toluene. Anal. Calcd for $C_{21}H_{15}Cl_2NO_3$: C, 63.02; H, 3.78; N, 3.50. Found: C, 62.88; H, 4.20; N, 3.96.

Alternate Synthesis of 3. To a rapidly stirred mixture of 1.23 g (10 mmol) of 2-amino-5-methylphenol, 100 mL of benzene, and 21 mL of 1 N NaOH was added in portions 3.71 g (20 mmol) of *p*-nitrobenzoyl chloride. After 1.5 h the crude **3** was filtered, washed with water, and weighed (3.64 g, 87%). Recrystallization of **3** from ethanol gave crystals melting at 240–242 °C.

Alternate Synthesis of 4. By employing the same procedure described above for the synthesis of **3**, compound **4** was prepared in 95% yield by admixing 0.620 g (5 mmol) of 2-amino-5-methylphenol, 25 mL of benzene, 10 mL of 1 N NaOH, and 1.75 g (10 mmol) of *p*-chlorobenzoyl chloride. Recrystallization of **4** from toluene gave crystals that melted at 203–204 °C.

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Registry No.—**3**, 66809-90-3; **4**, 66809-91-4; α-phenyl-*N*-*p*-tolylnitrone, 19064-77-8; *p*-chlorobenzoyl chloride, 122-01-0; 2-amino-5-methylphenol, 2835-98-5.

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4,5-Dihydropyridazines: X-ray Structure of a Dimer

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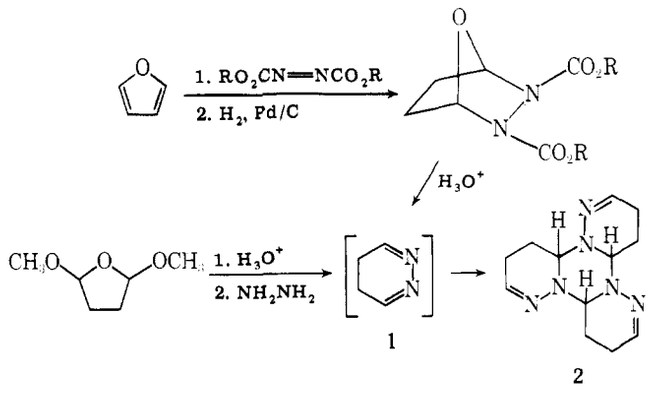
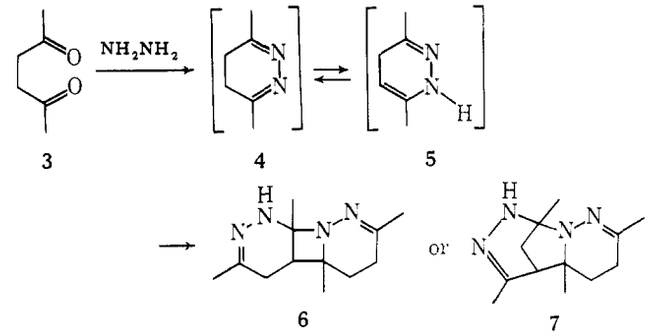
Our interest in 4,5-dihydropyridazines (**1**) as pseudodienes in Diels–Alder reactions prompted us to investigate the tautomerizations and self-condensations of this class of compounds.

Earlier[1] we reported the preparation and X-ray structure of a trimer (**2**) of 4,5-dihydropyridazine (**1**) obtained in ~5% overall yield from dialkyl azodicarboxylate and furan. We find that this trimer is more easily prepared by the aqueous hydrolysis of 2,5-dimethoxytetrahydrofuran, followed by addition of hydrazine to the hydrolysis mixture. Yields are 35–40% based on dimethoxytetrahydrofuran. Since the isolation of succinaldehyde from this hydrolysis is reported in 30% yield,[2] the conversion of aldehyde to trimer is reasonably good.



