Reaction of Cyclopropenones with Heteroaromatic Nitrogen Compounds

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Diphenylcyclopropenone reacts with a variety of heteroaromatic nitrogen compounds to give in good yield either (*a*) 1,2-diphenyl-3-indolizinyl *cis*-1,2-diphenyl acrylates and aza analogs, (*b*) 5,6-diphenyl-7-hydroxypyrrolo[1,2-*b*]pyridazines and similar structures, or (*c*) adducts in which cycloaddition takes place to an N=N bond. Proof of structure of the new heterocycles is based on deuterium labelling experiments, hydrogenolysis to known compounds, and the preparation of chloro and iminoether derivatives. Cycloheptenocyclopropenones in the examples studied form heterocycles of type *b*.

La diphénylcyclopropénone réagit avec une variété de composés hétéroaromatiques contenant de l'azote et conduit avec de bons rendements soit (*a*) aux *cis*-diphényl-1,2 acrylates (et leurs analogues azotés) de diphényl-1,2 indolizinyle-3, (*b*) aux diphényl-5,6 hydroxy-7 pyrrolo[1,2-*b*]pyridazines et structures similaires, ou (*c*) des composés d'addition dans lesquels la cycloaddition se fait sur le lien —N=N—. Les preuves de structure de ces composés sont basées sur des expériences impliquant des marquages par le deutérium, des hydrogénolyses conduisant à des composés connus et la préparation de dérivés chlorés et iminoéthers. Dans les cas examinés, les cyclohepténocyclopropénones conduisent à des hétérocycles du type *b*.

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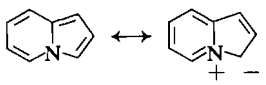
Indolizine (**1**) is one of the fundamental nitrogen heterocyclic systems which has been neglected in comparison to its isomer indole (*1*). Recently interest has been generated in this system since Boekelheide and co-workers have shown indolizine adds to activated acetylenes



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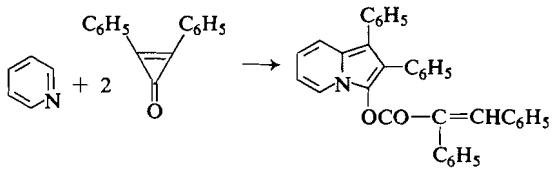
under dehydrogenating conditions to form the theoretically important class of cyclazines (2) in a reaction in which the indolizine reacts as an azomethine ylide, 1,3-dipole (3). Convenient synthetic routes to indolizines are few in number. There are also no synthetic routes which are readily adaptable to the preparation of aza-analogs of indolizine. An interest in the chemistry of cyclopropenones (4) led us to reinvestigate the suggested reaction of pyridine with diphenylcyclopropenone to form diphenylindolizinol derivatives (5) and to extend this reaction to include cycloheptenocyclopropenone and a variety of heteroaromatic nitrogen compounds. Breslow reports pyridine reacts with diphenylcyclopropenone in refluxing methanol to give a compound $C_{35}H_{25}NO_2$ tentatively assigned the indolizinol ester structure **2** or **3**. The product shows a prominent ester carbonyl absorption at 1730 cm^{-1} in the i.r. spectrum (5) like other similar adducts described below. We confirmed the implied cyclization step to the pyridine 2 position by examining the corresponding product obtained from pyridine-d_5. Accurate mass spectral peak measurement confirmed the incorporation of only four deuterons in the product.



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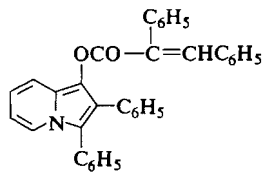

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The adduct yields 1 mol of *cis*-1,2-diphenylacrylic acid on mild alkaline hydrolysis. More vigorous basic hydrolysis leads to extensive decomposition which is not unexpected in view of the reported similar behavior of indolizine **4** (6). Hydrogenolysis of the pyridine adduct with an equimolar mixture of lithium aluminum hydride and aluminum chloride afforded the known 1,2-diphenylindolizine (**5**) isolated at the picrate

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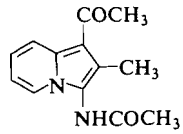

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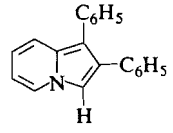

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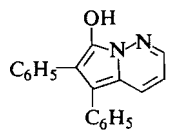
derivative thus proving the structure of the adduct as **2** unambiguously. Compound **5** was not isolated directly since the instability of indolizines unsubstituted in the 1 position has been noted previously (13).

