204. The Reaction of 1,3-Butadiene with Ethyl Diazopyruvate. Syntheses of Salicylates and of Nezukone

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The Rh-catalyzed reaction of 1,3-butadiene with ethyl 3-diazopyruvate leads, *inter alia*, to a dihydrooxepinecarboxylate whose oxidation and functional-group manipulation produce salicylates. *Wittig* reactions on the acylcyclopropane accompanying the dihydrooxepine yields acrylates whose pyrolyses afford cycloheptadienecarboxylates. Oxidation and functional-group transformation produces the natural tropone, nezukone.

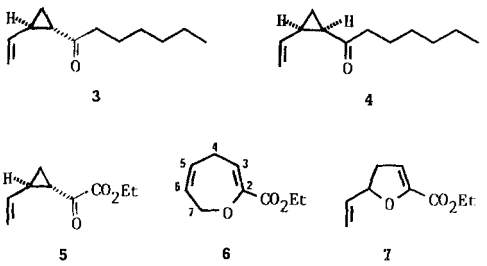
Introduction. – Whereas α-diazocarbonyl compounds are transformed normally into acylcyclopropanes on metal-assisted decomposition in the presence of olefins, diazopyruvates, *e.g.* **1**, are converted into 4,5-dihydro-2-furoates in this reaction with electron-rich olefins as, for example, enol ethers [1][1]). In the case of the reaction of ethyl diazopyruvate (**1**) with a conjugated dienol ether, the dihydrofuroate product was accompanied by a dihydrooxepine derivative [1e]. In order to ascertain the sequence of events responsible for this unusual result, a study of the reaction of ethyl diazopyruvate (**1**) with a simpler diene, *i.e.* 1,3-butadiene (**2**), was undertaken.

1 **2**

Results and Discussion. – As a point of reference, at first 1,3-butadiene (**2**) was caused to interact with 1-diazo-2-octanone under $Rh_2(OAc)_4$ catalysis, leading to a *ca.* 2:1 mixture of the expected acylcyclopropanes **3** and **4** (83% yield)[2]). The same reaction with ethyl diazopyruvate (**1**) afforded only one expected compound – the acylcyclopropane **5** (35%) – accompanied by dihydrooxepinecarboxylate **6** and dihydrofuroate **7** in 26 and 4% yields, respectively. The formation of the minor dihydrofuran derivative was in consonance with the production of such a side product on metal-induced decomposition of diazopyruvate in the presence of even unfunctionalized alkenes[1]), but the absence of the *cis* isomer of keto-ester **5** [2] [4] and the presence of the dihydrooxepine [1a] ester **6** among the products was unusual. On the assumption of the last two facts being interconnected, a simple explanation emerges. In analogy with the valence tautomerism of *cis*-2-vinylcyclopropanecarboxaldehyde (**8a**) and 2,5-dihydrooxepine (**9a**) [5], the unob-

[1]) There is one example of even an unfunctionalized olefin, (*Z*)-2-butene, being changed into a dihydrofuroate as a minor product (5% yield) on treatment with methyl diazopyruvate under $CuSO_4$ catalysis [2].

[2]) For the reaction of the diene with ethyl diazoacetate, see [3].



3 4

5 6 7

served acylcyclopropane (**8b**) can be in equilibrium with the dihydrooxepine **9b** (≡ **6**; *Scheme 1*). Whereas, however, the **8a**⇄**9a** equilibrium is 19:1 in favor of the cyclopropane [5], the coulombic repulsion of the α-dicarbonyl system of cyclopropane **8b** may be responsible for the dislocation of the **8b**⇄**9b** equilibrium in favor of the dihydrooxepine. *trans*/*cis*-Isomerization of ketone **5** (*i.e.* **5**→**8b** conversion) on photolysis [6] led to dihydrooxepinecarboxylate **6** (≡ **9b** in 80% yield).