1 2

It is known that the condensation of hexane-2,5-dione (acetonylacetone (**3**)) with hydrazine affords a dimer of 3,6-dimethyl-4,5-dihydropyridazine[3,4] rather than the monomer or trimer. More recently, De Mayo, Stothers, and Usselman[4] reduced the possible structures of the dimer to **6** and **7**, giving



3 4 5 6 7

preference to **7** on the basis of ^{13}C NMR data. Initial attempts to take X-ray structural data of the dimer itself were unsuccessful due to the instability of the dimer. However, the N-acetylated derivative of the dimer, originally reported by De Mayo, Stothers, and Usselman[4] as being more stable, was successfully used in the structure determination. We have found, in support of the ^{13}C NMR work, that **7** is the correct structure.

Crystal Data. $C_{14}H_{22}N_4O$: monoclinic, $P2_1/c$, a = 12.145 (1) Å, b = 8.132 (1) Å, c = 15.536 (2) β = 110.44 (1)°, Z = 4, D_c = 1.21 g/cm^3, Cu = Kα, λ 1.54178 Å. Of the 1050 data collected with a G.E. XRD-490 computer controlled system by the stationary counter, stationary-crystal method 971 were considered statistically significant. Balanced Ross filters with Cu Kα radiation were used to measure all reflections to a 2θ maximum of 90°. The structure was solved by a multisolution $\Sigma 2$ sign expansion and ultimately refined (nonhydrogens) anisotropic, hydrogens with fixed isotropic temperature factor) to R_w = 0.038. The surprising feature is that all 22 hydrogen atoms are prominently displayed on the difference map. The hydrogens of the five methyl groups are rigidly constrained by the proximity of the other molecules and by steric requirements of the molecule itself and hence are readily apparent in the maps generated.

It is interesting to note the different reaction paths taken by 4,5-dihydropyridazine (**1**) and 3,6-dimethyl-4,5-dihydropyridazine (**4**) in their self-condensation reactions. While the steric requirements of the axial groups in the central ring are important in blocking trimerization of **4**, the basic difference is that trimerization occurs from a 4,5-dihydrotautomer (**1**)[5] and dimerization appears to occur through a key 1,4-dihydro tautomer (**5**).[4]

To test how monosubstitution at position 3 might affect these reactions we synthesized 3-*tert*-butyl-4,5-dihydropyridazine (**9**) by condensation of 4-oxo-5,5-dimethylhexanal (**8**) with hydrazine. If the reaction is worked up without allowing the temperature to rise above room temperature, the product obtained is a viscous oil having a complex NMR similar to that

