The Reduction and Hydrolysis of Some 7,7-Diethylpyrazolo[1,2-*a*]-pyridazine-6,8(7*H*)dione Derivatives (1)

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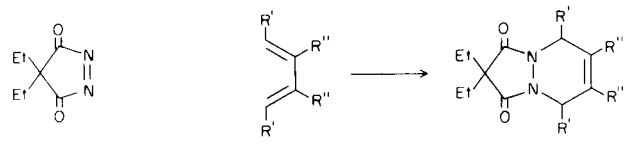
The chemistry of several of the Diels-Alder adducts formed by the reaction of 4,4-diethylpyrazoline-3,5-dione (**1**) with conjugated dienes was studied with respect to reduction (hydride and catalytic) and reaction with base. Reaction of the 2,3-dimethyl-1,3-butadiene adduct with lithium aluminum hydride followed by hydrogenation gave 1,3,5,6,7,8-hexahydro-*cis-endo*-6,7-dimethyl-2,2-diethylpyrazolo[1,2-*a*]pyridazine (**11**). Attempted conversion of this compound to 3,3-diethyl-*cis*-7,8-dimethyl-1,5-diazacyclononane (**12**) gave instead a compound which has been tentatively identified as *N*-(2,3-dimethyl-4-aminobutyl)-2-ethyl-2-methylbutanaldimine (**14**). Lithium aluminum hydride reduction of 4,4-diethylpyrazolidine-3,5-dione (**22**) or the adducts formed from **1** and cyclopentadiene or 1,3-cyclohexadiene gave good yields of 4,4-diethylpyrazolidine (**21**). This later reduction gave a new and efficient synthetic route to the pyrazolidine ring system. Lithium aluminum hydride reduction of 5,6,7,8-tetrahydro-5,8-ethano-2,2-diethylpyrazolo[1,2-*a*]pyridazine-1,3(2*H*)dione (**26**) followed by hydrogenolysis led to a high yield of 4,4-diethyl-2,6-diazabicyclo[5.2.2]undecane (**28**) which is the first reported example of this ring system. Reaction of several of the adducts with ethanolic potassium hydroxide resulted in the opening of the five-membered ring.

We have recently reported on the use of 4,4-diethylpyrazoline-3,5-dione (**1**) as an efficient reagent for obtaining derivatives of 5,8-dihydropyrazolo[1,2-*a*]pyridazine-1,3(2*H*)dione (**2**) *via* the Diels-Alder reaction (3).



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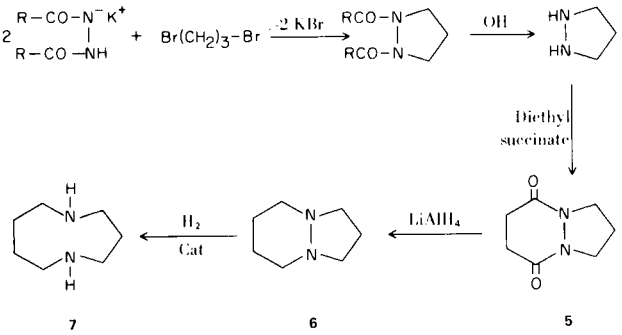
Since no reactions of ring system **2** have been reported, an investigation of the chemistry of this system was undertaken in order to determine some practical uses for the Diels-Alder adducts of **1**.

The reduction of several of the adducts was studied with the ultimate goal of obtaining saturated derivatives of the 1,5-diazacyclononane ring system (**7**). Compound **7** which was prepared through a multistep synthesis by Stetter and Spangenberger shown below is the only reported example of this system (4).

Reduction of 5,8-dihydro-6,7-dimethyl-2,2-diethylpyrazolo[1,2-*a*]pyridazine-1,3(2*H*)dione (**8**) with lithium aluminum hydride by the procedure of Stetter and Spangenberger (4) gave 1,3,5,8-tetrahydro-6,7-dimethyl-2,2-diethylpyrazolo[1,2-*a*]pyridazine (**10**). Compound **10** was further reduced by catalytic hydrogenation over 5% palladium-on-carbon or Raney nickel to give 1,3,5,6,7,8-hexahydro-*cis-endo*-6,7-dimethylpyrazolo[1,2-*a*]pyridazine (**11**) (5). Compound **11** was also prepared by lithium aluminum hydride reduction of **9**.



