, 141-79-7; CH_2=CHC(O)CH_3, 78-94-4; $NO_2(CH_2)_3C(O)OEt$, 2832-16-8; $NO_2(CH_2)_2CH(CH_2NO_2)C(O)OEt$, 106251-91-6; $NO_2CH_2CH(Ph)CH_2C(O)Ph$, 6277-67-4; $CH_3CH(NO_2)(CH_2)_2C(O)OEt$, 4093-53-2; $CH_3CH(NO_2)(CH_2)_2C(O)OBu$, 106251-92-7; $CH_3CH(NO_2)(CH_2)_2C(O)CH_3$, 35223-72-4; $CH_3CH_2CH(NO_2)(CH_2)_2C(O)OEt$, 59925-14-3; $CH_3CH_2CH(NO_2)CH(Ph)CH_2C(O)Ph$, 80460-05-5; $(CH_3)_2C(NO_2)(CH_2)_2C(O)OBu$, 91017-54-8; KF, 7789-23-3; nitrocyclohexane, 1122-60-7; 2-cyclohexen-1-one, 930-68-7; 3-(1-nitroethyl)cyclohexanone, 59969-93-6; 3-(2-nitroprop-2-yl)cyclohexanone, 4908-50-3; butyl 1-nitro-1-cyclohexanepropanoate, 106251-93-8; 3-(1-nitro-1-cyclohexyl)cyclohexanone, 106251-94-9; alumina, 1344-28-1.

Aldol-Equivalent Elaboration of Sterically Hindered Ketones: Methallylmagnesium Chloride as a Synthon for Acetone Enolate

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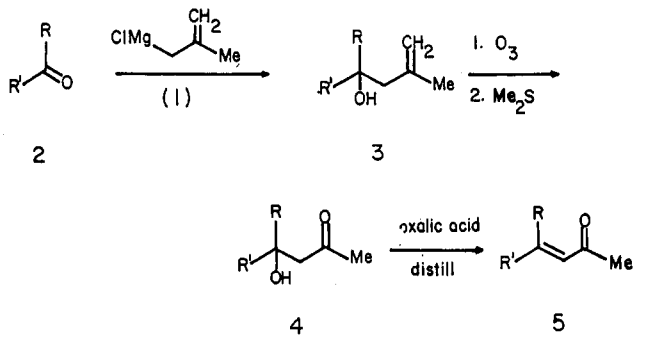
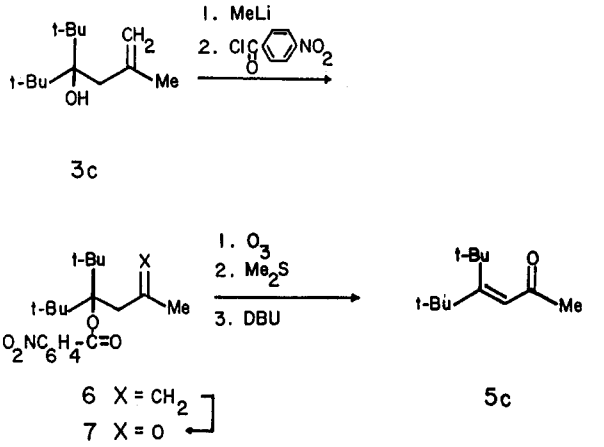
The aldol condensation has long been one of the most useful methods for the construction of carbon–carbon bonds. Modern variants on this venerable process, which allow the controlled cross-condensation of two dissimilar carbonyl compounds, have greatly extended the synthetic utility of the aldol reaction.[1] Nonetheless, important limitations still exist. For example, enolate additions to sterically hindered ketones are troublesome, presumably due to unfavorable equilibria for this reversible reaction. Likewise, additions to easily enolizable ketones often fail because of a kinetically preferred proton transfer.

Current interest in the preparation of organic compounds containing bulky substituents[2] led us to explore aldol-equivalent reactions which would be applicable to such hindered ketones. Bulky dialkyl ketones are readily available and would serve as useful starting materials for the preparation of such sterically encumbered molecules. We report here a successful procedure for the three-carbon,

Scheme I



Scheme II



aldol-equivalent homologation of ketones (Scheme I), which should be of particular value in the elaboration of sterically hindered and easily enolized ketones.