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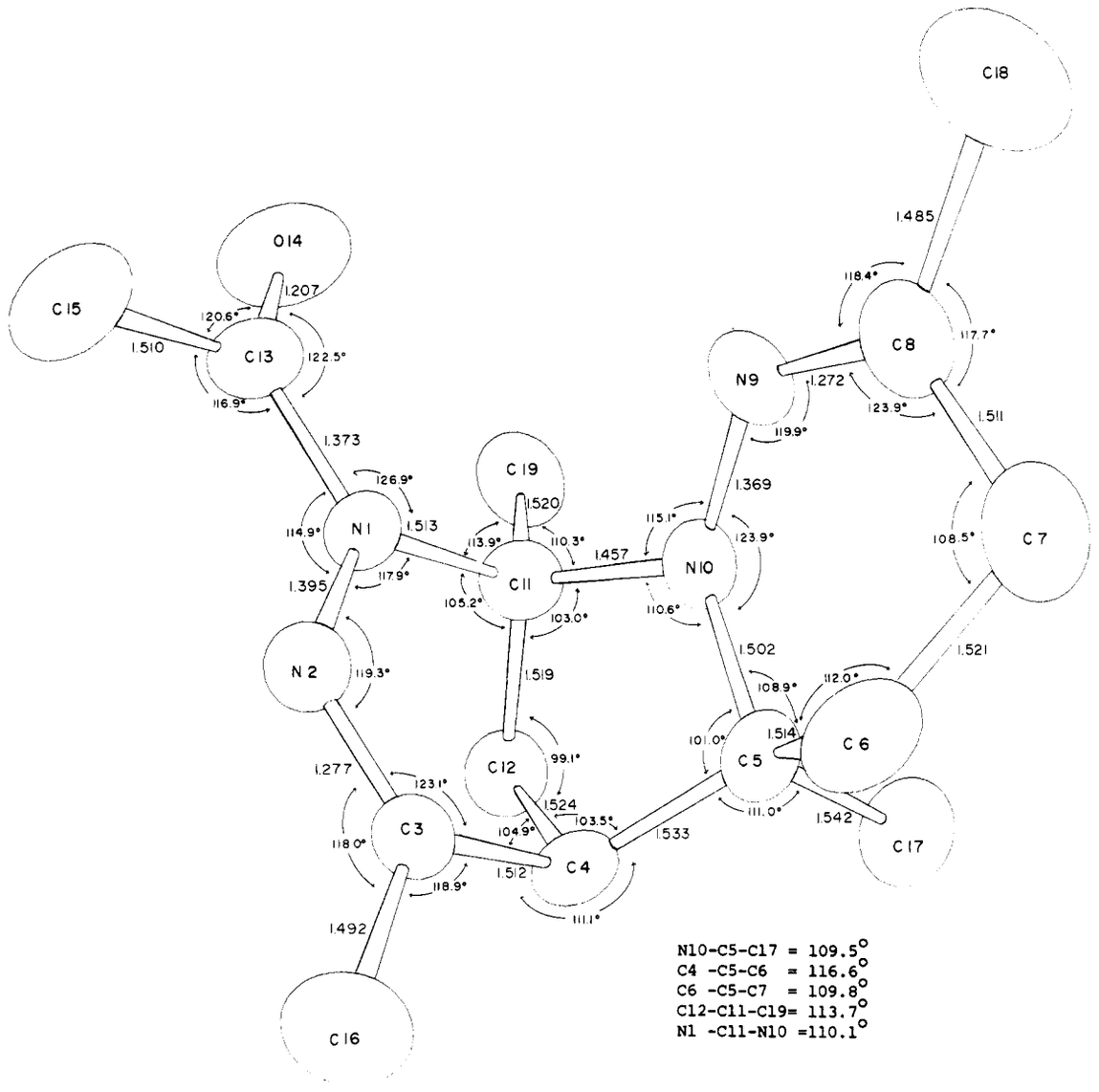
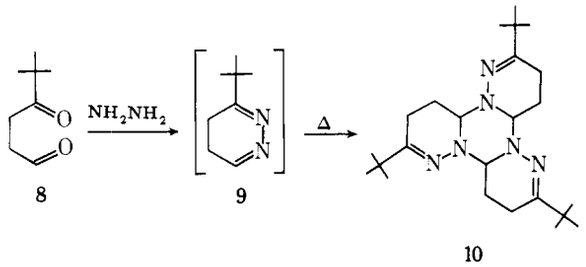


Figure 1.

of **7**. If heated in refluxing benzene prior to workup, a crystalline trimeric product (**10**) is obtained. If an attempt is made to distill the oil in vaccuo, some trimer (**10**) is produced along with substantial decomposition. This may indicate reversible formation of a dimer similar to **6** which goes back through the monomer **9** to trimer **10** upon heating.



8 9 10

In anticipation that both dimerization and trimerization might be sterically precluded we synthesized 3,6-di-*tert*-butyl-4,5-dihydropyridazine (**11**) from the corresponding diketone and hydrazine. Indeed it was found to be monomeric although it quickly aromatizes in the presence of air.

In this work we have attempted to clarify the reaction paths available to 4,5-dihydropyridazines in their self-condensation reactions. If unsubstituted at the 6 or 3,6 positions they can trimerize via a 4,5-dihydro tautomer. If substituted in the 3 and 6 positions they may still dimerize via a 1,4-dihydro tautomer. The 3-substituted dihydropyridazines may well go by either route although we have only spectroscopic evidence for the dimerization at this time.

Experimental Section

Melting points were taken in open capillaries on a Mel-temp melting point apparatus. Infrared spectra were obtained on a Perkin-Elmer 283. NMR spectra were obtained on a Varian A60 and a Hitachi Perkin-Elmer R20B. Elemental analyses were carried out by Galbraith Analytical Laboratories.

