yield obtained. Infrared showed NH, 3110–3220, N=O (asym), 1568 (sh), 1581, C=O, none.

Registry No.—1,1-Bis(formamido)-2,2,2-trifluoroethane, 26958-24-7; 1,1-bis(acetamido)-2,2,2-trifluoroethane, 27039-91-4; 1,1-bis(*N*-nitroformamido)-2,2,2-trifluoroethane, 26958-25-8; 1,1-dinitramino-2,2,2-trifluoroethane, 26958-26-9; 1,1-bis(formamido)ethane, 20602-52-2; 1,1-bis(*N*-nitroformamido)ethane, 26958-28-1; 1,1-dinitraminoethane, 26958-29-2.

Reactions of Dodecabromopentacyclo[5.3.0.0^{2,6}.0^{3,9}.0^{4,8}]decane with Sodium Methoxide

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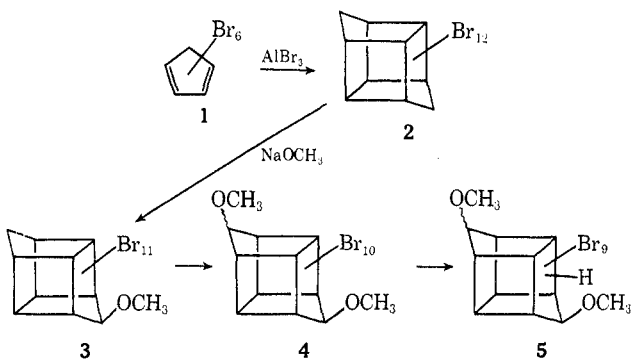
Hexabromocyclopentadiene (**1**) is dimerized by aluminum tribromide in refluxing bromine to give dodecabromopentacyclo[5.3.0.0^{2,6}.0^{3,9}.0^{4,8}]decane (**2**).[2] Examination of molecular models leads to the prediction that **2** would be very inert toward nucleophilic attack. The compound has a small cluster of carbon atoms at its center and a large protective outer armor of bromine atoms. Back-side attack at any carbon atom of **2** appears to be impossible. Nevertheless, bromocarbon **2** reacts with sodium methoxide in tetrahydrofuran to give a series of cage compounds.

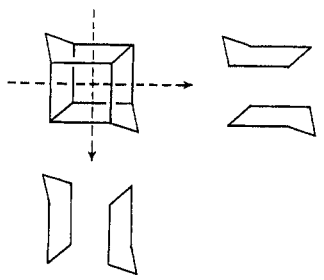
Kinetic control by slow addition of sodium methoxide and patient tlc analysis revealed initial formation of a monomethoxy derivative **3**, which was converted to a dimethoxy derivative **4**. Most of the starting material **2** and compound **3** disappeared before a third product **5** appeared along with several open cage products which had double bond adsorption in their infrared spectra. Compound **4** was prepared in 70–80% yield by following the reaction by tlc and quenching at a maximum concentration of **4**.



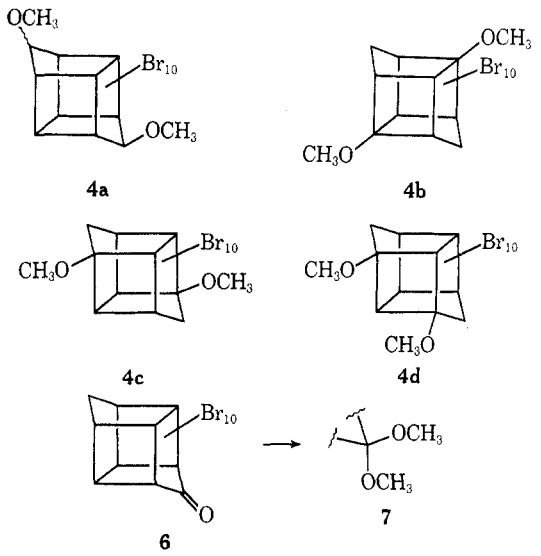
The structures of **3**, **4**, and **5** are assigned on the basis of their nmr, mass spectra, and relative reaction rates.

Nmr spectra of mixtures of **3** and **4** exhibit two poorly resolved lines at δ 3.97 in DMSO-d_6 with a separation of 0.009 ppm. Thus the environment of the single methyl of **3** is very similar to the environment of the two methyls of **4**. Although **5** appears pure by mass spectral analysis, its nmr can only be explained as a mixture. No attempt has been made for an assignment of various isomer ratios of **5** to the nmr spectrum, since the structure is tentative.

