Synthesis and Reactions of Some 5-Hydroxypyridazinium Hydroxide Inner Salts from 3(2*H*)-Furanones

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The synthesis of anhydro-5-hydroxypyridazinium hydroxide derivatives is presented. It is based on the reaction of 2-acetoxy-3(2*H*)-furanones with monosubstituted hydrazines. All structures are supported spectroscopically and from product studies of the alkylation reaction of the N-unsubstituted 1,4-dihydropyridazin-4-one **2a**. Sodium borohydride reduction of these pyradizinium betaines provides an easy entry to new 5-hydroxy-1,6-dihydropyridazine derivatives, which were alkylated, under basic conditions, to give 1,2-disubstituted 1,2,3,4-tetrahydropyridazin-4-one derivatives.

The ring transformations of 3(2*H*)-furanones with nucleophiles are the subject of studies in this laboratory. Previously, we demonstrated that the reaction of hydrazine hydrate with 2-acetoxy-3(2*H*)-furanones **1** produced, as main products, the 3,6-substituted-5-(ethoxycarbonyl)-4(1*H*)-pyridazinones **2**.[1] We have now investigated the reaction of the compounds **1** with unsymmetrical hydrazines which led to a novel, convenient synthesis of the anhydro bases of 1-alkyl-(or -phenyl)-3-aryl-4-(ethoxycarbonyl)-5-hydroxy-6-methylpyridazinium hydroxides **3**. Only two examples of this heterocyclic nitrogen ring system have been reported.[2,3]

Results and Discussion

Reaction of monosubstituted hydrazines with furanones **1** may result in the formation of several types of products as depicted in Scheme I. Phenylhydrazine gave the betaines **3a–c** in high yields (70–85%), in ether solution at room temperature, after a single filtration, along with a minor amount of pyrazole **4** (R = Ph) (<5%). Methylhydrazine and benzylhydrazine led to isomeric mixtures as summarized in Table I. Various attempts were made to improve the yield of these reactions through the use of different solvents. The product distribution was found to be dependent on the reaction solvent (Table I). In all cases, in acetonitrile solution, the anhydro bases could be readily removed from the product mixtures. The betaines obtained are described in Table II.

The reaction products can be explained by assuming a competing process via ring-opening and ring-closing sequences. The ratio (**3** + **4**)/(**5** + **6**) reflects the relative nucleophilicities of the two hydrazine nitrogen atoms toward the C-5 position of the furanone ring. The cyclodehydration of the open intermediate can occur in two possible directions to form a five-membered ring or a six-membered ring. By analogy to our previous study, one would expect the predominant formation of the six-membered ring with the acetoxy leaving group.[1] The present results essentially confirm this trend in path a. However, in path b, we see that five-membered-ring formation seriously interferes with that of the pyridazinones **5**. The formation of compounds **5** presumably requires the loss of acetate ion prior to the nucleophilic attack at C-2; the inductive effect of the substituent on nitrogen could stabilize the dipolar intermediate and thereby decrease the rate of proton transfer to oxygen, with a resultant increase in the relative reactivity of the carbonyl function. This interpretation can explain the improved yield of **5d** when the protic solvent alcohol was used.

Proofs of structure for compounds **3** were based firmly on their NMR, IR, and UV spectral behavior, elemental analyses, and chemical reactions.[4] The more obvious synthetic approach begins with an alkylation reaction of the preformed pyridazinone **2a**. The regiospecific conversion of the 4-chloropyridazine **7** by methoxide would

Table I. Reaction of 1a with Methylhydrazine and Benzylhydrazine[a]

solvent	substituents R	substituents Ar	% 3	% 4	% 5	% 6	% overall yield
CH_3CN	CH_3	C_6H_5	44		6	50	80
EtOH	CH_3	C_6H_5	35		35	30	74
CH_3CN	$C_6H_5CH_2$	C_6H_5	93	4		3	62
EtOH	$C_6H_5CH_2$	C_6H_5	82	6	4	8	45

[a] Product distribution in mole percent as estimated from the NMR spectra.

Table II. Anhydro-5-hydroxypyridazinium Hydroxide Derivatives 3a-g[a]

compd	R	Ar	mp, °C	% yield
3a	Ph	Ph	185[b]	70[e]
3b	Ph	4-CH_3Ph	218[b]	85[e]
3c	Ph	4-CH_3OPh	200[b]	85[e]
3d	CH_3	Ph	191[c]	36[f]
3e	CH_3	4-CH_3Ph	163[c]	28[f]
3f	CH_3	4-CH_3OPh	148[c]	20[f]
3g	CH_2Ph	Ph	110[d]	45[f]

[a] Satisfactory analytical data (±0.3%) for C, H, and N were reported for all compounds in this table. [b] Recrystallization solvent was ethanol. [c] Recrystallization solvent was water. [d] Recrystallization solvent was acetonitrile. [e] Reaction in ether. [f] Reaction in acetonitrile.