Synthesis of the Trimer of 4,5-Dihydropyridazine (2). To 75 mL of H_2O was added 4 drops of concentrated HCl and 10 mL (77 mmol) of 2,5-dimethoxytetrahydrofuran. After stirring 4 h at 40–50 °C, the mixture was allowed to cool to room temperature. Hydrazine (3.2 mL, 100 mmol) was added and stirring continued for 1 h. The reaction mixture was then extracted with 4 × 25 mL of ether and the extract dried over $MgSO_4$. The solvent was removed in vaccuo yielding 2.23 g (36% yield) of **2**. Recrystallization from ether gave white crystals, mp 138–140 °C (lit.[1] mp 139–140 °C).

Synthesis of Dimer 7. The dimer was synthesized by the method of Overberger and Kesslin,[3] mp 49–51 °C (lit. mp 52–53 °C).

Synthesis of the *N*-Acetyl Derivative of 7. This derivative was prepared by the method of DeMayo, Stothers, and Usselman, mp 153–155 °C (lit.[4] 153–153.5 °C).

Synthesis of 4-Oxo-5,5-dimethyhexanal. The Grignard reagent of 2-(2-bromoethyl)-1,3-dioxane was prepared according to the method of Stowell[6] using 15 g (76.9 mmol) of 2-(2-bromoethyl)-1,3-dioxane and 5.61 g (230 mmol) of Mg in 50 mL of THF. This Grignard

was added dropwise by syringe to a slight excess (12 mL, 97.4 mmol) of trimethylacetyl chloride in 50 mL of the THF while maintaining a positive N_2 pressure. The reaction mixture was stirred 0.5 h after addition was complete and then 15 mL of water was added. The THF was removed in vaccuo and the product was extracted with a 3 × 75 mL portion of hexane. The hexane extract was washed with dilute HCl and dried over $MgSO_4$.

Concentration of the hexane and distillation gave 2-(3-oxo-4,4-dimethylpentyl)-1,3-dioxane (12.34 g, 61.7 mmol): bp 115–122 °C (7 mm); IR (neat) 2962, 2851, 1708, and 1149 cm^{-1}; NMR (CCl_4) δ 1.11 (s, 9 H), 1.2–2.2 (m, 4 H), 2.3–2.7 (m, 2 H), 3.4–4.3 (m, 4 H), and 4.45 (t, 1 H).

This compound was hydrolyzed to 8 as follows. In a 50-mL flask equipped with magnetic stirring was placed 40 mL of H_2O and 5.34 g of 2-(3-oxo-4,4-dimethylpentyl)-1,3-dioxane and 1 g of oxalic acid. A Dean-Stark trap modified to return the bottom layer was attached and filled with water. The mixture was refluxed for 3 h, steam distilling 8 into the trap. The product was taken up in 10 mL of ether, dried over $MgSO_4$, concentrated, and distilled in vacuo (bp 88 °C (12 mm)). The yield was 2.30 g (6.12 mmol, 61%): IR (neat) 2968, 2825 (shoulder), 2718, 1725, and 1707 cm^{-1}; NMR (CCl_4) δ 1.14 (s, 9 H), 2.50 (s, 4 H), and 9.80 (s, 1 H).

Synthesis of the Trimer of 3-*tert*-Butyl-4,5-dihydropyridazine (10). In a 100-mL flask equipped with N_2 atmosphere, condenser, and magnetic stirring was placed 50 mL of benzene and 3.01 g (21.2 mmol) of 4-oxo-5,5-dimethylhexanal. Hydrazine (97%, 2 mL, 63 mmol) was added dropwise. After stirring at reflux for 1 h a Dean-Stark trap was attached and the water azeotroped off over a 2-h period. The benzene was removed in vaccuo and the oil produced was crystallized by addition of 95% ethanol. A second crop of crystals was obtained by addition of water to the ethanol. The yield was 1.30 g (9.4 mmol, 44%): mp 123–125 °C; IR ($CHCl_3$) 2960, 1624, 1475, and 1362 cm^{-1}; NMR δ 1.09 (s, 9 H), 1.9–2.6 (m, 4 H), and 3.2–3.6 (m, 1 H). Mass spectrum showed a large parent ion at 414 ± 1.

Anal. Calcd for $C_8H_{14}N_2$: C, 69.52; H, 10.21; N, 20.27. Found: C, 69.36; H, 10.34; N, 20.14.

