abstraction from one of the *N*-methyl groups rather than C-6. The result is formation of **1b** with preservation of the C-6 stereochemistry.

(16) (a) W. C. Wildman and D. T. Bailey, *J. Org. Chem.*, **33**, 3749 (1968); (b) G. A. Brine, Ph.D. Dissertation, Duke University, 1974.

(17) The *m*-chloroperbenzoic acid used was a technical grade containing 85% of the oxidant (Aldrich Chemical Co.).

(18) Use of fresh catalyst substantially reduced the amount required and the reaction time.

(19) Since the hydrochloride salt crystallizes as a hydrate, omission of the H_2O substantially reduces the quantity obtained.

(20) The reference sample was supplied by Regis Chemical Co., Morton Grove, Ill.

Synthesis and Reactivity Patterns of *meso*- and *dl*-Bistriquinacene. Efficient Route to the Diastereomeric Bivalvanes

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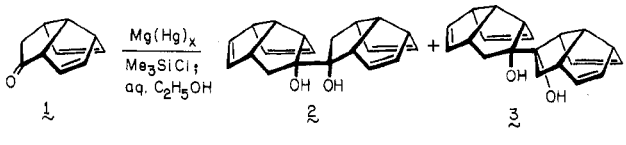
Pinacolic reduction of *dl*-2,3-dihydrotriquinacen-2-one and its tetrahydro derivative gives rise to an equal mixture of *dl* and meso diols. In order to effect the rapid, efficient, yet nondestructive separation of the two pairs of "dimers", the individual mixtures were dehydrated directly with (preferably) phosphorus oxychloride in pyridine and treated with 0.5 molar equiv of *N*-methyltriazolinedione at low temperature. Under these conditions, only the meso isomers enter into Diels–Alder reaction since the s-cis conformation of their conjugated diene moieties makes possible simultaneous exo bonding of the dienophile to both termini. In contrast, concerted $_{\pi}4_s$ bonding to a *dl* isomer requires concurrent exo,endo attack and is more sterically impeded. The *dl* isomers are consequently left in solution in a pure state. The homogeneous dihydro and tetrahydro adducts submit to hydrolysis–oxidation with formation of azo compounds which extrude nitrogen readily to return the meso hydrocarbons. By this procedure, nonimmolative chemical separation of the isomer pairs is conveniently effected. Their individual catalytic hydrogenation affords pure *dl*- and *meso*-bivalvane. The alkali metal–ammonia reduction of the dehydration products has been examined for its stereochemical outcome.

Because of the many exciting structural features inherent in the dodecahedrane molecule, among which may be cited the existence of a cavity of 2.0–2.5 Å diameter completely enclosed within the carbon network, we have developed an interest in the synthesis of this $(CH)_{20}$ polyhedron. In one approach based upon the concept of stepwise dimerization of two triquinacene halves,[1] the pinacolic reduction of *dl*-2,3-dihydrotriquinacen-2-one (**1**) was studied and shown to give the desired *dl* diol **2** admixed with an approximately equal

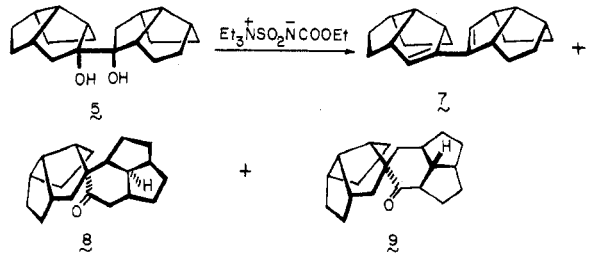


1 2 3

amount of meso isomer **3**.[2] When starting with enantiomerically pure (+)-**1**, **2** becomes the exclusive reductive coupling product because of enforced enantiomer recognition. Identical behavior was noted in the fully saturated series involving (±)- and (+)-hexahydrotriquinacen-2-one (**4**). However, the existing method for preparing optically pure **1** and **4** is laborious and nonconducive to scale-up. High-pressure liquid chromatographic separation of **2**, **3**, and their perhydro counterparts can be effected with somewhat greater efficiency, but we desired a rapid, high-yield, and nondestructive means of cleanly separating the *dl* and meso series. Were this goal to be achieved, rapid access to *dl*-bivalvane and its derivatives could be gained with limited expenditures of time and effort starting entirely with racemic **1** and **4**.

We now describe the successful adaptation of this plan to the preparation of *dl*- and *meso*-bistriquinacene and their octahydro counterparts, together with the conversion of these polyolefins to the respective bivalvanes and to diastereomeric "dimers" which have previously eluded synthesis.

The Perhydrotriquinancene Series. To gain information on the susceptibility of the four diols to directed twofold dehydration, preliminary studies were carried out on pure



5 7 8 9

samples of **5** and **6**. We desired introduction of the pair of double bonds into the less substituted sites (cf. **7** and **10**) and therefore made initial recourse to ethyl(carboxysulfamoyl) triethylammonium hydroxide inner salt because of its well-established propensity for directing cis elimination.[3] Reaction of **5** with this reagent in tetrahydrofuran at −5 °C for 2 h led to formation of **7** (68.5%) and a mixture of isomeric spiro ketones **8** and **9** (28%). With less polar solvents such as benzene and cyclohexane, dehydration proceeded less rapidly and required more elevated temperatures, but still gave a predominance of **7** (Table I). The definitive spectral data for **7** include a particularly revealing two-proton olefinic singlet at δ 5.27 and a ^{13}C NMR spectrum comprised of only ten signals. This last pattern is of course consistent only with strict maintenance of C_2 symmetry. Were dehydration to have occurred instead toward the bridgehead positions, the resulting fully substituted diene would also belong to this point group but would lack olefinic protons. No contamination from this product was seen. The electronic spectrum of **7** in isooctane consists of three absorption maxima at 237, 245, and 255 nm.

