Tetrahedron Letters, Vol.28, No.28, pp 3209-3212, 1987
Printed in Great Britain

0040-4039/87 \$3.00 + .00
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An Attempted Synthesis of Tricyclo[8.$2^{1,10}$.$0^{1,7}$.$0^{4,10}$]-1(7),4(10)-dodecadiene

by

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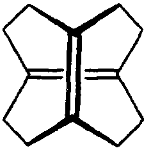
Abstract: Titanium-induced cyclization of diketone **4** yields diene **12**, presumably by Cope rearrangement of the desired tricyclo[8.$2^{1,10}$.$0^{1,7}$.$0^{4,10}$]-1(7),4(10)-dodecadiene (**1**). Molecular mechanics calculations support the belief that the rearrangement should be rapid.

Tricyclo[8.$2^{1,10}$.$0^{1,7}$.$0^{4,10}$]-1(7),4(10)-dodecadiene (**1**) has its double bonds disposed in a most unusual manner. Not only are the double bonds mutually perpendicular, they are also rigidly held in a proximity that should ensure a considerable degree of electronic interaction between them. Thus, molecular-mechanics calculations[1] on diene **1** indicate an expected distance between the two double bonds of 2.32 Å and an out-of-plane torsional deformation of 25.4° for each individual bond. Making the standard assumption that the internuclear stacking distance of 3.35 Å in graphite[2] represents the optimum spacing between p orbitals, it is clear that diene **1** should be strongly perturbed.



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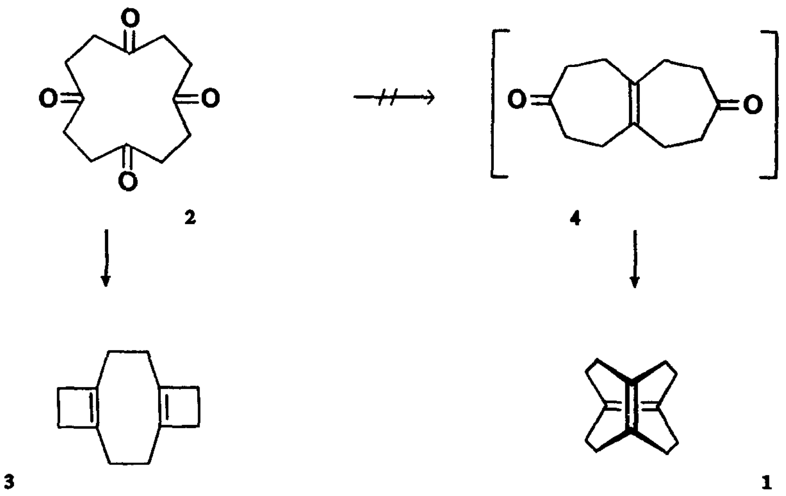
The most direct route for the synthesis of **1** would be a twofold titanium-induced cyclization[3] of the known[4] tetraketone **2**. If the first carbonyl coupling were to occur in a 1,7 sense to yield intermediate **4**, then a second coupling reaction might yield **1** in a single operation. Unfortunately, the desired reaction does not occur: Treatment of tetraketone **2** with $TiCl_3$/Zn-Cu according to our previously published conditions[3] gives only diene **3**,[5] the result of twofold 1,4-coupling.