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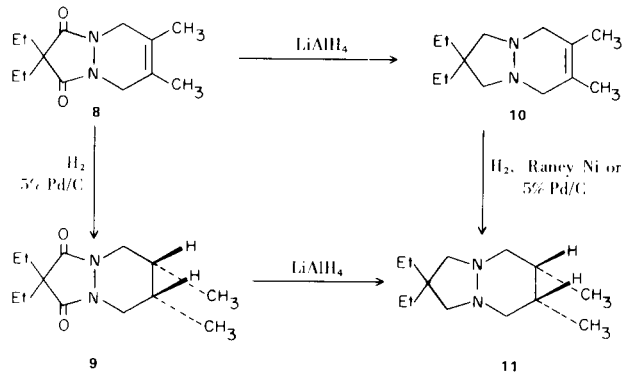
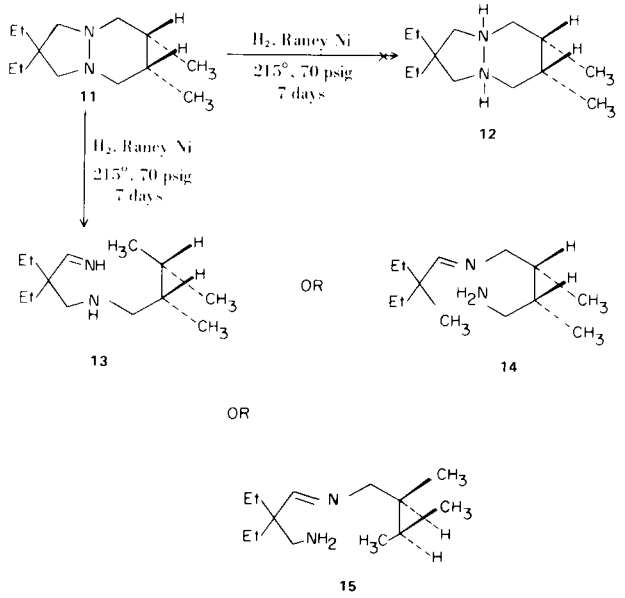
Compounds **10** and **11** were characterized on the basis of their spectral properties and elemental analysis. They both reacted with picric acid to form monopicrate salts.

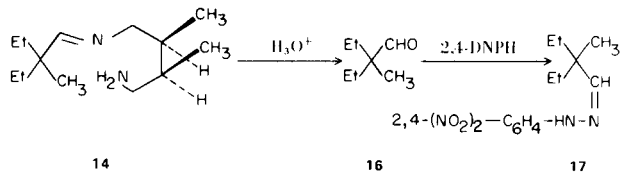
Attempts were made to effect hydrogenolysis of the nitrogen to nitrogen bond of **11** to yield 3,3-diethyl-*cis*-7,8-dimethyl-1,5-diazacyclononane (**12**). Heating a stirred mixture of **11** and Raney nickel in absolute ethanol under



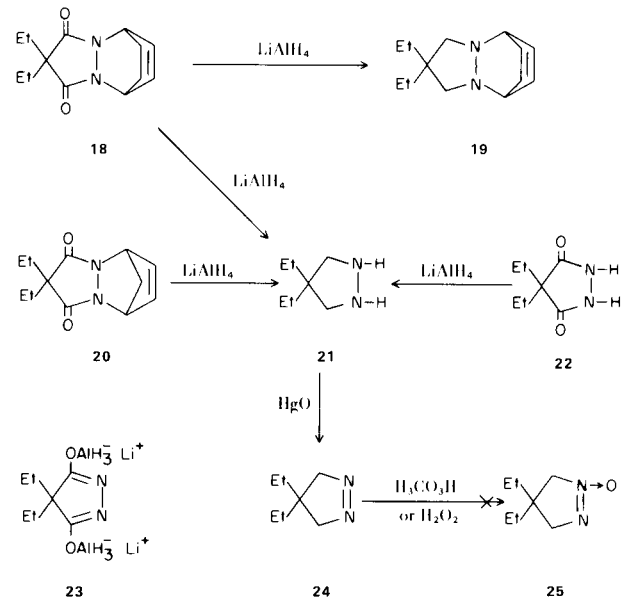
hydrogen at 110° and 48 psig for 42 hours resulted only in the recovery of unreacted starting material. The two ethyl and *cis*-methyl groups of **11** apparently inhibit the absorption of **11** onto the surface of the catalyst, for the unsubstituted ring system **6** reportedly underwent hydrogenolysis to give **7** at room temperature and atmospheric pressure (4). When the reaction was repeated under more