Table III. Alkylation of 2a

alkylating agent	base/solvent	% 3	% 5	% overall yield
CH_3I	$C_2H_5O^-/C_2H_5OH$	29	71	30
$(CH_3)_2SO_4$	$C_2H_5O^-/C_2H_5OH$	37	63	44
$(CH_3)_2SO_4$	K_2CO_3/Me_2SO	40	60	66
$C_6H_5CH_2Cl$	K_2CO_3/Me_2SO	28	62	57

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(2) Eichenberger K.; Romestsch, R.; Druey, J. *Helv. Chim. Acta* **1956**, *39*, 1755.
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(4) Pyrazoles **4a,g** and **6d,g** (Ar = Ph, R = CH_3 or CH_2Ph) are already described: Gelin, S.; Gelin, R.; Hartmann, D. *J. Org. Chem.* **1978**, *43*, 2665. According to our previous results, pyrazole **4a** (Ar = Ph, R = Ph) was prepared by action of phenylhydrazine with 4-(ethoxycarbonyl)-2-methoxy-2-methyl-5-phenyl-3(2*H*)-furanone: yield 43%; mp 132 °C; UV λ_{max} (EtOH) 239 nm (ϵ 20 100).

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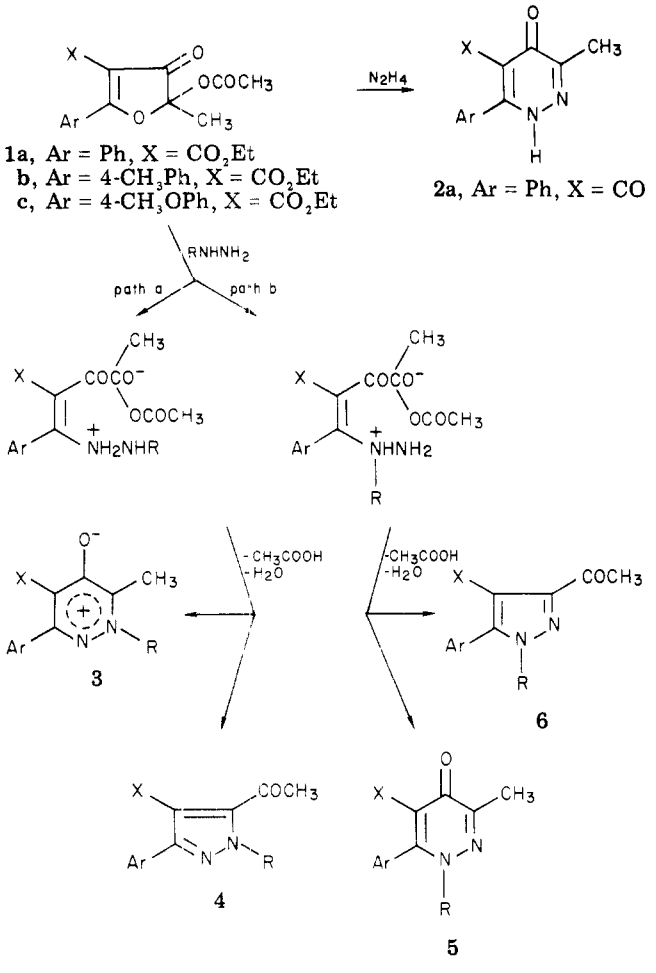
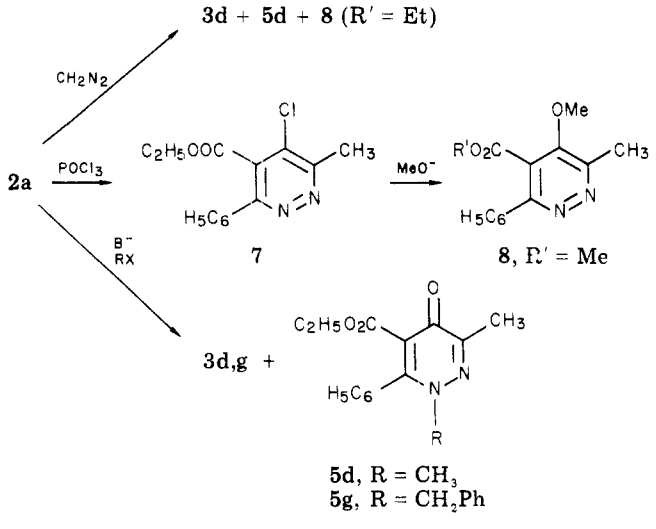
Scheme I



Scheme II



generate the 4-methoxypyridazine 8. On the other hand, methylation (or benzylation) of **2a**, under basic conditions, gave the *N*-alkyl derivatives **3d** (or **3g**) and **5d** (or **5g**) (Scheme II). With various base/solvent systems the nature of the medium and the base was not critical; the product distribution was chiefly affected by the nature of the alkylating agents (see Table III).

