Indenone Chemistry. 5.[1] Use of Indenones in the Synthesis of Indeno[1,2-*d*]pyridazine Derivatives and the Diazagibbane Skeleton

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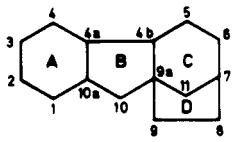
Treatment of 2,3-bis(bromomethyl)-6-methoxy-1-indenone (**3**) with sodium iodide in acetone yields the intermediate 2,3-dimethylene-6-methoxy-1-indenone (**4**), which can be trapped in situ with dialkyl azodicarboxylates. This leads to the formation of tetrahydroindeno[1,2-*d*]pyridazine derivatives **5**. The adduct **5b** can be hydrogenated and subsequently alkylated with allyl bromide. Treatment of the alkylated product **7c** with hydrogen bromide in glacial acetic acid and subsequent reaction with sodium *tert*-amylate affords the diazagibbane **2**.

Gibberellins are plant growth regulators[3] with a tetracyclic skeleton as depicted in **1**. The precise mode of their



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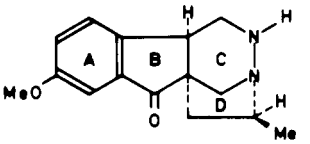

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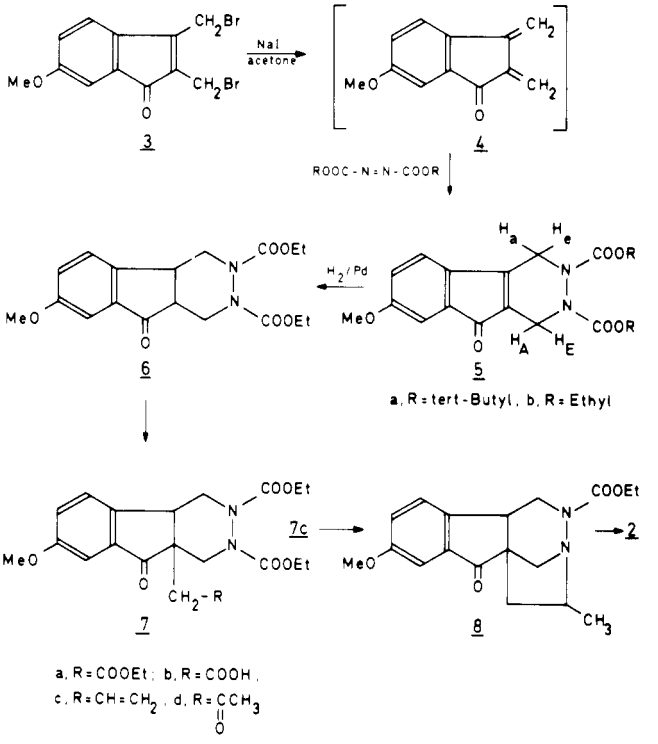
physiological action remains obscure; however, much effort on the problem of structure–activity relationships has been expended in testing the relative biological activities of gibberellins and structurally related molecules. So far, the only functional group found to be essential for activity is the B-ring β-carboxyl group. The more active gibberellins also possess a γ-lactone function fused to the A ring which, in the most active compounds, usually bears a 3 β-hydroxyl group.[4]

Our approach to the study of structure–activity relationships is to keep the general gibberellin skeleton as such and to introduce nitrogen atoms in the C and/or D ring. In this paper we describe a synthetic route to the analogue **2**, which can be considered as a precursor of a heterocyclic gibberellin. To our knowledge no aza analogues of the gibbane skeleton have been reported.

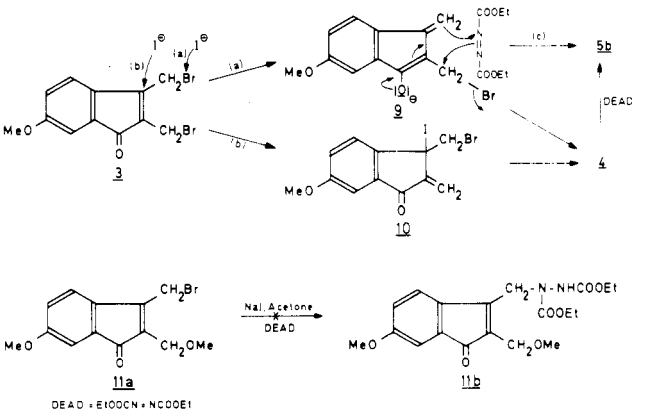
The multifunctional 2,3-bis(bromomethyl)-6-methoxy-1-indenone **3**[1,5] was used to prepare in two steps the indenohexahydropyridazine derivative **6**, from which the diazagibbane **8** was obtained in only two steps (Scheme I). The functional groups of the A and B rings of **8** (**2**) have been chosen with a view to their further elaboration to the characteristic A and B rings of natural gibberellins.[6]

The indenotetrahydropyridazines[7] **5** were obtained by treatment of the bis(bromomethyl)indenone **3** with dialkyl azodicarboxylates and sodium iodide in acetone. The reaction is presumed to occur by formation of the diene **4**[5] followed by trapping with the azo compound. Other

Scheme I



Scheme II



dienophiles such as maleic anhydride or methyl acrylate were unsuccessful in this respect, and only dimers of **4** were observed.[5]

Formation of adduct **5b** might also be explained by a γ-nucleophilic attack of the enolate **9** on the azo compound followed by ring closure (paths a and c, Scheme II).[8]

(1) Part 4: Lahousse, H; Martens, H; Hoornaert, G. *J. Org. Chem.* **1980**, *45*, 3451.