vigorous conditions (215° and 70 psig for one week), a product analyzing for $C_{13}H_{28}N_2$ was isolated in high yield. Although this is the correct analysis for the diazacyclononane **12**, the spectral properties of the isolated product ruled out the possibility of its formation. The presence of an imine moiety was observed in the infrared spectrum by a strong sharp band at 6.02 μ and verified in the nmr which showed a sharp singlet (1*H*) at δ 7.50. These results indicated that **13**, **14**, or **15** were possible structures for the product. The known instability of aldimines without *N*-substitution made **13** the least likely possibility (6). A solution of the compound in one molar phosphoric acid was heated to 80° for several minutes. Steam distillation of the reaction mixture separated a volatile component which formed a 2,4-dinitrophenylhydrazone derivative. The reaction mixture was made basic and the steam distillation continued, but no volatile amine could be detected in the distillate. The above chemical tests suggest that the compound is *N*-(2,3-dimethyl-4-aminobutyl)-2-methyl-2-ethylbutanaldimine (**14**) as it is the only compound of the three possibilities that could form a volatile carbonyl compound under the reaction conditions. However, since the desired diazacyclononane **12** was obviously not formed, attempts to more firmly establish the structure of the compound were not undertaken.



Lithium aluminum hydride reduction of the adduct **18** from **1** and cyclohexadiene did not give the expected product 1,3,5,8-tetrahydro-5,8-ethano-2,2-diethylpyrazolo[1,2-*a*]pyridazine (**19**). Instead 4,4-diethylpyrazolidine (**21**) was isolated in 61% yield. Analogous reduction of **20** led to a 75% yield of **21**. Although it is difficult to postulate a rational mechanism for this unusual cleavage (7), the intermediacy of hydrazide **22** or salt **23** would not be unexpected, for lithium aluminum hydride reduction of **22** led to a 53% yield of **21** despite its low solubility which may have caused it to be unreactive to reduction (8,9).



The lithium hydride reduction of adducts **18** and **20** and hydrazide **22** to form **21** represent new and efficient routes to the pyrazolidine ring system.

The pyrazolidine **21** readily formed a dibenzoyl derivative, and it was easily oxidized by air or yellow mercuric oxide to 4,4-diethyl-1-pyrazoline (**24**). Attempts to oxidize **24** to the *cis* azoxy compound **25** with peracetic acid or hydrogen peroxide were not successful.

Lithium aluminum hydride reduction of **26** did not result in ring cleavage. Instead the expected product 1,3,5,6,7,8-hexahydro-5,8-ethano-2,2-diethylpyrazolo-[1,2-*a*]pyridazine (**27**) was isolated. A monopicrate derivative of **27** was prepared. Hydrogenolysis of **27** under hydrogen at 120° and 45 psig for one week using Raney nickel as a catalyst gave a high yield of 4,4-diethyl-2,6-diazabicyclo[5.2.2]undecane (**28**) which is the first reported derivative of this ring system. Compound **28** was characterized by elemental analysis and its spectral properties. It formed a dihydrochloride salt and it reacted with excess *p*-toluenesulfonyl chloride to give a mono-*p*-toluenesulfonamide derivative.

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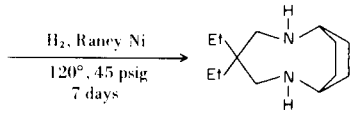

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Attempted hydride reduction of **29** did not yield the tricyclic compound 1,3,5,6,7,8-hexahydro-5,8-methano-2,2-diethylpyrazolo[1,2-*a*]pyridazine (**30**). An unidentified liquid analyzing for $C_{12}H_{24}N_2O_2$ was isolated that had an infrared spectrum indicative of an alcohol and a complex nmr spectrum.

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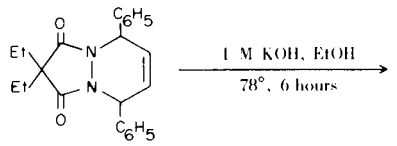
The reaction of several of the adducts with hydroxide ion was studied. Reaction of **31** with one molar potassium hydroxide at 78° for six hours resulted in the formation of 1-(diethylcarbethoxyacetyl)-1,4,5,6-tetrahydro-3,6-diphenylpyridazine (**32**) and 1-(diethylcarboxyacetyl)-1,4,-5,6-tetrahydro-3,6-diphenylpyridazine (**33**) in yields of 33% and 72% respectively. When the reaction time was extended to 42 hours, the yields of **32** and **33** were 27% and 71%. Presumably the longer reaction time resulted in partial saponification of **32**.