Pyridazine reacts readily with diphenylcyclopropenone to give a different type of product $C_{19}H_{14}N_2O$ as a green crystalline solid *i.e.* corresponding to the incorporation of only 1 equiv of the cyclopropenone and is assigned the 5,6-diphenyl-7-hydroxypyrrolo[1,2-*b*]pyridazine structure **6** which, like similar compounds



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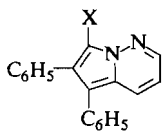
formed in this work, gave a positive color reaction for phenolic hydroxyl with ferric chloride and showed strong i.r. absorption at 3570 cm^{-1} typical of phenolic type hydroxyl shifted approximately 100 cm^{-1} by interaction with the chloroform solvent (7). Indolizinols and similar structures are reported to give a color reaction with ferric chloride (8). Structure **6**, which is an analog of a plausible intermediate in the formation of **2** and similar structures, receives support by its smooth conversion to the chloro compound **7***a*, $C_{19}H_{13}ClN_2$, by treatment with phosphorus oxychloride. Such reactions are



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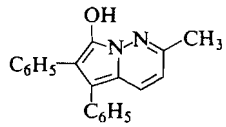
a X = Cl

b X = OCH_2CH_3

typical of amidic groups in heterocyclic systems, *e.g.* the conversion of α-pyridone to 2-chloropyridine (9). Compound **6** was also converted smoothly to the iminoether **7***b* in 87% yield with triethoxonium fluoroborate (*vide infra*). Nitrogen-1 in compound **6** would not be expected to react with a further equivalent of diphenylcyclopropenone since pyrrolopyridazines have been shown to be inert to quaternization (10).

Reaction of diphenylcyclopropenone in methanol with a first group of heteroaromatic nitrogen compounds resulted in the clean formation of either of the two types of adducts exemplified by **2** and **6**. In no case was a mixture of products obtained (see Tables 1 and 2). 3-Methylpyridazine reacted to give the pyrrolo[1,2-*b*]pyridazine (**8**), $C_{20}H_{16}N_2O$, in good yield which like **6** showed a strong phenolic hydroxyl absorption



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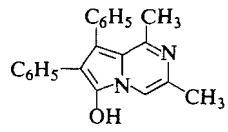

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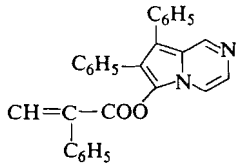

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in the i.r. The position of quaternization of pyridazines is dictated by the position of ring substituents (11). The expected initial attack by N-1 of 3-methylpyridazine on diphenylcyclopropenone is in accordance with the formation of **8**. Investigation of a series of alpha methyl substituted pyridines and isoquinolines revealed that no reaction took place with cyclopropenones presumably for similar reasons of steric hindrance.

2,6-Dimethylpyrazine gave 1,3-dimethyl-7,8-diphenyl-6-hydroxypyrrolo[1,2-*a*]pyrazine (**9**), $C_{21}H_{18}N_2O$, in contrast to the behavior of pyrazine itself which gave 7,8-diphenyl-6-pyrrolo[1,2-*a*]pyrazinyl *cis*-1,2-diphenylacrylate (**10**), $C_{34}H_{24}N_2O_2$, which like **2** shows a prominent ester absorption at 1730 cm^{-1} in the i.r. spectrum. Compounds **2** and **10** and similar structures all show a sharp singlet at 7.78 δ characteristic of the vinyl proton in the 1,2-diphenylacrylic acid moiety (4*b*, *c*). The difference in reactivity of 2,6-dimethylpyrazine and pyrazine cannot be accounted for at this time since repeated attempts to acylate **9** by reaction with *cis*-1,2-diphenylacryloyl chloride or excess diphenylcyclopropenone regenerated **9** unchanged. Paquette similarly reports that normal

TABLE 1. Reaction products of diphenylcyclopropenone with heteroaromatic compounds

Number	Reactant	Product type*	Melting point (°C)	Yield (%)	Observed (%) C	H	N	Molecular ion (mass spectrum)	Calculated (%) C	H	N	Molecular ion (mass spectrum)
2	Pyridine	B	178	50	85.47	5.23	2.77	491.1880	85.52	5.13	2.85	491.1885
34	3-Picoline	B	169	19	85.20	5.17	2.72	505.2043	85.52	5.37	2.77	505.2042
6	Pyridazine	A	158	83	79.82	4.86	9.69	286.1100	79.70	4.93	9.78	286.1106
8	3-Methylpyridazine	A	120	65	79.87	5.55	8.95	300.1257	79.98	5.37	9.33	300.1263
10	Pyrazine	B	173	31	82.23	4.96	5.15	492.1840	82.91	4.91	5.69	492.1838
14	2-Methylpyrazine	A	263	45	80.17	5.36	9.41	300.1255	79.98	5.37	9.33	300.1263
9	2,3-Dimethylpyrazine	A	216	80	80.04	5.63	8.86	314.1418	80.23	5.77	8.91	314.1419
35	Quinoxaline	A	285	26	81.52	4.68	8.10	336.1260	82.12	4.79	8.33	336.1263
16	Isoquinoline	B	178	25	—	—	2.75	541.2032	—	—	2.59	541.2042
17	Phthalazine	A	187	61	82.15	4.62	8.34	336.1258	82.12	4.79	8.33	336.1263
19	Quinazoline	A	248	65	82.16	4.70	8.11	336.1258	82.12	4.79	8.33	336.1263
18	2-Methylquinoxaline	A	240	63	82.27	5.26	7.59	350.1415	82.26	5.18	7.99	350.1419
24	Cinnoline	C	174	77	81.90	4.69	8.39	336.1261	82.12	4.79	8.33	336.1263
23	3,4-Benzocinnoline	C	264	74	83.48	4.52	7.17	386.1422	83.92	4.69	7.25	386.1419
36	4-Phenylpyrimidine	A	151	64	—	—	7.89	362.1415	—	—	7.73	362.1419