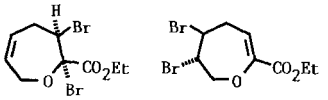
Scheme 1

8 9

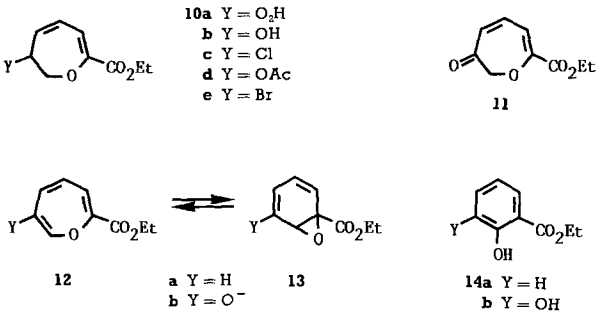
a R = H
b R = CO_2Et

In view of the ease of the dihydrooxepine synthesis and in view of the known, facile conversion of oxepines (*via* their valence tautomers – the benzene oxides) into phenols [7], the oxidation of dihydrooxepine **6** came under scrutiny. The compound proved to be surprisingly inert toward a variety of dehydrogenation agents[3]), but on exposure to the air (or, more efficiently, to O_2) was transformed into a hydroperoxide **10a** [8] whose reduction with Me_2S led to an alcohol of structure **10b**. Treatment of the latter with methanesulfonyl chloride, Ac_2O, and chromic acid afforded chloride **10c**, acetate **10d**, and ketone **11**, respectively. Despite various attempts of dehydrochlorination, the chloride **10c** could

[3]) Bromination/dehydrobromination yielded unusual results. Treatment of ester **6** with 1 equiv. of Br_2 in CCl_4 solution gave dibromide **i** [Yield 98%. M.p. 45–46°. IR (film): 1743*s* (C=O). ^{1}H-NMR ($CDCl_3$): 1.38 (*t*, *J* = 7, CH_3CH_2O); 2.81 (*ddd*, *J* = 16, 8, 5, 1 H–C(4)); 3.55 (*dt*, *J* = 16, 3, 1 H–C(4)); 4.30 (*q*, *J* = 7, CH_3CH_2O); 4.40 (*dd*, *J* = 16, 8, 1 H–C(7)); 4.59 (*ddd*, *J* = 16, 5, 5, 1 H–C(7)); 4.99 (*dd*, *J* = 5, 3, H–C(3)); 5.8–6.1 (*m*, H–C(5), H–C(6))]. Excess Br_2 yielded a mixture of stereoisomeric tetrabromides [IR (film): 1745*s*, 1765*s* (C=O)] whose short, mild exposure to Zn afforded the fully dehalogenated ester **6** (56%) and dibromide **ii** [Yield 37%, viscous liquid. ^{1}H-NMR (CCl_4): 1.31 (*t*, *J* = 7, CH_3CH_2O); 2.7–3.0 (*m*, CH_2(4)); 3.8–4.6 (*m*, H–C(5), H–C(6), CH_2(7)); 4.18 (*q*, *J* = 7, CH_3CH_2O); 6.21 (*t*, *J* = 6, H–C(3))]. Short treatment of the latter in Et_2O solution with diazabicycloundecene produced bromide **10e** [Yield 80%, liquid. ^{1}H-NMR ($CDCl_3$): 1.35 (*t*, *J* = 7, CH_3CH_2O); 4.2–4.6 (*m*, CH_2(7)); 4.29 (*q*, *J* = 7, CH_3CH_2O); 4.91 (*ddd*, *J* = 12, 3, 1, H–C(6)); 5.90 (*ddd*, *J* = 12, 6, 1, H–C(4)); 6.30 (*dd*, *J* = 12, 3, H–C(5)); 6.40 (*d*, *J* = 6, H–C(3))].

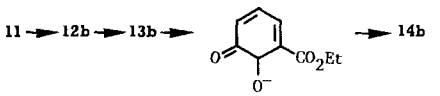


i ii

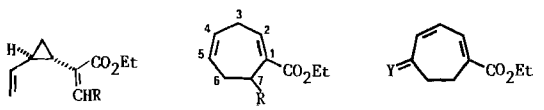


not be converted into the oxepinecarboxylate **12a**. However, pyrolysis of the acetate **10d** produced ethyl salicylate (**14a**; 29%), indicative of the transient presence of oxepine **12a**, its isomerization into the valence tautomer **13a**, and rearrangement of the latter. Treatment of ketone **11** with lithium diisopropylamide (LDA) yielded ethyl *o*-pyrocatechuate (**14b**; 74%), suggestive of the transformations depicted in *Scheme 2*.