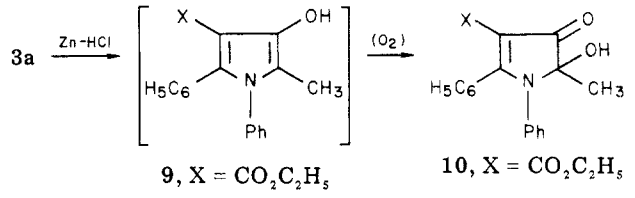
Both crystalline compounds **3d,g** and **5d,g** were isolated in the pure state by column chromatography on silica gel. The dipolar structure is proposed for the more polar *N*-alkyl derivatives. Determination of the position of the *N*-alkyl group in the isomeric compounds **3** and **5** was also

Table IV. *N*-Alkyl-1,4-dihydropyridazin-4-ones from Alkylation of **2a**[a]

compd	R	Ar	mp, °C	% yield[d]
5d	CH_3	Ph	158[b]	35
5g	CH_2Ph	Ph	153[c]	33

[a] Satisfactory analytical data (±0.2%) for C, H, and N were reported for these compounds. [b] Crystallization solvent was hexane-ethyl acetate (1:1). [c] Crystallization solvent was hexane-ethyl acetate (7:3). [d] With K_2CO_3/Me_2SO.

Scheme III



indicated by spectral comparison of each pair of isomers. In the NMR spectra, the chemical shift difference between the *N*-methyl groups is remarkably large. The *N*-methyl protons in compound **5d** are observed at higher field (δ 3.57) than those of the corresponding anhydro base **3d** (δ 4.26). This difference (0.69 ppm) between the two values is more important than that of the isomeric *N*-1- and *N*-2-methylcinnolones (0.18–0.28 ppm).[5,6] An upfield shift was also observed in going from **3g** to **5g** for the methylene protons of the *N*-benzyl groups (0.58 ppm). These differences reflect the greater polarization of the anhydro base than that of the 1-alkyl-1,4-dihydropyridazin-4-one (see Table V). The ultraviolet spectra are consistent with the assigned structures. Compounds **5** show a band at about 280 nm, according to the absorption of the parent N-unsubstituted compound **2a**;[1] in contrast, the zwitterions **3** exhibited a band at a longer wavelength (323–328 nm). A hypsochromic shift (33 nm) was also observed in going from 1-methyl-1,4-dihydropyridazin-4-one to the anhydro-1-methyl-5-hydroxypyridazinium hydroxide.[2] The IR spectra of compounds **3** showed an intense band near 1590–1600 cm^{-1}, whereas the isomeric pyridazinones **5** showed a carbonyl stretching (C-4) at 1615 cm^{-1} (see Table V).

Treatment of **2a** with ethereal diazomethane yielded a mixture of **3d**, **5d**, and **8** (with $CO_2C_2H_5$) in a ratio 37:42:21 as determined from its NMR spectrum (Scheme II).

The UV and IR spectra of compounds **3a–c** (R = Ph) are similar to those found for compounds **3d,g**. Chemical support for structure **3a** was also obtained by its N–N bond cleavage by zinc–hydrochloric acid. The reaction afforded a compound **10** identical with the 5-hydroxy-1,5-diphenyl-3-(ethoxycarbonyl)-6-methyl-4-oxo-4,5-dihydropyrrole produced by action of the aniline upon the furanone **1a**.[7] Reduction releases the unsubstituted nitrogen as ammonium chloride[8] giving the 3-hydroxypyrrole **9** [as determined by NMR: δ 2.02 (s, C-6 CH_3), 7.80 (broad, OH)], which rapidly autoxidized in air[7,9] (Scheme III).

Sodium borohydride reduction of compounds **3a**, **3d**, and **3g** afforded the dihydro compounds **11a**, **11d**, and **11g**, a class of nitrogen heterocycles hitherto unknown (Scheme IV).

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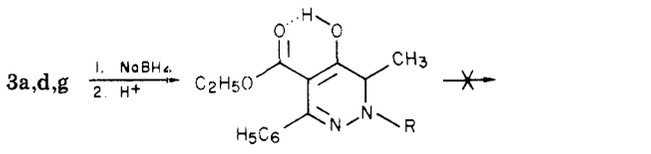
Table V. Pertinent Spectral Data of Compounds 3d,g, 5d,g, and 8

