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Studies of Diels-Alder-type Additions of Cyclic α-Carbonyl-Azo-Compounds[*1]

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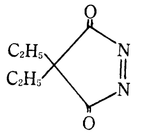
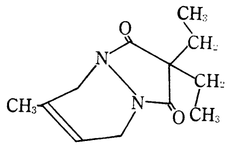
The unstable cyclic diacyl diimides[1–3] and dioxotriazoline,[4] which were generated from the corresponding dihydro-compounds by oxidation with lead tetraacetate or *t*-butyl hypochlorite, gave the Diels-Alder adducts in the presence of the conjugated dienes. In recent papers, it has been shown that 4,4-diethyl-3,5-dioxo-1-pyrazoline[5,6] prepared from diethylmalonic acid hydrazide was reactive as a dienophile.

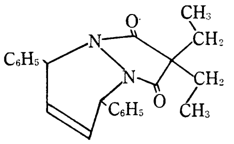
Several cyclic diacyl hydrazides were slowly oxidized with nickel peroxide[7] to prepare dicarbonyl-azo-compounds, they then gave the adducts by means of an *in situ* reaction with dienes. As the process was carried out in heterogeneous system, it was not so troublesome as with the above treatments to isolate the adducts from the degraded oxidants. Thus, the method provided a more convenient one-step synthesis of pyridazine derivatives. The proposed structure of the products is based on the molecular weights, the results of elemental analyses, and the IR and NMR spectra.



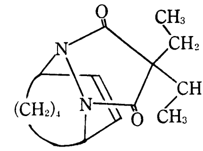
1c



2c



3c



4c

When maleic hydrazide and nickel peroxide were suspended in methylene chloride and stirred at room temperature, 3,6-dioxopyridazine (**1a**) was produced, and a small amount of nitrogen has evolved because of the partial decomposition of hydrazide. A reaction *in situ* with isoprene gave 1,4-dihydro-2-methyl-6,9-dioxopyridazino[1,2-*a*]pyridazine (**2a**) *via* the process shown by Equations (1) and (2). The IR (KBr) spectrum of **2a** showed a carbonyl absorption at 1638 cm^{-1}, but no imino absorption. The NMR ($CDCl_3$) spectrum exhibited signals at τ 8.10 (s, 3H, 2-CH_3), 5.56 (s, 2H, 1-CH_2), 5.75—5.35 (m, 2H, 4-CH_2), 4.24 (m, 1H, 3-olefinic H), and 3.05 (s, 2H, 7,8-olefinic H). The reactions with *trans,trans*-1,4-diphenyl-1,3-butadiene and 1,3-cyclooctadiene gave 1,4-dihydro-6,9-dioxo-1,4-diphenylpyridazino[1,2-*a*]pyridazine (**3a**) and 1,4-butano-1,4-dihydro-6,9-dioxopyridazino[1,2-*a*]pyridazine (**4a**) respectively.

$$R\begin{matrix}\diagup CO\text{-}NH\\ |\\ \diagdown CO\text{-}NH\end{matrix} \xrightarrow{\text{Ni-PO}} \underset{\mathbf{1}}{R\begin{matrix}\diagup CO\text{-}N\\ \|\\ \diagdown CO\text{-}N\end{matrix}} + H_2O \qquad (1)$$

$$\mathbf{1} + \text{diene} \longrightarrow \text{adduct} \qquad (2)$$

Ni-PO = nickel peroxide

R= a: -CH=CH-, b: o-$C_6H_4\langle$, c: $(C_2H_5)_2C\langle$

diene = 2: isoprene, 3: diphenylbutadiene,
4: cyclooctadiene

Adducts:

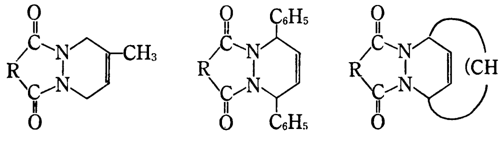


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TABLE 1. DIELS-ALDER ADDUCTS

Adduct	Yield %	Mp[d)] °C, (S)[e)]	Formula	Mw[j)]	Calcd. %			Found %		
					C	H	N	C	H	N
2a	33.7	117—118 (A)	$C_9H_{10}N_2O_2$	178	60.66	5.66	15.72	60.41	5.48	15.54
3a[a)]	62.5	225—226 (B)	$C_{20}H_{16}N_2O_2$	316	75.93	5.10	8.86	75.85	5.00	8.67
4a	22.5	171—172 (A)	$C_{12}H_{14}N_2O_2$	218	66.03	6.47	12.84	66.08	6.50	12.76
2b	23.7	151—154.5 (A)	$C_{13}H_{12}N_2O_2$	228	68.41	5.30	12.27	68.51	5.26	12.22
3b[b)]	79.2	217.5—218.5 (B)	$C_{24}H_{18}N_2O_2$	366	78.67	4.95	7.65	78.86	4.79	7.60
4b	89.5	200.5—201.0[f)] (C)	$C_{16}H_{16}N_2O_2$	268	71.62	6.01	10.44	71.85	6.08	10.38
2c[c)]	83.3	53—55[g)] (A)	$C_{12}H_{18}N_2O_2$	222	64.84	8.16	12.60	64.62	8.37	12.37
3c[c)]	55.6	154—156[h)] (A)	$C_{23}H_{24}N_2O_2$	360	76.64	6.71	7.77	76.89	6.64	7.85
4c	7.8	137—138[i)] (D)	$C_{15}H_{22}N_2O_2$		68.67	8.45	10.68	68.05	8.44	10.53

a) The reagents were refluxed in benzene.
b) The reaction was continued for 88 hr.
c) Lead tetraacetate was used as the oxidant of cyclic hydrazide.
d) Melting points are uncorrected.
e) Recrystallization from the following solvent: A, alcohol; B, benzene - alcohol; C, petroleum ether - *n*-hexane - ethanol; D, water.
f) Lit,[3)] mp 208—210°C.
g) Lit,[5)] mp 58.5—60°C.
h) Lit,[5)] mp 147—148°C.
i) Lit,[5)] mp 134—136°C.
j) Molecular weight determinations were made by analysis of the mass spectra.