The infrared spectra of several crops obtained by fractional crystallization of the ketone fraction showed pronounced variations in the intense 1410-cm^{-1} absorption characteristic of methylene groups adjacent to carbonyl, thereby indicating the presence of both **8** and **9**. Their ratio in the reaction mixture was determined by mass spectral analysis of their base-

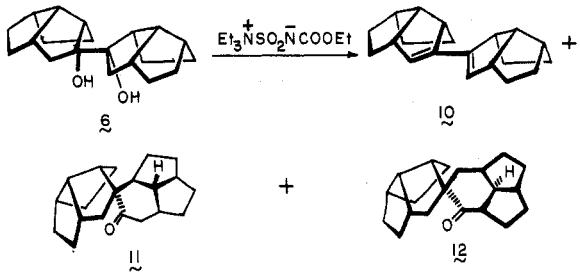
Table I. Summary of Dehydration Data Involving the Burgess Reagent

Diol	Solvent	Temp, °C	Time, h	Product composition, %[a] Diene	Ketone mixture
5	THF	−5	2	68.5	28
	C_6H_6	60	0.5	52	46
	Cyclohexane	65	1	70	25
6	THF	25	2	66	33
	C_6H_6	25	1	54	43
	CH_3CN	25	1	24	73
	CH_2Cl_2	0	3	36	59

[a] Isolated yields after column chromatography on silica gel.

promoted deuterium exchange products and supportive ^{13}C spectral analysis to be 73% of **8** (d_2 incorporation) and 27% of **9** (d_1 incorporation). The major component (**8**) was subsequently isolated in pure form by repeated recrystallization from hexane. The observed ketonic distribution is considered to be a reflection of the relative pinacolic migratory capabilities of secondary and tertiary carbon in the absence of steric inhibition to either shift.[4]

Dehydration of **6** with the Burgess reagent was examined over a wider range of solvent polarities (Table I). However, acetonitrile and methylene chloride promoted greater levels of pinacol rearrangement and were less satisfactory. That **10** was the diene produced was attested to by its ^1H (δ 5.28, s, 2 H) and ^{13}C NMR spectra (ten signals) and by the near identity of its uv spectrum with that of **7**. Interestingly, the ratio of ketones **11** and **12** (20:80) was reversed from that realized in

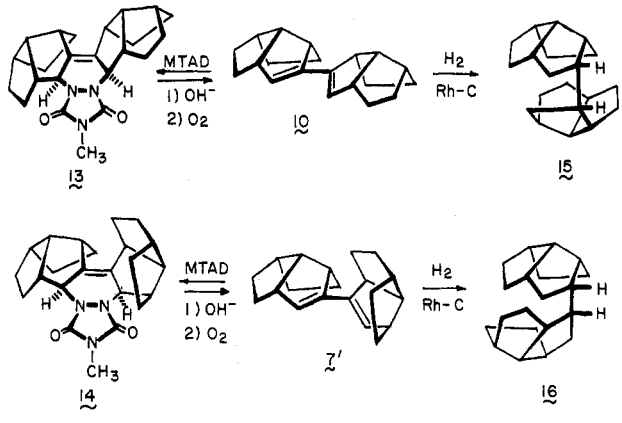


the *dl* series. More facile 1,2 shift of the lesser substituted carbon is herein encountered seemingly because of nonbonded steric interactions which develop between the neighboring methylene groups of the two halves in that antiperiplanar conformation necessary for migration of either tertiary carbon.[5]

Since complications presented by competing pinacol rearrangement were unwanted, conditions were sought which would preclude their operation. From available data,[6] it appeared that phosphorus oxychloride in pyridine is capable of dehydrating 1,2-glycols while apparently bypassing the incursion of rearrangement. Accordingly, when **6** was heated at steam bath temperatures with 2 molar equiv of this reagent for 6 h, there was observed high-yield conversion exclusively to **10**. Clearly, this was the procedure of choice since trans elimination of water also did not occur despite known examples to the contrary.[7]

The scheme now was critically dependent upon a sizable reactivity difference between **7** and **10** as 4π addends in the Diels–Alder reaction. The meso diene (**10**), earlier depicted in its s-cis conformation, is seen to make geometrically possible simultaneous bonding of the dienophile to the exo surfaces of both termini. Steric impedance to the cycloaddition should consequently be minimal. s-Cis conformational readjustment in **7** (see **7′**), a necessary prelude to its involvement in such chemistry, so orients the diene moiety that concerted $_\pi 4_s$ bonding requires concurrent exo,endo attack. Because of the rather sizable steric blockade to endo approach in such concave molecules, reduced reactivity was anticipated for the *dl* isomer. However, the magnitude of this kinetic gap remained on unknown quantity.