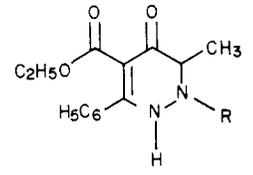
compd	R	^{1}H NMR δ ($CDCl_3$)	IR ν, cm^{-1} ($CHCl_3$)	UV λ_{max}, nm (ε) (ethanol)
3d	CH_3	2.66 (s, 3 H, C-6, CH_3), 4.26 (s, 3 H, NCH_3)	1735, 1595	332 (6650), 247 (14200), 209 (14550)
3g	CH_2Ph	2.62 (s, 3 H, C-6, CH_3), 5.70 (s, 2 H, NCH_2)	1735, 1600	328 (6900), 248 (17000), 216 (13200)
5d	CH_3	2.37 (s, 3 H, C-3, CH_3), 3.57 (s, 3 H, NCH_3)	1740, 1615	280 (13400), 233 (5550), 210 (8900)
5g	CH_2Ph	2.45 (s, 3 H, C-3, CH_3), 5.12 (s, 2 H, NCH_2)	1740, 1615	282 (17200), 215 (11900)
8[a]		2.77 (s, 3 H, C-3, CH_3), 4.08 (s, 3 H, OCH_3)[b]	1745	232 (14300)

[a] 8 with $COOCH_3$. [b] These values are similar to those found for 8 with $COOC_2H_5$ from the isomeric mixture of the diazomethane alkylation of 2a: δ 2.77 (C-3, CH_3), 4.10 (OCH_3).

Scheme IV

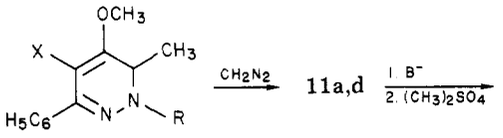


A
11a, R = Ph
d, R = CH_3
g, R = CH_2Ph

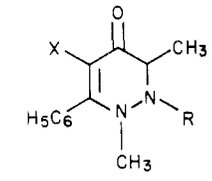


B
11a, R = Ph
d, R = CH_3
g, R = CH_2Ph

Scheme V



13a, R = Ph, X = CO_2Et
d, R = Me, X = CO_2Et



12a, R = Ph, X = CO_2Et
d, R = Me, X = CO_2Et

The structure of compounds **11** was inferred by their spectroscopic properties. For example, the NMR spectra exhibit a doublet for the methyl protons at C-6 and an enolic OH signal intramolecularly hydrogen bonded to the ester carbonyl at δ 12–13. The infrared spectra, in the solid state (KBr) or in solution ($CHCl_3$), showed the absence of a carbonyl ester function attributable to a tautomeric structure such as **11B**. A strong band at 1600–1625 cm^{-1} is characteristic of the stretching of an ester carbonyl group chelated to an enolic hydroxyl. Solid evidence for this assignment was also derived from the comparison of the absorption spectra of compounds **11d** and **11g** (315 nm) with that of **11a** (369 nm). The higher maximum of **11a** indicates the likely presence of a conjugated *N*-Ph group. The great stability of the enol form can be attributed to the extended conjugation of that form.

Surprisingly, we have observed that the NMR signals corresponding to the ethoxycarbonyl methylene groups in compounds **11** showed additional splitting, which indicated magnetic nonequivalence of these methylene protons. Spin decoupling proved that the multiplet centered at about 4 ppm and assigned to the methylene protons of **11a** is coupled to the three-proton triplet at 0.8 ppm. The parameters deduced by spectral analysis are as follows:

Parameters of the ABX_3 Ethyl Group of 11a ($CDCl_3$)

δ(X)	δ(A)	δ(B)	J_{AX}	J_{AB}
0.82	3.90	4.07	± 7 Hz	∓ 10.5 Hz

A more complicated situation is observed in the spectra of compounds **11d** and **11g**. Ester methylene protons and the dihydropyridazine ring proton (C-6) appear as a set of multiplets (14 lines). A quadruplet at δ 3.78 (**11d**) or at δ 3.83 (**11g**) is due to the proton at C-6. The assignment was substantiated by irradiating the signal of the methyl protons at C-6 at 1.25 ppm (**11d**) or at 1.20 ppm (**11g**) and simultaneously collapsing the quadruplet into a singlet. These phenomena can be interpreted in terms of restriction of rotation of the carbethoxy group, possibly due to the phenyl substituent and to the chelation of the hydroxyl group; thus, compounds **13a,d** (O-methylated) do not show this phenomenon. Magnetic nonequivalence of the signals from diastereotopical protons in methylene ester groups has recently received attention.[10-12]

Alkylation of compounds **11** can proceed on either the oxygen or the nitrogen atom. Methylation, under basic conditions, led to selective N-alkylation giving the 1,2-disubstituted 1,2,3,4-tetrahydropyridazin-4-one derivatives **12**. This reaction provides a new entry into this class of compounds of which very few examples have been reported in the chemical literature.[13] Methylation of **11a** with diazomethane afforded the *O*-methyl derivative **13a**, while compound **11d** yielded both isomeric compounds **12d** and **13d** in a ratio 55:45, respectively (Scheme V).