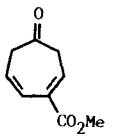
Scheme 2



The ready access to the seven-membered heterocyclic system by the interaction of ethyl diazopyruvate (**1**) with 1,3-butadiene (**2**) suggested that the same route may be applicable to a simple preparation of seven-membered carbocycles. Hence, keto-ester **5** was exposed to *Wittig* reactions, condensation with (methylidene)triphenylphosphorane yielding (73%) the acrylate **15a** [4] and with (benzylidene)triphenylphosphorane producing (76%) the cinnamate **15b**. Pyrolysis of the two α,β-unsaturated esters led to cycloheptadienecarboxylates **16a** (81%) and **16b** (92%), respectively [9]. As in the case of the dihydrooxepine, the diene **16a** underwent air (or O_2) oxidation, and the resultant hydroperoxide [8] was reduced with Me_2S, affording hydroxy-ester **17a** (46%) and the hydroperoxide-dehydration product, keto-ester **17b** (9%). *Jones* oxidation of **17a** gave **17b** in 80% yield.



Being a γ-substituted dihydrotropone, keto-ester **17b** seemed to be suited ideally for use in a synthesis of nezukone (**22**), a troponoid natural product whose seven-membered ring nucleus had not yet been constructed heretofore *via* a divinylcyclopropane-rearrangement route. However, a short reaction path was needed to overcome the necessity of ketone protection during side-chain modification, nucleus oxidation, and side-chain



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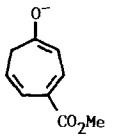

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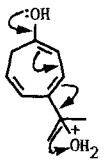

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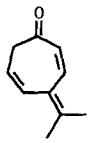

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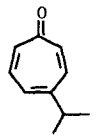

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reduction. The following two-step process, incorporating enolate formation as a mode of nuclear ketone masking, accomplished the task. Treatment of keto-ester **17b** with NaOMe/MeOH afforded keto-ester **18** (97%) [10]. Conversion of the latter into its enolate **19** with KH kept the keto group from being attacked by the next reagent, and interaction of the enolate ester with MeLi and subsequent protolysis (presumably *via* **20** and **21**) yielded nezukone (**22**; 68%)[4]) [12].

Conclusion. – The above observations reveal that the formation of dihydrooxepinecarboxylates in the metal-assisted interaction of diazopyruvates with 1,3-butadienes is the likely consequence of one of the two major primary products, *i.e.* the *cis*-1-acyl-2-vinylcyclopropane, undergoing rearrangement (*e.g.* **8b**→**9b**). Both major products of the reaction between ethyl diazopyruvate and 1,3-butadiene could be converted in few steps into compounds of general interest, dihydrooxepinecarboxylate **6** into salicylates **14**, and the acylcyclopropane **5** into the tropone nezukone (**22**).

Experimental Part

General. All reactions were performed under N_2 and the extracts of the crude reaction products dried over anh. $MgSO_4$. Column chromatography: on silica gel. M.p.: *Kofler* micro hotstage; uncorrected. UV spectra: MeOH solns.; λ in nm (log ε); *Perkin-Elmer-550* spectrophotometer. IR spectra: liquid films; in cm^{-1}; *Pye-Unicam-3-200* spectrophotometer. ^{1}H-NMR spectra: $CDCl_3$ solns.; δ in ppm, J in Hz, with Me_4Si as internal standard; *Varian-EM-390* spectrometer. ^{13}C-NMR spectra: $CDCl_3$ solns.; *Nicolet-QE-300* spectrometer, operating at 75.5 MHz in the *Fourier* transform mode; δ in ppm downfield from Me_4Si; $\delta(Me_4Si) = \delta(CDCl_3) + 76.9$ ppm.

*1-(*trans- *and* cis-*2'-Vinylcyclopropyl)heptanone* (**3** and **4**, resp.). The reaction of 1,3-butadiene (**2**) and 1-diazo-2-octanone was carried out as described for the reaction **1** + **2** (see below) and was followed by the same workup procedure: *ca.* 2:1 mixture **3**/**4** in 83% yield.