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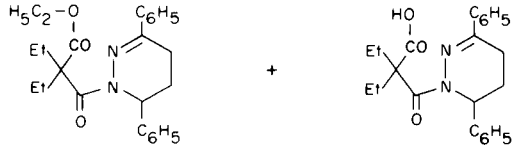

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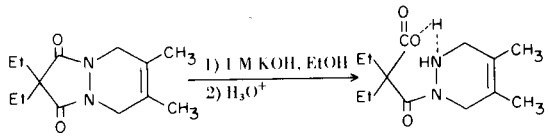
Reaction of **8** with one molar potassium hydroxide at 78° for 42 hours produced a 23% yield of 1-(diethylcarboxyacetyl)-1,2,3,6-tetrahydro-4,5-dimethylpyridazine (**34**) in its zwitterion form and a 74% recovery of starting material. The infrared spectrum of **34** showed the N-H absorption at 3.1 μ and the two carbonyl absorptions at 5.90 and 6.20 μ for the amide carbonyl and carboxylate anion. The nmr spectrum showed the presence of the two ethyl and two allylic methyl groups and absorptions at δ 5.25, 4.10, 3.37, and 2.87 in a ratio of 1-2-2-1. No absorption could be detected in the usual carboxyl region. This result suggests that the carboxyl proton does not completely protonate the basic nitrogen atom, but instead it is complexed between the carboxylate anion and nitrogen atom.



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Attempted reaction of **18** with potassium hydroxide at 78° led only to the recovery of starting material.

EXPERIMENTAL (10)

General Method for the Lithium Aluminum Hydride Reduction of the Diels-Alder Adducts (11).

A procedure similar to the method of Stetter and Spangenberger (4) was employed. To a slurry of 6.5 g. of powdered lithium hydride in 300 ml. of dry tetrahydrofuran at 0° was added dropwise over a 15 minute period a solution of 0.04 mole of the Diels-Alder adduct in 100 ml. of dry tetrahydrofuran with stirring. The resulting mixture was heated at reflux for 42 hours. After cooling the reaction mixture to 0°, the excess lithium aluminum hydride was decomposed by the cautious addition of

water and then 10% sodium hydroxide. The solids were removed by filtration and thoroughly washed with tetrahydrofuran. The filtrate was dried over sodium sulfate and the solvent removed under reduced pressure to give a liquid residue which was purified by distillation.

1,3,5,8-Tetrahydro-6,7-dimethyl-2,2-diethylpyrazolo[1,2-*a*]pyridazine (**10**).

From the reduction of 10.2 g. (0.043 mole) of 5,8-dihydro-6,7-dimethyl-2,2-diethylpyrazolo[1,2-*a*]pyridazine-1,3(2*H*)dione (**8**) with 6.5 g. of lithium aluminum hydride was obtained 7.1 g. of a liquid. Distillation of the liquid gave 5.5 g. (62%) of **10**, b.p. 127-135° (6 mm). Redistillation gave an analytical sample of **10**, b.p. 88-89° (1 mm); nmr (deuterochloroform) δ 3.05 (s, 4, pyridazine methylenes), 2.61 (s, 4, pyrazole methylenes), 1.61 (s, 6, allylic-C*H*$_3$), 1.55 (m, 4, -C*H*$_2$-), and 0.85 (t, 6, C*H*$_3$-).

Anal. Calcd. for $C_{13}H_{24}N_2$: C, 74.94; H, 11.61; N, 13.45. Found: C, 74.56; H, 11.37; N, 13.36.

M.p. of monopicrate derivative (recrystallized from ethanol-water) 117-118°.

Anal. Calcd. for $C_{19}H_{27}N_5O_7$: C, 52.17; H, 6.22; N, 13.46. Found: C, 52.28; H, 5.94; N, 16.36.

1,3,5,6,7,8-Hexahydro-*cis-endo*-6,7-dimethyl-2,2-diethylpyrazolo[1,2-*a*]pyridazine (**11**).