When equimolar amounts of pure **10** and *N*-methyltriazolinedione (MTAD) were allowed to react in anhydrous tetrahydrofuran solution at −65 °C, the red coloration due to the dienophile faded within 10 min. Solvent evaporation left adduct **13** (100%), structural assignment to which is based upon the highly symmetric nature of its ^1H and ^{13}C NMR spectra (see Experimental Section) and its clean reconversion to **10**



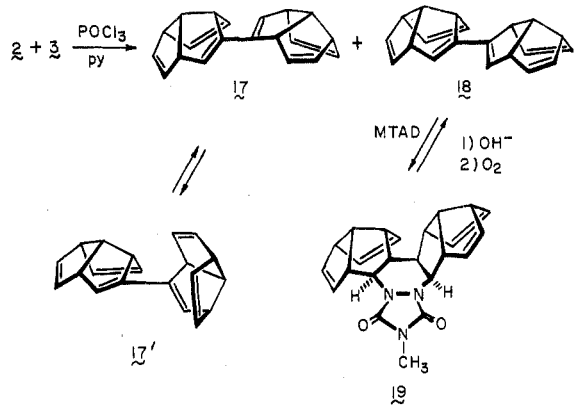
upon hydrolysis–oxidation.[8] Comparable treatment of **7** did not result in cycloaddition until the temperature was raised to −25 °C. The adduct so produced (**14**) was characterized by two different >CHN< signals (δ 4.28 and 4.00) as a consequence of their different spatial orientations and a 23-line ^{13}C pattern indicative of the inherent molecular dissymmetry. That **14** could readily be transformed back to **7** was also demonstrated.

When 0.5 molar equiv of MTAD was added to a 1:1 mixture of **7** and **10** dissolved in acetone at −65 °C, pure adduct **13** was isolated in 46% yield. The recovered hydrocarbon (53%) consisted of **7** contaminated by 6% of **10**. This impurity was completely removed by a second exposure to MTAD. It proved more efficient, however, to include a slight excess of MTAD at the outset of the cycloaddition. Thus, nonimmolative chemical separation of the two isomers was indeed possible!

Catalytic hydrogenation of **7** and **10** over 5% rhodium on carbon at 45 psig led in characteristically slow (6 days) but efficient fashion to diastereomerically pure crystalline samples of *dl*- (**16**) and *meso*-bivalvane (**15**), respectively.

***meso*- and *dl*-Bistriquinacene.** For comparative purposes, pure **3** was subjected to parallel experiments with $POCl_3$/pyridine and with the inner salt. In agreement with the earlier observations, the first set of conditions led exclusively and in high yield to **18** while the Burgess reagent gave **18** (53%) admixed and spiro ketones (41%). Accordingly, a mixture of **2** and **3** was dehydrated in the preferred manner and subse-

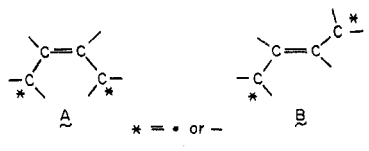
quently treated directly at −78 °C with MTAD. The relative molar quantity of the dienophile was controlled to provide an amount adequate for reaction only with *meso*-bistriquinacene (**18**), the percentage of which in the mixture was ascertained by prior VPC analysis. Gleaned from control experiments was the observation that the reactivity difference between **17** and **18** was less than that which distinguished **7** from **10.** This is because of the lack of endo protons in **17** which serve in its more saturated counterpart (**7**) to more effectively deter approach of the dienophile (see **17'**). Nevertheless, **18** is selectively consumed under these conditions with formation of adduct **19.** Over the course of several experiments, the unreacted hydrocarbon fraction was noted to be consistently greater than 98% enriched in **17.** Adduct **19** was converted by



hydrolysis–oxidation[8] back to **18,** thereby accomplishing efficient separation of the title compounds.

The ^{1}H NMR spectra of both **17** and **18** bear close similarity to that of triquinacene,[9] being characterized by a downfield multiplet of area 10 in the δ 5.6–5.8 region and an upfield pseudosinglet at 3.80 (8 H) attributable to the various methine protons. Both polyolefins expectedly show ten-line ^{13}C NMR spectra in agreement with maintenance of intrinsic C_2 and C_s symmetry, respectively.

Stereochemistry of Alkali Metal Reduction. Although the capacity of 1,3-dienes for alkali metal reduction has been recognized for many years,[10] only limited attention has been given to stereochemical control of the 1,4-addition process.[11,12] This earlier work suggests that cis,trans isomer ratios are somewhat sensitive to solvent, alkali metal, and the homogeneity or heterogeneity of the latter reagent. Also at play is a delicate balance of stereoelectronic and steric factors. The cis radical anion and its dianion (A) presumably derive their stability from ion pairing with the metal, a phenomenon which should gain importance in nonpolar solvents but be critically dependent as well upon the coordinative capacity of the cation and prevailing steric effects. The trans intermediate B, on the other hand, does not suffer as greatly from repulsion of the two



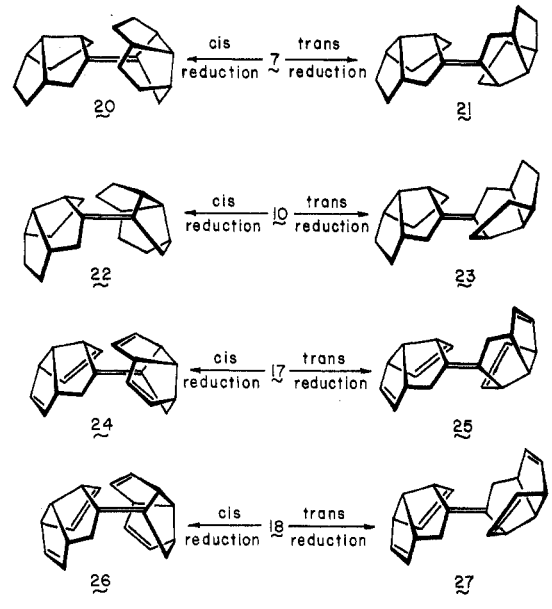
negative charges and a preference for this species should be noted in polar solvent systems where stabilization by the gegenion is less effective by virtue of increased solvation.