The same process, when applied to 1,4-dioxophthalazine (**1b**) generated from phthalic acid hydrazide by nickel peroxide oxidation and isoprene, gave 1,4-dihydro-2-methyl-6,11-dioxopyridazino[1,2-*b*]phthalazine (**2b**). In the reaction of *trans,trans*-1,4-diphenyl-1,3-butadiene or 1,3-cyclooctadiene with **1b**, 1,4-dihydro-6,11-dioxo - 1,4 - diphenylpyridazino [1,2 - *b*] phthalazine (**3b**) or 1,4-butano-1,4-dihydro-6,11-dioxopyridazino[1,2-*b*]phthalazine (**4b**) respectively was isolated.

The procedure in which nickel peroxide was used as the oxidant of diethylmalonic acid hydrazide gave a small of the reaction product, or no yield at all, with diene. On the other hand, 4,4-diethyl-3,5-dioxo-1-pyrazoline (**1c**) prepared by oxidation with lead tetraacetate gave the 1,4-adducts in a high yield. They were 2,2-diethyl-2,3,5,8-tetrahydro-7-methyl-1,3-dioxo-1*H*-pyrazolo[1,2-*a*]pyridazine (**2c**), 2,2-diethyl-2,3,5,8-tetrahydro-1,3-dioxo-5,8-diphenyl-1*H*-pyrazolo-[1,2-*a*]pyridazine (**3c**), and 5,8-butano-2,2-diethyl-2,3,5,8-tetrahydro-1,3-dioxo-1*H*-pyrazolo[1,2-*a*]-pyridazine (**4c**).

Experimental

General Procedure for the Reaction of Cyclic Diacyl Diimide with Dienes. The reagents, cyclic hydrazide (0.01 mol) and diene (0.01—0.03 mol), were slurried in methylene chloride (50 m*l*) at room temperature. A large excess of diene should be avoided. Fine powder of nickel peroxide (1.2—2.0 times the theoretical amount, as determined on available oxygen[7a)]) was added, little by little, with magnetic stirring. Stirring was continued for *ca.* 20—40 hr at room temperature after the addition of the nickel peroxide. The loss of the methylene chloride was compensated for according to circumstances. The reaction mixture was then filtered, and the filtrate was evaporated on a rotary evaporator at <40°C to yield a crude adduct. The residue was purified by crystallization or by distillation under reduced pressure to give an analytical sample.

The Diels-Alder adducts thus prepared, along with their physical properties, yields and analyses, are listed in Table 1. The yields, based on the cyclic hydrazide, were determined from the weight of the raw crystals from the first recrystallization.

IR and NMR Spectra of Adducts. 3a: 1632 cm^{-1} (C=O); τ 3.67 (s, 4H, 2,3,7,8-olefinic H), 3.02 (s, 2H, methyne), 2.82 (s, 10H, phenyl). **4a**: 1637 cm^{-1}; τ 8.90—7.40 (m, 8H, methylene), 4.45 (m, 2H, methyne), 3.85 (m, 2H, 2,3-olefinic H), 3.10 (s, 2H, 7,8-olefinic H). **2b**: 1630 cm^{-1}; τ 8.08 (s, 3H, CH_3), 5.46 (s, 2H, 1-CH_2), 5.60—5.25 (m, 2H, 4-CH_2), 4.24 (m, 1H, 3-CH), 2.21 (m, 2H, 8,9-aromatic H), 1.70 (m, 2H, 7,10-aromatic H). **3b**: 1640 cm^{-1}; τ 3.61 (m, 2H, methyne or olefinic H), 3.50 (m, 2H, methyne or olefinic H), 2.81 (s, 10H, phenyl), 2.17 (m, 2H, 8,9-aromatic H), 1.68 (m, 2H, 7,10-aromatic H). **4b**: 1630 cm^{-1}; τ 8.70—7.30 (m, 8H, methylene), 4.20 (m, 2H, methyne), 3.80 (m, 2H, olefinic H), 2.23 (m, 2H, 8,9-aromatic H), 1.70 (m, 2H, 7,10-aromatic H). **2c**: 1725 and 1685 cm^{-1}; τ 9.16 (t, 6H, $C\underline{H}_3CH_2$), 8.20 (quar, 4H, $CH_3C\underline{H}_2$), 8.12 (s, 3H, 7-CH_3), 5.97 (s, 2H, 8-CH_2), 6.10—5.76 (m, 2H, 5-CH_2), 4.43 (m, 1H, 6-CH). **3c**: 1689 cm^{-1}; τ 9.71 (t, 3H, $C\underline{H}_3CH_2$), 9.15 (t, 3H, $C\underline{H}_3CH_2$), 8.65—8.00 (quin, 4H, $2CH_3C\underline{H}_2$), 4.40 (m, 2H, 2CH), 4.08 (m, 2H, olefinic H), 2.80—2.30 (m, 10H, phenyl). **4c**: 1717 and 1666 cm^{-1}; τ 9.45—8.85 (m, 6H, $2C\underline{H}_3CH_2$), 8.60—7.60 (m, 12H, methylene), 5.15—4.75 (m, 2H, 2CH), 4.00—3.80 (m, 2H, olefinic H).