(m, 11 H); IR (KBr) ν_{NH} 3250, $\nu_{C_Ar H}$ 3100–3000, $\nu_{as\ gem\ CH_3}$ and $\nu_{s\ gem\ CH_3}$ 2962, 2860, $\nu_{as\ CH_2}$ 2930; $\nu_{C_Ar C_Ar}$, $\nu_{C=C}$, $\nu_{C=N}$ 1630–1450, $\gamma_{C_Ar H\ monosubst}$ 750, $\gamma_{C_Ar C_Ar\ monosubst}$ 690; $\gamma_{C_Ar H}$ 770 cm^{-1}; mass spectrum *m/e* 276 (M^+).

Registry No. 1 (R^1 = R^4, R^2 = H, R^3 = Ph), 102651-36-5; 1 (R^1 = Ph, R^2 = R^3 = CO_2Et), 5292-53-5; 1 (R^1 = R^3 = Ph, R^2 = H), 588-59-0; 1 (R^1 = *i*-Pr, R^2 = R^3 = CO_2Et), 5652-68-6; 1 (R^1 = R^3 = CO_2Et, R^2 = H), 623-91-6; 1 (R^1 = R^2 = CO_2Et, R^3 = H), 141-05-9; 1 (R^1 = R^2 = 1,4-butylene, R^3 = H), 110-83-8; 2 (R^1 = R^4), 102651-37-6; 2 (R^1 = Ph), 100-52-7; 2 (R^1 = *i*-Pr), 78-84-2; 2 (R^1 = CO_2Et), 924-44-7; 1,6-hexadial, 1072-21-5; 2,2,4-trimethyl-1*H*-1,5-benzodiazepine, 24107-34-4.

Fragmentation of 2-Benzyl-3-(tosylazo)cyclohex-2-en-1-one to Methyl 7-Phenyl-5-heptynoate

R. Friary* and V. Seidl

Schering Research, Schering-Plough Corporation, Bloomfield, New Jersey 07003

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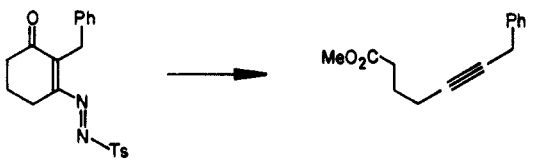
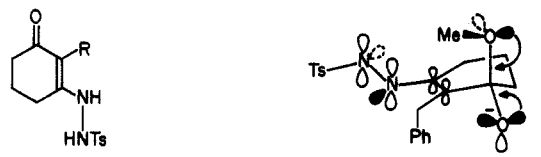
To test a hypothesis that 7-aryl-5-heptynoic acids might inhibit biosynthesis of peptidoleukotrienes, we needed a source of the acids which are not commercially available. Save for one bond, their carbon–carbon connectivity corresponds to that of enolized 2-(arylmethyl)-1,3-cyclohexanediones. The common connectivity suggested that an invented cleavage of the uncommon bond should transform the diones into the acids. Here we report that compound 1 fragmented to **2**, breaking the C_1–C_2 bond of 1.



1 **2**

Known reactions changed 2-benzyl-1,3-cyclohexanedione[1] to 1. (Toluenesulfonyl)hydrazine condensed with the dione forming **3** (16%),[2] and HIO_4 oxidized **3** to the unstable 1 (92%).[4] The geometry of azo group substituents of 1 is presumably trans.[4] Such an arrangement would facilitate concerted Grob fragmentation of presumptive intermediate **4** (vide infra).[6,7]



3, R=CH_2Ph
7, R=H

4

Treatment of 1 with NaOMe in hot MeOH yielded 52% of **2** after distillation. Assignment of structure followed from IR, ^1H NMR, and mass spectra. Identity of spectra of **2** with those of a sample that was synthesized independently from **5** confirmed our assignment. Separate saponifications of both ester samples and spectral and chromatographic comparisons of the resulting acid samples also supported assignments of structures. Contrasting spectra of both samples of 7-phenyl-5-heptynoic acid to those of 2-benzyl-1,3-cyclohexanedione established that the latter had *not* been obtained unwittingly.[8]

$$(MeO)_3C(CH_2)_3C{\equiv}CH \rightarrow \underset{5}{}$$

$$(MeO)_3C(CH_2)_3C{\equiv}CCH_2Ph \rightarrow \mathbf{2}$$

In hot, (initially) neutral EtOH solution, the 2-unsubstituted compound **6** underwent low-yielding (4%) addition–elimination to 3-ethoxycyclohex-2-en-1-one. Neither IR nor ^1H NMR spectra of the black, complex (TLC) product mixture detected ethyl 5-hexynoate. Treatments of **6** with NaOMe in MeOH as well as with $(MeO)_3CH$ in MeOH also gave complex mixtures. Clean, high-yielding fragmentation of **6** was elusive.