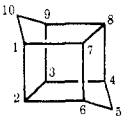
The normal fragmentation pattern observed in mass spectra of bishomocubane compounds is cleavage to two five-carbon rings by the two routes illustrated below.[3]



The most intense ion in the mass spectrum of **4** is *m/e* 407 from $C_5Br_4OCH_3^+$. An important feature is the lack of any C_5 fragments from **4** with two OCH_3 groups. Thus the methoxy groups must not be placed on the same five-carbon ring. Compounds **4a–d** satisfy the mass spectrum and the symmetry requirement necessary to give a single line nmr. An alternate structure is the dimethyl ketal **7**, which is readily prepared from ketone **6**, but **7** has ir, nmr, and mass spectra which are quite different from the spectra of **4**.



The structure of **3** is based primarily on its conversion to **4** and on its mass spectrum. Structure **4a** is assigned to **4** on the basis of the reaction rate data. A monomethoxy derivative is formed which reacts with methoxide at about the same rate as bromocarbon **2**. Further reaction with methoxide is slower than formation of the first two products. If reaction occurs first at C-10 the activity at C-5 would not be altered, and the product would readily react at C-5 to form **4**. After forma-



(1) To whom inquiries should be addressed: Textile Department, Clemson University, Clemson, S. C. 29631.

(2) C. W. Roberts and M. B. Chenoweth, U. S. Patent 3,212,973 (1965).

(3) W. L. Dilling and M. L. Dilling, *Tetrahedron*, **23**, 1225 (1967).

tion of **4** all of the remaining carbons are quite different from C-5 and C-10. A difference in rate would be expected and is observed.

If reaction occurs first at C-1, the second OCH_3 might become attached to C-6, C-9, or C-4. If C-1 and C-4 are substituted, further reaction at C-6 or C-9 would be expected to give trimethoxy products just as fast as dimethoxy products are formed. This is not observed. Similar arguments can be developed against initial attack at any carbon other than C-5 or C-10.

Compound **4** is most likely a mixture of cis and trans isomers. Separation of the two isomers by the isolation methods used and nmr resolution of the different methyls is unlikely. Conformation of the structures of **3** and **4** requires cleavage of the ethers to form ketones. If the methoxyls are on the bridgehead carbons, alcohols will be formed. At this time a satisfactory cleavage procedure has not been found.

Compound **5** exhibits mass spectral peaks at *m/e* 407 and 329 from fragments $C_5Br_4OCH_3$ and $C_5HBr_3OCH_3$. If the third reaction step had been introduction of a third OCH_3, a peak at *m/e* 359 from $C_5Br_3(OCH_3)_2$ would be expected, but it is not present in the mass spectrum. The hydrogen atom is presumably introduced during aqueous work-up of the reaction. Attempts to separate the isomers of **5** by tlc and recrystallization were unsuccessful.

The mechanism of the displacement reaction is speculative at this point. As discussed previously, backside attack on the bridgehead carbons is impossible and similar attack on the bridge carbons appears to be hindered by the bromine atoms. Formation of a carbonium ion at the bridgehead carbons is unlikely since they cannot become planar, and formation of carbonium ions at bridge carbons has not been observed with perhalogenated bishomocubyl compounds except under extreme conditions.[4] If the reaction occurs through a carbonium ion at C-5, dimethyl ketal **7** would be expected to form faster than **4**. Ketal **7** is not a major product.[5]

Experimental Section

Infrared spectra were obtained with Beckman IR-9 and Perkin-Elmer 137 spectrometers. The mass spectra were obtained on a CEC-21-110B (Direct Probe) instrument. Nuclear magnetic resonance spectra were obtained on Varian A60 and HA100 spectrometers. Thin layer chromatography (tlc) plates were prepared from silica gel G containing 0.04% of Rhodamine 6G.

Hexabromocyclopentadiene (**1**) was prepared by the method of Straus[7] or by a modification of West's[8] procedure. Recrystallization from hexane or methanol yielded a product melting at 86.5–88°.