(2) (a) Scholar of the Instituut tot aanmoediging van Wetenschappelijk Onderzoek in Nijverheid en Landbouw (IWONL). (b) Leuven. (c) Diepenbeek.

(3) Hedden, P; MacMillan, J; Phinney, B. O. *Annu. Rev. Plant Physiol.* **1978**, *29*, 149.

(4) Brian, P. W.; Grove, J. F. *Phytochemistry* **1967**, *6*, 1475.

(5) Martens, H; Hoornaert, G. *Tetrahedron* **1974**, *30*, 3641.

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(7) The only reported indeno[1,2-*d*]pyridazine derivative was obtained by vapor-phase pyrolysis of 4,5,8-triphenylpyridazine[4,5-*d*]triazine: Gilchrist, T. L.; Gymer, G. E.; Rees, C. W. *J. Chem. Soc.*, Perkin *Trans. 1* **1975**, 1747.

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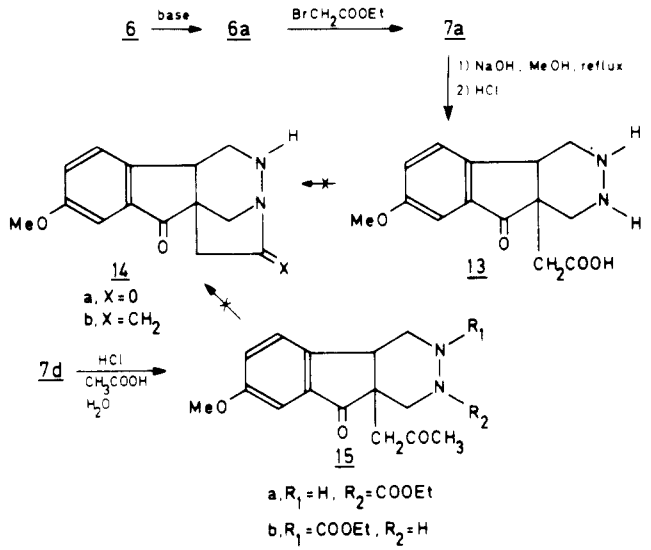
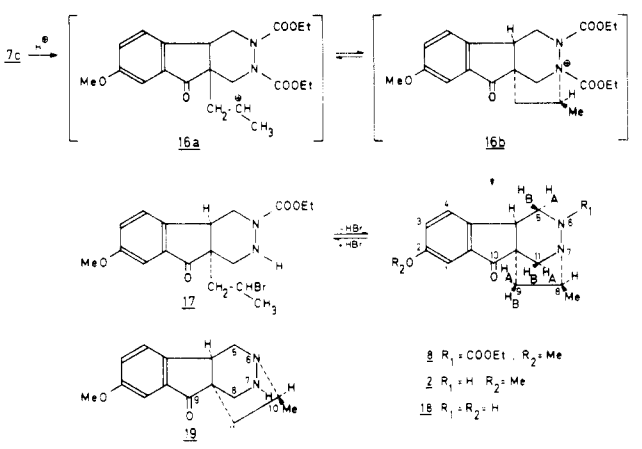
Scheme III



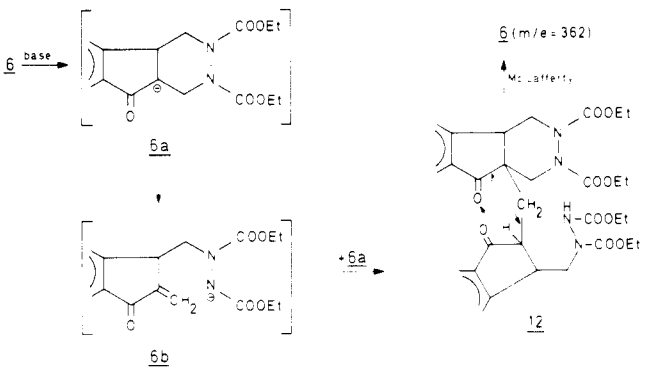
Scheme IV



However, the reaction of **3** with nucleophiles generally involves attack at the β-carbon (path b) to give intermediates[1] such as **10**, which is a plausible precursor of **4**. To test the alternative possibility (path a, c), we treated the indenone **11a**[1] with NaI in the presence of DEAD. No addition compound such as **11b** was found, but the starting products were recovered. We feel that this result makes the trapping of an intermediate **9** by DEAD (path c) less plausible. In our opinion the good leaving group Br^- in the 2-bromomethyl group of **3** plays a decisive role in the generation of **4** and of **5b** in the presence of DEAD.

Catalytic hydrogenation of the adduct **5b** yielded the indenohexahydropyridazine compound **6**. The D-ring elaboration was pursued via an alkylation at the 9a-position of **6**, followed by a ring closure.

Treatment of **6** with equivalent amounts of potassium *tert*-butoxide and ethyl bromoacetate in dry *tert*-butyl alcohol gave compound **12** instead of the desired product



7a. Its mass spectrum (M^+, m/e 724) is in agreement with a dimer of **6**. On the grounds of its degradation pattern we propose the depicted structure. The most important ion is m/e 362, which probably arises from a McLafferty rearrangement. No further effort has been made to confirm the structure of **12**, but its formation can be explained by a ring opening of the carbanion **6a** to the α,β-unsaturated ketone **6b**, which is subsequently attacked by another carbanion, **6a**.