*A, 1:1 Adduct exemplified by pyridazine product 6; B, 1:2 adduct exemplified by pyridine product 2; C, 1:1 adduct exemplified by cinnoline product 24.

TABLE 2. Spectroscopic data on indolizines and aza analogs

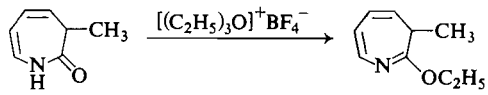
Number	Infrared spectrum (Nujol)	Nuclear magnetic resonance spectrum (δ) Solvent*	Indolizine ring, aryl and vinyl H	Methyl protons	Absorption spectrum (CH_3CN) λ_{max}	log ε
2	1728	$CDCl_3$	7.93(1H)s, 7.78(1H)bs, 7.0–7.5(21H)m, 6.1–6.7(2H)m		249 268(sh) 330(sh)	5.50 5.41 4.76
34	1733	$CDCl_3$	7.88(1H)s, 7.63(1H)bs, 6.9–7.5(21H)m, 6.3–6.6(1H)m	2.15(3H)s	250 267(sh) 320(sh)	5.52 5.44 4.94
6	3200(br) 1617	TFA	8.0–9.0(3H)m, 7.2–7.7(10H)m, 6.66(1H)s keto-form		253 276(sh) 430	5.18 5.07 4.54
8	3430(br) 1610	$CDCl_3$	6.5–8.2(13H)m	3.38(3H)s	250(sh) 290(sh) 333(sh) 465	5.13 4.93 4.68 4.25

TABLE 2. (*Concluded*)

Number	Infrared spectrum (Nujol)	Nuclear magnetic resonance spectrum (δ)			Absorption spectrum (CH_3CN)	
		Solvent*	Indolizine ring, aryl and vinyl H	Methyl protons	λ_{max}	log ε
10	1729	TFA	8.26(1H)s, 7.0–7.8(23H)m		286 417	5.44 4.48
14	2500(br) 1623	TFA	8.63(1H)d, 6.9–7.8(11H)m J = 7 Hz	2.40(3H)s	271(sh) 318 390	5.07 5.00 4.87
9	2500(br) 1623	TFA	10.15(1H)br, 6.7–8.0(10H)m	2.35(3H)bs 3.05(3H)bs	280(sh 325 388	5.00 5.04 4.85
35	2500(br) 1615	TFA	8.82(1H)d, 7.0–7.8(14H)m J = 7.5 Hz		362 480(sh)	4.82 3.72
16	1729	$CDCl_3$	7.86(1H)s, 6.61 and 7.75(2H)ABq, 7.0–7.6(24H)m J = 7.5 Hz		268 313(sh) 395(sh)	5.75 5.55 4.08
17	3540 2700 1620	TFA	9.33(1H)s, 8.2–8.6(3H)m, 7.2–7.8(11H)m, 6.83(1H)s keto-form		259 296 328(sh) 395(sh)	5.29 5.41 5.05 4.13
19	2600(br)	TFA	9.12(1H)s, 8.45(1H)bs, 7.0–8.0(14H)m		269 330 364	5.61 5.01 4.48
18	1640	TFA	7.0–8.3(14H)	3.16(3H)s	255 271 310(sh) 352 466	5.38 5.36 4.96 4.77 4.24
24	1641	$CDCl_3$	7.0–7.7(14H)m, 5.93 and 6.86(2H)ABq 9.4(1H)d J = 7.5 Hz J = 8 Hz		255 297(sh) 378	5.37 4.91 5.12
23	1655	$CDCl_3$	8.94(1H)q, 6.1–7.9(17H)m J = 7.5, 2.5 Hz		252(sh) 285(sh) 290 350	5.54 5.19 5.21 5.22
36	3100(br)	TFA	8.03 and 8.62(2H)ABq, 6.8–7.9(14H)m, 6.61(1H)s J = 7 Hz 8.2–8.5(1H)m, keto-form		266 281 295(sh) 340 404 450	5.32 5.32 5.31 4.93 4.59 4.39

