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# SOME PREPARATION METHODS OF A TRICYCLO[4.1.0.0$^{2,7}$]HEPT-4-EN-3-ONE SKELETON

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ABSTRACT: β-Elimination of acetic acid was elaborated in our synthetic method of a tricyclo[4.1.0.0$^{2,7}$]hept-4-en-3-one (tropovalene) skeleton. Presented was a new synthetic method of this skeleton, which consists of a reaction sequence of 1,4-addition of propanethiol to bicyclo[3.2.0]hepta-3,6-dien-2-one, photochemical construction of bicyclobutane skeleton, oxidation, and thermal elimination of sulfenic acid.

The procedure which consists of photochemical construction of a bicyclo[3.2.0]hept-6-en-2-one skeleton, oxa-di-π-methane rearrangement and elimination of acetic acid is a facile strategy for the synthesis of tricyclo-[4.1.0.0$^{2,7}$]hept-4-en-3-one **1**, a valene-type valence isomer[1] of cyclohept-2,4,6-

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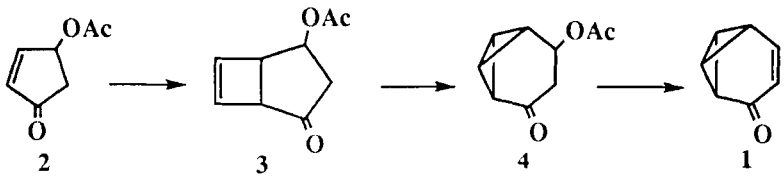


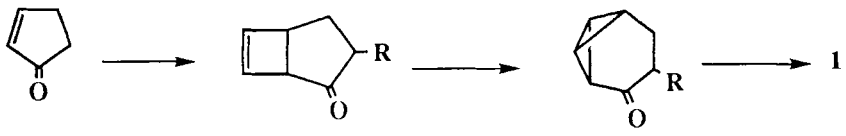

Scheme 1.



trien-1-one (tropone) (Scheme 1).[2] Starting from this work, we have achieved chemistries of some valene-type isomers of nonalternant hydrocarbons.[3] Other groups have made use of this photolysis and have developed the troponoid and alicyclic chemistries.[4] Recently, we have reported anomalous thermal bond-reorganization of **1**,[5] which forced us to provide alternative synthetic methods of derivatives bearing a substituent on the desired site of **1**.

Success of construction of the tricyclo[4.1.0.$0^{2,7}$]hept-4-en-3-one skeleton was dependent upon the final step in Scheme 1, since this skeleton was often labile with the reaction conditions and repeated purification procedures. Another problem in Scheme 1 was that the general method of synthesizing β-acetoxyketone moiety which served as an equivalent of α,β-unsaturated ketone has not yet been established.

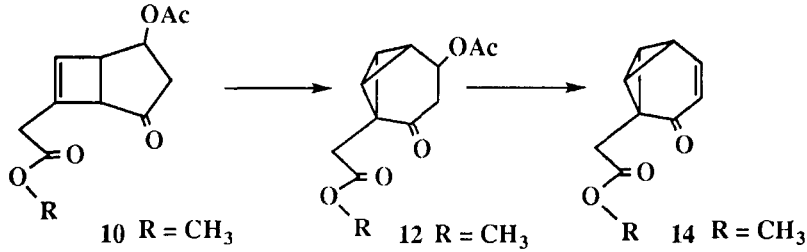
Sulfenylation followed by oxidation and thermal elimination of sulfenic acid has been established for the construction of α,β-unsaturated ketones.[6] As reported,[3, 5] this method was useful for producing **1** of high purity (Scheme 2). The applicability of the method to tricyclo[4.1.0.$0^{2,7}$]heptan-3-one skeletons




Scheme 2.

should be worthy to note, since the labile bicyclobutane ring was not decomposed with sulfenic acid or species generated during disproportionation of sulfenic acid.