Alkali metal reduction of **7, 10, 17,** and **18** represents a potentially simple and convenient method for positioning a double bond between the two structural halves without danger of concomitant overreduction in the fully unsaturated series. Since all four syn "dimers" (**21, 22, 25,** and **26**) have been previously prepared in unequivocal fashion,[2] the stereochemical course of these reactions could be readily ascertained. Furthermore, it was presumed that access to the synthetically important but heretofore unknown anti "dimers" could be realized as well. Noteworthily, while cis reduction of the meso dienes will give rise to syn products, formation of the analogous diastereomers in the *dl* series requires trans addition. Within this series of molecules, therefore, the opportunity is available for acquisition of new information on those factors which govern the geometrical outcome of conjugate addition to 1,3-dienes.

Table II. Reduction of Meso Hydrocarbons 10 and 18 in Liquid Ammonia

Compd	Metal	Temp, °C	Composition, % Trans-1,4	Cis-1,4	1,2
10	Li	−33	44	11	45
		−78	61	20	19
	Na	−33	69	18	13
		−78	75	17	8
	K	−33	62	19	19
		−78	73	23	4
18	Li	−33	77	*a*	23
		−78	72	*a*	28
	Na	−33	82	*a*	18
		−78	77	*a*	23
	K	−33	68	*a*	32
		−78	84	*a*	16

[a] Pentaene **26** was only incompletely resolved during VPC analysis. Control experiments showed that the level of **26** never exceeded the 5–10% level. The percentage compositions cited do not give weight to this minor product.



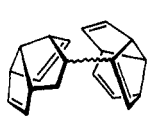
Although the initial intent was to conduct the alkali metal reductions in various solvents, preliminary indications that aprotic media such as tetrahydrofuran were inefficient and necessitated unduly long reaction times caused us to focus attention exclusively upon the various alkali metals in liquid ammonia at two different temperatures. The results realized for meso hydrocarbons **10** and **18** are summarized in Table II. The prevalance of anti "dimers" **23** and **27,** respectively, in these product mixtures denotes that reduction in the trans configuration is favored in these stereoisomers and that in most, but not all, cases an increase in temperature acts to favor this reaction channel. Such temperature-dependent behavior, previously noted in the case of butadiene,[11] does not appear to be the result of olefin isomerization under the reaction

Table III. Reduction of *dl* Hydrocarbons 7 and 17 in Liquid Ammonia

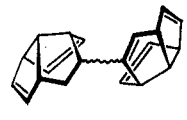
Compd	Metal	Temp, °C	Composition, % Trans-1,4	Cis-1,4	1,2
7	Li	−33	68		32
		−78	61		39
	Na	−33	67		33
		−78	49		51
	K	−33	91		9
		−78	61		39
17	Li	−33	72	8	20
		−78	75	8	17
	Na	−33	73	8	19
		−78	74	8	18
	K	−33	87	5	8
		−78	81	9	10

conditions. However, the data necessary to conclusively establish this point could not be obtained.[13] In both instances, 1,2 reduction was found to occur competitively, but at a generally lesser level. The identity of pure **23** and **27** rests inter alia on their ^{13}C NMR spectra which are comprised of ten signals, the chemical shifts being sufficiently distinctive from those of the known isomers **22** and **26** to be characteristic. In contrast, **28a** and **28b** each exhibit the full complement of 20 peaks because of annihilation of the C_2 symmetry axis.

Whereas **10** did undergo rather significant levels of cis-1,4 reduction, its *dl* counterpart **7** was not detectably transformed to **20.** Rather, the product mixture consisted only of **21** and **29b** under all conditions studied (Table III). Hexaene **17** behaved comparably, delivering the known **25** by trans reduction. Small levels of cis-1,4 reduction were now observed, but these were invariably lower than competitive 1,2 reduction.



28a, as drawn
b, tetrahydro counterpart



29a, as drawn
b, tetrahydro counterpart

Our findings indicate that the recognizable levels of 1,4 reduction which occur from the available trans conformations exceeds those which take place from the cis forms irrespective of the metal and temperature. Undoubtedly, a combination of steric and stereoelectronic factors are responsible for the observed stereoselectivity. The results for **7,** where a distinction between less sterically encumbered conformation **7** and the more crowded cisoid option **7′** can be made simply with Dreiding models, are especially telling. Owing to this presumed thermodynamic preference and to the anticipated predilection for generation of charge separated dianions of type B in ammonia solution, the product distribution can expectedly be skewed heavily, if not exclusively, in favor of trans reduction. Owing to the higher degree of unsaturation in **17** and the resulting elimination of several endo protons, the trans ground state conformational preference should be somewhat subdued. The data in Table III which indicate the incursion of some cis-1,4 reduction in this case are commensurate with this thinking.

The reduction of meso diene **10** is still less discriminatory. The implication is that its cis diene conformation probably enjoys a greater thermodynamic advantage than those in the *dl* series such that the driving force underlying the preferred formation of trans 1,4 dianions could be partially nullified. Our study of molecular models is again supportive of this hypothesis.

It is therefore clear that synthetic access to **23** and **27** can be profitably achieved by this methodology. Moreover, the two-step conversion of **2** to **25** which is now made possible represents a procedure vastly superior to that heretofore available.

Experimental Section

Infrared spectra were obtained with a Perkin-Elmer Model 467 spectrometer. The ^1H NMR spectra were determined on Varian T-60 and A-60A instruments and apparent splittings are given in all cases. A Bruker 90 spectrometer was employed for the recording of ^{13}C spectra. Microanalyses were performed by the Scandinavian Microanalytical Laboratory, Herlev, Denmark. Mass spectral measurements were made on an AEI-MS9 spectrometer at an ionizing potential of 70 eV.