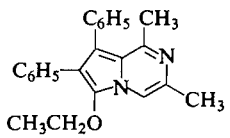
*TF = Trifluoroacctic acid.

acylating reagents (*e.g.* dimethyl sulfate and benzene sulfonyl chloride) are ineffective in the conversion of the amide function in **11** to an imino derivative but that the Meerwein reagent triethoxonium fluoroborate was immediately effective (12). Treatment of compound **9** with



11 **12**

triethoxonium fluoroborate gave the imino ether **13** in good yield. The iminoethers **14** and **15** were similarly prepared quite smoothly from the parent enol compounds in good yield (see Tables 3 and 4).



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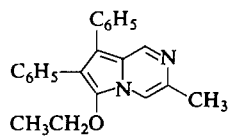

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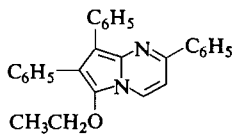

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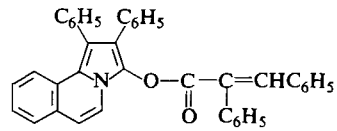
A difference in the reactivity of aza groups in nitrogen heterocycles towards cyclopropenones is exemplified by the ready reaction of isoquinoline to form 1,2-diphenyl-3-pyrrolo[1,2-*a*]-isoquinolinyl *cis*-1,2-diphenylacrylate (**16**), $C_{39}H_{27}NO_2$, in contrast to the complete lack of reactivity of quinoline under similar conditions. In compound **16** cyclization of the first diphenylcyclopropenone moiety to the quinoline 1-position is confirmed by the observation of a 7.5 Hz AB quartet due to protons-5 and -6 centered at 7.75 and 6.61 δ. The chemical shift of proton-5 relative to that in the corresponding adduct **24** obtained from cinnoline favors the orientation shown.

Phthalazine and 2-methylquinoxaline in contrast reacted readily with diphenylcyclopropenone but with the formation of the 1:1 adducts **17**, 1,2-diphenyl-3-hydroxypyrrolo-[1,2-*a*]-phthalazine, $C_{23}H_{16}N_2O$, and **18**, 4-methyl-2,3-diphenyl-1-hydroxypyrrolo[1,2-*a*]quinoxaline, $C_{24}H_{18}N_2O$, both of which showed prominent



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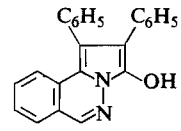

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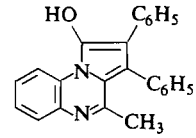

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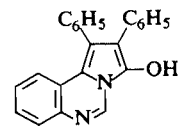
hydroxyl absorption in the i.r. spectrum. The latter evidence together with the correct integration of the aromatic region of the n.m.r. spectrum precludes addition across the N=N bond of phthalazine as occurred in the case of benzocinnoline and cinnoline (*vide infra*). In these additions as in the case of pyridazine there was no tendency for reaction of diphenylcyclopropenone with the second nitrogen.

The corresponding third product, isomeric with **17**, obtained from quinazoline is assigned the 1,2-diphenyl-3-hydroxypyrrolo[1,2-*c*]quinazoline structure **19** because of the susceptibility



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of N-3 of quinazoline to quaternize readily and the general reactivity of the 3,4-bond towards addition (14). Also there have been no cases reported of alkylation of the N-1 position in quinazoline (15). Structures **17**–**19** receive support by their conversion into the corresponding iminoethers **20**–**22** with triethoxonium fluoroborate.

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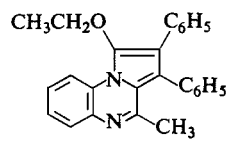

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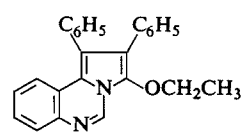

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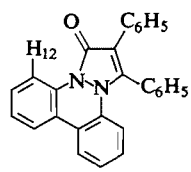
TABLE 3. Iminoethers of indolizines and aza analogs