However, **6** reacted with sodium hydride in benzene and a five-fold excess of ethyl bromoacetate to give **7a** in 90% yield (Scheme III). The alkylation was expected to give a cis junction between the B and C rings as was the case for a similar alkylation with carbocyclic analogues.[9] On treatment of **7a** with sodium hydroxide under different reaction conditions, either the acid **7b** or the acid **13** was obtained. The acid **13** slowly decomposed, probably by air oxidation,[10] and so we could only ascertain its structure via the acid **7b** (see Experimental Section). All attempts (e.g., treatment of **13** with dicyclohexylcarbodiimide in $CHCl_3$ or heating **13** under vacuum up to 250 °C) to cyclize **13** to the bridgehead amide **14a** failed. This can be explained by the high reactivity of bridgehead amides toward hydrolysis[11] or by their difficult formation.[12] We tried a second approach based on the report of a successful synthesis of a bridgehead enamine system.[13] This was the cyclization of the ketone **7d** to the diazagibbane **14b** (Scheme III). The ketone **7d** was obtained by alkylation of **6** with alkyl bromide, followed by oxidation of the double bond with $PdCl_2$–$CuCl_2$.[14] Treatment of **7d** with HCl, dissolved in aqueous acetic acid, provided equal amounts of the monodecarboxylated products **15a** and **15b**. Attempts to perform a cyclization with this product mixture (e.g., heating it up to 250 °C in a sealed tube with different solvents and acid catalysts) were unsuccessful.

Ultimately the following approach to the diazagibbane skeleton **8** was successful. When the alkylated compound **7c** was treated with a 40% solution of HBr in glacial acetic acid at room temperature, a mixture of four products was formed. Preparative TLC of this mixture afforded two fractions, each containing two products. The ^{13}C NMR spectrum of the first fraction showed methine carbon absorptions at 68.8 and at 42.52 ppm, which can be attributed, respectively, to methine carbons linked to a nitrogen and to a bromine atom. The mass spectrum of this same fraction showed a molecular ion at m/e 410 containing a bromine atom together with an ion at m/e 330. The latter can be attributed either to M^+ of **8** or to a fragment ion of **17** (loss of HBr). Taking into account these results, we have assigned the structures **8** and **17** to the two products (Scheme IV). According to its mass spectrum the second fraction contained the demethylated counterparts of **8** and **17**. The reaction of **7c** with HBr was then repeated and

(8) This was suggested by a referee.

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(10) Horwell, D. C.; Deyrup, J. A. *J. Chem. Soc., Chem. Commun.* **1972**, 485.
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(12) Brouillette, W. J.; Smissman, E. E.; Grunenwald, G. L. *J. Org. Chem.* **1979**, *44*, 839.
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(14) Tsuji, J.; Shimizu, I.; Yamamoto, K. *Tetrahedron Lett.* **1976**, 2975.

Table I. ^{1}H NMR Spectral Data of C- and D-Ring Protons of the Diazagibbane 2 as Depicted in Scheme IV

atom	shift,[a] δ	Δδ,[b]	coupled H and J,[c] Hz
H_{4b}	3.16		H_{5A}, 7.4; H_{5B}, 11; H_4, 0.8
H_{5A}	3.39	−0.27	H_{4b}, 7.4; H_{5B}, 11.9
H_{5B}	2.76	−0.32	H_{4b}, 11; H_{5A}, 11.9
H_6	4-4.5		
H_8	3.48	−0.67	Me_8, 6.9; H_{9A}, 7.4; H_{9B}, 6.2; H_{11B}, 1.3
Me_8	1.29	−0.25	H_8, 6.9
H_{9A}	2.08	−0.28	H_8, 7.4; H_{9B}, 12.1; H_{11B}, 2.2
H_{9B}	1.88	−0.32	H_8, 6.2; H_{9A}, 12.1
H_{11A}	2.75	−0.69	H_{11B}, 12
H_{11B}	3.17	−0.61	H_8, 1.3; H_{9A}, 2.2; H_{11A}, 12

[a] δ in parts per million relative to Me_4Si in $CDCl_3$. [b] $\Delta\delta = \delta_{CDCl_3} - \delta_{CDCl_3 + CF_3COOD}$. [c] Some J values are detected by decoupling experiments.

the product mixture was treated with sodium *tert*-amylate in *tert*-amyl alcohol (to convert **17** into **8**) and with 5% NaOH in water (to remove the remaining carboethoxy group at the 6-position). This led to the expected product **2** (33%) and the demethylated compound **18**. Treatment of **18** with diazomethane provided **2** quantitatively; the overall yield of the cyclization reaction was thus 71%. The absence of a product with structure **19** points to the preference for ring closure leading to a five-membered D ring, as has also been observed for carbocyclic analogues.[15]

The formation of **8** directly from **7c** on addition of HBr/CH_3COOH reveals a rather novel acid-catalyzed intramolecular C–N bond formation. The HBr/CH_3COOH system should play a role in the selective loss of the 7-carboethoxy group. The following reaction paths are proposed (Scheme IV). By analogy with the known acid-catalyzed addition of urethanes on unsaturated bonds,[16] attack of the 2-NCOOEt group on the intermediate carbenium ion **16a** could generate the quaternary ammonium salt **16b**. These salts are also formed in the acylation of tertiary amines ($R_3N + XCOOEt \rightleftarrows R_3N^+COOEtX^-$). This equilibrium is shifted to the left when the nucleophilic character of the counter ion X^- is more pronounced.[17] Decomposition of the quaternary ammonium salt **16b** in the same way with Br^-[17,18] or acetic acid[17] should lead to **8**. The formation of **17** is then explained by an attack of Br^- at the 8-position of the N-protonated compound **8**.