Stereoelectronic control explained fragmentation of 1 to **2** via **4**, according to a Deslongchampsien conformational analysis. Neither formation nor fragmentation of **4** required any conformational or rotational changes for **4** to attain needed antiperiplanar orbital alignment. In contrast, at least one such change would have been needed for any intermediate to convert 1 to 3-methoxycyclohex-2-en-1-one in an addition–elimination reaction.

Experimental Section[11]

2-Benzyl-3-[[(4-methylphenyl)sulfonyl]azo]cyclohex-2-en-1-one (1). Prepared from **3** according to ref 3, compound 1 was obtained as a bright orange solid, mp 89–91 °C, in a yield of 92%. Rapid decomposition ensued when 1 was allowed to dry in air on a filter; unrecrystallized but pure 1 was used directly in the next step: IR 1680 s (CO), 1600 m (vinyl), 1494 m (N=N), 1455 br (N=N), 1345 s (SO_2), 1160 s (SO_2); ^1H NMR 7.78 (d, *J* = 9, 2 H, Ar), 7.30 (d, *J* = 9, 2 H, Ar), 7.10 (m, 3 H, Ar), 6.75 (m, 2 H, Ar), 3.77 (s, 2 H, -$CH_2C_6H_5$), 2.54 (m, 4 H, -CH_2CO- and -CH_2CN_2-), 2.40 (s, 3 H, CH_3), 2.00 (m, -CH_2)-); MS, 368 (4, M^+), 213 (44, M – $O_2SC_6H_4CH_3$), 185 (29, M – $N_2SO_2C_6H_4CH_3$), 91 (100, $C_7H_7^+$).

Anal. Calcd for $C_{20}H_{20}N_2O_3S$: C, 65.19; H, 5.47; N, 7.60; S, 8.70. Found: C, 64.97; H, 5.10; N, 7.72; S, 8.48.

Methyl 7-Phenyl-5-heptynoate (2). A. From Fragmentation of 1. NaOMe (0.460 g, 8.5 mmol) was added to a solution of 1 (3.00 g, 8.15 mmol) in MeOH (50 mL), and the resulting orange mixture was heated over 30 min to reflux. MeOH was evaporated from the cooled orange solution and the residue was

(1) Stetter, H.; Dierichs, W. *Chem. Ber.* **1958**, *85*, 1061–1067.
(2) The illustrated vinylogous tosylhydrazide structure (**3**) is that expected.[3,4] Misinterpretation of ^1H NMR data accounted for misassignment of an unconjugated tosylhydrazone structure in a closely related case.[5]
(3) Teuber, H.-J.; Braun, R. *Chem. Ber.* **1967**, *100*, 1353–1366.
(4) Fatiadi, A. J. *J. Org. Chem.* **1970**, *35*, 831–835.
(5) Hiegel, G. A.; Burk, P. *J. Org. Chem.* **1973**, *38*, 3637–3639.
(6) Grob, C. A. *Angew. Chem., Int. Ed. Engl.* **1969**, *8*, 532–622.
(7) (a) Deslongchamps, P. *Stereoelectronic Effects in Organic Chemistry*; Pergamon Press: Toronto, 1983; p 257; (b) p 106; (c) p 210; (d) p 222.
(8) Failure to increase yields of **3** despoiled hopes to exploit fragmentation of 1 to **2**. Several attempts to apply published conditions[3-5,9,10] to preparation of vinylogous arylsulfonylhydrazides from 2-(arylmethyl)-1,3-cyclohexanediones were unsuccessful.
(9) Corey, E. J.; Sachdev, H. S. *J. Org. Chem.* **1975**, *40*, 579–581.
(10) Bertz, S. H.; Dabbath, G. *J. Org. Chem.* **1983**, *48*, 116–119.
(11) Uncorrected melting points were taken on a Fisher Digital Melting Analyser (Model 355) or on a Kofler block (Thomas Model 40). Boiling points are also uncorrected. IR spectra (in CH_2Cl_2 solution or in other media as noted) were obtained on Perkin-Elmer 727B or 1320 spectrophotometers; ν values are in cm^{-1}. ^1H NMR spectra (in $CDCl_3$ or other solvents as noted) were recorded on a Varian EM-390 instrument; δ values are in ppm downfield from internal Me_4Si. *J* values of coupling constants are in hertz. High-resolution MS were determined on a MAT-312, double-focusing instrument operating at 70 sV. Medium-resolution MS were measured on a Varian CH5 spectrometer. Parenthesized numbers following *m/z* values are relative ion intensities. E. Merck (Darmstadt) supplied F-254 silica gel plates for TLC, as did Analtech. Developed plates were visualized in UV light, in I_2 vapor, or (Analtech plates) by spraying with phosphomolybdic acid followed by heating. E. Merck as well as Baker provided 60–200-mesh silica gel for column chromatography.