Number	Original *N*-compound	Melting point (°C)	Yield (%)	Observed (%)				Calculated (%)			
				C	H	N	Molecular ion (mass spectrum)	C	H	N	Molecular ion (mass spectrum)
7*b*	Pyridazine	303	87	79.50	5.55	8.21	314.1409	80.25	5.79	8.92	314.1419
14	2-Methylpyrazine	157	91	79.68	5.96	8.59	328.1574	80.46	6.14	8.53	328.1578
13	2,6-Dimethylpyrazine	62	97	80.70	6.20	8.09	342.1727	80.67	6.48	8.18	342.1732
20	Phthalazine	130	83	—	—	7.78	364.1574	—	—	7.69	364.1575
22	Quinazoline	121	90	—	—	7.81	364.1579	—	—	7.69	364.1575
21	2-Methylquinoxaline	152	93	82.46	5.86	7.36	378.1727	82.51	5.86	7.40	378.1732
37	4-Phenylpyrimidine	120	70	83.30	5.28	6.90	390.1728	83.05	5.08	7.17	390.1732

TABLE 4. Spectroscopic data on iminoethers of indolizines and aza analogs

Number	Nuclear magnetic resonance spectra ($CDCl_3$) δ					Absorption spectra (CH_3CN)	
	Aryl protons		OCH_2	CH_3	CH_3 Aromatic	λ_{max}	log ε
7b		7.0–7.6(13H)m	3.75(2H) 7 Hz	1.25(3H)t 7 Hz		256 314 455	5.43 5.33 4.96
14		7.0–7.6(12H)m	3.94(2H)q 7 Hz	1.26(3H)t 7 Hz	2.29(3H)s	252 282(sh) 325(sh) 360(sh)	5.50 5.37 4.56 4.47
13		7.0–7.5(11H)m	3.73(2H)q 6.5 Hz	1.22(3H)t 6.5 Hz	2.27(3H)s, 2.81(3H)s	252 270(sh) 329	5.51 5.39 4.63
20	8.32(1H)d 8.10(1H)s 4 Hz	7.0–7.8(13H)m	3.81(2H)q	1.27(3H)t 7 Hz		261 292 320(sh) 387	5.40 5.61 5.18 4.02
22	8.46(1H)s	7.0–8.4(14H)m	3.81(2H)q 7 Hz	1.28(3H)t 7 Hz		271 308(sh) 327 355(sh)	5.64 5.05 5.02 4.46
21		6.8–8.0(14H)m	3.77(2H)q 7 Hz	1.23(3H)t 7 Hz	2.89(3H)s	254 346	5.55 4.95
37		6.7–8.3(17H)m	3.90(2H)q 7 Hz	1.25(3H)t 7 Hz		281 340 390(sh)	5.50 5.12 4.66

In all cases examined so far reaction has involved initial attack by an aza nitrogen on the carbonyl group of the cyclopropenone (which is supported by the observed lack of reactivity of all alpha substituted nitrogen heterocycles) followed by cyclization to an adjacent carbon (confirmed in the case of pyridine by the deuterium labelling experiment). Reaction of diphenylcyclopropenone with 3,4-benzocinnoline which lacks a free carbon alpha to the aza nitrogen resulted in the formation of a third type of adduct **23** formulated as the 2,3-diphenyl-1-ketopyrazolo[1,2-*a*]cinnoline, $C_{27}H_{18}N_2O$, in which addition occurs across the N=N double bond. The n.m.r. spectrum of **23** shows all the aromatic protons are intact and the i.r. spectrum shows a strong tertiary amidic carbonyl absorption at 1660 cm^{-1} but no hydroxyl group. The absence of any enolizable hydrogen is confirmed by the recovery of **23** unchanged after treatment with phosphorus oxychloride (contrast **5** and **7**). Similarly **23** is unaffected by treatment with trifluoroacetic acid unlike adducts of types **6**, **8**, **9**, **17**, and **18**, all of which undergo keto-enol displacements as the p*H* is altered. Observation of an 8 Hz doublet at 8.94 δ in the n.m.r. spectrum



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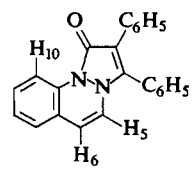

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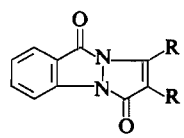

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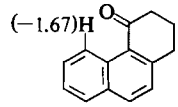
of **23** assigned to H-12 (the paramagnetic shift of which *ca.* −1.4 p.p.m. is in accordance with the *peri* effect exemplified by model compounds **26** and **27** (16)) allows an unambiguous assignment of structure **24** to the analogous cinnoline adduct. The n.m.r. spectrum of **24** shows H-10



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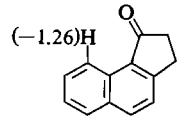

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TABLE 5. Reaction products of cycloheptenocyclopropenone with heteroaromatic nitrogen compounds