General Procedure for Dehydration of 5 with the Burgess Reagent. A solution of **5**[2] (272 mg, 0.9 mmol) in anhydrous tetrahydrofuran (3 ml) was added dropwise under a nitrogen atmosphere to a stirred solution of ethyl(carboxysulfamoyl)triethylammonium hydroxide inner salt[3] (850 mg, 3.9 mmol) in 8 ml of the same solvent cooled to −10 °C. After 2 h at −5 °C, the reaction mixture was poured into water (20 ml), extracted with ether (2 × 10 ml), dried, and evaporated. The residue was chromatographed on silica gel. Elution with petroleum ether gave 163 mg (68.5%) of **7,** while elution with petroleum ether–ether (9:1) led to isolation of the mixture of spiro ketones **8** and **9** (79 mg, 28%).

Recrystallization of **7** from ethanol furnished colorless crystals: mp 37–38 °C; ^1H NMR δ ($CDCl_3$) 5.27 (s, 2), 2.8–3.3 (m, 4), 2.0–2.6 (m, 2), and 0.8–1.8 (m, 18); ^{13}C NMR ($CDCl_3$) 142.68, 130.33, 53.06, 50.69, 50.15, 46.10, 32.88, 32.56, 31.54, and 30.35 ppm; ν_{max} (neat) 3035, 902, and 840 cm^{-1}; λ_{max} (isooctane) 237 nm (ϵ 19 000), 245 (23 400), and 255 (14 100).

Anal. Calcd for $C_{20}H_{26}$: C, 90.16; H, 9.84. Found: C, 89.99; H, 9.91.

Recrystallization of the ketone mixture from hexane resulted in isolation of dominant isomer **8** in pure form: mp 125–126 °C; ^{13}C NMR ($CDCl_3$) 215.06, 62.51, 54.25, 52.04, 48.15, 44.24, 44.03, 43.16, 41.79, 41.30, 38.23, 35.02, 34.15, 33.24, 32.80, 32.29, 31.99, 30.75, 30.43, and 27.11 ppm; ν_{max} (KBr) 1690, 1468, 1410, and 1188 cm^{-1}.

Anal. Calcd for $C_{20}H_{28}O$: C, 84.45; H, 9.92. Found: C, 84.45; H, 10.04.

A larger sample of the **8/9** mixture (350 mg) was thrice recrystallized from hexane such that three crops were obtained: A, 75 mg (pure **8**); B, 65 mg; C, 154 mg (total recovery 84%). A mixture of pure **8** (10 mg) and potassium carbonate (30 mg) in a dioxane (1 ml)–deuterium oxide (0.5 ml) solvent system[14] was gently refluxed for 5 h. A white solid was separated by filtration, the filtrate was extracted with ether, and the organic phase was evaporated to dryness. The combined solids were subjected to mass spectral analysis and >95% d_2 incorporation was thereby indicated. This procedure was repeated on the mixture of crops B and C, the result being 70% d_2 and 30% d_1 incorporation. On this basis, the ratio of **8** to **9** was computed to be approximately 73:27.

General Procedure for Dehydration of 6 with the Burgess Reagent. A solution of **6**[2] (302 mg, 1.0 mmol) in anhydrous tetrahydrofuran (4 ml) was added dropwise at 25 °C under nitrogen to a stirred solution of the inner salt (940 mg, 4.3 mmol) in 10 ml of the same solvent. After 2 h, the reaction mixture was processed as above. Concentration left a residue which was chromatographed directly on silica gel. Elution with petroleum ether gave 178 mg (66%) of **10,** while elution with petroleum ether–ether (9:1) afforded 94 mg (33%) of a mixture of **11** and **12.**

Recrystallization of **10** from ethanol furnished colorless crystals: mp 97–98 °C; ^1H NMR δ ($CDCl_3$) 5.28 (s, 2), 2.8–3.3 (m, 4), 2.0–2.6 (m, 2), and 0.8–2.0 (m, 18); ^{13}C NMR ($CDCl_3$) 142.90, 130.43, 53.28, 51.34, 50.15, 46.05, 33.10, 32.29, 31.75, and 30.08 ppm; ν_{max} (KBr) 3020, 905, and 842 cm^{-1}; λ_{max} (isooctane) 237 nm (ϵ 15 100), 245 (19 400), and 255 nm (13 300).

Anal. Calcd for $C_{20}H_{26}$: C, 90.16; H, 9.84. Found: C, 90.04; H, 9.80.

Recrystallization of the ketone mixture from hexane afforded pure **12:** mp 129.5–131 °C; ^{13}C NMR ($CDCl_3$) 216.17, 58.46, 53.98, 50.69, 50.55, 47.05, 46.24, 44.38, 41.65, 38.52, 38.04, 35.10, 34.02, 32.37, 32.24, 32.18, 32.13, 31.51, 31.00, and 27.44 ppm; ν_{max} ($CHCl_3$) 1685, 1468, and 1196 cm^{-1}.

Anal. Calcd for $C_{20}H_{28}O$: C, 84.45; H, 9.92. Found: C, 84.23; H, 9.91.

When pure **12** and an unpurified mixture of **11** and **12** were subjected to deuterium exchange in the predescribed manner, the resulting levels of d_2 and d_1 incorporation denoted an approximate ratio of 20:80 in favor of **12**.