trans-Isomer **3**: Liquid. IR: 1691*s* (C=O); 1639*w* (C=C). ^{1}H-NMR: 0.90 (*t*, J = 7, CH_3); 0.98–1.05, 1.41–1.47, 1.58–1.66, 1.97–2.05 (4*m*, H–C(1'), H–C(2'), CH_2(3')); 1.28–1.38 (*m*, 4 CH_2); 2.53 (*t*, J = 7, CH_2(2)); 4.90–5.45 (12-line *ABX*, CH=CH_2). ^{13}C-NMR: 13.8 (C(7)); 17.2 (C(3')); 22.3 (C(6)); 23.8 (C(3)); 28.0 (C(2')); 28.7 (C(4)); 29.3 (C(1')); 31.4 (C(5)); 43.7 (C(2)); 114.3 (CH_2=); 138.3 (CH=); 208.9 (C(1)). Anal. calc. for $C_{12}H_{20}O$ (180.28): C 79.94, H 11.18; found: C 80.04, H 11.11.

cis-Isomer **4**: Liquid. IR: 1691*s* (C=O); 1635*w* (C=C). ^{1}H-NMR: 0.87 (*t*, J = 7, CH_3); 1.15–1.22, 1.40–1.43, 1.98–2.09, 2.25–2.32 (4*m*, H–C(1'), H–C(2'), CH_2(3')); 2.50 (*t*, J = 7, CH_2(2)); 4.98–5.75 (14-line *ABX*, CH=CH_2). ^{13}C-NMR: 13.9 (C(7)); 14.5 (C(3')); 22.4 (C(6)); 23.7 (C(3)); 27.3 (C(2')); 28.1 (C(1')); 28.7 (C(4)); 31.4 (C(5)); 44.6 (C(2)); 115.5 (CH_2=); 135.1 (CH=); 207.8 (C(1)). Anal. calc. for $C_{12}H_{20}O$ (180.28): C 79.94, H 11.18; found: C 79.74, H 11.35.

*Ethyl 2-Oxo-2-(*trans-*2'-vinylcyclopropyl)acetate* (**5**), *Ethyl 4,7-Dihydrooxepine-2-carboxylate* (**6**), *and Ethyl 4,5-Dihydro-5-vinylfuroate* (**7**). A soln. of ethyl 3-diazopyruvate (**1**) (5.00 g, 35.0 mmol) in dry CH_2Cl_2 (400 ml) was added dropwise within 8 h into a stirred suspension of $Rh_2(OAc)_4$ (20 mg) in dry CH_2Cl_2 (100 ml), in which an excess of liquid 1,3-butadiene (**2**; *i.e.* gaseous **2** liquefied in a dry-ice/acetone condenser) has been dissolved. More **2** was added periodically, and the reaction (at r.t.) was monitored by TLC (SiO_2; hexane/AcOEt 4:1) for the

[4]) A major study of this type of reaction as applicable to general organic synthesis is described in [11].

disappearance of **1**. The mixture was concentrated to a 10-ml volume and chromatographed on a silica-gel column with hexane/AcOEt 12:1 to give 2.06 g (35%) of colorless, liquid **5**. IR: 1735*s*, 1720*s* (C=O); 1637*m* (C=C). ^{1}H-NMR: 1.2–1.4, 1.6–1.7, 2.1–2.3, 2.7–2.9 (4*m*, H–C(1'), H–C(2'), CH_2(3')); 1.36 (*t*, *J* = 7, CH_3CH_2O); 4.23 (*q*, *J* = 7, CH_3CH_2O); 5.04, 5.08, 5.18, 5.24, 5.42, 5.45, 5.66, 5.70, 5.72 (9-line *ABX*, CH=CH_2). Anal. calc. for $C_9H_{12}O_3$ (168.19): C 64.27, H 7.19; found: C 63.98, H 7.30.

Further elution yielded 230 mg (4%) of colorless liquid **7**. IR: 1737*s* (C=O); 1632*m* (C=C). ^{1}H-NMR (CCl_4): 1.30 (*t*, *J* = 7, CH_3CH_2O); 2.3–3.1 (*m*, CH_2(4)); 4.17 (*q*, *J* = 7, CH_3CH_2O); 4.8–5.2 (*m*, H–C(5)); 5.05, 5.18, 5.33, 5.68, 5.79, 5.83, 5.90, 5.95, 6.01, 6.10 (10-line *ABX*, CH=CH_2); 5.70 (*s*, H–C(3)). Anal. calc. for $C_9H_{12}O_3$ (168.19): C 64.27, H 7.19; found: C 64.36, H 7.30.