The structure of the diazagibbane **2** was confirmed by a 360-MHz ^{1}H NMR analysis (Table I). An alternative structure, **19**, was rejected on the basis of the following arguments.

(1) A long-range W coupling of $^4J = 1.3$ Hz was observed between H_8 and H_{11B}. For structure **19** this would imply a coupling along five bonds.

(2) A comparison of the ^{1}H NMR spectra in $CDCl_3$ and C_6D_6 afforded the following ASIS values[19] ($\Delta\delta = \delta_{CDCl_3} - \delta_{C_6D_6}$): H_{9A}, $\Delta\delta = 0.68$ ppm; H_{9B}, $\Delta\delta = 0.22$ ppm. In structure **2**, H_{9A} is more remote from the carbonyl dividing plane compared with H_{9B} which is located very close to this plane. This should give larger Δδ value for H_{9A} than for H_{9B}, as is observed. In structure **19** the position of H_{9A} and H_{9B} with respect to this plane is approximately the same.

(3) On addition of a few drops of CF_3COOD to the $CDCl_3$ solution, a deshielding of 0.69 ppm for H_{11A}, 0.61 ppm for H_{11B}, and 0.67 ppm for H_8 is observed. The other C- and D-ring protons are deshielded about 0.30 ppm (Table I). Large deshielding effects are expected only for the protons α to the protonated nitrogen atom. The observed shifts are therefore fully in agreement with structure **2** preferably protonated at N_7.

(4) A 200-MHz ^{1}H NMR spectrum of the derivative **8**, obtained by acylation of **2** with ethyl chloroformate, further confirmed the gibbane structure of the product **2**. Two protons, H_{5A} and H_{5B}, of the AMX spin system are markedly deshielded by the carbethoxy group at N_6. The "equatorial" proton H_{5A} ($^3J_{H_{5A}-H_{4b}} = 7.6$ Hz) undergoes a downfield shift of more than 1 ppm, whereas the "axial" proton H_{5B} ($^3J_{H_{5B}-H_{4b}} = 11$ Hz) is deshielded by about 0.2 ppm. This difference may be ascribed to the magnetic anisotropy of the carbonyl group at N_6. The coupling constants of the various protons are similar to those measured for product **2**, the conformations of both products being similar. Finally, four-bond coupling constants between H_{11B} and, respectively, H_{9A} and H_8 were measured on a resolution-enhanced spectrum. As both ^4J values are higher than 1 Hz (respectively, 2.2 and 1.3 Hz), and exo position of the 8-CH_3 group can be assumed.

From the above results it can be concluded that the indenone **3** is a suitable precursor in the synthesis of a series of indeno[1,2-*d*]pyridazines. One of these can be easily transformed into a diazagibbane skeleton by using an acid-catalyzed regiospecific cyclization of the allyl derivative **7c**.

Experimental Section

The IR spectra were recorded with a Perkin-Elmer 257 grating spectrophotometer. The ^{1}H NMR (internal Me_4Si) spectra were obtained with Varian XL-100, Varian XL-200, and Bruker WH-360 spectrometers; the ^{13}C NMR spectra were run of a Bruker WP-80 spectrometer. For the mass spectra an AEI MS-12 was used; the ionization energy was 70 eV, and the samples were injected directly at a temperature between 100 and 200 °C. Silica gel for preparative layer and column chromatography was Merck type 60 (70–230 mesh). All melting points are uncorrected. 2,3-bis(bromomethyl)-6-methoxy-1-indenone (**3**) was synthesized according to an earlier described method.[5]

2,3-Bis(*tert*-butoxycarbonyl)-7-methoxy-1,2,3,4-tetrahydroindeno[1,2-*d*]pyridazin-9-one (5a). Compound **3** (5 mmol, 1.73 g) and 50 mmol (11.5 g) of di-*tert*-butyl azodicarboxylate are dissolved in 75 mL of dry acetone. To the ice-cooled solution is added dropwise a solution of 11 mmol (1.66 g) of NaI dissolved in 50 mL of dry acetone. After an additional 15 min, the mixture is filtered, and the filtrate is poured into 100 mL of water. This solution is extracted three times with 100 mL of ether. The extracts are treated with a $Na_2S_2O_3$ solution until the remaining I_2 is removed. The ether layer is dried over $MgSO_4$, filtered, and evaporated in vacuo. Preparative TLC on silica gel with chloroform–hexane (50/50) affords **5a** as a red oil: 0.624 g (1.5 mmol, yield 31%); IR ($CHCl_3$) 1710, 1610 cm^{-1}; NMR (Me_2SO) 1.44 (br s, 18 H, 2 *tert*-butyl), 3.95 (dt, 1 H, $J_{ae} = 17$ Hz, $J_{aE} = 3.25$ Hz, $J_{aA} = 3.5$ Hz, 4-CH_a), 4.30 (dt, 1 H, $J_{AE} = 19$ Hz, $J_{aA} = 3.5$ Hz, $J_{eA} = 3.2$ Hz, 1-CH_A), 4.37 (dd, 1 H, $J_{ae} = 17$ Hz, $J_{eA} = 3.25$ Hz, $J_{eE} = 0$ Hz, 4-CH_e), 4.74 (dd, 1, $J_{AE} = 19$ Hz, $J_{aE} = 3.25$ Hz, $J_{eE} = 0$ Hz, 1-CH_E), 6.87 (dd, 1 H, $J_o = 8$ Hz, $J_m = 2$ Hz, 6-H), 6.96 (d, 1 H, $J_m = 2$ Hz, 8-H), 7.02 (d, 1 H, $J_o =$ Hz, 2-H); mass spectrum, *m/e* (relative intensity) 416 (7), 316 (4), 304 (20), 287 (12), 260 (100), 216 (23), 215 (17), 188 (6), 186 (38); calcd for M^+ *m/e* 416.1947, found *m/e* 416.1943.