From the reduction of 11.9 g. (0.05 mole) of 5,6,7,8-tetrahydro-*cis-endo*-6,7-dimethyl-2,2-diethylpyrazolo[1,2-*a*]pyridazine-1,3(2*H*)dione (**9**) with 8.0 g. of lithium aluminum hydride was obtained 9.6 g. of a liquid. Distillation of this liquid gave 7.9 g. (75%) of **11**, b.p. 120-127° (12 mm). Redistillation gave an analytical sample of **11**, b.p. 104-105° (5 mm); nmr (deuterochloroform) δ 2.67 (m, 6, pyridazine-*H*), 2.10 (m, 4, pyrazole-*H*), 1.50 (m, 4, -C*H*$_2$-), and 0.86 (m, 12, C*H*$_3$-).

Anal. Calcd. for $C_{13}H_{26}N_2$: C, 74.22; H, 12.46; N, 13.32. Found: C, 74.12; H, 12.50; N, 13.17.

M.p. of the monopicrate derivative (recrystallized from ethanol-water) 136-137°.

Anal. Calcd. for $C_{19}H_{29}N_5O_7$: C, 51.93; H, 6.65; N, 15.93. Found: C, 52.12; H, 6.73; N, 15.87.

Catalytic reduction of **10** in 95% ethanol with either 5% palladium-on-carbon or Raney nickel under hydrogen at room temperature and atmospheric pressure also gave **11**.

4,4-Diethylpyrazolidine (**21**).

From the reaction of 11.7 g. (0.05 mole) of 5,8-dihydro-5,8-ethano-2,2-diethylpyrazolo[1,2-*a*]pyridazine-1,3(2*H*)dione (**18**) with 8.0 g. of lithium aluminum hydride was obtained 6.8 g. of a liquid. Distillation of this liquid gave 3.9 g. (61%) of **21**, b.p. 67-69° (5 mm); ir (neat) 3.03 μ (N-H) and 11.85 μ; nmr (deuterochloroform) δ 4.55 (s, 2, N-H); 3.08 (s, 4, ring-C*H*$_2$-), 1.33 (m, 4, -C*H*$_2$-), and 0.75 (t, 6, C*H*$_3$-).

Anal. Calcd. for $C_7H_{16}N_2$: C, 65.57; H, 12.58; N, 21.85. Found: C, 65.62; H, 12.36; N, 21.75.

A dibenzoyl derivative was prepared and recrystallized from ethanol-water: m.p. 141-142°; uv max (95% ethanol) 223 mμ (ε, 15,000).

Anal. Calcd. for $C_{21}H_{24}N_2O_2$: C, 74.97; H, 7.19; N, 8.33. Found: C, 74.85; H, 7.04; N, 8.45.

From the reduction of 7.7 g. (0.035 mole) of 5,8-dihydro-5,8-methano-2,2-diethylpyrazolo[1,2-*a*]pyridazine-1,3(2*H*)dione (**20**) with 6.5 g. of lithium aluminum hydride was obtained 3.60 g. (75%) of **21**.

In a similar manner, reduction of 12.4 g. (0.08 mole) of 4,4-diethylpyrazolidine-3,5-dione (**22**) with 12.3 g. of lithium aluminum hydride gave 5.4 g. (53%) of **21**. A reflux time of 72 hours was employed in this reaction. When the reaction time was shortened to 37 hours, 3.95 g. (39%) of **21** was isolated.

1,3,5,6,7,8-Hexahydro-5,8-ethano-2,2-diethylpyrazolo[1,2-*a*]-pyridazine (**27**).

From the reduction of 9.6 g. (0.04 mole) of 5,6,7,8-tetrahydro-5,8-ethano-2,2-diethylpyrazolo[1,2-*a*]pyridazine-1,3(2*H*)dione (**26**) with 6.5 g. of lithium aluminum hydride was obtained 9.2 g. of a liquid. Distillation of this liquid gave 7.35 g. (86%) of **27**, b.p. 87-97° (1 mm). Redistillation gave an analytical sample of **27**, b.p. 89-90° (1 mm); nmr (deuterochloroform) δ 2.76 and 2.67 (two singlets, 6, bridgehead-*H* and pyrazole-C*H*$_2$-), 2.2-1.3 (m, 12, C*H*$_2$-), and 0.86 (t, 6, C*H*$_3$-).

Anal. Calcd. for $C_{13}H_{24}N_2$: C, 74.94; H, 11.61; N, 13.45. Found: C, 74.85; H, 11.70; N, 13.30.