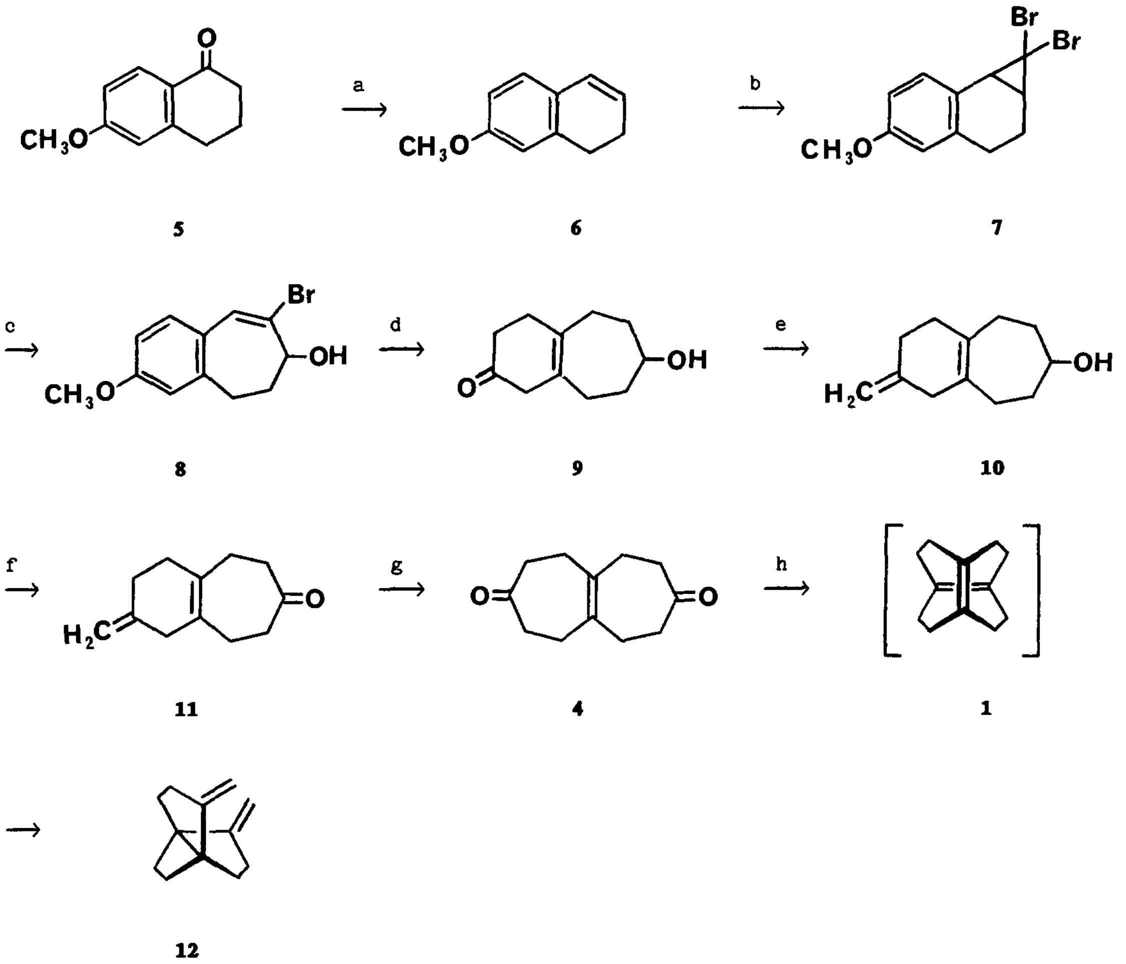


An alternative, though less direct, route for the preparation of diene **1** is by explicit synthesis and subsequent carbonyl coupling of diketone **4**. Though disarmingly simple in appearance, diketone **4** proved unusually difficult to prepare. Ultimately, however, we devised the route shown in Scheme I. Reduction and dehydration of 6-methoxytetralone (**5**), followed by dibromocarbene addition to the resultant olefin, gave dibromocyclopropane **7**, which underwent silver-ion assisted rearrangement[6] to yield **8**. Reduction of **8** with lithium in alcoholic liquid ammonia accomplished several transformations and resulted in formation of hydroxy enone **9** after hydrolysis of the initial reduction product with mild aqueous acid.

Although numerous attempts at diazomethane-induced ring expansion of enone **9** were unsuccessful, we were ultimately able to produce diketone **4** using the cyanogen azide method[7] we reported some years ago. Thus, conversion of **9** to diene **10** occurred smoothly and without rearrangement on treatment with the Tebbe reagent;[8] oxidation of **10** gave dienone **11**; and reaction of **11** with cyanogen azide followed by treatment with aqueous acid gave **4**. Surprisingly, none of the regioisomeric ring-expanded product was detected.

Slow addition of diketone **4** over a 48-hour period to a slurry of Ti(0) prepared by reduction of $TiCl_3$ with Zn-Cu in refluxing dimethoxyethane gave a crude mixture that was purified by kugelrohr distillation (100°, 1.5 mm) to provide a single hydrocarbon product in 50% yield. Unfortunately, the NMR spectra[9] of this hydrocarbon were unambiguously those of the known[10] Cope rearrangement product **12** rather than the desired diene **1**.

Careful NMR analysis of the reaction mixture prior to completion of the coupling showed only rearrangement product **12**. Thus, the Cope rearrangement must be an unusually easy one since **1** is not even transiently detectable. Indeed, molecular-mechanics calculations show why this should be.



Scheme I: Attempted Synthesis of Tricyclo[8.$2^{1,10}$.$0^{1,7}$.$0^{4,10}$]-1(7),4(10)-dodecadiene (1)
(a) $LiAlH_4$, then p-TsA, PhH, 98%; (b) $CHBr_3$, KOtBu, pentane, 80%; (c) $AgClO_4$, H_2O, acetone, 80%; (d) Li, NH_3, ethanol, then CH_3COOH, H_2O, 50%; (e) $(C_5H_5)_2Ti{=}CH_2$, 61%); (f) $(COCl)_2$, DMSO; (g) CNN_3, CH_3CN, then H_3O_+; (h) $TiCl_3$, Zn-Cu, dimethoxyethane, 48 hr. addition, 50%.

Molecular-mechanics calculations predict that Cope rearrangement product **12** should be some 22 kcal/mol more stable than diene **1** (ΔH_f = 67.64 kcal/mol for **1**; ΔH_f = 45.65 kcal/mol for **12**). This large thermodynamic driving force, in addition to a perfect orbital alignment for rearrangement, makes it unlikely that diene **1** will be isolable at normal temperatures.

Acknowledgement: This work was supported by the donors of the Petroleum Research Fund, administered by the American Chemical Society (Grant 15406-AC1).

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9. ^{1}H NMR ($CDCl_3$, 300 MHz) δ 4.77 (m, 2 H), 4.61 (br. s, 2 H), 2.98-2.86 (m, 2 H), 2.55-2.47 (m, 2 H), 1.99-1.88 (m, 4 H), 1.80-1.73 (m, 2 H), 1.58-1.44 (m, 2H).
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(Received in USA 7 April 1987)