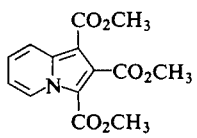
Number	Reactant	Product type*	Melting point (°C)	Yield (%)	Observed (%)				Calculated (%)			
					C	H	N	Molecular ion (mass spectrum)	C	H	N	Molecular ion (mass spectrum)
32	2-Methylpyrazine	A	170	49	72.23	7.39	12.37	216.1267	72.19	7.46	12.95	216.1263
31	2-Dimethylpyrazine	A	217	50	—	—	11.73	230.1415	—	—	12.16	230.1419
33	3-Methylpyridazine	A	145	81	—	—	12.66	216.1267	—	—	12.95	216.1263

*See footnote to Table 1.

as an 8 Hz doublet at 9.4 δ (corresponding to a paramagnetic *peri* shift of *ca.* −1.6 p.p.m.) and a clear 8 Hz AB quartet due to H-5 and -6 centered at 5.93 and 6.86 δ thus defining the orientation of addition of the diphenylcyclopropenone moiety (contrast structure **16**). This is in accordance with expectation since cinnolines without exception quaternize at N-1 (17) and also indicates that in the reaction of nitrogen heterocycles with cyclopropenones attack by the nitrogen occurs at the carbonyl carbon, a result which is consistent with the formation of **2** from pyridine. Compound **24** shows a strong amide carbonyl at 1640 cm^{-1} in the i.r. spectrum and shows no hydroxyl or evidence of an enolizable proton.

Structures containing a fused pyrazolone ring are well documented, *e.g.* **25** (18).

It has been remarked elsewhere that diphenylcyclopropenone in certain of its reactions behaves like a more reactive form of diphenylacetylene (4*a*). The analogy is useful here since pyridine, pyridazine, and a pyrazinium ylide react with activated acetylenes to afford indolizine structures and aza analogs of the indolizine skeleton *e.g.* **28–30** respectively (19, 10, 20).



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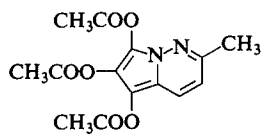

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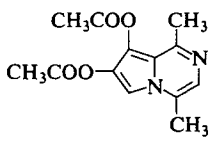

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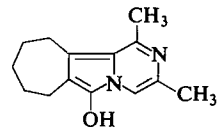
Cycloheptenocyclopropenone (5) reacts readily with 2,6-dimethylpyrazine to give a 1:1 adduct which shows a strong hydroxyl band at 3570 cm^{-1} and is similar in properties to those of adducts **6**, **8**, **9**, and **17–19** and is assigned structure **31**. Similarly adducts **32** and **33** are obtained from 2-methylpyrazine and 3-methylpyridazine respectively (see Table 5).



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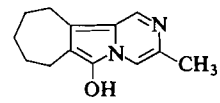

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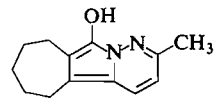

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Experimental

Melting points were determined on a Fisher–Johns apparatus and are uncorrected. The i.r. spectra were recorded on a Perkin–Elmer model 421 spectrophotometer, and only the principal, sharply defined peaks are reported. The n.m.r. spectra were recorded on Varian A-60 and A-100 analytical spectrometers. The spectra were measured on approximately 10–15% (w/v) solutions in $CDCl_3$, with tetramethylsilane as a standard. Line positions are reported in p.p.m. from the reference. Absorption spectra were recorded in 'spectro'-grade solvents on a Beckman DB recording spectrophotometer. Mass spectra were determined on an Associated Electrical Industries MS-9 double focusing high resolution mass spectrometer. The ionization energy, in general, was 70 eV. Peak measurements were made by comparison with perfluorotributylamine at a resolving power of 15000. Kieselgel DF-5 (Camag, Switzerland) and Eastman Kodak precoated sheets were used for t.l.c. Microanalyses were carried out by Dr. C. Daesslé, Organic Microanalysis Ltd., Montreal, Quebec and by Mrs. D. Mahlow of this department.

Reaction of Diphenylcyclopropenone with Heteroaromatic Nitrogen Compounds

The reaction conditions and purification procedures are illustrated by the following examples. The analytical and spectroscopic properties of other compounds similarly prepared are summarized in Tables 1 and 2.

(a) Reaction of Diphenylcyclopropenone with Pyridine

A solution of 4.12 g (0.02 mol) of diphenylcyclopropenone (5) and 1.6 g (0.02 mol) of pyridine in 50 ml of methanol was heated under reflux for 2 h during which time the solution became dark yellow and a green precipitate formed. After cooling, 2.01 g of a 1,2-diphenyl-3-indolizinyl *cis*-1,2-diphenylacrylate were collected (40% yield) and purified by recrystallization from chloroform–ethanol.

Anal. Calcd. for $C_{35}H_{25}NO_2$ (mol. wt. 491.1885): C, 85.52; H, 5.13; N, 2.85. Found (491.1880 (mass spectrum)): C, 85.47; H, 5.23; N, 2.77.