Dodecabromopentacyclo[5.3.0.0^{2,6}.0^{3,9}.0^{4,8}]decane (**2**).—The procedure previously described[2] was modified as follows. Hexabromocyclopentadiene (473 g, 0.88 mol), 2500 g (800 ml) of anhydrous bromine, and 105 g (0.39 mol) of aluminum bromide were mixed at 25° and heated at reflux under anhydrous conditions for 72 hr. After decomposing the aluminum bromide with water, the bromine was steam distilled off. The granular residue was collected and washed with water and hexane to give 454 g (96%), mp 330–340° dec. Recrystallization with charcoal decolorization from ethylene dibromide, toluene, or *m*-xylene gave 440 g (93%) of **2**, mp 340° dec, mass spectrum P^+ at *m/e* 1068 (Br^{79}).

5,10-Dimethoxydecabromopentacyclo[5.3.0.0^{2,6}.0^{3,9}.0^{4,8}]decane (**4**).—Bromocarbon **2** (19.7 g, 0.018 mol) was dissolved in 300 ml of tetrahydrofuran, and sodium methoxide (3 g, 0.055 mol) was added. The mixture was stirred at room temperature under nitrogen and followed by periodic tlc analysis of the liquid phase. An additional 3 g of sodium methoxide was added after 17 hr. After 89 hr ice was added slowly until the base dissolved. Water was added dropwise with stirring at a rate which gave a granular precipitate. The product was collected by suction filtration, washed with water, and dried under vacuum at 65° (20 mm) to yield 15.7 g of **4** (84% crude) as an off-white solid. Tlc analysis indicated a purity of 95% or better. Recrystallization from boiling toluene gave 12.5 g of white crystals which slowly decomposed above 280° without melting: ir OCH_3 at 2958, 2852, 1446, and 1263 cm^{-1}, no double bond absorption; nmr (DMSO-d_6) single line δ 4.00; nmr (benzene-d_6) single line δ 3.74; mass spectrum P^+ at *m/e* 972 with ten bromine atoms, most intense peak at *m/e* 407 from $C_5Br_4OCH_3^+$, no peaks from C_5 fragments bearing two methoxy groups were observed.

Anal. Calcd for $C_{12}H_6Br_{10}O_2$: mol wt, 981.3; C, 14.69; H, 0.62; Br, 81.44. Found: C, 15.0; H, 0.63; Br, 81.3.

5-Methoxyundecabromopentacyclo[5.3.0.0^{2,6}.0^{3,9}.0^{4,8}]decane (**3**).—Following the procedure above, the reaction was stopped when a small amount of starting material **2** and a moderate amount of **3** were present. A sample of **3** was collected by tlc for a mass spectrum: P^+ at *m/e* 1020 with 11 bromine atoms (weak); $P^+ - Br$ at *m/e* 941 with ten bromines is strong (insufficient material was collected for an infrared spectrum). An nmr spectrum of the product mixture from a similar run with only **2**, **3**, and **4** present had two poorly resolved lines at δ 3.97 in DMSO-d_6 with a separation of 0.009 ppm and a ratio of 1.4:1. The ir spectrum of this mixture did not have double bond adsorption.

Dimethoxynonabromopentacyclo[5.3.0.0^{2,6}.0^{3,9}.0^{4,8}]decane (**5**).—Following the procedure above the reaction was stopped when **2**, **3**, and **4** had disappeared. The crude product was eluted from a silica gel column with hexane–benzene. The first fraction gave only one spot on tlc. Recrystallization from hexane–chloroform gave white crystals which decomposed without melting above 260°: nmr ($CDCl_3$) major δ 3.83 and 4.01, minor δ 3.9, 4.0, and 4.5, ratios uncertain from overlap of signals; ir (KBr) OCH_3 at 2960, 2860, 1449, and 1280 cm^{-1}, no double bond absorption; mass spectrum P^+ at *m/e* 894 (weak), $P^+ - Br$ at 815 (strong), fragments at 407 and 392.

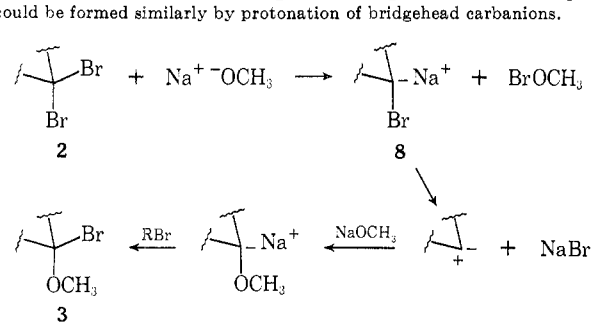
Anal. Calcd for $C_{12}H_7Br_9O_2$: mol wt, 902.3; Br, 79.70. Found: Br, 79.4.