2,3-Dicarbethoxy-7-methoxy-1,2,3,4-tetrahydroindeno[1,2-*d*]pyridazin-9-one (5b). Compound **3** (5 mmol, 1.73 g) and 25 mmol (4.15 g) of diethyl azodicarboxylate are dissolved in 50

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(19) Williams, D. H.; Bhacca, N. S. *Tetrahedron* **1965**, *21*, 2021.

mL of dry acetone. To the ice-colled solution is added dropwise 11 mmol (1.66 g) of NaI dissolved in 40 mL of dry acetone. After an additional 15 min, the mixture is filtered, and the filtrate is concentrated in vacuo. The excess of diethyl azodicarboxylate is removed by three extractions of the oily residue with 100 mL of hexane. The residue is dissolved in ether and treated with a $Na_2S_2O_3$ solution until the remaining I_2 is removed, and then the solution is washed with water. The ether layer is dried over $MgSO_4$, filtered, and evaporated in vacuo. Recrystallization from benzene–pentane (20/80) gives orange red crystals of **5b**: 1.56 g (4.35 mmol, 87%); mp 112 °C; IR ($CHCl_3$) 1715, 1610 cm^{-1}; NMR ($CDCl_3$) δ 1.26 and 1.28 (2 t, 3 H each, 2 OCH_2CH_3), 3.80 (s, 3 H, 7-OCH_3), 4.20 and 4.22 (2 q, 2 H each, 2 OCH_2CH_3), 4.00–4.38 and 4.60–5.10 (hidden absorption and m, 2 H each, 1- and 4-CH_2), 6.75 (dd, 1 H, J_o = 8 Hz, J_m = 2 Hz, 6-H), 6.90 (d, 1 H, J_o = 8 Hz, 5-H), 7.06 (d, 1 H, J_m = 2 Hz, 8-H); mass spectrum, *m/e* (relative intensity) 360 (96), 288 (55), 287 (63), 214 (56), 186 (100); calcd for M^+ *m/e* 360.1321, found *m/e* 360.1315. Anal. Calcd for $C_{18}H_{20}N_2O_6$: C, 59.99; H, 5.59; N, 7.77. Found: C, 60.17; H, 5.61; N, 7.62.

2,3-Dicarbethoxy-7-methoxy-1,2,3,4,4a,9a-hexahydroindeno[1,2-*d*]pyridazin-9-one (6). Compound **5b** (20 mmol, 7.2 g) is dissolved in 50 mL of ethyl acetate. To the solution is added 1 g of Pd (10% on $CaCO_3$), and the mixture is shaken for 12 h in a Parr apparatus (3 atm) at room temperature. The mixture is then filtered and evaporated in vacuo. Purification by silica gel column chromatography with benzene–ethyl acetate (90/10) affords 13.4 mmol (4.85 g, 67%) of **6**. Recrystallization from benzene–pentane gives white crystals of **6**: mp 110 °C; IR ($CHCl_3$) 1720, 1615 cm^{-1}; NMR ($CDCl_3$) δ 1.5 (2 t, 3 H each, 2 OCH_2CH_3), 3.86 (s, 3 H, 7-OCH_3), 4.3 (2 q, 2 H each, 2 OCH_2CH_3), 2.4–5.1 (m, 6 H, 1-CH_2, 4-CH_2, 1a-H, 4a-H), 7.10–7.50 (m, 3 H, 5-H, 6-H, 8-H); mass spectrum, *m/e* (relative intensity) 362 (76), 290 (84), 289 (46) 218 (10) 217 (48), 188 (21) 174 (100); calcd for M^+ *m/e* 362.1477, found *m/e* 362.1468. Anal. Calcd for $C_{18}H_{22}N_2O_4$: C, 59.66; H, 6.12; N, 7.73. Found: C, 59.77; H, 6.25; N, 7.60.

9a-(Carbethoxymethyl)-2,3-dicarbethoxy-7-methoxy-1,2,3,4,4a,9a-hexahydroindeno[1,2-*d*]pyridazin-9-one (7a). To a solution of 10 mmol (3.62 g) of **6** and 30 mmol (5.01 g) of ethyl bromoacetate in 70 mL of dry benzene is added 11 mmol (0.270 g) of NaH. The mixture is stirred for 12 h at room temperature and then treated with dry ethanol to remove the excess of NaH. The solution is extracted two times with 20 mL of water; the benzene layer is dried over $MgSO_4$ and evaporated in vacuo. Silica gel column chromatography with benzene–ethyl acetate (90/10) affords **7a** as a colorless oil: 4.03 g (9 mmol, 90%); IR ($CHCl_3$) 1725, 1615 cm^{-1}; NMR ($CDCl_3$) δ 1.00–1.40 (m, 9 H, 3 OCH_2CH_3), 2.80 and 3.1 (2 d, 1 H each, J_{AB} = 16 Hz, 9a-CH_2COOEt), 2.5–4.8 (m, 5 H, 1-CH_2, 4-CH_2, 4a-H) 3.78 (s, 3 H, 7-OCH_3), 3.8–4.24 (m, 6 H, 3 OCH_2CH_3), 7.00–7.40 (m, 3 H, 5-H, 6–H, 8-H); mass spectrum, *m/e* (relative intensity) 448 (100), 403 (36), 402 (25), 376 (43), 375 (16), 361 (26), 348 (8), 303 (8), 274 (34), 260 (96); calcd for M^+ *m/e* 448.1845, found *m/e* 448.1838.