The i.r. spectrum $\nu_{max}(CHCl_3)$: 1728 cm^{-1} (ester C=O). The n.m.r. $\delta_{TMS}(CDCl_3)$: 7.0–7.5 (21H, multiplet, aromatic and indolizine ring protons) 7.93 (1H, singlet, vinyl proton). The absorption spectrum $\lambda_{max}(CH_3CN)$: 249 (log ε 5.50); 268 (sh) (log ε 5.41); 330 mμ (sh) (log ε 4.76).

(b) Control Reaction of Diphenylcyclopropenone with Pyridine-d_5

A solution of 3.0 g (0.015 mol) of diphenylcyclopropenone and 1.2 g (0.015 mol) of pyridine-d_5 (99%, Merck, Sharpe and Dohme of Canada Ltd.) in 50 ml of methanol was heated under reflux for 1.5 h. After cooling the green solid was collected and purified by recrys-

tallization from chloroform–ethanol, 1.55 g (43% yield) m.p. 188°.

Mol. Wt. Calcd. for $C_{35}H_{21}D_4NO_4$: 495.2198. Found: 495.2192.

(c) Reaction of Diphenylcyclopropenone with Pyridazine

A solution of 2.06 g (0.01 mol) of diphenylcyclopropenone and 0.8 g (0.01 mol) of pyridazine in 40 ml of methanol was heated under reflux for 2 h. Upon cooling and setting aside for 24 h, a mass of green crystals precipitated and was collected and purified by recrystallization from methanol affording 5,6-diphenyl-7-hydroxypyrrolo[1,2-*b*]pyridazine, 2.37 g (83% yield), m.p. 158° (dec.).

Anal. Calcd. for $C_{19}H_{14}N_2O$ (mol. wt. 286.1106): C, 79.70; H, 4.93; N, 9.78. Found (286.1100 (mass spectrum)): C, 79.82; H, 4.86; N, 9.69.

The i.r. spectrum ν_{max}(Nujol): 3200 cm^{-1} (br) (OH). The n.m.r. spectrum $\delta_{TMS}(CF_3COOH)$: 6.66 (1H, singlet enolizable proton); 7.2–7.7 (10H, multiplet, aromatic protons); 8.0–9.0 (3H, multiplet, indolizine ring protons). The absorption spectrum $\lambda_{max}(CH_3CN)$: 253 (log ε 5.18); 276 (sh) (log ε 5.07); 430 mμ (log ε 4.54).

(d) Reaction of Diphenylcyclopropenone with 2,6-Dimethylpyrazine

A solution of 2.06 g (0.01 mol) of diphenylcyclopropenone and 1.08 g (0.01 mol) of 2,6-dimethylpyrazine in 40 ml of methanol was allowed to stand at room temperature for 3 days. The initially orange solution gradually turned dark red and a yellow solid which had precipitated was collected and purified by recrystallization from methanol giving 1,3-dimethyl-7,8-diphenyl-6-hydroxypyrrolo-[1,2-*a*]-pyrazine, 2.52 g (80% yield), m.p. 216° (dec.). This material shows only one spot on silica t.l.c. in 1:4 methanol–benzene which moved to a different position in acidic eluants. When exposed to air the yellow solid turned orange and finally red, but when the latter red material was recrystallized from methanol, the yellow form, m.p. 216°, was recovered unchanged. The sensitivity of this product to p*H* like others of similar structure described in this paper is attributed to facile keto–enol tautomerizations.

Anal. Calcd. for $C_{21}H_{18}N_2O$ (mol. wt. 314.1419): C, 80.23; H, 5.77; N, 8.91. Found (314.1418 (mass spectrum)): C, 80.04; H, 5.63; N, 8.86.

The i.r. spectrum ν_{max}(Nujol), 3500 br (OH), 1623 cm^{-1} (C=O). The n.m.r. spectrum $\delta_{TMS}(CF_3COOH)$ 2.35 (3H, broad singlet, CH_3), 3.05 (3H, broad singlet, CH_3); 6.7–8.0 (10H, aromatic protons), 10.15 (1H, broad singlet, 4-indolizine ring proton). The absorption spectrum $\lambda_{max}(CH_3CN)$ 280 (sh) (log ε 5.00); 325 (log ε 5.04); 388 mμ (log ε 4.84).

(e) Reaction of Cycloheptenocyclopropenone with 2-Methylpyrazine

A solution of 2.44 g (0.02 mol) of cycloheptenocyclopropenone (5) and 1.88 g (0.02 mol) of 2-methylpyrazine in 50 ml of methanol was heated under reflux for 2 h and set aside at room temperature overnight. A green crystalline solid precipitated and was collected and purified by recrystallization from methanol–dimethoxyethane giving 7,8-cyclohepteno-3-methyl-6-hydroxypyrrolo[1,2-*a*]pyrazine, 2.15 g (49% yield), m.p. 170° (dec.).

