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FACILE SYNTHESES OF BICYCLO[4.2.2]DECA-2,4,7,9-TETRAENES

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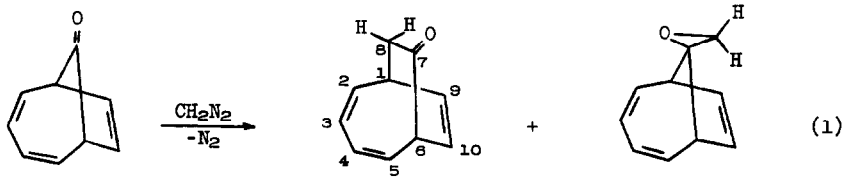
We should like to report two excellent synthetic methods for preparing bicyclo[4.2.2]-deca-2,4,7,9-tetraenes based on ring expansion of bicyclo[4.2.1]nona-2,4,7-trien-9-one[1] (1) to bicyclo[4.2.2]deca-2,4,9-trien-7-one (2) and subsequent transformations. Bicyclo[4.2.2]deca-2,4,7,9-tetraenes have been previously prepared by (1) isomerization of bullvalene,[2a-c] 9,10-dihydronaphthalenes,[2d-g] bicyclo[6.2.0]deca-2,4,6,9-tetraene,[2h] and their derivatives, (2) decomposition of 9-(diazomethyl)bicyclo[6.1.0]nona-2,4,6-triene,[2i] and (3) reaction of acetylenes with tricarbonylcyclooctatetraeneiron.[2j] Such tetraenes are of interest with respect to isomerization, addition reactions with electrophilic[2c,3] and with carbenic reagents, and conversion to higher homologous bicyclic polyenes.

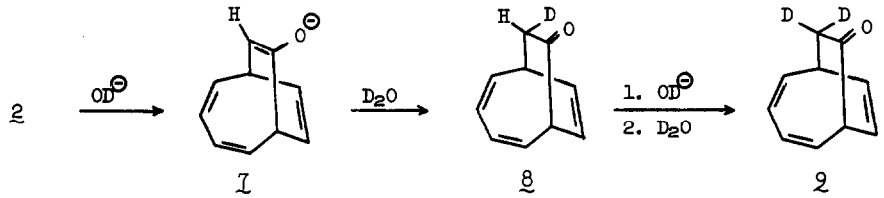
Bicyclo[4.2.1]nona-2,4,7-trien-9-one (1) is prepared readily by addition of dimethylcarbamoyl chloride to dilithium cyclooctatetraenide at 0° and hydrolysis of the reaction product.[1] Reaction of 1 with diazomethane (2.5 equiv) in methanol-chloroform-ether at 0° (2.5 hr) containing lithium chloride (Equation 1) yields 2[4] (63%) and spiro[bicyclo[4.2.1]nona-2,-4,7-trien-9,2'-oxirane] (3, 22%). Separation of 2 from 3 is effected with Girard's T reagent in aqueous ethanolic acetic acid and subsequent hydrolysis of the hydrazone derivative with hydrochloric acid. The structure of 2 is established from its analysis and spectral proper-



1 2 3 (1)

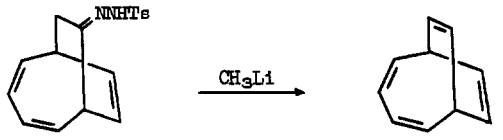
ties, by its hydrogenation to bicyclo[4.2.2]decan-7-one,[21] and by preparation of its oxime (4), 2,4-dinitrophenylhydrazone (5), and tosylhydrazone (6) derivatives. NMR analysis in chloroform-d did not reveal tautomerization in either ketone 2 or its derivatives 4, 5, and 6. Apparently the bicyclic delocalization in their possible bicyclo[4.2.2]deca-2,4,7,9-tetraenyl isomers is insufficient to cause extensive tautomerism of 2, 4, 5, and 6.

Ketone 2 undergoes base-catalyzed enolization to 7 readily. In carbon tetrachloride at 25°, monodeuteration of 2 by sodium deuteroxide in deuterium oxide (massive excess) occurs in ~ 12 hr to give 8-deuteriobicyclo[4.2.2]deca-2,4,9-trien-7-one (8). Under conditions identical for preparing 8 except that the sodium deuteroxide is more concentrated, dideuteration of 2 to 8,8-dideuteriobicyclo[4.2.2]deca-2,4,9-trien-7-one (9) occurs relatively slowly (~ 215 hr). The difference in rates of mono and dideuteration of 2 is such that 8 and 9 were preparable; the structures and deuterium contents of 8 and 9 were determined by nmr and mass spectral methods. It is likely, because of steric factors, that proton removal from 2 and deuterium incorporation into its enolate 7 (Equation 2) occur selectively syn rather than anti to the C_9-C_{10} bridge to give 8 of indicated stereochemistry. Dideuterio ketone 9 is synthetically useful in preparing deuterium labeled bicyclo[4.2.2]deca-2,4,7,9-tetraenes by adaptation of the methods subsequently described.