More elution gave 1.50 g (26%) of colorless, liquid **6**. UV: 234 (1.69). IR: 1720*s* (C=O); 1650*s* (C=C). ^{1}H-NMR (CCl_4): 1.28 (*t*, *J* = 7, CH_3CH_2O); 3.00 (*dd*, *J* = 6, 3, CH_2(4)); 4.13 (*q*, *J* = 7, CH_3CH_2O); 4.4–4.6 (*m*, CH_2(7)); 5.7–5.9 (*m*, H–C(5), H–C(6)); 6.18 (*t*, *J* = 6, H–C(3)). Anal. calc. for $C_9H_{12}O_3$ (168.19): C 64.27, H 7.19; found: C 64.45, H 7.23.

A soln. of 200 mg (1.2 mmol) of **5** in 10 ml of benzene was irradiated in a quartz tube in a *Rayonet* photoreactor at 257 nm for 3 h. It was then evaporated and the residue chromatographed with hexane/AcOEt 9:1 to give 134 mg (67%) of **6**.

Ethyl 6,7-Dihydro-6-hydroxyoxepine-2-carboxylate (**10b**). A stream of dry O_2 was passed through liquid **6** (830 mg, 4.9 mmol) for 24 h and the material then chromatographed. Elution with hexane/AcOEt 9:1 led to the recovery of 581 mg (70%) of **6** and 247 mg (25%; 83%, based on consumed **6**) of hydroperoxide **10a**. IR: 3380*s* (br., OH); 1710*s* (C=O); 1650*m*, 1600*m* (C=C). ^{1}H-NMR: 1.32 (*t*, *J* = 7, CH_3CH_2O); 4.24 (*q*, *J* = 7, CH_3CH_2O); 4.38 (*t*, *J* = 4, CH_2(7)); 4.78 (*dt*, *J* = 4, 4, H–C(6)); 5.9–6.4 (*m*, H–C(3), H–C(4), H–C(5)). A mixture of **10a** and Me_2S (1 ml) in MeOH (20 ml) was stirred at r.t. for 45 min. The solvent and excess Me_2S were removed by vacuum distillation, and a hexane soln. of the residue was passed through a short *Florisil* column to give 216 mg (95%) of colorless, viscous **10b**. UV: 281 (3.75). IR: 3440*s* (br., OH); 1715*s* (C=O); 1640*m*, 1600*m* (C=C). ^{1}H-NMR (CCl_4): 1.33 (*t*, *J* = 7, CH_3CH_2O); 3.9–4.5 (*m*, H–C(6), CH_2(7)); 4.20 (*q*, *J* = 7, CH_3CH_2O); 5.78 (*ddd*, *J* = 12, 8, 2, H–C(4)); 6.1–6.3 (*m*, H–C(5)); 6.29 (*d*, *J* = 8, H–C(3)). HR-MS: 184.0743 ($C_9H_{12}O_4$, calc. 184.0735).

Ethyl 6-Chloro-6,7-dihydrooxepine-2-carboxylate (**10c**). Et_3N (208 mg, 2.0 mmol) and methanesulfonyl chloride (255 mg, 1.7 mmol) were added sequentially to a stirred soln. of **10b** (250 mg, 1.4 mmol) in dry CH_2Cl_2 (10 ml) at 0°. The stirring was continued at r.t. for 0.5 h and the mixture extracted with 1N HCl, 10% NaOH soln., and brine. It was then dried, concentrated, and passed through a pad of *Florisil*, leading to 221 mg (78%) of liquid **10c**. UV: 285 (4.10). IR: 1717*s* (C=O); 1638*w*, 1600*w* (C=C). ^{1}H-NMR: 1.32 (*t*, *J* = 7, CH_3CH_2O); 4.0–4.9 (*m*, H–C(6), CH_2(7)); 4.28 (*q*, *J* = 7, CH_3CH_2O); 5.8–6.3 (*m*, H–C(4), H–C(5)); 6.38 (*d*, *J* = 8, H–C(3)). HR-MS: 202.0386 ($C_9H_{11}ClO_3$, calc. 202.0397).