However, we could not practically obtain **7**[7] in a satisfactory amount. Namely, in contrast to 4-acetoxycyclopent-2-en-1-one **2**, cyclopent-2-en-1-one **5** was, quite interestingly, fairly inert to photochemical [2+2] cycloaddition with acetylene using 100-W high pressure mercury lamp in acetone at dry ice/acetone temperature.[2] A further attempt to obtain tricyclo[4.1.0.$0^{2,7}$]heptan-3-one **7** at one try by photolysis of **5** with acetylene using 450-W high pressure mercury lamp resulted in failure. In addition, compounds **6** and **7** are of low boiling point. Hence separation from the solvent in the reported procedure[7] sometimes reduced the yield of **6** and **7**. Introduction of phenylthio group to **6** followed by photochemical bond reorganization to **9** resulted in failure, since photolysis of **8** in acetone gave an intractable mixture.



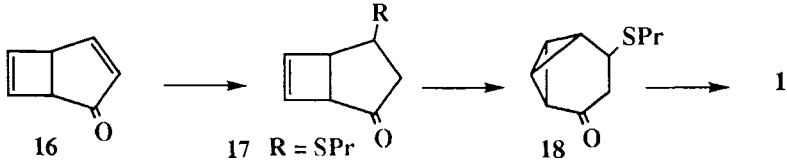

**10** R = $CH_3$ **12** R = $CH_3$ **14** R = $CH_3$

**11** R = Ph **13** R = Ph **15** R = Ph

Scheme 3.

While the 4-acetoxycyclopent-2-en-1-one system was the effective chromophore for photochemical cycloaddition, β-elimination of acetic acid in 5-acetoxytricyclo[4.1.0.$0^{2,7}$]hept-4-en-3-one skeleton often led to destruction of a bicyclobutane ring of the product. Hence, the method of β-elimination of acetic acid should have been elaborated. For this study, good choices of substrates were 2-[(methoxycarbonyl)methyl]-5-acetoxy- **12** and 2-[(phenoxycarbonyl)methyl]-5-

acetoxytricyclo[4.1.0.0$^{2,7}$]heptan-3-one **13**, since the tropovalene skeletons in **14** and **15** possess a substituent which may be useful for the construction of more sophisticated derivatives of **1** and the substituent on a bicyclobutane ring has sometimes caused destruction[8] of this ring (Scheme 3). Compounds **10**[9, 10] and **11**[11, 12] in acetone were photolyzed smoothly to yield **12** and **13**, respectively. Both compounds **12** and **13** resisted β-elimination of acetic acid with deactivated alumina (10 % $H_2O$). Forced conditions, for example, use of activated alumina led to decomposition or conversion to isomers containing a cyclobutene ring (Dewar type isomer). Many attempts with bases[13] in various solvents resulted in failure. Ultimately, β-elimination of acetic acid of **12** and **13** was successful with basic alumina. Thus, filtration of **12** on alumina containing aqueous ammonia (4 %) by 3 % with a mixture of benzene and ether (9:1 v/v) and chromatographic separation over deactivated silica gel (10 % $H_2O$) gave the desired product **14** (70.0 % yield). Similarly, compound **13** quantitatively underwent β-elimination to yield **15** when a fairly excess amount of the same alumina was used (15 times the amount of **13**).




Scheme 4.

The last improvement is functionalization at a 4-position of the bicyclo-[3.2.0]hept-6-en-2-one skeleton (Scheme 4). Thus, due to a ring strain, β-elimination of acetic acid in this skeleton required forced conditions (aluminum containing 3 % $H_2O$), compared with the 5-acetoxytricyclo[4.1.0.0$^{2,7}$]heptan-3-

one system. The fact made our procedure in Scheme 1 successful, since pure 4-acetoxybicyclo[3.2.0]hept-6-en-2-ones could be photolyzed. Repeated purification by column chromatography, however, often resulted in β-elimination even in this skeleton, forming a photochemically inert bicyclo[3.2.0]hept-3,6-dien-2-one skeleton. To exclude the problem, we synthesized 4-propylthiobicyclo[3.2.0]hept-6-en-2-one **17**. Thus, bicyclo[3.2.0]hept-3,6-dien-2-one **16**[15] was treated with lithium propanethiolate in THF at –78 °C to yield **17** (70.1% yield). As expected, compound **17** was easily purified by chromatography over deactivated silica gel (6% $H_2O$) and, furthermore, was converted to a bicyclobutane isomer **18** upon photolysis. Bicyclobutane **18** could completely be purified as well by chromatography over deactivated silica gel (20% $H_2O$) (35% ). Compound **18** was oxidized with *m*-chloroperbenzoic acid at –78 °C and then thermolyzed in carbon tetrachloride at 70 °C to yield **1** (71.3% based on **18**).