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partitioned between Et_2O and H_2O. Combined Et_2O extracts were washed with 1 N $NaHCO_3$ (4 × 50 mL) and with H_2O and were dried ($MgSO_4$) and filtered. Evaporation of solvent followed by distillation of the oily residue (1.28 g) gave **2** (1.10 g, 52%), bp 135–145 °C at 0.4 mm. Chromatography over silica gel and elution with $CHCl_3$–hexanes (60:40) gave a purer sample: IR 2950 s, 1950 w (C≡C), 1730–1720 s (ester CO), 1220 br s (CO_2CH_3), 1180–1160 br s (CO_2CH_3); ^1H NMR 7.30 (br s, 5 H, Ar), 3.65 (s, 3 H, -OCH_3), 3.57 (m, 2 H, -C$H_2C_6H_5$), 2.47 (m, 2 H, -C$H_2CO_2CH_3$), 2.25 (m, 2 H, -CH_2C≡C-), 1.90 (m, 2 H, -CH_2-); MS, 216 (1, M^+), 105 (100).

Anal. Calcd for $C_{14}H_{16}O_2$ (M^+): 216.1150. Found: 216.1144.

IR, ^1H NMR, and mass spectra as well as side-by-side and co-spotted thin-layer chromatograms of **2** were compared with those of an authentic sample. Comparisons showed the samples to be identical.

B. From Benzylation and Hydrolysis of 6,6,6-Trimethoxy-1-hexyne. Benzylation of **5**[12] and hydrolysis of the product also gave **2** as follows.

A mixture of **5** (1.34 g, 7.80 mmol) and CuI (0.670 g, 3.50 mmol) in dry THF (8 mL) was cooled to −70 °C under dry N_2. *n*-Butyllithium (7.76 mmol from a 1.15 M solution in hexanes) was added slowly. After 30 min at −70 °C, benzyl chloride (0.854 g, 6.70 mmol) in THF (8 mL) was added. After refluxing 5 h, the cooled reaction mixture was poured into cold H_2O (200 mL). Et_2O (200 mL) was added, and the mixture was filtered. Layers of the filtrate were separated, and the aqueous layer was extracted with Et_2O. Combined Et_2O solutions were dried ($MgSO_4$) and evaporated to give crude 7-phenyl-1,1,1-trimethoxy-5-heptyne (1.94 g): IR 2940 s, 2825 s, 2190 w (C≡C), 1100 s (COC); ^1H NMR 7.25 (s, 5 H, Ar), 3.53 (m, 2 H, -C$H_2C_6H_5$), 3.21 (s, 9 H, -OCH_3), 2.25 (m, 2 H, -CH_2C(OMe)$_3$), 1.8 (m, 2 H, -CH_2C≡C-), 1.53 (m, 2 H, -CH_2-). The product was used directly in the next step.

A solution of 7-phenyl-1,1,1-trimethoxy-5-heptyne (1.70 g, 6.50 mmol), pyridinium *p*-toluenesulfonate (80.4 mg), and MeOH (25 mL) was heated 40 min at 40 °C, after which solvent was evaporated. Distillation of the residue (1.4 g) gave **2** (53%), bp 105 °C at 0.2 mm, pure according to TLC and to ^1H NMR spectroscopy.