Our approach to this problem is based on the synthetic equivalence of methallylmagnesium chloride (1) with the enolate of acetone.[3,4] Upon addition of the organometallic reagent to a ketone, the latent carbonyl group of 1 can be unmasked by ozonolytic cleavage of the terminal alkene. Several ketones were investigated. The results are summarized in Table I. In all cases, addition of methallylmagnesium chloride was accomplished in a straightforward manner and in high yield. The well-documented reversibility of allyl organometallics to hindered ketones[5] poses no problem—the equilibrium strongly favors the addition product. Even readily enolizable ketones such as cyclopentanone and camphor undergo efficient addition of the methallyl Grignard reagent, in accord with the observation that allylic organometallics rarely cause enolization of carbonyl substrates.[6] Only a single stereoisomeric product was detected in the addition to camphor. This is formulated as the exo alcohol **3e**, by analogy to the literature precedent.[7]

Ozonolysis of the homoallylic alcohols **3a–e** proceeds quite cleanly and in excellent yield to give the corre-

(1) (a) Wittig, G. *Top. Curr. Chem.* **1976**, 67, 1. (b) Mukaiyama, T. *Org. React. (N.Y.) 1976*, 28, 203.
(2) Tidwell, T. T. *Tetrahedron* **1978**, 34, 1855.
(3) Allylic organometallic compounds have been used occasionally as aldehyde enolate equivalents, but we are not aware of any application as ketone enolate synthons. See: (a) Braude, E. A.; Wheeler, O. H. *J. Chem. Soc.* **1955**, 320. (b) Hoffman, R. W. *Angew. Chem., Int. Ed. Engl.* **1982**, *21*, 555.
(4) Other organometallic synthons for acetone enolate have been developed: (a) Trost, B. M.; Stanton, J. L. *J. Am. Chem. Soc.* **1975**, *97*, 4018. (b) Friedrich, L. E.; de Vera, N.; Hamilton, M. *Synth. Commun.* **1980**, *10*, 637.
(5) Benkeser, R. A.; Siklosi, M. P.; Mozdzen, E. C. *J. Am. Chem. Soc.* **1978**, 100, 2134.
(6) Courtois, G.; Miginiac, L. *J. Organomet. Chem.* **1974**, *69*, 1.
(7) Coxon, J. M.; Steel, P. J.; Coddington, J. M.; Rae, I. D.; Jones, A. J. *Aust. J. Chem.* **1978**, *31*, 1223.

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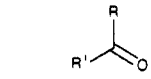
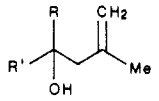
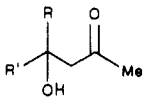
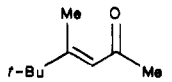
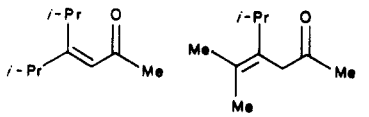
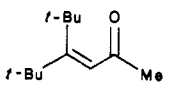
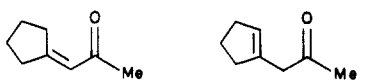
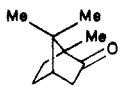
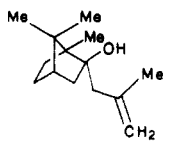
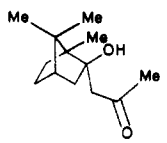
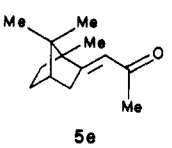
Table I. Three-Carbon Ketone Homologation with Methallylmagnesium Chloride

ketone	homoallylic alcohol	% yield[a]	hydroxy ketone	% yield[b]	enone	% yield[a]
 **2a**, R = Me, R' = *t*-Bu	 **3a**	83	 **4a**	100	 **5a**	74
2b, R = R[1] = *i*-Pr	**3b**	93	**4b**	95	 **2:1 5b**	78[c]
2c, R = R[1] = *t*-Bu	**3c**	87	**4c**	95[a]	 **5c**	30[d]
2d, R, R[1] = $(CH_2)_4$	**3d**	87	**4d**	100	 **1:2 5d**	60[c]
 **2e**	 **3e**	97	 **4e**	98	 **5e**	91

[a] Yield indicated is for distilled material. [b] Yield for crude, isolated product; material is unstable to distillation. [c] Total distilled yield for the indicated mixture. Ratios determined by GC analysis at 100 °C on OV-101. [d] Overall yield from **3c**—see text.