Anal. Calcd. for $C_{13}H_{16}N_2O$ (mol. wt. 216.1263): C, 72.19; H, 7.46; N, 12.95. Found (216.1267 (mass spectrum)): C, 72.23; H, 7.39; N, 12.37.

The i.r. spectrum ν_{max}(Nujol): 3500 (br) OH, 1619 cm^{-1} (C=O). The n.m.r. spectrum $\delta_{TMS}((CD_3)_2SO)$ 0.8–2.0 (10H, multiplet, cycloheptено protons), 3.07 (3H, singlet, CH_3), 6.5–8.5 (3H, multiplet, aromatic protons). The absorption spectrum $\lambda_{max}(CH_3CN)$: 303 (log ε 4.93); 365 mμ (log ε 4.65).

Hydrogenolysis of 1,2-Diphenyl-3-indolizinyl cis-1,2-Diphenylacrylate with Lithium Aluminum Hydride and Aluminum Chloride (21)

To a suspension of 1.23 g (2.5 mmol) of 1,2-diphenyl-3-indolizinyl *cis*-1,2-diphenylacrylate and 1.17 g (12 mmol) of aluminum chloride in 200 ml of dry ether was added with stirring a solution of 0.17 g (4.4 mmol) of lithium aluminum hydride in 50 ml of dry ether. The mixture was heated under reflux for 24 h with continued stirring. The excess lithium aluminum hydride was decomposed cautiously with methanol and a slight excess of 20% aqueous sodium carbonate was added with cooling. The ether layer was washed with water and dried ($MgSO_4$). The filtered ether solution was concentrated to *ca.* 50 ml, a saturated solution of picric acid in ethanol was added, and the mixture set aside for 2 days during which time a green solid precipitated. The collected 1,2-diphenylindolizine picrate, 0.15 g (12% yield), had m.p. 149–150° (ethanol) (lit. m.p. 146–148° (22)). The mass spectrum showed a base peak at *m/e* 269 corresponding to $C_{20}H_{15}N$ for diphenylindolizine.

Preparation of Iminoethers from Indolizinol Analogs with Triethoxonium Fluoroborate

Reaction conditions and purification procedures are exemplified for the preparation of the iminoether from the phthalazine adduct (see also Tables 3 and 4).

To a dried solution of 0.168 g (0.5 mmol) of 1,2-diphenyl-3-hydroxypyrrolo[1,2-*a*]phthalazine in 10 ml of chloroform was added with stirring at room temperature a freshly prepared solution of 2 mmol triethoxonium fluoroborate (23) in 10 ml of methylene chloride. After the addition was completed, stirring was continued for 2 h and the solution was set aside overnight. The mixture was treated with 50% aqueous potassium carbonate solution and filtered. The filtrate was washed with water and dried ($MgSO_4$). Evaporation of the solvent and trituration of the residual oil with 60% aqueous methanol afforded 1,2-diphenyl-3-methoxypyrrolo[1,2-*a*]phthalazine, 0.15 g (83% yield), m.p. 129–130° (aqueous methanol).

Anal. Calcd. for $C_{25}H_{20}N_2O$ (mol. wt. 364.1575): N, 7.69; Found: (364.1574 (mass spectrum)): N, 7.78%.

The n.m.r. spectrum $\delta_{TMS}(CDCl_3)$: 1.27 (3H, triplet CH_3); 3.81 (2H, quartet, J = 7 Hz CH_2CH_3); 7.0–7.8 (12H, multiplet, aromatic protons), 8.10 (1H, singlet, 6 proton); 8.32 (1H, doublet, J = 8 Hz, 10 proton). Absorption spectrum $\lambda_{max}(CH_3CN)$: 261 (log ε 5.40); 292 (sh) (log ε 5.61); 320 (sh) (log ε 5.18); 387 mμ (log ε 4.02).

Preparation of 7-Chloro-5,6-diphenylpyrrolo[1,2-b]-pyridazine

A mixture of 1.43 g (5 mmol) of 5,6-diphenyl-7-hydroxypyrrolo[1,2-*b*]pyridazine and 20 ml of phosphorus oxychloride was heated under reflux for 2 h and the

excess phosphorus oxychloride was removed *in vacuo*. Trituration of the residual oil with ethyl acetate gave a brown solid which was recrystallized from chloroform and ethanol giving 7-chloro-5,6-diphenylpyrrolo[1,2-*b*]-pyridazine, 1.03 g (68% yield), m.p. 164°.

Mol. Wt. Calcd. for $C_{19}H_{13}N_2Cl$: 304.0767. Found (mass spectrum): 304.0760.

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