The choice of **12** or **13** as correct structures was supported from their comparative spectral analyses. In the IR spectra, the nonchelated stretching carbonyl ester was observed in each case at its normal position (≃1720 cm^{-1}); while the spectra of the two isomers were different, they were not particularly revealing as to structural assignment. The ultraviolet spectra suggested that their chromophoric systems were different. Comparing the change occurring with the nature of the substituent (R = Ph or CH_3), we can see that the position of the UV maximum is very similar in the compounds **12a** and **12d**. In contrast compound **13a** (R = Ph) shows its principal absorption maximum at a longer wavelength than compound **13d** (R = CH_3). Such a hypsochromic shift is characteristic of a conjugated system. The dissimilarity between the two

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Table VI. Chemical Analyses of Compounds

compd	molecular formula	% calcd			% found		
		C	H	N	C	H	N
3a	$C_{20}H_{18}N_2O_3$	71.84	5.43	8.38	71.78	5.64	8.16
3b	$C_{21}H_{20}N_2O_3$	72.39	5.79	8.04	72.22	5.90	8.05
3c	$C_{21}H_{20}N_2O_4$	69.21	5.53	7.69	69.25	5.45	7.70
3d	$C_{15}H_{16}N_2O_3$	66.16	5.92	10.29	66.24	5.88	10.11
3e	$C_{16}H_{18}N_2O_3$	67.11	6.34	9.78	67.10	6.37	9.98
3f	$C_{16}H_{18}N_2O_4$	63.56	6.00	9.27	63.28	6.03	9.27
3g	$C_{21}H_{20}N_2O_3$	72.39	5.79	8.04	72.41	5.79	8.09
5d	$C_{15}H_{16}N_2O_3$	66.16	5.92	10.29	66.16	5.99	10.28
5g	$C_{21}H_{20}N_2O_3$	72.39	5.79	8.04	72.57	5.82	8.01
7	$C_{14}H_{13}N_2ClO_2$[a]	60.76	4.73	10.12	60.65	4.95	10.11
8	$C_{14}H_{14}N_2O_3$	65.10	5.46	10.85	65.40	5.42	10.78
11a	$C_{20}H_{20}N_2O_3$	71.41	5.99	8.33	71.47	6.02	8.27
11d	$C_{15}H_{18}N_2O_3$	65.67	6.61	10.21	65.60	6.50	9.96
11g	$C_{21}H_{22}N_2O_3$	71.98	6.33	8.00	72.15	6.43	8.02
12a	$C_{21}H_{22}N_2O_3$	71.98	6.33	8.00	72.06	6.40	7.97
12d	$C_{16}H_{20}N_2O_3$	66.64	6.99	9.72	66.26	7.04	9.60
13a	$C_{21}H_{22}N_2O_3$	71.98	6.33	8.00	71.91	6.34	7.85
13d	$C_{16}H_{20}N_2O_3$	66.64	6.99	9.72	66.46	7.05	9.43

[a] % Cl Calcd: 12.81. Found: 12.58.

isomers appeared in the NMR signals of their *O*- or *N*-methyl group. The methyl signal at lower field (δ 4.00 for **13a** and δ 3.92 for **13d**) is attributed to the methoxy group, whereas the signal at higher field (δ 3.06 for **12a** and δ 3.33 or 3.38 for **12d**) can be clearly related to the *N*-methyl group.

Compounds **3** do not appear useful for the synthesis of heterocycles via 1,3-dipolar cycloadditions. Treatment with dimethyl acetylenedicarboxylate under forcing conditions gave tarry material. Thiation with phosphorus pentasulfide failed.

Experimental Section

Melting points were determined on a Kofler hot plate. Infrared and ultraviolet spectra were recorded with Beckman Model Acculab 2 and DB spectrophotometers. ^{1}H NMR spectra were run in $CDCl_3$ on Varian A-60 and Varian HA-100 spectrometers with Me_4Si as an internal standard. Elemental analyses were performed by Microanalytical Laboratory, Centre National de la Recherche Scientifique, Villeurbanne, France.

Compounds **1**[7] and **2a**[1] were prepared as previously described.

General Preparation of Anhydro-5-hydroxy-1-phenylpyridazinium Hydroxides (3a–c). To a solution of **1** (0.01 mol) in 50 mL of ether was added 1.1 g (0.012 mol) of phenylhydrazine. This solution was allowed to stand for 2 h to give white crystals. The crystals were filtered, washed with ether (2 × 5 mL), and recrystallized to yield pure compounds **3a–c**. Yields and melting points are given in Table II.