Table II. Selected Characterization Data for Enones 5a–e

compd	mol form.[a]	IR $\nu_{C=O}$, cm^{-1}	^1H NMR, δ		
			$CH_3C(=O)$	$CH=C$	R; R′
5a	$C_9H_{16}O$	1685	2.21	6.12	2.11 (CH_3); 1.11 (*t*-Bu)
5a (α,β)	$C_{10}H_{18}O$	1679	2.20	6.04	3.97 (Me_2CH); 2.58 (Me_2CH)
5b (β,γ)	$C_{10}H_{18}O$	1710	2.14		2.92 (Me_2CH); 1.73, 1.60 nMe_2C=C)
5c	$C_{12}H_{22}O$	1693	2.25	5.87	1.30 (*t*-Bu); 1.24 (*t*-Bu)
5d (α,β)	$C_8H_{12}O$	1689	2.17	6.26	2.77, 2.43 (allyl CH_2's)
5d (β,γ)	$C_8H_{12}O$	1709	2.20	5.51	3.19 (CH_2C=O)
5e	$C_{13}H_{20}O$	1689	2.20	5.99	2.82, 2.40 (each 1 H, m, allyl CH_2)

[a] Compounds **5a** and **5c** gave satisfactory analytical data (C, H); satisfactory exact mass spectra were obtained for each of the isomers of **5b** and **5d** and for **5e**.

sponding β-hydroxy ketones **4a–e**. With the exception of the di-*tert*-butyl compound **4c**, these β-ketols could not be purified completely, suffering partial dehydration on attempted distillation. The intentional dehydration of the ketols was accomplished more effectively by steam distillation from aqueous oxalic acid. The known[4a] enone **5a** was formed as a single isomer (*E* stereochemistry), as was **5e**, tentatively assigned the *E* configuration on the basis of steric considerations. Dehydration of **4b** or **4d** led in each case to a mixture of α,β- and β,γ-unsaturated isomers, as determined by GC and NMR analysis. For **5d**, the product mixture favored the β,γ-isomer by a 2:1 ratio. Treatment of this mixture with KO-*t*-Bu/*t* BuOH led rapidly to a mixture in which the α,β-unsaturated isomer predominated, in accord with the reported[8] equilibrium ratio for **5d** (73:27, favoring the conjugated enone). The enone **5b** was obtained as a 2:1 mixture favoring the conjugated isomer. This ratio was not affected significantly by equilibration with base.

Ketol **4c** was resistant to dehydration. Instead, enone **5c** was prepared via the following modified sequence (Scheme II). Ene alcohol **3c** was taken to its *p*-nitrobenzoate ester **6** by using standard methodology.[9] Ozonolysis of **6** produced the β(*p*-nitrobenzoyl)oxy ketone **7**, which on treatment with 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) in refluxing benzene was converted to enone **5c** (30% overall from **4c**, not optimized).

The methodology described herein is well suited for the elaboration of hindered and enolizable ketones. The overall process corresponds to an aldol-type reaction and should be particularly useful in precisely those applications where traditional methods fail.

Experimental Section

Melting points were determined on a Fisher-Johns hot stage and are uncorrected. Proton magnetic resonance spectra of solutions in $CDCl_3$ were obtained on a JEOL FX90Q spectrometer (90 MHz). Chemical shifts are reported in parts per million downfield of internal tetramethylsilane. IR spectra (of neat liquid

(8) Svata, V.; Prochazka, M. *Collect. Czech. Chem. Commun.* **1975**, *40*, 2315.

(9) Kaiser, E. M.; Woodruff, R. A. *J. Org. Chem.* **1970**, *35*, 1198.

films unless noted otherwise) were recorded on a Nicolet 20DXB spectrometer. Mass spectra were determined on a Kratos MS 25 spectrometer. Elemental analyses were performed by MicAnal, Tucson, AZ.

Di-*tert*-butyl ketone was synthesized by using the procedure of DuBois and Bauer.[10] A stock soluton of methallylmagnesium chloride in THF was prepared by analogy to the method of Otto and Van Zanten.[11] All other reagents were obtained commercially and used as received. THF was distilled from Na/benzophenone.