Ethyl 6-Acetoxy-6,7-dihydrooxepine-2-carboxylate (**10d**). Et_3N (2 ml), Ac_2O (0.8 ml), and 2 crystals of 4-(dimethylamino)pyridine were added to a stirred soln. of **10b** (216 mg, 1.2 mmol) in dry CH_2Cl_2 (5 ml) and stirring was continued for 45 min. The mixture was washed sequentially with 1N HCl, 10% KOH soln., and brine, dried, and evaporated. Passage of a hexane soln. of the residue through a *Florisil* pad and evaporation of the solvent yielded 229 mg (88%) of liquid **10d**. IR: 1735*s*, 1720*s* (C=O); 1640*w*, 1602*w* (C=C). ^{1}H-NMR: 1.32 (*t*, *J* = 7, CH_3CH_2O); 2.10 (*s*, CH_3CO); 4.1–4.4 (*m*, CH_2(7)); 4.25 (*q*, *J* = 7, CH_3CH_2O); 5.4–6.5 (*m*, H–C(3), H–C(4), H–C(5)). HR-MS: 226.0840 ($C_{11}H_{14}O_4$, calc. 226.0840).

Ethyl 6-Oxo-6,7-dihydrooxepine-2-carboxylate (**11**). A soln. of **10a** (200 mg, 1.0 mmol) and Ac_2O (2 ml) in dry pyridine (5 ml) was stirred at r.t. until all hydroperoxide had disappeared (iodometric analysis). Evaporation of the mixture and chromatography of the residue with hexane/AcOEt 9:1 led to 82 mg (45%) of viscous liquid **11**. IR (CCl_4): 1725*s*, 1671*s* (C=O); 1628*w* (C=C). ^{1}H-NMR: 1.33 (*t*, *J* = 7, CH_3CH_2O); 4.22 (*q*, *J* = 7, CH_3CH_2O); 4.46 (*s*, CH_2(7)); 6.3–6.9 (*m*, H–C(3), H–C(4), H–C(5)). HR-MS: 182.0579 ($C_9H_{10}O_4$, calc. 182.0579).

Alternatively, a soln. of 3 ml of *Jones* reagent [prepared from CrO_3 (70 g) in H_2O (100 ml) and conc. (18M) H_2SO_4 (112 mg, 61 ml) in H_2O (200 ml)] was added dropwise within 5 min to a stirred soln. of **10b** (304 mg, 1.65 mmol) in acetone (10 ml) at 0°. The mixture was then stirred at r.t. for 5 h, filtered through a *Celite* pad, and Et_2O was added to the filtrate. The soln. was washed with H_2O, 5% $NaHCO_3$ soln., and brine, dried, and evaporated. Chromatographic workup as above yielded 210 mg (70%) of liquid **11**.

Salicylates **14**. Pyrolysis of **10d** by distillation at 610° under vacuum (*ca.* 5 Torr) through a hot cylindrical tube into a dry-ice trap and extensive chromatographic purification of the pyrolysate produced *ethyl salicylate* (**14a**; 28%), identical in all respects with an authentic sample.

A soln. of **11** (38 mg, 0.2 mmol) in dry THF (5 ml) was added to a preformed LDA (1.0 mmol) soln. in dry THF (5 ml) at −78°. The mixture was stirred at −78° for 2 h and thereafter at r.t. for 7 h. It was then acidified with a few drops of conc. HCl and evaporated under vacuum. The residue was taken up in $CHCl_3$ and the mixture

filtered through a *Florisil* pad. Evaporation of the filtrate gave 28 mg (74%) of crystalline *ethyl o-pyrocatechuate* (= *ethyl 1,2-dihydroxybenzoate*; **14b**), m.p. 68–69°, identical in all respects with an authentic sample.

*Ethyl 2-(*trans-*2'-Vinylcyclopropyl)acrylate* (**15a**). Reaction of (methyl)triphenylphosphonium bromide (3.57 g, 10.0 mmol) with LDA and then with **5** under the conditions and workup of the **5**→**15b** transformation (see below) yielded 1.17 g (73%) of colorless, liquid **15a**. UV: 233 (sh, 3.76). IR: 1725*s* (C=O); 1638*s* (C=C). ^{1}H-NMR (CCl_4): 0.8–1.9 (*m*, H–C(1'), H–C(2'), CH_2(3')); 1.30 (*t*, *J* = 7, CH_3CH_2O); 4.20 (*q*, *J* = 7, CH_3CH_2O); 4.75, 4.78, 4.89, 4.92, 5.07, 5.10, 5.20, 5.23, 5.33, 5.36, 5.42, 5.52, 5.55, 5.64 (14-line *ABX*, $CH=CH_2$); 5.30 (*s*, H–C(3) *trans* to CO_2Et); 6.04 (*s*, H–C(3) *cis* to CO_2Et). Anal. calc. for $C_{10}H_{14}O_2$ (166.21): C 72.26, H 8.49; found: C 72.10, H 8.51.