7 8 9 (2)

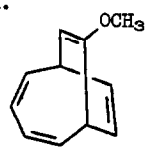
Tosylhydrazone 6 is of value in that it is converted efficiently (Equation 3) by methyllithium (4 equiv)[5] in hexane at 25° (3 hr) to bicyclo[4.2.2]deca-2,4,7,9-tetraene[6a] (10, > 81%); minor products are cis-9,10-dihydronaphthalene[6a] (1%) and naphthalene. Analogously the tosylhydrazone (11) of 8-methylbicyclo[4.2.2]deca-2,4,9-trien-7-one, as prepared from 1 and



6 10 (3)

diazoethane, is converted by methyllithium to 7-methylbicyclo[4.2.2]deca-2,4,7,9-tetraene (12).[6b] This method represents a more advantageous overall route to 10 and 12 than other preparations previously reported as well as that yet found for elimination of bicyclo[4.2.2]-deca-2,4,9-trien-7-ol[7] and 7-methylbicyclo[4.2.2]deca-2,4,9-trien-7-ol[7] and their derivatives by a variety of methods.

Base-catalyzed O-alkylation, silylation, and acylation of 2 result in facile syntheses of 7-substituted bicyclo[4.2.2]deca-2,4,7,9-tetraenes. Thus addition of potassium t-butoxide (3 equiv; reaction time, 4 min) and then methyl fluorosulfonate[8] (3 equiv; reaction time, 3 min) to 2 in hexamethylphosphoramide at 5°, rapid aqueous extraction of the product, and distillation yields 7-methoxybicyclo[4.2.2]deca-2,4,7,9-tetraene (13, 93-95%). In less polar environments methylation of enolate 7 is less efficient and also results in significant C-alkylation. In glyme containing potassium t-butoxide (1.25-3 equiv) at 25°, 2 reacts with excess methyl fluorosulfonate to give 13 in only 29-42% conversion; exo-8-methylbicyclo[4.2.2]deca-2,4,9-trien-7-one (14, 3- < 1%) and 8,8-dimethylbicyclo[4.2.2]deca-2,4,9-trien-7-one (15, 0-30%) are also produced.



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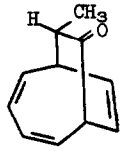

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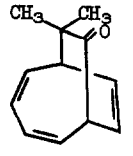

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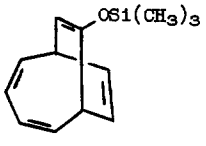

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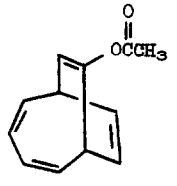

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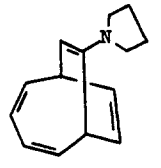

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O-Silylation and O-acylation of enolate 7 also occur efficiently. In glyme at 25° 2 reacts with potassium t-butoxide (3 equiv; 3 min) and then trimethylsilyl chloride (4 equiv; 5 min) to give, after vacuum distillation, 7-trimethylsiloxybicyclo[4.2.2]deca-2,4,7,9-tetraene (16, 61%). Similarly addition of acetyl chloride (excess) to 2 and potassium t-butoxide (3 equiv) in glyme at 20° yields 7-acetoxybicyclo[4.2.2]deca-2,4,7,9-tetraene (17, 83%). Although quite unstable to acids, 2 is converted however via its enol by p-toluenesulfonic acid

and refluxing excess isopropenyl acetate to 17 (86%). Further, 2 reacts with pyrrolidine (2 equiv) in refluxing benzene containing p-toluenesulfonic acid (catalytic amount) to produce 7-pyrrolidinobicyclo[4.2.2]deca-2,4,7,9-tetraene (18, > 90%). Tetraenes 13, 16, 17, and 18 are hydrolytically sensitive, particularly in acidic environments, giving 2 essentially quantitatively. The structures of 13, 16, and 18 were assigned on the basis of their exact masses and by their nmr and ir spectra. At glc temperatures up to 200°, 13, 16, 17, and 18 do not undergo thermally allowed isomerization to 3-substituted bicyclo[4.2.2]deca-2,4,7,9-tetraenes.[2f,9]

The methods presently described allow rapid synthesis of substituted bicyclo[4.2.2]deca-2,4,7,9-tetraenes in preparative quantities. Various electrophilic, carbenic, and ring-expansion reactions of these tetraenes are being studied in these laboratories.

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3. H. Loeffler and G. Schroeder, Tetrahedron Lett., 2119 (1970).

4. All new compounds reported gave satisfactory analyses except where indicated; the nmr and ir spectra of all compounds described are consistent with their assigned structures.

5. R. Shapiro and M. Heath, J. Amer. Chem. Soc., 89, 5734 (1967).

6. (a) Identical with authentic samples obtained from Dr. M. J. Broadhurst of these laboratories. (b) Private communication from M. J. Broadhurst.

7. Prepared by reactions of 2 with sodium borohydride and with methyl Grignard reagents.

8. Purchased from Aldrich Chemical Co. Inc., Milwaukee, Wis.

9. Fluxional isomerism of this type has also been described by W. von Philipsborn, J. Altman, E. Babad, J. J. Bloomfield, D. Ginsburg, and M. B. Rubin, Helv. Chim. Acta, 53, 725 (1970).