Dehydration of 6 with Phosphorus Oxychloride. A pyridine solution (1 ml) of **6** (190 mg, 0.63 mmol) was treated with phosphorus oxychloride (196 mg, 1.26 mmol) and heated on a steam bath for 6 h. The black reaction mixture was extracted with pentane (3 × 5 ml) and the combined extracts were washed with 3 N hydrochloric acid and water, dried, and evaporated. There remained a white solid (165 mg) which was purified by column chromatography on silica gel. There was obtained 140 mg (84%) of pure **10**, mp 97–98 °C.

MTAD Addition to 10. A cold (−78 °C) stirred solution of **10** (133 mg, 0.5 mmol) in anhydrous tetrahydrofuran (8 ml) was treated dropwise with a solution of *N*-methyltriazolinedione (56 mg, 0.5 mmol) in acetone (2 ml). After 10 min at −65 °C, the red coloration had completely faded. The solvent was removed in vacuo to give pure **13** (189 mg, 100%). Recrystallization from ethanol furnished colorless crystals: mp 218.5–219 °C; ^{1}H NMR δ ($CDCl_3$) 3.95 (d, J = 6.5 Hz, 2, >CHN<), 3.04 (s, 3, methyl), and 0.8–3.4 (br m, 24, methylenes and methines); ^{13}C NMR ($CDCl_3$) 153.53, 134.32, 60.02, 53.55, 49.29, 45.02, 44.43, 32.99, 32.83, 32.72, 31.21, and 24.79 ppm.

Anal. Calcd for $C_{23}H_{29}N_3O_2$: C, 72.79; H, 7.70; N, 11.07. Found: C, 72.66; H, 7.70; N, 11.04.

Hydrolysis–Oxidation of 13. A stream of argon was bubbled for 30 min into a mixture of **13** (379 mg, 1.0 mmol), potassium hydroxide (1.2 g), ethylene glycol (10 ml), and distilled water (10 ml) contained in a Claisen distilling flask fitted with a condenser and 10-ml receiver. The receiver was cooled in a dry ice–acetone bath. With continued argon purging, the flask was heated strongly with a Bunsen burner flame until approximately 10 ml of distillate was collected in the receiver. The distillate and pot residue were combined and diluted with 30 ml of water. The aqueous solution was extracted with methylene chloride (3 × 20 ml) and the combined extracts were oxygenated for 30 min. The solution was washed with water and brine, dried, and evaporated. Column chromatography of the residue on silica gel provided 165 mg (62%) of pure **10**, mp 97–98 °C.

MTAD Addition to 7. Solutions of **7** (133 mg, 0.5 mmol) in anhydrous tetrahydrofuran (4 ml) and of *N*-methyltriazolinedione (56 mg, 0.5 mmol) in acetone (2 ml) were mixed at −78 °C. With continued magnetic stirring, the temperature of this solution was gradually increased until at −25 °C slow consumption of dienophile was noted (fading of red color). After 20 min at this temperature, the solvent was removed by evaporation and the residue was recrystallized from hexane to give 158 mg (85%) of **14**. The mother liquor contained unreacted **7**. Further recrystallization from ethanol gave colorless crystals: mp 145.5–147 °C; ^{1}H NMR δ ($CDCl_3$) 4.28 (m, 1, >CHN<), 4.00 (m, 1, >CHN<), 3.05 (s, 3, methyl), and 1.0–3.5 (br m, 24, methylenes and methines); ^{13}C NMR ($CDCl_3$) 152.99, 152.34, 136.91, 131.24, 61.21, 59.32, 53.44, 52.63, 49.12, 47.07, 44.92, 44.75, 43.51, 43.14, 35.64, 33.48, 32.88, 32.67, 32.08, 31.86, 31.16, 27.44, and 24.74 ppm.

Anal. Calcd for $C_{23}H_{29}N_3O_2$: C, 72.79; H, 7.70; N, 11.07. Found: C, 72.54; H, 7.81; N, 11.09.

Hydrolysis–Oxidation of 14. When a 110-mg (0.3 mmol) sample of **14** was subjected to the hydrolysis–oxidation conditions described above for **13**, there was isolated after chromatographic (silica gel) purification 38 mg (75%) of **7**, mp 37–38 °C.

MTAD Addition to a Mixture of 7 and 10. To a cold (−65 °C) solution of a **7/10** mixture (composition 1:1, 1.34 g, 5.0 mmol) in tetrahydrofuran (200 ml) was added dropwise a solution of MTAD (280 mg, 2.5 mmol) in acetone (20 ml) during 30 min. The mixture was slowly allowed to warm to room temperature whereupon the solvent was evaporated before chromatography of the residue on silica gel. Elution with petroleum ether returned 720 mg (53%) of diene, VPC analysis of which revealed the composition to be 94% of **7** and 6% of **10**. Elution with petroleum ether–ether gave 900 mg (46%) of pure **13**, mp 218–219 °C.

***meso*-Bivalvane (15).** A 100-mg (0.37 mmol) sample of **10** dissolved in ethyl acetate (10 ml) was hydrogenated in the presence of 5% rhodium on carbon (50 mg) at a pressure of 45 psig in a Paar apparatus for 6 days. The catalyst was separated by filtration and the filtrate evaporated to leave a white solid which was recrystallized from ethanol. There was obtained 90 mg (89%) of **15**, the melting point and ^{13}C NMR spectrum of which were identical with those of an authentic sample.

***dl*-Bivalvane (16).** Catalytic hydrogenation of **7** (100 mg, 0.37 mmol) as above afforded 87 mg (86%) of pure **16** which proved identical in all respects with an authentic sample.[2] VPC analysis indicated no contamination by a different stereoisomer.