General Preparation of Anhydro-1-alkyl-5-hydroxypyridazinium Hydroxides (3d–g). To a solution of **1** (0.01 mol) in 20 mL of acetonitrile was slowly added methylhydrazine (0.46 g, 0.01 mol) or benzylhydrazine (1.23 g, 0.01 mol). The mixture was allowed to stand at room temperature for 3 h and then the solvent was removed by rotary evaporation. The resulting residue was kept at 100 °C for 1 h. Trituration of the residue with 50 mL of ether produced a white precipitate which was collected and recrystallized to give **3d–g**. Yields and melting points are given in Table II. Spectroscopic data of **3d** and **3g** are listed in Table V.

General Preparation of 1-Alkyl-5-(ethoxycarbonyl)-3-methyl-6-phenyl-1,4-dihydropyridazin-4-ones (5d,g). A mixture containing 2.58 g (0.01 mol) of **2a**, 1.38 g (0.01 mol) of anhydrous potassium carbonate, and 1.70 g (0.012 mol) of methyl iodide, 1.51 g (0.012 mol) of dimethyl sulfate, or 1.53 g (0.012 mol) of benzyl chloride in 50 mL of dimethyl sulfoxide was stirred at room temperature for 4 h. The reaction mixture was poured into water (75 mL) and extracted with chloroform (5 × 10 mL). The combined extracts were washed with 10 mL of 5% NaOH and 10 mL of water. Drying (Na_2SO_4) and concentrating gave a mixture of isomeric *N*-alkyl compounds **3d** and **5d** or **3g** and **5g**, which were chromatographed on silica gel. Elution with ethyl acetate gave the less polar compounds **5d** or **5g** as white crystalline material; the more polar compounds **3d** or **3g** were then eluted with ethanol. Spectra (IR and NMR) were identical with those of products **3d** and **3g** obtained from **1a** and methylhydrazine or benzylhydrazine. Yields and melting points are given in Tables III and IV. Spectroscopic data are listed in Table V.

4-Chloro-5-(ethoxycarbonyl)-3-methyl-6-phenylpyridazine (7). A solution of **2a** (2.58 g, 0.01 mol) in 20 mL of phosphoryl chloride (0.22 mol) was heated on a steam bath for 1 h and then poured into an ice-cold solution of sodium acetate (30 g) in water (500 mL). The reaction mixture was extracted with benzene (4 × 20 mL), dried (Na_2SO_4), and concentrated in vacuo. Hexane (60 mL) was added to the residue and the mixture was heated to reflux followed by hot filtration; a dark oil separated. The hexane extract was concentrated to 10 mL and allowed to cool, whereupon **7** separated as pale yellow needles (1.8 g, 51%): mp 74 °C; IR ($CHCl_3$) 1750, 1500 cm^{-1}; UV (EtOH) (ϵ) 227 (10 000), 242 nm (12 800); ^{1}H NMR ($CDCl_3$) δ 1.18 (t, 3 H, J = 7 Hz), 2.87 (s, 3 H), 4.43 (q, 2 H, J = 7 Hz), 7.57–8.05 (m, 5 H).

4-Methoxy-5-(methoxycarbonyl)-3-methyl-6-phenylpyridazine (8). A solution of **7** (1.38 g, 5 mmol) in 5 mL of methanol was added to a sodium methoxide solution [from sodium (0.3 g) and methanol (20 mL)]. The mixture was refluxed for 2 h. After evaporation of the solvent and addition of water (10 mL), the solution was extracted with methylene chloride. Rotoevaporation of the solvent and then recrystallization from hexane–ethyl acetate (7:3) gave the product (1.5 g, 58%): mp 97 °C; IR ($CHCl_3$) 1745, 1575 cm^{-1}; UV (EtOH) (ϵ) 232 nm (14 300); ^{1}H NMR ($CDCl_3$) δ 2.77 (s, 3 H), 3.78 (s, 3 H), 4.08 (s, 3 H), 7.62–7.97 (m, 5 H).

3-(Ethoxycarbonyl)-5-hydroxy-5-methyl-1,2-diphenyl-2-pyrrolin-4-one (10). Zinc–Hydrochloric Acid Reduction of 3a. A stirred mixture of **3a** (1.67 g, 5 mmol), zinc dust (2 g, 0.025 g-atom), and acetic acid (20 mL) were refluxed, and then concentrated hydrochloric acid (6 mL) was added in 10 equal portions of 0.6 mL over a period of 3 h. After dilution with 5% $NaHCO_3$, the mixture was extracted with methylene chloride to give an oily residue which was exposed to air in a thin film for 1 week, being converted into solid mass which was washed with ether (30 mL); the solid compound was filtered and recrystallized from acetonitrile to yield (0.34 g, 20%) **10**. The IR and NMR spectra of this compound were identical with the product **10** previously described.[7]

General Preparation of 4-(Ethoxycarbonyl)-5-hydroxy-6-methyl-1-phenyl(or -alkyl)-3-phenyl-1,6-dihydropyridazines (11a,d,g). A mixture containing compounds **3a,d,g** (0.01 mol) and 1.89 g (0.05 mol) of sodium borohydride in 50 mL of isopropyl alcohol was stirred at room temperature for 24 h. The solvent was removed by rotary evaporation. The cooled residue was diluted with ice–water (75 mL), acidified with an excess of 6 N hydrochloric acid, and then extracted with methylene chloride.

