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Generation of Four Five-Membered Rings in a One Pot Process. Studies Directed Toward the Synthesis of Dicyclopenta[a,d]pentalene via the Tandem Pauson-Khand Reaction

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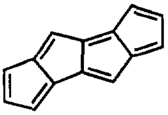
Abstract: *The synthesis of the four five-membered rings of a suitably functionalized parent system 15 of dicyclopenta[a,d]pentalene 2 has been accomplished via a tandem Pauson-Khand reaction in a one pot process.* Copyright © 1996 Elsevier Science Ltd

Recently interest in our laboratory has involved the synthesis of polyquinane natural products as well as some polyquinenes of computational interest.[1,2] Among the latter nonnatural products, the dicyclopentapentalenes **1** and **2** remain as attractive synthetic targets since these polyquinenes contain a system of 4n+2 π electrons with alternating single and double bonds. Controversy exists as to whether these 14π annulenes are delocalized, exhibit aromatic Hückel "type" stability or exist as alternant hydrocarbons that behave as highly reactive olefins.



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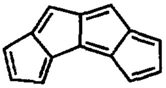
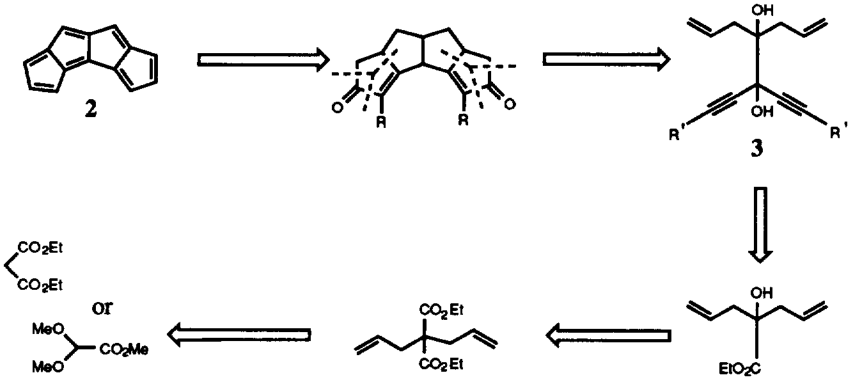


2

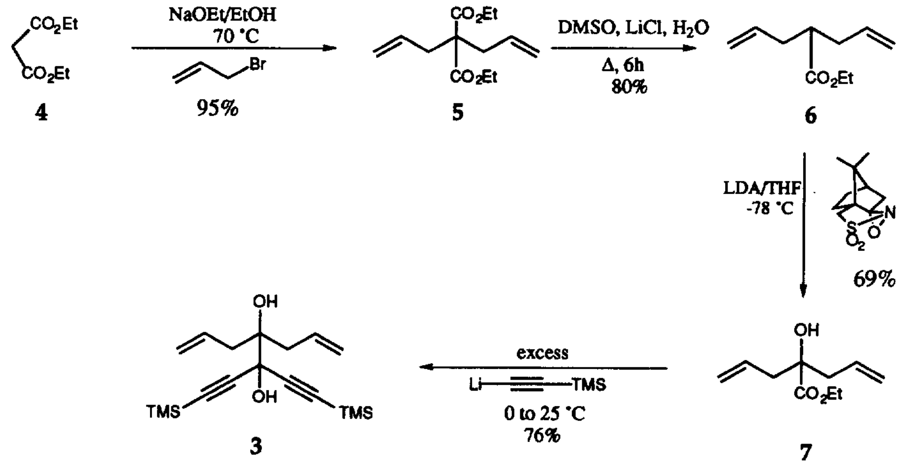
Nakajima and Toyota[3] reported theoretical calculations on these two annulenes stating if **1** and **2** exhibited aromatic character as postulated,[3] then the resonance energy for **1** would be 6.8 kcal/mol as compared to 1.2 kcal/mol for 14π annulene **2**. These results are in contrast to Hess and Schaad[4] who much earlier reported that both annulenes might be aromatic with heptaene **2** exhibiting more delocalization of π electrons than heptaene **1**. *Ab initio* calculations recently indicated that annulene **2** should be slightly more stable than **1** by 0.33 kcal/mol.[5] Since Hafner[6] has isolated and characterized the tetra-t-butyl analog of **1**, support for the existence of molecules such as annulene **2** has increased. For this reason the construction of systems related to **2** has been revisited in our laboratory. Described in the present paper is the most recent approach towards the rapid construction of the parent angular system related to **2** which employed a tandem Pauson-Khand reaction. Several years ago the preparation of the perhydroanalogs of **1** and **2** via the Weiss reaction were reported;[7] however, the appearance of four different olefinic isomers on dehydration prevented a practical route to either **1** or **2**. Consequently, a regiospecific approach to a functionalized dicyclopenta[a,d]pentalene related to **2** was developed. A retrosynthetic analysis of this approach is illustrated in Scheme 1. A key feature of this route would be the facile construction of an appropriately funtionalized acyclic system such as **3** which could be subjected to a tandem Pauson-Khand reaction to generate the tetracyclic framework in a one pot process. The functionalized unit **3** would carry the appropriate functionality for a later approach to annulene **2**. In the design of this sequence the inherent symmetry present in **2** was readily recognized, moreover the Pauson-Khand reaction was chosen for it has proven an effective means to generate fused five-membered rings.[8-11] The diol **3** was chosen as the precursor for the Pauson-Khand reaction and two complementary routes to this molecule **3** were developed.