*Ethyl α-(*trans-*2'-Vinylcyclopropyl)cinnamate* (**15b**). (Benzyl)triphenylphosphonium bromide (4.40 g, 10.0 mmol) was added to a dry THF soln. (150 ml) of 10.0 mmol of LDA (prepared by adding the requisite amount of a hexane soln. of BuLi to a soln. of 11.0 mmol of $(i\text{-Pr})_2$NH in dry THF at −78°) at −78°, and kept at −40° for 2 h. The soln. was allowed to reach r.t. and then stirred for another 2 h. A soln. of **5** (1.63 g, 9.7 mmol) in dry THF (10 ml) was added at 0°, the stirred mixture permitted to warm to r.t., and the stirring continued for 4 h. The mixture was acidified with 1N HCl and extracted with Et_2O. The extract was washed with H_2O and brine, dried, and evaporated. Chromatography of the residue with hexane/AcOEt 20:1 afforded 1.80 g (76%) of colorless liquid (*E*)/(*Z*)-**15b** (*ca.* 2:1). IR: 1710*s* (C=O); 1635*m* (C=C). ^{1}H-NMR: 0.7–1.8 (*m*, H–C(1'), H–C(2'), CH_2(3')); 4.8–5.7 (*m*, $CH=CH_2$); 7.1–7.6 (*m*, arom. H); (*E*)-**15b**: 1.08 (*t*, *J* = 7, CH_3CH_2O); 4.04 (*q*, *J* = 7, CH_3CH_2O); 6.45 (*s*, H–C(*β*)); (*Z*)-**15b**: 1.32 (*t*, *J* = 7, CH_3CH_2O); 4.19 (*q*, *J* = 7, CH_3CH_2O); 7.56 (*s*, H–C(*β*)). HR-MS: 242.1302 ($C_{16}H_{18}O_2$, calc. 242.1307).

Ethyl 1,4-Cycloheptadiene-1-carboxylate (**16a**). A pyrolysis of **15a** (1.17 g, 7.1 mmol) according to the conditions and workup of the **15b**→**16b** transformation (see below) led to 942 mg (81%) of colorless, liquid **16a**. UV: 223 (3.90). IR: 1710*s* (C=O); 1648*m* (C=C). ^{1}H-NMR: 1.24 (*t*, *J* = 7, CH_3CH_2O); 2.0–2.4, 2.5–2.7 (2*m*, CH_2(6), CH_2(7)); 2.95 (*t*, *J* = 5, CH_2(3)); 4.12 (*q*, *J* = 7, CH_3CH_2O); 5.3–5.8 (*m*, H–C(4), H–C(5)); 6.95 (*t*, *J* = 5, H–C(2)). HR-MS: 166.0991 ($C_{10}H_{14}O_2$, calc. 166.0994).

Ethyl 7-Phenyl-1,4-cycloheptadiene-1-carboxylate (**16b**). A soln. of **15b** (1.80 g, 7.4 mmol) in degassed CCl_4 (15 ml) was heated at 250° under a *ca.* 0.7-Torr vacuum for 10 h and then evaporated. Chromatography of the residue and elution with hexane/AcOEt 20:1 gave 1.65 g (92%) of colorless, liquid **16b**. IR: 1710*s* (C=O); 1640*w*, 1600*w* (C=C). ^{1}H-NMR (CCl_4): 1.15 (*t*, *J* = 7, CH_3CH_2O); 2.4–2.7 (*m*, CH_2(6)); 2.8–3.1 (*m*, CH_2(3)); 4.08 (*q*, *J* = 7, CH_3CH_2O); 4.20 (*t*, *J* = 5, H–C(7)); 5.4–5.7 (*m*, H–C(4), H–C(5)); 7.01 (*t*, *J* = 6, H–C(2)); 7.15 (*s*, arom. H). HR-MS: 242.1293 ($C_{16}H_{18}O_2$, calc. 242.1307).