General Procedure for Homoallyl Alcohols 3a–e. A 30-mL portion of stock methallyl magnesium chloride solution (0.94 M, in THF) was stirred at 0 °C under an N_2 atmosphere. A solution of ketone **2** (25 mmol) in dry THF (10 mL) was added dropwise over 15 min. The solution was then allowed to stir at 20 °C for 40 min, at which time the reaction was quenched with saturated aqueous NH_4Cl. The organic phase was separated and the aqueous phase extracted with pentane. The combined organics were dried over $MgSO_4$, filtered, and concentrated. The residue was purified by bulb-to-bulb distillation.

Ozonolysis: Preparation of β-Ketols 4a–e. A solution of homoallylic alcohol **3** (24 mmol) in CH_2Cl_2 (30 mL) was cooled to −70 °C. Ozone was bubbled through the solution until a blue color developed. After 5 min, the excess ozone was removed with an O_2 purge, and dimethyl sulfide (30 mmol) was added. The solution was allowed to warm to 20 °C and stirred for 8 h. The solvent was removed under vacuum, and the residue partitioned between pentane and saturated brine. The organic phase was dried, filtered, and concentrated to give the crude ketol **4**, which was generally not purified further.

Dehydration: Enones 5a,b,d,e. Ketol **4** (3.2 g) was combined with oxalic acid (3.2 g) and 50 mL of water. The mixture was heated at reflux for 30 min and then distilled until no more organic material came over. The distillate was extracted with pentane (3 × 10 mL). The extracts were dried over $MgSO_4$, filtered, and concentrated. The crude material was purified by bulb-to-bulb distillation.

4-*tert*-Butyl-2,5,5-trimethyl-4-[(4-nitrobenzoyl)oxy]hex-1-ene (6). The ester, prepared from alcohol **3c** by the procedure of Kaiser and Woodruff,[10] was obtained as pale yellow needles from methanol (77%): mp 97.5–98.5 °C; IR (KBr) ν 1708, 1525, 1280, 890 cm^{-1}; ^1H NMR δ 8.26 (m, 4 H), 4.84 (m, 2 H), 3.30 (br s, 2 H), 1.70 (br s, 3 H), 1.30 (s, 18 H). Anal. Calcd for $C_{20}H_{29}O_4$: C, 69.14; H, 8.41; N, 4.03. Found: C, 69.35; H, 8.41; N, 4.10.

4-*tert*-Butyl-5,5-dimethyl-4-[(4-nitrobenzoyl)oxy]hexan-2-one (7). A solution of ene ester **6** in CH_2Cl_2 was ozonized as above. The crude product was purified by column chromatography (CH_2Cl_2 eluent), followed by crystallization from methanol, to provide white needles of **7** (45%): mp 121.5–122 °C; IR (KBr) ν 1730, 1719, 1523, 1285 cm^{-1}; ^{1}HNMR δ 8.23 (m, 4 H), 3.51 (s, 2 H), 2.20 (s, 3 H), 1.23 (s, 18 H). Anal. Calcd for $C_{19}H_{27}NO_5$: C, 65.31; H, 7.79; M, 4.01. Found: C, 64.99; H, 7.82; N, 3.94.

4-*tert*-Butyl-5,5-dimethyl-3-hexen-2-one (5c). A solution of keto ester **7** (27.8 mg) in benzene (1 mL) and DBU (50 mg) was heated at 80 °C for 2.5 hours. The yellow mixture was diluted with 2 mL of benzene and washed with 0.3 M H_2SO_4 (5 mL). The organic phase was filtered through $MgSO_4$ and concentrated. Pure enone was obtained by bulb-to-bulb distillation [97 °C (20mm)] yielding 13.5 mg (91%) of **5c**: see Table II.

Acknowledgment is made to the donors of the Petroleum Research Fund, administered by the American Chemical Society, for the support of this work.

Registry No. **2a**, 75-97-8; **2b**, 565-80-0; **2c**, 815-24-7; **2d**, 120-92-3; **2e**, 76-22-2; **3a**, 107035-96-1; **3b**, 107035-97-2; **3c**, 107035-98-3; **3d**, 67570-15-4; **3e**, 107035-99-4; **4a**, 42095-30-7; **4b**, 107036-00-0; **4c**, 107036-01-1; **4d**, 38134-31-5; **4e**, 107036-02-2; **5a**, 23732-21-0; **5b** (isomer 1), 107036-03-3; **5b** (isomer 2), 107036-04-4; **5c**, 107036-05-5; **5d** (isomer 1), 933-02-8; **5d** (isomer 2), 823-91-6; **5e**, 107036-06-6; **6**, 106140-00-5; **7**, 106140-07-2; 4-$NO_2C_6H_4COCl$, 122-04-3; methallylmagensium chloride, 5674-01-1; acetone enolate, 71695-00-6.