It is noteworthy here that **17** was photochemically converted to the desired product, since the compound having both a sulfur atom and carbonyl chromophore, upon photolysis, sometimes formed a charge transfer complex and this complex was converted to a mixture of rearrangement or fragmentation products.[16] Photolysis of 4-propylsulfonylbicyclo[3.2.0]hept-6-en-2-one **19** and 4-*p*-toluenesulfonylbicyclo[3.2.0]hept-6-en-2-one **20** was attempted, yielding a complex mixture. These facts show that the alkylthio group can serve as a protecting group of α,β-unsaturated ketones in the photolysis.

## EXPERIMENTAL

**2-[(methoxycarbonyl)methyl]tricyclo[4.1.0.0$^{2,7}$]hept-4-en-3-one 14**

Basic alumina was prepared by adding 3 % weight of 4 % aqueous ammonia to

commercially available alumina. Compound **12** (1.50 g, 6.30 mmol) was filtered through basic alumina (7.5 g) with a mixture of benzene and ether (1 : 1 v/v). Chromatography over deactivated silica gel (10 % $H_2O$)with a mixture of benzene and ether (9 : 1) gave **14** (785 mg, 4.41 mmol, 70 %) as a colorless oil.

**14**: bp 70–90 °C/0.3 Torr (1 torr = 133.322 Pa); IR (neat) 1735 and 1670 $cm^{-1}$; $^1H$ NMR ($CDCl_3$) δ 6.95 (dd, 1H, $J$ = 9.6 and 4.8 Hz), 5.50 (dd, 1H, $J$ = 9.6 and 1.4 Hz), 3.73 (s, 3H), 3.38 (d, 2H, $J$ = 2.4 Hz), 2.57 (s, 2H), 2.70–2.43 (m, 1H).

**2-[(phenoxycarbonyl)methyl]tricyclo[4.1.0.0$^{2,7}$]hept-4-en-3-one 15**

Basic alumina was prepared in the same manner as the case of formation of **14**. Compound **13** (18.9 g, 6.30 mmol) was filtered through basic alumina (7.5 g) with a mixture of benzene and ether (9 : 1 v/v). Removal of solvent gave a crystalline solid **15** (1.51 g) which was practically pure based on $^1H$ NMR spectrum. Recrystallization from ether gave **15** (755 mg, 3.15 mmol, 50 %) as colorless crystals.

**15**: mp 76.0–77.1 °C; IR (KBr) 1740 and 1650 $cm^{-1}$; $^1H$ NMR ($CDCl_3$) δ 7.44–7.05 (m, 5H), 6.97 (dd, 1H, $J$ = 9.6 and 4.6 Hz), 5.55 (dd, 1H, $J$ = 9.6 and 1.3 Hz), 3.45 (d, 2H, $J$ = 2.4 Hz), 2.77 (s, 2H), 2.58 (dtd, 1H, $J$ = 4.6, 2.4, and 1.3 Hz).

**4-propylthiobicyclo[3.2.0]hept-6-en-2-one 17**

To a solution of 1-propanethiol (0.44 ml, 4.9 mmol) in THF (5 ml) was added 1.5 N *n*-butyllithium in *n*-hexane (3.2 ml, 4.8 mmol) at –78 °C. After stirring for 30 min, bicyclo[3.2.0]hept-3,6-dien-2-one **16** (430 mg, 4.1 mmol) in THF (1 ml) was added and stirring was continued for 30 min. Extraction with ether and column chromatography over deactivated silica gel (6 % $H_2O$, 10 g) with benzene gave **17** (524 mg, 2.87 mmol, 70.1 %) as a faint violet oil.