Ethyl 5-Oxo-1,3-cycloheptadiene-1-carboxylate (**17b**). A soln. of **16a** (500 mg, 0.30 mmol) in CH_2Cl_2 (10 ml) was stirred under O_2 at r.t. for 96 h. MeOH (5 ml) and Me_2S (2 ml) were added, and the stirring was continued for 4 h. The soln. was evaporated and the residue chromatographed. Elution with hexane/AcOEt 5:1 led to the recovery of 125 mg (25%) of **16a** as well as to the isolation of 45 mg (9%) of **17b** (see below) and 250 mg (46%) of colorless, liquid *ethyl 5-hydroxy-1,3-cycloheptadiene-1-carboxylate* (**17a**). UV: 272 (4.14). IR: 3590*m*, 3460*m* (OH); 1680*s* (C=O); 1630*m*, 1605*m* (C=C). ^{1}H-NMR: 1.32 (*t*, *J* = 7, CH_3CH_2O); 1.7–3.0 (*m*, CH_2(6), CH_2(7)); 4.15 (*q*, *J* = 7, CH_3CH_2O); 4.2–4.5 (*m*, H–C(5)); 5.93 (*dd*, *J* = 12, 6, H–C(3)); 6.0–6.3 (*m*, H–C(4)); 7.02 (*d*, *J* = 6, H–C(2)).

Jones oxidation of **17a** (300 mg, 1.65 mmol) under the exact conditions and workup of the **10b**→**11** conversion (see above) afforded 237 mg (80%) of **17b**. UV: 296 (3.99). IR: 1710*s*, 1665*s* (C=O); 1630*m*, 1587*w* (C=C). ^{1}H-NMR: 1.32 (*t*, *J* = 7, CH_3CH_2O); 2.70 (*t*, *J* = 11, CH_2(7)); 2.73 (*t*, *J* = 11, CH_2(6)); 4.28 (*q*, *J* = 7, CH_3CH_2O); 6.25 (*d*, *J* = 13, H–C(4)); 6.72 (*dd*, *J* = 13, 7, H–C(3)); 7.15 (*d*, *J* = 7, H–C(2)). HR-MS: 180.0781 ($C_{10}H_{12}O_3$, calc. 180.0786).

Methyl 4-Oxo-1,6-cycloheptadiene-1-carboxylate (**18**). A soln. of **17b** (95 mg, 0.53 mmol) in abs. MeOH (5 ml) was added dropwise within 1 h to a stirred soln. of dry NaOMe (130 mg, 2.4 mmol) in abs. MeOH (5 ml) at 0°. The mixture was stirred at r.t. for 4 h, then neutralized with cold 10% HCl soln. and extracted with Et_2O. The extract was washed with H_2O and brine, dried, and evaporated, yielding 84 mg (97%) of liquid **18** (whose SiO_2 chromatography causes slow decomposition). UV: 321 (3.49). IR: 1722*s*, 1706*s* (C=O); 1630*m*, 1601*s* (C=C). ^{1}H-NMR: 3.19 (*d*, *J* = 7, CH_2(5)); 3.23 (*d*, *J* = 7, CH_2(3)); 3.82 (*s*, CH_3O); 6.05 (*dt*, *J* = 10, 7, H–C(6)); 6.75 (*d*, *J* = 10, H–C(7)); 7.05 (*t*, *J* = 7, H–C(2)). Anal. calc. for $C_9H_{10}O_3$ (166.17): C 65.20, H 6.03; found: C 65.05, H 6.07.

Nezukone (= *4-Isopropyl-2,4,6-cycloheptatrienone*; **22**). A soln. of **18** (35 mg, 0.21 mmol) in dry THF (2 ml) was added dropwise within 5 min to a stirred suspension of KH (20 mg, 0.49 mmol; rinsed first with dry THF and dried under vacuum) in dry THF (2 ml) at 0° and the mixture stirred at 5° for 15 min and then at r.t. for 2 h. A 0.83M MeLi (0.60 ml, 0.50 mmol) soln. in Et_2O was added slowly by syringe at −78° and the mixture stirred at −78° for 15 min. It was then allowed to warm to r.t., and AcOEt (0.5 ml) was added. The mixture was poured into 1 ml of 10% H_2SO_4 at 0°, neutralized with 1N NaOH, and extracted exhaustively with AcOEt. The extract was washed with

brine, dried, and evaporated. Chromatography of the residue on *Florisil* with hexane/AcOEt 10:1 led to 21 mg (68%) of liquid **22**. UV, IR, and ^{1}H-NMR: identical with the data in [12].

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