7-Phenyl-5-heptynoic Acid. Saponifications (1 equiv of KOH, H_2O, MeOH, 3 h at 20 °C of **2** followed by standard workups gave the desired acid (79%) as a semisolid: IR 3470 and 2940–2900 (OH), 1945 (C≡C), 1700 br s (CO_2H); ^1H NMR 10.0 (br s, 1 H, ex, -CO_2H), 7.33 (br s, 5 H, Ar), 3.56 (br t, 2 H, -C$H_2C_6H_5$), 2.52 (t, J = 6, 2 H, -CH_2CO_2H), 2.32 (m, 2 H, -CH_2C≡C), 1.92 (m, 2 H, -CH_2-); MS, 202 (5, M^+), 91 (100, $C_7H_7^+$).

Anal. Calcd for $C_{13}H_{14}O_2$ (M^+): 202.0933. Found: 202.0981.

2-Benzyl-3-[[(4-methylphenyl)sulfonyl]hydrazino]cyclohex-2-en-1-one (3). A mixture of 2-benzyl-1,3-cyclohexanedione (17.25 g, 82.5 mmol),[1] (*p*-toluenesulfonyl)hydrazine (16.25 g, 0.880 mmol), concentrated HCl (1 mL), and MeOH (290 mL) was allowed to stand 60 h at 25 °C. The mixture was treated with charcoal, filtered, and concentrated. A solution of the residue in $CHCl_3$ was also filtered, and $CHCl_3$ was then evaporated. The oily residue crystallized on trituration with Et_2O, and the crystals were collected, washed with Et_2O, and dried to give impure **3** (26.1 g, mp 122–125 °C). Several crystallizations from MeOH gave pure **3** (15.8%), mp 172.5–173.5 °C; IR (mineral oil) 3350 (NH), 1568 (CO), 1330, 1300, 1160; ^1H NMR (Me_2SO-d_6): 9.73 and 8.14 (2 NH, ex), 7.43 (d, 2 H, J = 7.5, Ar), 7.30 (d, 2 H, J = 7.5, Ar), 7.17 (m, 5 H, Ar), 3.5 (s, 2 H, -C$H_2C_6H_5$), 2.38 (s, 3 H, -$C_6H_4CH_3$), 2.14 (m) and 1.67 (m) (total of 6 H); MS, 370 (10, M^+), 215 (100, M − $SO_2C_6H_4CH_3$), 185 (14, M − NHNHS$O_2C_6H_4CH_3$).

Anal. Calcd for $C_{20}H_{22}N_2O_3S$: C, 64.84; H, 5.99; N, 7.56; S, 8.65. Found: C, 64.71; H, 6.13; N, 7.69; S, 8.74.

2-Benzyl-3-[[(4-methylphenyl)sulfonyl]hydrazino]cyclohex-2-en-1-one [(4-Methylphenyl)sulfonyl]hydrazone. Initial filtration of the MeOH reaction mixture from which **3** was obtained (vide supra) gave a byproduct (1.33 g, 2.9%), mp 192–195 °C.

Anal. Calcd for $C_{27}H_{30}N_4S_2O_4$: C, 60.20; H, 5.61; N, 10.40; S, 11.90. Found: C, 60.18; H, 5.35; N, 10.23; S, 12.04.

3-[[(4-Methylphenyl)sulfonyl]azo]cyclohex-2-en-1-one (6). Prepared from **7** according to ref 4, compound **6** was obtained as a bright orange solid, mp 59–60 °C, in a yield of 89%. Rapid decomposition ensued when **6** was allowed to dry in air on a funnel: IR 1670 (CO), 1590, 1460, 1380, 1160; ^1H NMR 7.78 (d, J = 7.5, Ar), 7.37 (d, J = 7.5, 2 H, Ar), 6.66 (s, 1 H, vinyl H), 2.47 (br s, 7 H, overlapping resonances of 2 -CH_2- and -CH_3), 2.15 (m, -CH_2-); MS, 278 (11, M^+), 91 (100, $C_7H_7^+$). Instability of **6** precluded recrystallization, and acceptable microanalytical data for N were not obtained despite analyses of two different samples.