5,5-Dimethoxydecabromopentacyclo[5.3.0.0^{2,6}.0^{3,9}.0^{4,8}]decane (**7**) was prepared from the methyl hemiketal[9] of ketone **6** in 70–90% yields by reaction with diazomethane in ether[4] or by reaction with powdered sodium hydroxide and dimethyl sulfate in ether. Recrystallization from hexane–chloroform gave white crystals which decomposed above 260° without melting: ir (OCH_3) at 2949, 2841, 1459, 1443, 1435, and 1229 cm^{-1}; nmr ($CDCl_3$) one line at δ 3.64.

Anal. Calcd for $C_{12}H_6Br_{10}O_2$: mol wt, 981.3; C, 14.69; H, 0.62; Br, 81.44. Found: C, 14.7; H, 0.53; Br, 81.2.

(4) G. W. Griffin and A. K. Price, *J. Org. Chem.*, **29**, 3192 (1964); W. L. Dilling, Ph.D. Thesis, Purdue University, 1962.

(5) A possible reaction of bromocarbon **2** is displacement on bromine to form a carbanion **8**. Dr. K. Scherer (personal communication) has proposed the following mechanism to account for the formation of **3** and **4**. This mechanism is consistent with the observed rate data and the expected carbanion stabilities based on analogous chlorocage carbanions.[6] Compound **5** could be formed similarly by protonation of bridgehead carbanions.



(6) G. A. Ungefug, Ph.D. Thesis, University of California, Berkeley, Calif., 1968.

(7) F. Straus, L. Kollek, and W. Heyn, *Ber.*, **63b**, 1868 (1930).

(8) P. T. Kwitowski and R. West, *J. Amer. Chem. Soc.*, **88**, 4541 (1966); **90**, 4697 (1968).

(9) R. G. Pews and C. W. Roberts, *J. Org. Chem.*, **34**, 2029 (1969).

CAUTION: Prolonged skin contact with ketone **6** and its derivatives may be fatal.

Registry No.—**2**, 5144-46-7; **3**, 26932-22-9; **4**, 26932-23-0; **5**, 26913-18-8; **7**, 26932-24-1.

Acknowledgments—The authors are grateful to L. Shadoff for the mass spectral data, to R. Nyquist for the infrared spectra, to J. Heeschen and T. Evans for the nmr data, and to L. Swim and P. North for the elemental analyses.

Synthesis and Certain Reactions of 1-Aryl-4-(2-quinolyl)-1,3-butanediones, a New Class of β-Diketones[1]

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In connection with the synthesis of potential new antimalarial agents, a series of 1-aryl-4-(2-quinolyl)-1,3-butanediones (**4**) were required as key intermediates. In spite of their seemingly simple array of functionality, β-diketones of type **4** have not been reported. Moreover, their preparation *via* standard Claisen condensations of a 2-quinolineacetic acid ester with substituted acetophenones appeared to hold little promise of success, owing to the probability that the basic reagents commonly employed in such reactions would preferentially abstract one of the highly acidic methylene hydrogens of the ester.

We now wish to describe a general method for the preparation of this new class of β-diketones as exemplified by the synthesis of five such compounds from readily available starting materials (see Scheme I). The present sequence involved metalation of quinaldine (**1**) with *n*-butyllithium in tetrahydrofuran–hexane at room temperature to afford lithio derivative **2**, which was then acylated with ethyl acetate to give 2-acetonylquinoline (**3**).[3] Completion of the β-dicarbonyl side chain was then accomplished by selective aroylation at the methyl position of **3** using the appropriate aromatic ester and excess sodium hydride in refluxing 1,2-dimethoxyethane as the condensing agent (see Table I). The rather unusual tendency for ketone **3** to undergo preferential aroylation at the less acidic methyl site may be due to the fact that the azomethine function imparts