9a-(Carboxymethyl)-2,3-dicarbethoxy-7-methoxy-1,2,3,4,4a,9a-hexahydroindeno[1,2-*d*]pyridazin-9-one (7b). Compound **7a** (1 mmol, 0.448 g) and 10 mmol (0.4 g) of NaOH are dissolved in 15 mL of ice-cooled methanol. The solution is stirred for 1 h and filtered. The white precipitate is dissolved in water, and the solution is acidified with a 10% HCl solution to pH 3. The mixture is extracted three times with 50 mL of CH_2Cl_2, and the extracts are evaporated in vacuo. Preparative TLC on silica gel with chloroform–methanol (90/10) affords **7b** as a colorless oil: 0.399 g (0.95 mmol, 95%); IR ($CHCl_3$) 3200–2600, 1715, 1610 cm^{-1}; NMR ($CDCl_3$) δ 1.00–1.40 (m, 6 H, 2 OCH_2CH_3), 2.84 and 3.04 (2 d, 1 H each, J_{AB} = 16 Hz, 9a-CH_2COOH), 2.5–5.00 (m, 5 H, 1-CH_2, 4-CH_2, 4a-H), 3.80 (s, 3 H, 7-OCH_3), 3.8–4.30 (m, 4 H, 2 OCH_3), 7.05–7.45 (m, 3 H, 5-H, 6-H, 8-H), 9.85 (br s, 1 H, COOH); mass spectrum, *m/e* (relative intensity) 420 (100), 375 (7), 361 (7), 348 (35), 347 (83), 303 (60), 289 (27), 275 (17).

9a-(Carboxymethyl)-7-methoxy-1,2,3,4,4a,9a-hexahydroindeno[1,2-*d*]pyridazin-9-one (13). Compound **7a** (5 mmol, 2.24 g) and 50 mmol (2 g) of NaOH are dissolved in 30 mL of methanol–water (90/10). The solution is degassed three times. After being refluxed for 24 h under a N_2 atmosphere, the mixture is cooled in an ice bath. The solution is acidified with 40 mL of a 10% HCl solution and extracted three times with 30 mL of CH_2Cl_2. The water layer is evaporated in vacuo, leaving a product which is considered to be the HCl salt of **13**. The structure of **13** could not be ascertained as oxidation occurred (*m/e* of the decomposition product equals *m/e* of **13** minus 2) on treatment of the HCl salt with base. When the salt is stirred for 2 h in a solution of 10 mmol (1.08 g) of ethyl chloroformate in 25 mL of $CHCl_3$ the acid, **7b** is obtained (yield 65%).

9a-Allyl-2,3-dicarbethoxy-7-methoxy-1,2,3,4,4a,9a-hexahydroindeno[1,2-*d*]pyridazin-9-one (7c). Compound **6** (10 mmol, 3.62 g) and 30 mmol (3.63 g) of freshly distilled allyl bromide are dissolved in 70 mL of dry benzene. NaH (11 mmol, 0.270g) is added, and the mixture is stirred for 12 h at room temperature. After completion of the reaction, the excess NaH is removed by treatment with dry ethanol. The solution is washed two times with 20 mL of water, and the benzene layer is dried over $MgSO_4$ and evaporated in vacuo. Silica gel column chromatography of the residue with benzene–ethyl acetate (90/10) affords **7c** as a colorless oil: 3.65 g 9.1 mmol, 91%); IR ($CHCl_3$) 1725 cm^{-1}; NMR ($CDCl_3$) δ 1.0–1.33 (m, 6 H, two OCH_2CH_3), 2.10–3.80 and 3.8–4.9 (m and hidden absorption, 7 H, pyridazine ring protons and 9a-$CH_2CH{=}CH_2$), 3.82 (s, 3 H, 7-OCH_3), 3.82–4.32 (m, 4 H, 2 OCH_2CH_3), 5.04 (d, 1 H, J_{AC} = 9 Hz, H_C), 5.10 (d, 1 H, J_{AB} = 16 Hz, H_B) 5.28–5.80 (m, 1 H, H_A), 7.10–7.52 (m, 3 H, 5-H, 6-H, 8-H); mass spectrum, *m/e* (relative intensity) 402 (100), 361 (11), 357 (4), 330 (57), 329 (67), 289 (41), 285 (21), 257 (19), 186 (26); calcd for M^+ *m/e* 402.1790, found *m/e* 402.1786.