M.p. of the monopicrate derivative (recrystallized from ethanol-water) 141-142°.

Anal. Calcd. for $C_{19}H_{27}N_5O_7$: C, 52.17; H, 6.22; N, 16.01. Found: C, 52.20; H, 6.41; N, 15.84.

Lithium Aluminum Hydride Reduction of 5,6,7,8-Tetrahydro-5,8-methano-2,2-diethylpyrazolo[1,2-*a*]pyridazine-1,3(2*H*)dione (**29**).

From the reduction of 8.4 g. (0.038 mole) of **29** with 7.1 g. lithium aluminum hydride was obtained a liquid residue. Distillation gave 1.4 g. of a liquid, b.p. 96-126° (5 mm). Redistillation gave a fraction, b.p. 101-106° (4 mm) which analyzed for $C_{12}H_{24}N_2O_2$ and gave a negative 2,4-dinitrophenylhydrazine test: ir (neat) 2.90 μ (OH) and 9.3 μ.

Anal. Calcd. for $C_{12}H_{24}N_2O_2$: C, 63.12; H, 10.59; N, 12.27. Found: C, 63.00; H, 10.47; N, 12.42.

Hydrogenolysis of 1,3,5,6,7,8-Hexahydro-*cis-endo*-6,7-dimethyl-2,2-diethylpyrazolo[1,2-*a*]pyridazine (**11**).

A mixture of 2.0 g. (0.095 mole) of **11** in 50 ml. of absolute ethanol and 12 ml. of settled activated Raney nickel (12) was heated under hydrogen at 215° and 70 psig for one week with stirring. The catalyst was removed by filtration and the solvent removed under reduced pressure to give 1.8 g. (90%) of a liquid. Distillation of the liquid gave an analytical sample which had an ir spectrum identical to that of the crude product and which analyzed for $C_{13}H_{28}N_2$, b.p. 88-90° (1 mm); ir (neat) 3.3 μ (NH) and 6.02 μ (C=N); nmr (deuterochloroform) δ 7.50 (s, 1, N=C-*H*), 3.2-2.0 (m, 8), and 2.0-0.7 (m, 19).

Anal. Calcd. for $C_{13}H_{28}N_2$: C, 73.52; H, 13.29; N, 13.19. Found: C, 73.43; H, 13.02; N, 13.23.

A solution of 0.2 g. of this compound in six ml. of 1 *M* phosphoric acid was heated at 70° for 10 minutes. Distillation of the mixture gave three ml. of distillate containing a sweet smelling organic substance. Addition of a saturated aqueous solution of 2,4-dinitrophenylhydrazine which was 1 *M* in hydrochloric acid precipitated a small amount of α-methyl-α-ethylbutyraldehyde 2,4-dinitrophenylhydrazone (**17**), m.p. 116-120° (lit. (13) 122.8-123.5°). The reaction mixture was made basic with 6 *M* sodium hydroxide, and the solid which was formed was removed by filtration. Further distillation did not separate any volatile amine.

4,4-Diethyl-2,6-diazabicyclo[5.2.2]undecane (**28**).

A mixture of 2.4 g. (0.012 mole) of 1,3,5,6,7,8-hexahydro-5,8-ethano-2,2-diethylpyrazolo[1,2-*a*]pyridazine (**27**) in 75 ml. of absolute ethanol and 10 ml. of settled activated Raney nickel was heated under hydrogen at 120° and 45 psig for one week with

stirring. The catalyst was removed by filtration and the solvent removed under reduced pressure to give 2.0 g. (83%) of **28**. Distillation gave an analytical sample of **28** which had an ir spectrum identical to that of the crude product, b.p. 119-121° (3.7 mm); ir (neat) 3.02 μ (N-H); nmr (deuterochloroform) δ 3.03 (s, 2, bridgehead-*H*), 2.62 (s, 2, N-H), 2.35 (m, 4, 3,5-C*H*$_2$-), 2.0-1.1 (m, 12), and 0.78 (t, 6, C*H*$_3$-).

Anal. Calcd. for $C_{13}H_{26}N_2$: C, 74.22; H, 12.46; N, 13.32. Found: C, 74.06; H, 12.35; N, 13.21.

M.p. of the dihydrochloride derivative (recrystallized from ethanol-water) 214-218° dec.

Anal. Calcd. for $C_{13}H_{28}N_2Cl_2$: C, 55.12; H, 9.96; N, 9.89. Found: C, 55.33; H, 9.22; N, 10.03.