The extract was dried and evaporated. The residue was recrystallized to give pure compounds 11.

4-(Ethoxycarbonyl)-5-hydroxy-6-methyl-1,3-diphenyl-1,6-dihydropyridazine (11a): 80%; mp 84 °C (ethanol); IR ($CHCl_3$) 2800–2600, 1655, 1610 cm^{-1}; UV (EtOH) (ϵ) 246 (19400), 304 (8900), 369 nm (5200); ^1H NMR ($CDCl_3$) δ 0.82 (t, 3 H, J = 7 Hz), 1.23 (d, 3 H, J = 7 Hz), 3.75–4.28 (m, 16 lines, 2 H), 4.94 (q, 1 H, J = 7 Hz), 6.76–7.20 (m, 8 H), 12.70 (broad, 1 H).

4-(Ethoxycarbonyl)-5-hydroxy-1,6-dimethyl-3-phenyl-1,6-dihydropyridazine (11d): 65%; mp 123 °C (CH_3CN); IR ($CHCl_3$) 2800–2600, 1650, 1610 cm^{-1}; UV (EtOH) (ϵ) 247 (13100), 307 nm (7400); ^1H NMR ($CDCl_3$) δ 0.86 (t, 3 H, J = 7 Hz), 1.25 (d, 3 H, J = 7 Hz), 3.11 (s, 3 H), 3.78 (q, 1 H, J = 7 Hz), 3.73–4.23 (m, 2 H), 7.16–7.60 (m, 5 H), 12.5 (broad, 1 H).

1-Benzyl-4-(ethoxycarbonyl)-5-hydroxy-6-methyl-3-phenyl-1,6-dihydropyridazine (11g): 50%; mp 117 °C (hexane); IR ($CHCl_3$) 2800–2600, 1640, 1610 cm^{-1}; UV (EtOH) (ϵ) 244 (13800), 310 nm (8500); ^1H NMR ($CDCl_3$) δ 0.83 (t, 3 H, J = 7 Hz), 1.20 (d, 3 H, J = 7 Hz), 3.83 (q, 1 H, J = 7 Hz), 3.75–4.31 (m, 2 H), 4.46 and 4.78 (d, AB, 2 H, J_{AB} = 14.5 Hz), 7.25–7.55 (m, 10 H), 13.0 (broad, 1 H).

General Preparation of 5-(Ethoxycarbonyl)-3-methyl-6-phenyl-1,2-disubstituted-1,2,3,4-tetrahydropyridazin-4-ones (12a and 12d). Dimethyl sulfate (1 mL, 1.35 g, 10.6 mmol) was added to a stirred solution of **11a** or **11d** (5 mmol) in 2 N potassium hydroxide (10 mL, 20 mmol). After 35 min of stirring, the mixture was extracted with methylene chloride (3 × 15 mL). The organic phases were washed with 2 N potassium hydroxide, followed by water, and dried ($MgSO_4$). Evaporation of the solvent afforded the crude compounds which were recrystallized.

5-(Ethoxycarbonyl)-1,3-dimethyl-2,6-diphenyl-1,2,3,4-tetrahydropyridazin-4-one (12a): 50%; mp 128 °C [hexane–ethyl acetate (1:1)]; IR ($CHCl_3$) 1715, 1650, 1600 cm^{-1}; UV (EtOH) (ϵ) 243 (17300), 314 nm (11000); ^1H NMR ($CDCl_3$) δ 0.70 (t, 3 H, J = 7 Hz), 1.50 (d, 3 H, J = 7 Hz), 3.06 (s, 3 H, 3.73 (q, 2 H, J = 7 Hz), 4.18 (q, 1 H, J = 7 Hz), 6.87–7.58 (m, 10 H).

5-(Ethoxycarbonyl)-1,2,3-trimethyl-6-phenyl-1,2,3,4-tetrahydropyridazin-4-one (12d): 49%; mp 187 °C (acetone); IR ($CHCl_3$) 1710, 1625 cm^{-1}; UV (EtOH) (ϵ) 247 (14200), 315 nm (8600); ^1H NMR ($CDCl_3$) δ 0.78 (t, 3 H, J = 7 Hz), 1.50 (d, 3 H, J = 7 Hz), 3.33 (s, 3 H), 3.48 (s, 3 H), 3.78 (q, 1 H, J = 7 Hz), 3.97 (q, 2 H, J = 7 Hz), 7.57 (s, 5 H).