9a-(Acetylmethyl)-2,3-dicarbethoxy-7-methoxy-1,2,3,4,4a,9a-hexahydroindeno[1,2-*d*]pyridazin-9-one (7d). Compound **7c** (10 mmol, 4.02 g) is dissolved in a mixture of 8 mL of dimethylformamide and 42 mL of water. To the solution are added 1 mmol (0.177 g) of $PdCl_2$ and 1 mmol (0.14 g) of Cu Cl_2, and the slurry is stirred for 12 h at 60 °C under an O_2 atmosphere. The mixture is filtered, and the filtrate is extracted three times with 20 mL of CH_2Cl_2. The extracts are concentrated in vacuo. Silica gel column chromatography of the residues with benzene–ethyl acetate (85/15) affords 7.4 mmol (3.09 g, 74%) of the ketone **7d**. Recrystallization from benzene–hexane gives white crystals: mp 153 °C; IR ($CHCl_3$) 1710 cm^{-1}; NMR ($CDCl_3$) δ 1.00–1.40 (m, 6 H, 2 OCH_2CH_3), 2.18 (s, 3 H, $COCH_3$), 2.6–5.00 (m and hidden absorption, 7 H, pyridazine ring protons and 9a-CH_2COCH_3), 3.84 (s, 3 H, 7-OCH_3), 3.90–4.30 (m, 4 H, 2 OCH_2CH_3), 7.22–7.60 (m, 3 H, 5-H, 6-H, 8-H); mass spectrum, *m/e* (relative intensity) 418 (72), 361 (55), 360 (37), 346 (34), 345 (40), 288 (77), 244 (36), 230 (45), 187 (100); calcd for M^+ *m/e* 418.1739, found *m/e* 418.1736. Anal. Calcd for $C_{21}H_{26}N_2O_7$: C, 60.28; H, 6.26; N, 6.69. Found: C, 60.41; H, 6.19; N, 6.77.

Monodecarboxylated Products 15a,b. Compound **7d** (2.5 mmol, 1.04 g) is dissolved in 10 mL of acetic acid, and 10 mL of a 10% HCl solution in water is added. The mixture is refluxed for 12 h under a N_2 atmosphere. The solution is cooled in an ice bath and treated with a Na_2CO_3 to pH 7. The solution is extracted three times with 30 mL of CH_2Cl_2, and the extracts are evaporated in vacuo. Preparative TLC on silica gel with benzene–ethyl acetate (75/25) affords 1.9 mmol (0.657 g, 76%) of a mixture of **15a** and **15b**. The products **15a** and **15b** are not stable and slowly decompose: IR ($CHCl_3$) 1720 cm^{-1}; NMR ($CDCl_3$) 1.20–1.40 (m, 3 H, OCH_2CH_3), 2.16 (s, 3 H, $COCH_3$), 2.8–4.85 (m, 7 H, pyridazine ring protons and 9a-CH_2COCH_3), 3.80 (s, 3 H, 7-OCH_3), 4.00–4.40 (m, 2 H, OCH_2CH_3), 7.20–7.50 (m, 3 H, 5-H, 8-H); mass spectrum, *m/e* (relative intensity) 346 (29), 331 (5), 274 (23), 272 (7), 186 (100).

6,7-Diaza-2-methoxy-8-methylgibban-10-one (2). Compound **7c** (2 mmol, 0.804 g) is dissolved in a 40% HBr solution in glacial acetic acid (20 mL), and the mixture is stirred for 12 h at room temperature under a N_2 atmosphere. After completion of the reaction, 30 mL of water is added, and the mixture is extracted three times with 50 mL of CH_2Cl_2. The extracts are dried over $MgSO_4$ and evaporated in vacuo. The residue is dried in vacuo for 24 h and is then dissolved in 15 mL of dry *tert*-amyl alcohol. To the solution is added 2 mmol (0.049 g) of NaH, and the mixture is stirred for 10 h at room temperature under a N_2 atmosphere. The mixture is cooled in an ice bath and is treated dropwise with a 5% NaOH solution to pH 12. After repeated (four times) extractions with 50 mL of CH_2Cl_2, the extracts are evaporated in vacuo, and the residue is purified by preparative TLC on silica

gel with chloroform–acetonitrile (70:30). This affords 0.66 mmol (0.170 g, 33%) of **2** and 0.76 mmol (0.185 g, 38%) of **18**. Additional treatment of **18** with an equivalent amount of CH_2N_2 in dry ether affords quantitatively the product **2**: IR ($CHCl_3$) 1705, 1620 cm^{-1}; NMR ($CDCl_3$, 360 MHz; for the spectral data of the C- and D-ring protons see Table I) δ 3.85 (s, 3 H, 2-OCH_3), 4.00–4.50 (br s, 1 H, NH), 7.18–7.27 (m, 3 H, 1-H, 3-H, 4-H); mass spectrum, *m/e* (relative intensity) 258 (100), 243 (3), 230 (24), 216 (9), 215 (6); calcd for M^+ *m/e* 258.1368, found *m/e* 258.1368.