M.p. of mono-*p*-toluenesulfonamide derivative (recrystallized from ethanol-water) 102-103°.

Anal. Calcd. for $C_{20}H_{32}N_2O_2S$: C, 65.89; H, 8.85; N, 7.68. Found: C, 66.16; H, 8.72; N, 7.59.

4,4-Diethyl-1-pyrazoline (**24**).

To a slurry of 11.2 g. (0.051 mole) of yellow mercuric oxide in 50 ml. of hexane at 0° was added dropwise a solution of 5.4 g. (0.042 mole) of 4,4-diethylpyrazolidine (**21**) in 25 ml. of hexane. Stirring was continued for three hours at room temperature. The reaction mixture was filtered, dried over sodium sulfate, and evaporated under reduced pressure to give a liquid mixture. Distillation gave 3.2 g. (60%) of **24**, b.p. 62-68°. Redistillation gave an analytic sample of **24**, b.p. 58-59° (5 mm); ir (neat) 1550 cm^{-1} (-N=N-); nmr (deuterochloroform) δ 4.07 (s, 4, ring-C*H*$_2$-), 1.33 (m, 4, -C*H*$_2$-), and 0.74 (t, 6, C*H*$_3$-).

Anal. Calcd. for $C_7H_{14}N_2$: C, 66.62; H, 11.18; N, 22.20. Found: C, 66.49; H, 11.18; N, 22.20.

Reaction of 5,8-Dihydro-5,8-diphenyl-2,2-diethylpyrazolo[1,2-*a*]-pyridazine-1,3(2*H*)dione (**31**) with Potassium Hydroxide.

A solution containing 2.0 g. (0.0056 mole) of **31** and 5.0 g. of potassium hydroxide in 50 ml. of 95% ethanol was heated at reflux for six hours. On cooling, the reaction mixture was added to 200 ml. of water to cause the precipitation of a white solid. Recrystallization from ethanol-water gave 0.75 g. (33%) of 1,4,5,6-tetrahydro-1-(diethylcarbethoxyacetyl)-3,6-diphenylpyridazine (**32**), m.p. 112.5-113.5°; ir (nujol) 5.75 and 6.0 μ (ester and amide carbonyls); uv max (95% ethanol) 284 mμ (ε, 22,300) and 293 mμ (ε, 21,300); nmr (deuterochloroform) δ 7.86-7.00 (m, 10, aromatic-H), 5.98 (s, 1, bridgehead-*H*), 4.07 (m, 2, O-C*H*$_2$-), 2.13 (m, 8, -C*H*$_2$-), 1.14 (t, 3, OCH$_2$C*H*$_3$), and 0.80 (t, 6, C*H*$_3$-).

Anal. Calcd. for $C_{25}H_{30}N_2O_3$: C, 73.86; H, 7.44; N, 6.89. Found: C, 74.10; H, 7.54; N, 6.81.

The aqueous solution was acidified with dilute nitric acid to give 1.3 g. (62%) of 1,4,5,6-tetrahydro-1-diethylcarboxyacetyl)-3,6-diphenylpyridazine (**33**). Recrystallization from ethanol-water gave pure **33**, m.p. 208-209.5°; ir (nujol) 3.0-4.0 μ (O-H), 5.85 and 6.0 μ (carboxyl and amide carbonyls); uv max (95% ethanol) 283 mμ (ε, 25,500) and 292 mμ (ε, 25,000); nmr (deuterochloroform) δ 11.92 (s, 1, COO*H*), 7.86-7.00 (m, 10, aromatic-*H*), 5.98 (s, 1, bridgehead-*H*), 2.14 (m, 8, -C*H*$_2$-), and 0.80 (t, 6, C*H*$_3$-).

Anal. Calcd. for $C_{23}H_{26}N_2O_3$: C, 72.99; H, 6.92; N, 7.40. Found: C, 73.04; H, 7.06; N, 7.59.

When the reaction time was extended to 72 hours, 27% of **32** and 72% of **33** were isolated.

Reaction of 5,8-Dihydro-6,7-dimethyl-2,2-diethylpyrazolo[1,2-*a*]-pyridazine-1,3(2*H*)dione (**8**) with Potassium Hydroxide.