Scheme 1



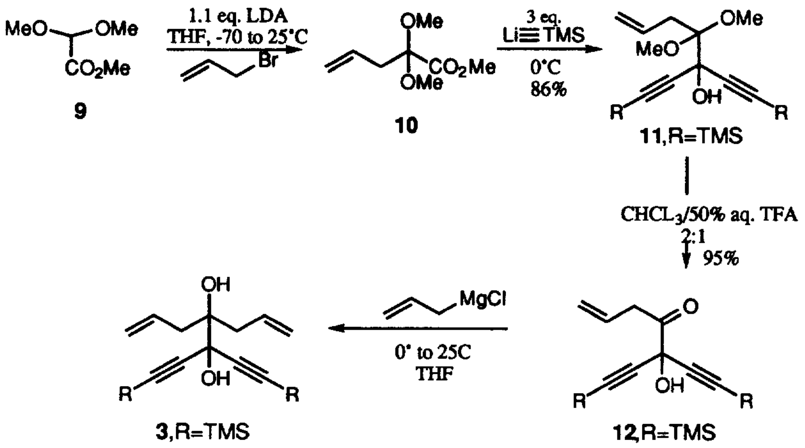
As illustrated in Scheme 2, the addition of the sodium salt of diethyl malonate **4**, generated *in situ* by treating diethyl malonate with sodium ethoxide in ethanol, to allyl bromide at 70°C resulted in the preparation of 2,2-diallyl diethyl malonate **5** in 95% yield. The diester **5** was then converted into the monoester **6** in good yield under the standard conditions of Krapcho.[12] When diester **5** was stirred in refluxing dimethyl sulfoxide in the presence of lithium chloride, monoester **6** was obtained. Ester **6** was treated with lithium diisopropyl amide, the anion of which was quenched with the Davis reagent, (+)(2R,8aS)-camphor sulfonyl oxaziridine,[13] to provide the alpha hydroxy ester **7**. This ester **7** was then stirred with four equivalents of lithium trimethylsilylacetylide to provide the desired diol **3** in 76% yield. The second route to diol **3** involved the use of methyl dimethoxyacetate, as shown in Scheme 3. Treatment of acetal **9** with lithium diisopropyl amide was followed by addition of allyl bromide to furnish the alkylated ketal **10**.[14] The ester **10** was then stirred with excess

Scheme 2



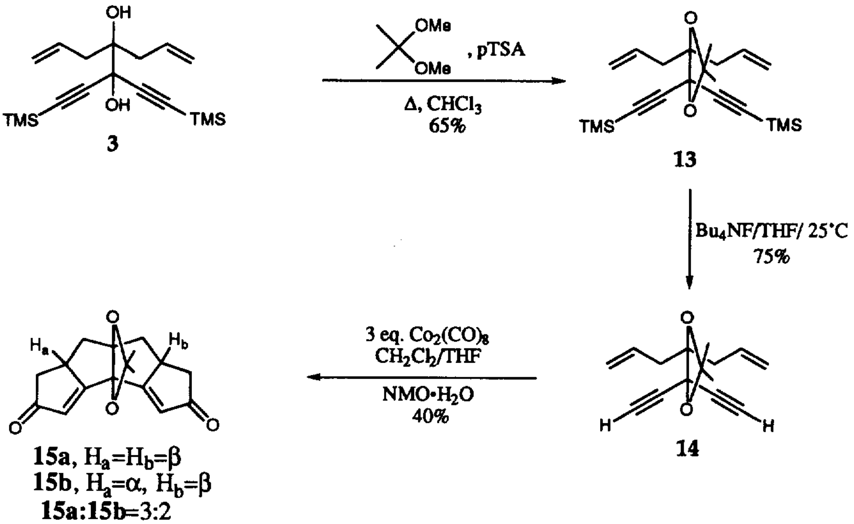
lithium trimethylsilylacetylide to provide the bisacetylinic ketal **11**. Ketal **11** was smoothly converted into the ketone **12** on stirring with aqueous trifluoracetic acid in chloroform. Allyl magnesium chloride [4eq., 2M] was then added to ketone **12** to provide diol **3** in good overall yield.

Scheme 3



With the key diol **3** in hand, this material **3** was treated with 2,2-dimethoxypropane in refluxing chloroform in the presence of pTSA[15] to constrain the diene-diyne in the eclipsed conformation to facilitate the formation of the tetracyclic skeleton. The silyl groups were then removed from acetonide **13** on exposure to tetrabutylammonium fluoride to give diene-diyne **14**.