**17**: bp 100–110 °C/0.1 Torr; IR (neat) 1730 $cm^{-1}$; $^1H$ NMR ($CDCl_3$) δ 6.35 (d like, 1H, $J$ = 2.4 Hz), 6.20 (d, 1H, $J$ = 2.4 Hz), 3.63–3.17 (m, 4H), 2.80–2.27 (t and m, 3H, $J$ = 6.6 Hz), 1.97–1.30 (sextet like, 2H, $J$ = 6.6 Hz), 1.00 (t, 3H, $J$ = 6.6 Hz); MS, m/z 182 ($M^+$, 23%), 154 ($M^+$–CO, 14%). Anal. C, H, S.

**5-propylthiotricyclo[4.1.0.0$^{2,7}$]heptan-3-one 18**

A solution of **17** (120 mg, 0.659 mmol) in dry acetone (100 ml) was bubbled with nitrogen. The solution was irradiated using 450-W high pressure mercury lamp through Pyrex with ice cooling for 1.3 h. After removal of acetone *in vacuo*, ether was added and ether layer was washed with water. Column chromatography over deactivated silica gel (20 % $H_2O$, 4 g) with a mixture of *n*-hexane and benzene (1 : 1 v/v) gave **18** (42 mg, 0.231 mmol, 35 %) as a colorless oil.

**18**: IR(neat) 1705 $cm^{-1}$; $^1H$ NMR ($CCl_4$) δ 3.37–2.07 (m, 9 H), 1.87–1.30 (sextet like, 2H, $J$ = 6.6 Hz), 1.03 (t, 3H, $J$ = 6.6 Hz); MS, m/z 182 ($M^+$, 10%), 154 ($M^+$ – CO, 5%).

**tricyclo[4.1.0.0$^{2,7}$]hept-4-en-3-one 1**

To a solution of **18** (106 mg, 0.582 mmol) in dichloromethane dichloride (3 ml) was added *m*-chloroperbenzoic acid (125 mg, 0.581 mmol) in dichloromethane (2 ml) at –78 °C. After stirring for 40 min, the mixture was extracted with ether. The organic layer was washed with diluted aqueous sodium sulfite, water and brine, and dried ($MgSO_4$). The solvent was removed and a residue was heated in carbon tetrachloride (4 ml) at 70 °C for 1 h. Column chromatography over deactivated silica gel (20 % $H_2O$, 1 g) with a mixture of benzene and ether (8 : 2 v/v) gave **1** (44 mg, 0.415 mmol, 71.3%).

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8) For example, 1-*t*-butyltricyclo[4.1.0.$0^{2,7}$]hept-4-en-3-one was obtained as a mixture with its Dewar type isomer in a good yield. Column chromatography resulted in isomerization of this desired product to the Dewar type isomer rather than purification of the former.

9) Compound **10** was prepared by photocycloaddition of **2** and methyl 3-butynoate[10] in acetone as a sole cycloaddition product in a yield of 63.2 %.

10) 3-Butynoic acid was prepared by addition of carbon dioxide at dry ice/ethanol temperature to a Grignard compound made from propagyl bromide, and was

purified by recrystallization from a mixture of benzene and ligroin. Methyl 3-butynoate was prepared by esterification of the acid with diazomethane.

11) Compound **11** was prepared by photocycloaddition of **2** and phenyl 3-butynoate[12] in acetone as a crystalline compound in a 13 % yield, which was a sole cycloaddition product.

12) Phenyl 3-butynoate was prepared by treatment of a mixture of 3-butynoic acid and phenol in trifluoroacetic anhydride at 80 °C for 40 h in a yield of 23 %.

13) We examined here sodium hydride, potassium carbonate, triethylamine, 1,8-diazabicyclo[5.4.0]undecene, tetramethylammonium 2,4,6-trimethylbenzene-carboxylate,[14] and diisopropylethylamine

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15) Compound **16** was prepared by elimination of acetic acid of **3** with deactivated alumina (3 % $H_2O$).

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