A solution containing 5.0 g. (0.037 mole) of **8** and 5.0 g. of potassium hydroxide in 50 ml. of 95% ethanol was heated at reflux for 42 hours. On cooling, the reaction mixture was added to 200 ml. of water. Acidification with dilute nitric acid caused the precipitation of 2.7 g. of a white solid. Recrystallization from benzene gave 1.2 g. (23%) of 1,2,3,6-tetrahydro-1-diethylcarboxyacetyl)-4,5-dimethylpyridazine (**34**), m.p. 147-148°; ir (nujol) 3.1 μ (N-H), 5.90 μ (amide carbonyl), 6.20 μ (carboxylate anion); uv max (95% ethanol) end absorption; nmr (deuterochloroform) δ 5.25 (s, 1), 4.10 (s, 2), 3.37 (s, 2), 2.87 (s, 1), 1.94 (m, 10), and 1.05 (t, 6).

Anal. Calcd. for $C_{13}H_{22}N_2O_3$: C, 61.42; H, 8.66; N, 11.02. Found: C, 61.56; H, 8.47; N, 10.83.

The benzene solution from the recrystallization of **34** was evaporated to dryness to give 1.5 g. of starting material **8** as identified by its infrared spectrum. The aqueous solution containing the original reaction mixture was washed twice with 100-ml. portions of methylene chloride. The methylene chloride washings were dried over sodium sulfate and evaporated to dryness under reduced pressure to give 2.1 g. of **8** (72% recovery of **8**).

Reaction of 5,8-Dihydro-5,8-ethano-2,2-diethylpyrazolo[1,2-*a*]-pyridazine-1,3(2*H*)dione (**18**) with Potassium Hydroxide.

A solution containing 3.0 g. of **18** and 4.0 g. of potassium hydroxide in 40 ml. of 95% ethanol was heated at reflux for 45 hours. On cooling, the reaction mixture was added to 200 ml. of water. Acidification with dilute nitric acid did not produce a precipitate. The aqueous solution was washed twice with 100-ml. portions of methylene chloride. The methylene chloride washings were dried over sodium sulfate and evaporated under reduced pressure to give 1.8 g. of a solid residue. Sublimation (0.1 mm) gave pure **18**, m.p. 105-106°.

REFERENCES

(1) Alternatively these may be classified as 1,6-diazabicyclo-[4.3.0]nonane derivatives.

(2) Present address: Indiana University of Pennsylvania, Indiana, Pennsylvania 15701.

(3) B. T. Gillis and R. A. Izydore, *J. Org. Chem.*, 34, 3181 (1969).

(4) H. Stetter and H. Spangenberger, *Chem. Ber.*, 91, 1982 (1958).

(5) The *cis-endo*-configuration of **11** which would arise from *cis*-addition of hydrogen from the least hindered *exo* side of the molecule is mechanistically implied but without proof. The nmr spectrum of the compound was too complex to make a definite assignment.

(6) P. A. S. Smith, "The Chemistry of Open-Chain Nitrogen Compounds," Vol. I, W. A. Benjamin, Inc., N. Y., 1965, pp. 293-294.

(7) The possibility that the reductions proceeded *via* a reverse Diels-Alder reaction was ruled out experimentally. Heating a solution of **18** in refluxing tetrahydrofuran for 48 hours (reaction conditions minus lithium aluminum hydride) gave after workup a quantitative recovery of **18**. If a reverse Diels-Alder reaction were operating, some of the characteristic decomposition products of the azo dienophile **1** (see reference (3)) would have been detected.

(8) R. Renaud and L. C. Leitch, *Can. J. Chem.*, 32, 545 (1954).

(9) R. L. Hinman, *J. Am. Chem. Soc.*, 78, 1645 (1956).

(10) Melting points are corrected. Microanalysis were per-

formed by Dr. Alfred Bernhardt, Mulheim, Germany or Dr. H. W. Galbraith, Knoxville, Tennessee. Infrared spectra were taken with a Perkin-Elmer Model 137 double beam spectrophotometer. The nmr spectra were taken with a Varian Model A-60 using deuterochloroform as a solvent and tetramethylsilane as an internal standard. The ultraviolet spectra were taken with a Cary Model 14 Spectrophotometer.

(11) The preparation and properties of the various Diels-Alder adducts cited herein can be obtained by consulting reference (3).

(12) A. A. Pavlic and H. Adkins, *J. Am. Chem. Soc.*, 68, 1471 (1946).

(13) S. Sarel and M. S. Newman, *ibid.*, 78, 5416 (1956).