Acknowledgment. The authors thank the Army Research Office (J.W.T.) and the Warner Lambert Co. (L.M.T.) for partial support of this research.

Registry No.—**2**, 37819-05-9; **7**, 36046-77-2; **7** *N*-acetyl derivative, 36046-34-1; **8**, 66662-24-6; **10**, 66842-46-4; 2,5-dimethoxytetrahydrofuran, 696-59-3; hydrazine, 302-01-2; 2-(2-bromoethyl)-13-dioxane, 33884-43-4; trimethylacetyl chloride, 3282-30-2; 2-(3-oxo-4,4-dimethylpentyl)-1,3-dioxane, 66842-47-5; 4,5-dihydropyridazine, 56962-82-4.

Supplementary Material Available: Table I listing final refined coordinates and anisotropic temperature factors (isotropic for hydrogen atoms) (3 pages). Ordering information is given on any current masthead page.

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Kinetics of the Rearrangement of *N*-Nitroso(2-methylamino)acetonitrile in Basic Methanol by Differential Pulse Polarography

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Daeniker[2] had reported earlier that *N*-nitroso(2-methylamino)acetonitrile (I) undergoes an interesting rearrangement in basic methanol solution to yield α-isonitroso-*N*-methylaminoacetonitrile (II) (eq 1). During the course of electroanalytical studies on I and other *N*-nitrosamines we observed that the kinetics of this reaction could be studied by differential pulse polarography. A similar application of this technique had been used by us to study the anchimeric role of the nitroso group in the aqueous basic hydrolysis of I.[3] The current study lends support to the mechanism of rearrangement proposed by Daeniker and, in addition, outlines an isolation procedure for II that gives considerably improved yields.

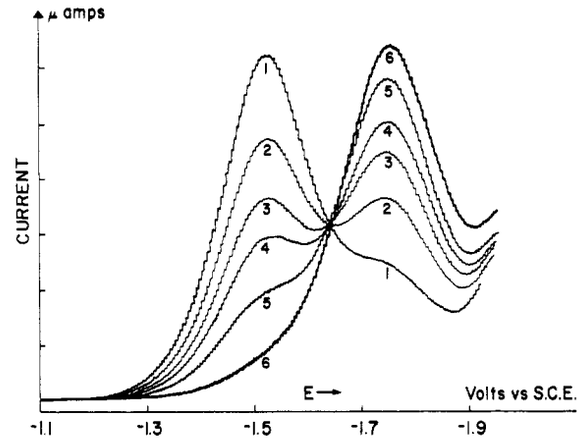

Figure 1. Differential pulse polarograms of rearrangement of *N*-nitroso-2(methylamino)acetonitrile in basic methanol solution: Supporting electrolyte 0.1 M Et_4NClO_4; temperature 22 °C; [OH^-] = 0.006 M; scan rate 5 mV/s; drop time 1.0 s; pulse amplitude 50 mV (p-p); Hg flow rate 1.20 mg/s. Curve 1: 0 min. Curve 2: 6 min. Curve 3: ~12 min. Curve 4: ~20 min. Curve 5: ~32 min. Curve 6: ~105 min.

$$\underset{\underset{N{=}O}{|}}{CH_3NCH_2CN} \xrightarrow[\text{Base}]{\text{ROH}} \underset{\underset{NOH}{\|}}{CH_3NHCCN} \qquad (1)$$

I II

In neutral methanol, I displays a single, diffusion-controlled, differential pulse polarographic peak at −1.52 V vs. SCE. In the presence of methoxide ion, however, the expected peak is followed by a second peak (−1.74 V), an unusual result for a nitrosamine.[4] The heights of the two peaks vary in a regular fashion as a function of time. Typical results are shown in Figure 1; curves 1–6 were recorded on the same solution over a period of approximately 100 min. The species giving rise to the second peak is stable; once it is fully formed the peak height remains constant over a period of 12 h.

The most logical explanation for the observed polarographic results is that proposed by Daeniker (Scheme I). To insure that the reaction described by eq 1 is occurring in the polarographic cell and that II is the species giving rise to the second peak, the solution conditions used in the polarographic cell were repeated on a preparative scale. The physical and spectral data for the sublimed product isolated were identical

Scheme I