6-Carbethoxy-6,7-diaza-2-methoxy-8-methylgibban-10-one (8). Compound **2** (1 mmol, 0.258 g), 1 mmol (0.108 g) of ClCOOEt, and 1 mmol (0.101 g) of NEt_3 are dissolved in 15 mL of dry CH_2Cl_2. The solution is stirred for 3 h at room temperature. The mixture is filtered, and the filtrate is evaporated in vacuo. The residue is purified by preparative TLC on silica gel with chloroform–acetonitrtile (85/15), which affords 0.90 mmol (0.297 g) of **8**. Recrystallization from benzene–hexane gives white crystals: mp 149 °C; IR ($CHCl_3$) 1725 cm^{-1}; NMR ($CDCl_3$, 200 MHz) δ 1.35 (t, 3 H, OCH_2CH_3), 1.42 (d, 3 H, 8-CH_3), 1.98 (dd, 1 H, $J_{9_A9_B}$ = 12 Hz, J_{9_B8} = 7.2 Hz, 9_B-H), 2.12 (ddd, 1 H, $J_{9_A9_B}$ = 12 Hz, J_{9_A8} = 7.5 Hz, $J_{9_A11_B}$ = 2.2 Hz, 9_A-H), 2.97 (t, 1 H, $J_{5_B5_A}$ = 11.5 Hz, J_{5_B4b} = 11 Hz, 5_B-H), 2.97 (d, 1 H, $J_{11_A11_B}$ = 12.5 Hz, 11_A-H), 3.10 (dt, 1 H, $J_{11_B11_A}$ = 12.5 Hz, $J_{11_B9_A}$ = 2.2 Hz, J_{11_B8} = 1.3 Hz, 11_B-H), 3.30 (m, 1 H, 8-H), 3.32 (dd, 1 H, J_{4b5_B} = 11 Hz, J_{4b5_A} = 7.6 Hz, 4b-H), 3.72 (s, 3 H, 2-OCH_3), 4.16 and 4.32 (**ABX**$_3$ pattern, 2 H, J_{AB} = 11 Hz, OCH_2CH_3), 4.51 (dd, 1 H, $J_{5_A5_B}$ = 11.5 Hz, J_{5_A4b} = 7.6 Hz, 5_A-H), 7.2–7.5 (m, 3 H, 1-H, 3-H, 4-H); ^{13}C NMR ($CDCl_3$, 20.1 MHz) 14.9 (OCH_2CH_3), 21.6 (8-CH_3), 41.7 (5-CH_2), 43.2 (9-CH_2), 45.4 (4b-CH), 55.2 (11-CH_2), 55.9 (2-OCH_3), 58 (9a-C), 62.1 (OCH_2CH_3), 68.9 (8-CH), 105.8 (1-CH), 125 (3-CH), 126.4 (4-CH), 138.4 (4a-C), 145.6 (10a-C), 155.8 (6-NCO), 160.7 (2-C), 204 (10-CO); mass spectrum, *m/e* (relative intensity) 330 (63), 257 (10), 215 (22), 214 (24), 200 (100); calcd for M^+ *m/e* 330.1579, found *m/e* 330.1581.

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Registry No. 2, 81097-50-9; **3**, 55288-51-2; **5a**, 81097-51-0; **5b**, 81097-52-1; **6**, 81097-53-2; **7a**, 81120-70-9; **7b**, 81097-54-3; **7c**, 81097-55-4; **7d**, 81097-56-5; **8**, 81097-57-6; **13**·HCl, 81120-71-0; **15a**, 81097-58-7; **15b**, 81097-59-8; **18**, 81097-60-1; di-*tert*-butyl azodicarboxylate, 870-50-8; diethyl azodicarboxylate, 1972-28-7; ethyl bromoacetate, 105-36-2; allyl bromide, 106-95-6; ethyl carbonochloridate, 541-41-3.

Rearrangements in the Halogenation of Tetraalkylethylenes with *N*-Halosuccinimides and *tert*-Butyl Hypochlorite

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The reaction of *N*-halosuccinimides and *tert*-butyl hypochlorite with tetraalkylethylenes has been investigated. Halo-cation addition to the double bond occurs in a fast reaction, followed by abstraction of an allylic proton, resulting in a double bond shift. In tetraalkylethylenes lacking for structural reasons the possibility of a double bond shift, a homoallylic halogenation occurs to produce in the case of adamantylideneadamantane the 4(e)-halo derivative. The electrophilic halogenation of tetraalkylethylenes with *N*-halosuccinimides and *tert*-butyl hypochlorite is compared with the well-known radical-chain allylic halogenation of mono-, di-, and trialkylethylenes with these reagents and the reaction of chlorine with olefins. The halogenations described here are strongly reminiscent of the singlet oxygen ene reaction and the causes of this resemblance are discussed.

In this paper we describe the remarkable halogenation[1,2] of tetraalkylethylenes with *N*-halosuccinimides and *tert*-butyl hypochlorite. These reagents are well-known to give allylic halogenation in a radical-chain reaction.[3] We have found that with tetraalkylethylenes these reagents react cleanly in an ionic manner to give products that deviate in structure from the normally expected halogenation products of *N*-halosuccinimides and *tert*-butyl hypochlorite with mono-, di-, and trialkylethylenes. These conclusions were derived from the observations made during the halogenation of adamantylideneadamantane (**1**). We have found that **1** reacts with chlorine and benzenesulfenyl chloride to give 4(e)-chloroadamantylideneadamantane (**2**) via an ionic pathway without any addition to the double bond.[4,5] In an attempt to carry out radical chlorination, **1** was treated with 1 equiv of *N*-chlorosuccinimide (NCS) in boiling CCl_4 containing a radical initiator. To our surprise the sole product was **2**. When this reaction was repeated in CH_2Cl_2 in the absence of radical initiators at room temperature, a rapid (<5 min) reaction occurred and **2** was formed in quantitative yield. The reaction takes place also in CCl_4, $CHCl_3$, or CH_2Cl_2/CH_3COOH and the rate increases with increasing solvent polarity.[6] The same product **2** was obtained when

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