Scheme 4



Recently Keese[16] has reported a tandem Pauson-Khand reaction to furnish a [5.5.5.5] fenestrane system under the modified conditions of Schreiber.[17] Under these conditions acetonide **14** was stirred with 3 equivalents of $Co_2(CO)_8$ in CH_2Cl_2/THF followed by addition of excess N-methyl morpholine N-oxide monohydrate to provide the tetracyclic system **15** in a one pot process. Both isomers **15a** and **15b** of the tetracyclic system should serve as functionalized precursors to an annulene such as **2**.

In summary, the diol **3** was converted (via acetonide **14**) into the tetracyclic polyquinane **15**[18] in a one pot process. The related system **13** did not undergo the Pauson-Khand reaction under similar conditions; however, attempts at this conversion have been minimal with **13** to date. The preparation of **15** provides, for the first time, a suitably functionalized dicyclopentapentalene for further assault on the target **2** and is readily available via the tandem Pauson-Khand process described here.

References and Notes:

1. Fu, X.; Cook, J.M. *Aldrichimica Acta.* **1992**, *25*, 42.
2. Gupta, A.K.; Fu, X.; Snyder, J.P.; Cook, J.M. *Tetrahedron* **1991**, *47*, 3665.
3. (a) Toyota, A.; Nakajima, T. *Tetrahedron* **1981**, *37*, 2572. (b) Nakajima, T.; Toyota, A.; Kataoka, M. *J. Am. Chem. Soc.* **1982**, *104*, 5610.
4. Hess, Jr., B. A.; Schaad, L.J. *J. Org. Chem.* **1971**, *36*, 3418.
5. Koehler, K.; Van Ornum, S.G.; Cook, J.M. unpublished results. Energies for **1** and **2** were calculated using Gaussian 94 (Rev B.2) at the 6-31G* basis set.
6. Stowasser, B.; Hafner, K. *Angew. Chem. Int. Ed. Engl.* **1986**, *25*, 466.
7. Lannoye, G.; Sambasivarao, K.; Wehrli, S.; Weiss, U.; Cook, J.M. *J. Org. Chem.* **1988**, *53*, 2327.
8. (a) Khand, I. U.; Knox, G. R.; Pauson, P.L.; Watts, W. E. *J. Chem. Soc., Chem. Commun.* **1971**, *36*. (b) Khand, I. U.; Knox, G. R.; Pauson, P.L.; Watts, W. E. *J. Chem. Soc., Perkin Trans.1* **1973**, 975.
9. Krafft, M. E.; Scott, I. L.; Romero, R. H.; Feibelmann, S.; Van Pelt, C. E. *J. Am. Chem. Soc.* **1993**, *115*, 7199
10. Schore, N. E. *Org. React.* John Wiley & Sons, Ed. Paquette, L. A. Academic Press, N.Y. **1991**, *40*, 1.
11. Gybin, A. S.; Smit, W. A.; Caple, R.; Veretenov, A. L.; Shashkov, A. S.; Vorontsova, L. G.; Kurella, M.G.; Chertkov, V. S.; Carapetyan, A. A.; Kosnikov, A. Y.; Alexanyan, M. S.; Lindeman, S. V.; Panov, V. N.; Maleev, A. V.; Struchkov, Y. T.; Sharpe, S. M. *J. Am. Chem. Soc.* **1992**, *114*, 5555.
12. Battersby, A.R.; Westwood, W. *J. Chem. Soc. Perkin. Trans. I* **1987**, 1679.
13. Davis, F. A.; Haque, M. S.; Ulatowski, T. G.; Towson, J. C. *J. Org. Chem.* **1986**, *51*, 2404.
14. Huet, F.; Pellet, M.; Conia, J.M. *Synthesis*, **1979**, 33.
15. Rosini, C.; Scamuzzi, S.; Focati, M. P.; Salvadori, P. *J. Org. Chem.* **1995**, *60*, 8289.
16. Thommen, M.; Veretenov, A. L.; Guidetti-Grept, R.; Keese, R. *Helv. Chem. Acta.* **1996**, *79*, 461.
17. Shambayati, S.; Crowe, W. E.; Schreiber, S. L. *Tetrahedron Lett.* **1990**, *31*, 5289.
18. **15a,** ^{13}C NMR (62.5 MHz, CDCl3): δ 208.41, 179.57, 128.54, 117.27, 106.93, 88.15, 46.03, 43.01, 42.92, 28.89 MS (CI): 287 (M+1, 100%), 271(42), 258(7), 243(7), 229(17).
    15b, ^{13}C NMR(62.5 MHz, CDCL3): δ 208.73, 208.17, 182.90, 181.48, 127.14, 126.65, 117.60, 104.13, 89.21, 44.14, 43.58, 42.96, 42.64, 42.39, 41.91, 28.62, 28.02 MS(CI) 287 (M+1, 100%), 271(70), 258(17), 243(15), 229(11), 211(7).

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