SCHEME I

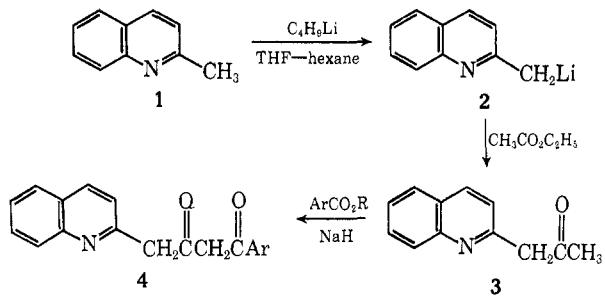


TABLE I[a]

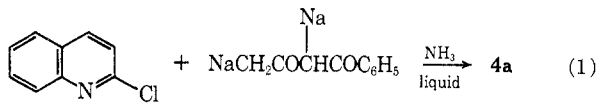
AROYLATIONS OF 2-ACETONYLQUINOLINE (**3**) TO PRODUCE β-DIKETONES **4**

β-Diketone Ar	No.	Reaction period, hr	Yield, %	Mp, °C
C_6H_5	**4a**	24	56	138–139.5[b]
C_6H_4Cl-*p*	**4b**	12	62	158–160[c]
3,4-$C_6H_3(Cl)_2$	**4c**	4	64	186–188[c]
p-$C_6H_4OCH_3$	**4d**	22	45	145–147[c]
3,4,5-$C_6H_2(OCH_3)_3$	**4e**	24	30	158–160[c]

[a] Satisfactory analytical data (±0.3 for C, H, N, and when present Cl) were found for all compounds: Ed. [b] Recrystallized from methanol. [c] Recrystallized from 95% ethanol.

to **3** chemical characteristics similar to those of a β-diketone. Consequently, these condensations may then proceed by one of the possible mechanistic pathways recently proposed to account for the conversion of β-diketones to 1,3,5-triketones under similar reaction conditions.[4] Incidentally, alkali amides, which have also been used to effect terminal aroylations of β-diketones,[5] were found to be much less satisfactory than sodium hydride for the conversion of **3** to **4a**.

Structural assignments for new β-diketones **4a–e** were confirmed by analyses (Table I), spectral data, and, in the case of **4a**, independent synthesis from 2-chloroquinoline and disodiobenzoylacetone (eq 1).[6] The nmr



(1)

spectra of **4a–e** (Table II), which had multiple peaks in the vinyl proton region, were consistent with the presence of several enolic forms for each of these compounds in solution. Comparison of the integrated intensity of the methylene proton absorption to that of the aromatic resonance in the spectrum of **4a** indicated the total enol content of this ketone to be approximately 75% in $CDCl_3$.

In order to test the feasibility of utilizing the β-dicarbonyl function of the above ketones for the construction of a second heterocyclic moiety, we examined the cyclization of several of these compounds with hydrazine and urea. Treatment of β-diketones **4a–c** and **4e** with the

* To whom correspondence should be addressed.

(1) (a) This is Contribution No. 807 from the Army Research Program on Malaria and was supported by Contract No. DA-49-193-MD-3024 from the U. S. Army Research and Development Command. (b) Presented before the Medicinal Chemistry Division of the American Chemical Society, New York, N. Y., Sept 1969.

(2) Abstracted from the Ph.D. Dissertation of T. P. M., Virginia Polytechnic Institute, Oct 1969.

(3) This procedure utilizing commercial *n*-butyllithium and ethyl acetate for the synthesis of **3** was found to be much more satisfactory than the method of M. J. Weiss and C. R. Hauser [*J. Amer. Chem. Soc.*, **71**, 2023 (1949)], in which alkali amides and acetic anhydride are employed as the metalating and acylating agents, respectively. It also gives a comparable yield and is less tedious than the procedure of N. N. Goldberg and R. Levine [*ibid.*, **74**, 5217 (1952)], which involves the preparation of phenyllithium as the metalating agent.

(4) See M. L. Miles, T. M. Harris, and C. R. Hauser, *J. Org. Chem.*, **30**, 1007 (1965).

(5) R. J. Light and C. R. Hauser, *ibid.*, **25**, 538 (1960).

(6) The possibility of utilizing 1,3-dialkali salts of other β-diketones in a one-step route to quinolyl β-diketones of type **4** did not pass unnoticed. However, numerous unsuccessful attempts to increase the low yield of **4a** obtained in the above reaction forced us to abandon this approach.