(10) Dubois, J. E. Bauer, P. *J. Am. Chem. Soc.* **1976**, *98*, 6993.
(11) Otto, P. Ph. H. L.; Van Zanten, B. *Recl. Trav. Chim. Pays-Bas* **1962**, *81*, 380.

Structural Elucidation of a Novel Deoxynivalenol Analogue

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Deoxynivalenol (3α,7α,15-trihydroxy-12,13-epoxytrichothec-9-en-8-one, vomitoxin) is one of the predominant trichothecene mycotoxins associated with infection of cereal grains by certain *Fusarium* species[1] and is cause for concern from the viewpoint of both animal and human health.[2]

Recently, a number of studies[3] have focused on the fate of deoxynivalenol during food processing. In a baking study[4] with contaminated flour, we reported the conversion of deoxynivalenol to a diosphenol isomer. This isomer was identified by comparison of its spectral characteristics with an acetylated analogue formed during acetylation studies with deoxynivalenol. While pursuing synthetic studies aimed at a large-scale preparation of the diosphenol isomer, we isolated a new oxidative analogue of deoxynivalenol. In this paper, we report the preparation and structural elucidation of the new compound.

Results and Discussion

As reported previously,[4] when deoxynivalenol (**1**) is refluxed vigorously with acetic anhydride, it is converted in high yield to the triacetylated diosphenol (**2**) (Scheme I). Workup of the reaction involves neutralization with aqueous sodium bicarbonate prior to extraction with chloroform and preparative thin-layer chromatography of the chloroform residue. When a large-scale batch from the described reaction was subjected to preparative thin-layer chromatography, the presence of a slightly more mobile (than compound **2**) pale yellow component became apparent. Extraction and crystallization of this component furnished pale yellow homogeneous crystals with physical and spectral properties that did not correlate with those of any previously reported derivative of deoxynivalenol (**1**). Molecular weight data for the compound determined by fast atom bombardment mass spectrometry was 378 (MH^+ at m/z 379), 2 mass units less than that of 3,15-diacetoxydeoxynivalenol. Its infrared spectrum revealed the presence of four carbonyl groups and absorption in the ultraviolet showed a strong maximum at 248 nm, indicating that the α,β-enone system was still intact. The ^1H NMR spectrum (Table I) confirmed loss of the C-7 proton, and a downfield shift of H-11 suggested greater polarization of the conjugated α,β-enone system. In its ^{13}C NMR spectrum (Table I), the normal C-7 absorption (ca. 70 ppm)

(1) Yoshizawa, T.; Morooka, N. *Agric. Biol. Chem.* **1973**, *37*, 2933. Vesonder, R. F.; Ciegler, A.; Jenson, A. H. *Appl. Microbiol.* **1973**, *26*, 1008. Blight, M. M.; Grove, J. F. *J. Chem. Soc., Perkin Trans. 1* **1974**, 1691. Ueno, Y. In *Advances in Nutritional Research*; Draper, H. H., Ed.; Plenum: New York, 1980; Vol. 3, pp 301–353.
(2) Ueno, Y., Ed. In *Developments in Food Science. 4. Trichothecenes—Chemical, Biological and Toxicological Aspects*; Elsevier: New York, 1983.
(3) Kamimura, H.; Nishijima, M.; Saito, K.; Yasuda, K.; Ibe, A.; Nagayama, T.; Ushiyama, H.; Naoi, Y. *J. Food Hyg. Soc. Jpn.* **1979**, *20*, 352. Scott, P. M.; Kanhere, R.; Lau, P. Y.; Dexter, J. E.; Greenhalgh, R. *Cereal Chem.* **1983**, *60*, 421. Abbas, H. K.; Mirocha, C. J.; Pawlosky, R. J.; Pusch, D. J. *Appl. Environ. Microbiol.* **1985**, *50*, 482.
(4) Greenhalgh, R.; Gilbert, J.; King, R. R.; Blackwell, B. A.; Startin, J. R.; Shepherd, M. J. *J. Agric. Food Chem.* **1984**, *32*, 1416.

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