***meso*-Bistriquinacene (18). A. Dehydration of 3 with $POCl_3$ in Pyridine.** A solution of **3** (400 mg, 1.36 mmol) and phosphorus oxychloride (810 mg, 5.4 mmol) in pyridine (5 ml) was heated on a steam bath for 24 h. The black reaction mixture was slowly poured into ice water (10 ml) and extracted with pentane–ether (1:1, 3 × 10 ml). The combined extracts were washed with 3 N hydrochloric acid, saturated sodium bicarbonate solution, and brine before drying. Evaporation left a white solid which was passed through a short silica gel column. There was obtained 275 mg (80%) of **18**: mp 165–167 °C (from ethanol); ^{1}H NMR δ ($CDCl_3$) 5.58–5.78 (m, 10, olefinics) and 3.80 (s, 8, methines); ^{13}C NMR ($CDCl_3$) 142.14, 133.75 (2 C), 133.16, 132.97, 130.27, 58.08, 57.68, 57.43, and 48.59 ppm; λ_{max} (cyclohexane) 245 nm (ϵ 12 700), 253 (17 300), and 262 (13 300).

Anal. Calcd for $C_{20}H_{18}$: C, 92.08; H, 7.02. Found: C, 92.58; H, 7.07.

B. Dehydration of 3 with the Burgess Reagent. A mixture of **3** (294 mg, 1.0 mmol) and the inner salt (880 mg, 4.0 mmol) in anhydrous ether (20 ml) was refluxed for 30 min and processed as described above. The product mixture was chromatographed on silica gel. Elution with petroleum ether afforded 136 mg (53%) of **18**, while elution with petroleum ether–ether (9:1) led to isolation of a mixture of spiro ketones (115 mg, 41%) which were not further characterized.

***dl*-Bistriquinacene (17).** A solution of **2** and **3** (880 mg, 3.0 mmol) and phosphorus oxychloride (1.71 g, 9.0 mmol) in pyridine (10 ml) was heated on a steam bath for 24 h and yielded 600 mg (79%) of the **17/18** mixture.

To a cold (−78 °C) solution of a **17/18** mixture (220 mg, 0.85 mmol) comprising 75% of the *dl* isomer and 25% of the meso form (VPC analysis on a 10 ft × 0.25 in. 15% Carbowax 20M column packed on Chromosorb P, 250 °C) in 30 ml of anhydrous tetrahydrofuran was added dropwise with stirring under nitrogen a solution of MTAD (24 mg, 0.21 mmol) in acetone (2 ml) during 1 h. The mixture was allowed to slowly warm to room temperature and the solvents were evaporated to leave a solid residue. Chromatography of this material on silica gel provided first 168 mg (76%) of **17** (>98% purity by VPC analysis) and then 72 mg (24%) of adduct **19**.

Recrystallization of **17** from ethanol gave colorless crystals: mp 74–76 °C; ^{1}H NMR δ ($CDCl_3$) 5.58–5.87 (m, 10, olefinics) and 3.80 (s, 8, methines); ^{13}C NMR ($CDCl_3$) 142.17, 133.56, 133.32, 132.99, 132.89, 129.52, 57.87, 57.73, 57.51, and 48.75 ppm; λ_{max} (cyclohexane) 245 nm (ϵ 12 000), 253 (17 200), and 262 (12 000).

Anal. Calcd for $C_{20}H_{18}$: C, 92.98; H, 7.02. Found: C, 92.57; H, 7.18.

Adduct **19** was also recrystallized to analytical purity from ethanol: mp 292–293 °C; ^{1}H NMR δ ($CDCl_3$) 6.10 (br d, J = 5.5 Hz, 2, olefinics), 5.78 (br d, J = 5.5 Hz, 4, olefinics), 5.28 (br d, J = 5.5 Hz, 2, olefinics), 3.23–4.02 (m, 10, methines), and 3.07 (s, 3, methyl); ^{13}C NMR ($CDCl_3$) 153.28, 135.96, 134.67, 133.59, 133.37, 129.95, 61.24, 57.81, 55.01, 50.39, 49.39, and 24.87 ppm.

Anal. Calcd for $C_{23}H_{21}N_3O_2$: C, 74.37; H, 5.70; N, 11.31. Found: C, 74.01; H, 5.67; N, 10.95.

Hydrolysis–Oxidation of 19. Submission of **19** (111 mg, 0.3 mmol) to the hydrolysis–oxidation conditions described for **13** led to the isolation of 30 mg (59%) of **18**, mp 165–167 °C, identical with the prior sample.

Generalized Reduction Procedure. Typically, 25 mg of the hydrocarbon dissolved in 0.5 ml of anhydrous tetrahydrofuran containing 20 μl of *tert*-butyl alcohol was added dropwise to an excess of the metal (ca. 25 mg) in distilled liquid ammonia (25 ml). The mixture was stirred for 1 h at the specified temperature before addition of saturated ammonium chloride solution and extraction with dichloromethane. The organic phase was dried and reduced to small volume before VPC analysis (12 ft × 0.125 in. 5% SE-30 column, 200 °C). With but one exception, the product peaks were completely resolved and Gaussian in nature. Ratios were obtained by triangulation.

Monoene **23** was obtained crystalline (mp 88–90 °C) directly upon elution from the column: ^{13}C NMR ($CDCl_3$) 138.06, 55.90, 48.92, 45.12, 43.91, 37.52, 34.63, 34.33, and 32.66 ppm (2 C); calcd *m/e* 268.2197, found 268.2196.

Anal. Calcd for $C_{20}H_{28}$: C, 89.49; H, 10.51. Found: C, 89.13; H, 10.54.