Anal. Calcd for $C_{13}H_{14}N_2O_3S$: C, 56.10; H, 5.07; N, 10.06; S, 11.52. Found: C, 56.46; H, 5.01; N, 9.39; S, 11.86.

3-[[(4-Methylphenyl)sulfonyl]hydrazino]cyclohex-2-en-1-one (7). Prepared from 1,3-cyclohexanedione according to ref 3, compound **7** was obtained in a yield of 88%, had mp 205–207 °C, and was pure (^1H NMR): IR (mineral oil) 3280 (NH), 1580–1520 br s (CO), 1350, 1320, 1180; ^1H NMR (Me_2SO-d_6) 9.72 (br s, NH), 8.50 (br s, NH), 7.81 (d, J = 7.8, 2 H, Ar), 7.40 (d, J = 7.8, 2 H, Ar), 5.12 (s, 1 H, vinyl H), 2.6–1.6 (overlapping resonances of CHD_2SOCD_3, -(CH_2)$_3$-, and CH_3 (s at 2.35)); MS, 280 (22, M^+), 125 (100), 91 (76, $C_7H_7^+$).

Anal. Calcd for $C_{13}H_{16}N_2O_3S$: C, 55.70; H, 5.75; N, 9.99; S, 11.44. Found: C, 56.26; H, 5.74; N, 9.83; S, 11.73.

3-Ethoxycyclohex-2-en-1-one. A solution of **6** (12 g, 43 mmol) and EtOH (50 mL) was stirred 5 h at 25 °C under N_2. The dark red solution became black, depositing a precipitate (3.2 g; uninvestigated). EtOH was evaporated from the filtered mixture, and a solution of the residue (6.2 g) in $CHCl_3$ was washed with 1 M aqueous Na_2CO_3 (2 × 200 mL) and with H_2O (200 mL). The dried ($MgSO_4$) solution was filtered through diatomaceous earth containing activated carbon and was concentrated to give an oily black residue (1.5 g) of several components (TLC). Flash chromatography over 150 g of Merck silica gel (230–400 mesh) and elution with $CHCl_3$ followed by distillation afforded 3-ethoxycyclohex-2-en-1-one (0.25 g, 4%) as a yellow liquid, bp 85 °C at 1 mm. Side-by-side and co-spotted thin-layer chromatograms of synthetic and commercial (Aldrich) samples were identical in two solvent systems. Indentity of the samples was confirmed by comparisons of ^1H NMR, IR, and mass spectra. Both samples contained a trace of the same, unidentified impurity (TLC, ^1H NMR).

Acknowledgment. We are grateful to Dr. D. Andrews (Schering-Plough) for criticism and to Prof. M. K. Kaloustian (Fordham University) for encouragement. We also thank Analytical Research Services (Schering-Plough) for microanalyses and spectra, as well as Mr. J. H. Schwerdt (Schering-Plough) for preliminary experiments.

Registry No. **1**, 102921-09-5; **2**, 88255-19-0; **3**, 102940-19-2; **5**, 82709-37-3; **6**, 102940-20-5; **7**, 102921-12-0; $PhCH_2C$≡C-$(CH_2)_3C(OMe)_3$, 102921-10-8; $PhCH_2C$≡$C(CH_2)_3CO_2H$, 88255-07-6; 2-benzyl-1,3-cyclohexanedione, 22381-56-2; 2-benzyl-3-[2-[(4-methylphenyl)sulfonyl]hydrazino]cyclohex-2-en-1-one [(4-methylphenyl)sulfonyl]hydrazone, 102921-11-9; 3-ethoxycyclohex-2-en-1-one, 5323-87-5.

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Preparation of Secondary and Tertiary Cyclic and Polycyclic Hydrocarbon Azides[1]

G. K. Surya Prakash, Maurice A. Stephenson, Joseph G. Shih, and George A. Olah*

Donald P. and Katherine B. Loker Hydrocarbon Research Institute and Department of Chemistry, University of Southern California, Los Angeles, California 90089-1661

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The azido functionality is one of the progenetorial groups for the synthesis of nitrogen-containing organic compounds.[2] In polycyclic bridgehead compounds such

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