4-(Ethoxycarbonyl)-5-methoxy-6-methyl-1,3-diphenyl-1,6-dihydropyridazine (13a). To a solution of **11a** (1.67 g, 5 mmol) in 5 mL of methanol was added an excess of ethereal diazomethane. After 2 h, TLC indicated complete disappearance of the starting material. Evaporation of the solvent and then recrystallization afforded **13a** (1.12 g, 56%): mp 92 °C (hexane); IR ($CHCl_3$) 1720, 1635 cm^{-1}; UV (EtOH) (ϵ) 247 (22600), 290 (5150), 373 nm (10600); ^1H NMR ($CDCl_3$) δ 0.85 (t, 3 H, J = 7 Hz), 1.23 (d, 3 H, J = 7 Hz), 4.00 (s, 3 H), 4.03 (q, 2 H, J = 7 Hz), 5.08 (q, 1 H, J = 7 Hz), 6.97–8.00 (m, 10 H).

4-(Ethoxycarbonyl)-5-methoxy-1,6-dimethyl-3-phenyl-1,6-dihydropyridazine (13d). Evaporation of the solvent as described for **13a** afforded an isomeric mixture of **13d** and **12d** in a ratio 45:55 (from its NMR spectra). The mixture was chromatographed on silica gel. Elution with ethyl acetate gave only **13d** as a viscous oil (0.30 g, 20%): IR ($CHCl_3$) 1720, 1630 cm^{-1}; UV λ_{max} (EtOH) (ϵ) 246 (13400), 336 nm (2700); ^1H NMR ($CDCl_3$) δ 0.80 (t, 3 H, J = 7 Hz), 1.12 (d, 3 Hz, J = 7 Hz), 3.17 (s, 3 H), 3.92 (s, 3 H), 3.97 (q, 2 H, J = 7 Hz), 4.03 (q, 1 H, J = 7 Hz), 7.32–7.75 (m, 5 H).

Satisfactory analytical data (±0.3%) for C, H, and N were recorded for compounds **7**, **8** 11, 12, and 13.

Registry No. **1a**, 53252-56-5; **1b**, 62879-96-3; **1c**, 62879-97-4; **2a**, 62538-35-6; **3a**, 70864-67-4; **3b**, 70864-68-5; **3c**, 70864-69-6; **3d**, 70864-70-9; **3e**, 70864-71-0; **3f**, 70864-72-1; **3g**, 70864-73-2; **4g**, 65942-86-1; **5d**, 70864-74-3; **5g**, 70864-75-4; **6d**, 65942-85-0; **6g**, 65942-87-2; **7**, 70864-76-5; **8**, 70864-77-6; **10**, 66823-25-4; **11a**, 70864-78-7; **11d**, 70864-79-8; **11g**, 70864-80-1; **12a**, 70864-81-2; **12d**, 70864-82-3; **13a**, 70864-83-4; **13d**, 70864-84-5; phenylhydrazine, 100-63-0; benzylhydrazine, 555-96-4; methylhydrazine, 60-34-4.

Supplementary Material Available: Spectroscopic data (UV, IR, ^1H NMR) for **3a–c,e,f** (1 page). Ordering information is given on any current masthead page.

Mono- and Bishomobenzotropones. 1. Synthesis and Nuclear Magnetic Resonance Spectra of 2,3-Benzo-6,7-monohomotropone and 2,3-Benzo-*trans*-4,5:6,7-bishomotropone

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The reaction of 2,3-benzotropone with dimethyloxosulfonium methylide has been observed to be nonselective and affords as the major products 2,3-benzo-6,7-monohomotropone and 2,3-benzo-*trans*-4,5:6,7-bishomotropone in yields of 35 and 28%, respectively. Structural characterization of these compounds has been established by extensive NMR analysis. Determination of the mechanism for this nonselective addition of Corey's reagent to an unsymmetrical seven-membered-ring conjugated ketone has also been attempted.

Synthesis

In 1962 Corey reported[1c] the first reaction of dimethyloxosulfonium methylide (1) with a seven-membered-ring conjugated ketone, eucarvone (2), and isolated, as the only product from this reaction, the cyclopropyl ketone 3 (eq 1). Corey[1e] used the results of this reaction to establish the selectivity of 1 as a methylene-transfer agent, since methylene transfer occurred only to the α,β rather than the γ,δ double bond. He qualified the selectivity observed for 1 in this reaction indicating that a partial shielding effect of the *gem*-dimethyl groups at C_δ may have prevented methylene transfer to the γ,δ double bond. Since this initial report by Corey, dimethylsulfonium methylides (4)[2] have been added to unsym-

(1) (a) E. J. Corey and M. Chaykovsky, *J. Am. Chem. Soc.*, 84, 866 (1962); (b) *ibid.*, 84, 867 (1962); (c) *ibid.*, 84, 3782 (1962); (d) *ibid.*, 87, 1345 (1965); (e) *ibid.*, 87, 1353 (1965).

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