Monoene **28b** was not obtained crystalline: ^{13}C NMR ($CDCl_3$) 147.13, 127.38, 54.92, 54.22, 53.14, 49.64, 48.02, 45.86, 44.99, 44.51, 43.11, 35.72, 33.02, 32.26 (2 C), 31.62 (2 C), 31.08, 30.64, and 27.30 ppm; calcd *m/e* 268.2197, found 268.2196.

Pentaene **27** was isolated in crystalline from (mp 123–125 °C) directly upon elution from the column: ^{13}C NMR ($CDCl_3$) 138.18,

134.35, 133.92, 132.92, 130.61, 58.49, 54.91, 50.82, 49.35, and 38.73 ppm; calcd *m/e* 260.1565, found 260.1569.

Pentaene **28a** proved not to be crystalline: ^{13}C NMR ($CDCl_3$) exhibits most intense peaks at 133.60, 132.75, 131.91, 57.74, 56.76, 48.96, and 37.72 ppm; calcd *m/e* 260.1565, found 260.1569.

Monoene **29b** was obtained crystalline: mp 70.5 °C (after sublimation); ^{13}C NMR ($CDCl_3$) 142.33, 126.41, 54.49, 53.31, 52.23, 49.37, 46.67, 45.91, 44.67, 43.65 (2 C), 34.48, 33.02, 32.32 (2 C), 31.67 (2 C), 30.97, 30.59, and 26.28 ppm; calcd *m/e* 268.2197, found 268.2196.

Anal. Calcd for $C_{20}H_{28}$: C, 89.49; H, 10.51. Found: C, 89.42; H, 10.74.

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Registry No.—**2,** 57700-83-1; **3,** 57760-88-0; **5,** 57700-82-0; **6,** 57760-87-9; **7,** 59938-99-7; **8,** 59939-00-3; **10,** 59981-13-4; **12,** 59939-01-4; **13,** 60018-67-9; **14,** 59939-02-5; **17,** 59939-03-6; **18,** 59981-14-5; **19,** 59939-04-7; **23,** 57700-86-4; **27,** 57700-87-5; **28a,** 59939-05-8; **28b,** 59953-49-0; MTAD, 13274-43-6.

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lin-Benzoguanine. Synthesis by Two Independent Methods

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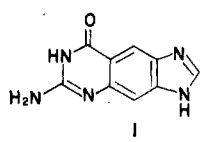
lin-Benzoguanine, 6-aminoimidazo[4,5-*g*]quinazol-8-one (1), has been synthesized by two independent methods, both starting with an intact central benzenoid ring. In one route, the substituted benzimidazole moiety was elaborated before closure of the pyrimidine ring. In the other, the substituted quinazolone was synthesized prior to imidazole ring closure. The title compound is fluorescent and represents a version of guanine that has been widened by 2.4 Å.

Recent work in these laboratories has centered on the synthesis and biochemical implications of benzologs of the purine bases,[1] specifically *lin*-benzoadenine (**2**). We have



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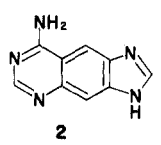

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extended this series to include *lin*-benzoguanine, 6-aminoimidazo[4,5-*g*]quinazol-8-one (1), and report here its synthesis by two independent methods. The syzygial nature of these two pathways allows specific substitution in either the imidazole or the pyrimidine portions of the system toward the conclusion of the respective sequences. In the route of primary interest, path A, the extensive use of acyl and hydrochloride derivatives of tri- and tetrasubstituted aromatics avoided some of the problems foreseen[1] in the discussion of synthetic approaches to the "stretched-out" bases. Path A, however, does not easily allow for the unequivocal substitution at the 3 position (analogous to 9 in guanine), which is needed for assignment of the desired site of ribosidation by comparison of uv spectra. Thus, a second route, path B, was established by modification of the procedure used for *lin*-benzoadenine, which provides unequivocal substitution of the 3 position by nucleophilic aromatic substitution of a modified 4-quinazolone.

Path A has the decided advantage of allowing the synthesis of a variety of purine analogues in one step from a common benzimidazole intermediate. The addition of isocyanates, isothiocyanates, and substituted cyanamides, analogous to the preparation of substituted quinazolines and pyrimidones,[2] should lead to benzologs of xanthines, 2-thioxanthines, and N^2-alkyl and 1-alkylguanines, respectively. The use of substituted cyanamides may be limited by the ambiguity of substitution, but this could be avoided by use of 2-alkylthiohypoxanthine intermediates.

Results and Discussion

Path A. Compound **3** was easily obtained by esterification of 4-nitroanthranilic acid in 95% yield. Reduction of **3** with hydrogen over Pd/C followed by acetylation with acetic anhydride afforded **4** in 94% yield. Nitration of **4** to give **5** was best accomplished at −10 °C with concentrated sulfuric acid and fuming nitric acid, the low temperature being necessary to prevent hydrolysis of the acyl groups of the product. Compound **5** was subjected to a series of reactions without isolation of the intermediates to give **9** in 85% yield. First, the acyl protecting groups were removed by heating in ethanolic HCl to give **6,** which proved to be unstable to air on long standing, even as its hydrochloride salt. Dissolution of **6** in 98% formic acid, followed by reduction with hydrogen over Pd/C and heating, gave **8,** which was identified by its NMR spectrum. Unfortunately, the formyl group was cleaved on prolonged standing,[3] both in air and under a nitrogen atmosphere, to give a mixture of fluorescent products. Cleavage of the formyl group with retention of purity, however, could be accomplished by heating with ethanolic HCl to afford the di-