Reaction of a Highly Spiro-activated Cyclopropane with Pyridines. A Novel Intramolecular Charge Transfer Interaction of the Product

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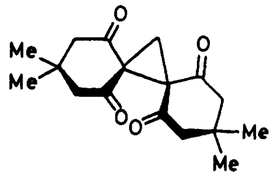
The reaction of 3,3,10,10-tetramethyldispiro[5.0.5.1]trideca-1,5,8,12-tetraone (1) with pyridines afforded a yellow crystalline product under very mild conditions. The structure of the product was assigned as a derivative of the pyridinium β-keto-enolate (2a) in which the cyclopropane ring of (1) is cleaved by heterolysis giving a β-keto-enolate anion. In its electronic spectrum the absorption maximum at longer wavelength (charge transfer band) for (2a) showed solvatochromic shifts. The transition energes (E_{ct}) of (2a) measured in various solvents give linear plots against the Kosower Z valves and Taft–Kamlet α-scales, with slopes of 0.62 and 15.70, respectively. Also, there is a linear relationship between E_{ct} and the Hammett σ-value for each substituent of the heteroaromatic ring in (2a—g), the ρ-value being −16.8. The structure and properties of (2a) have been described from these results.

THE chemistry of activated cyclopropanes has been examined from the points of view of nucleophilic ring opening as well as synthetic utilization.[1-3] Thus, mechanistic studies on these ring opening reactions have been reported by Cram *et al.* and Berkowitz and Grenotz,[2] and also some natural products have been synthesized by employing activated cyclopropane derivatives.[3] Here, we report the reactions of 3,3,10,10-tetramethyldispiro-[5.0.5.1]trideca-1,5,8,12-tetraone (1) (TACP) with pyridines, and the structure and properties of the products.[4]

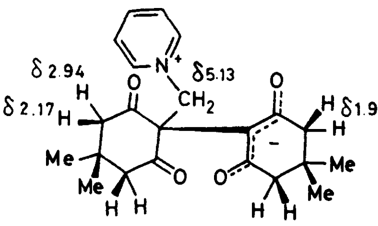
RESULTS AND DISCUSSION

Characterization of Reaction Product by N.m.r.—We considered that the cyclopropane ring in TACP (1) was favourably arranged for interaction with the four carbonyl groups.[5] For this reason, TACP smoothly reacted with excess of pyridine in various solvents even at room temperature to afford yellow crystals, m.p. 181—182° C, in high yield. The product could be recrystallized from chloroform or benzene, but the crystals were labile on heating a solution, and so hygroscopic that the yellow colour faded on exposure to the atmosphere to furnish a colourless solid. Elemental analysis gave a satisfactory result for $C_{22}H_{27}NO_4$ after a sample was dried for a day at 100 °C under nitrogen.



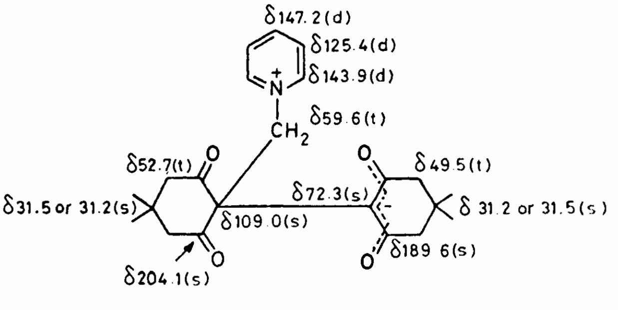
(1)

In the ^{1}H n.m.r. spectrum in $CDCl_3$, there were observed the following characteristic signals, δ 5.13 (2 H, s), 1.95 (4 H, s), and 2.17 and 2.94 (4 H, ABq, J 12 Hz), together with signals for four methyl groups and for five heteroaromatic protons. It may be deduced from the ^{1}H n.m.r. spectrum that the cyclopropyl methylene protons in TACP shifted downwards by *ca.* 2.5 p.p.m. in the product and four methylene protons out of eight in the two cyclohexane rings of TACP shifted upwards by *ca.* 0.7 p.p.m. (*cf.* the corresponding ^{1}H n.m.r. signals of TACP).[6] The structure of the product was assigned as the pyridinium β-keto-enolate (2a), a zwitterion.



(2a)

To confirm this assignment ^{13}C Fourier transform n.m.r. measurements were performed. In the spectrum, six singlets and three triplets were observed in addition to the signals for the four methyl groups and the pyridine carbons. The lowest singlet at δ 204.1 and the second lowest at 189.6 p.p.m. were assigned to the carbonyl carbons and to the enolate carbonyl carbons, respectively. The two singlets at δ 31.5 and 31.2 p.p.m. were attributed to the two quaternary carbon atoms with methyl groups attached. The singlets at δ 72.3 or 109.0 p.p.m. can be assigned to either the quaternary carbon atom between the two carbonyl groups or the central carbon atom in the β-keto-enolate. The lowest triplet at δ 59.6 p.p.m. was assigned to a methylene carbon atom adjacent to the positively charged nitrogen in the pyridinium ion. The triplet at δ 52.7 p.p.m. was attributed to the two methylene carbons in the neutral cyclohexanedione structure and similarly the triplet at δ 49.5 p.p.m. to the two methylene carbons in the negatively charged cyclohexanedione ring. Some of these δ values are comparable with those in TACP.[6] Thus the δ value (31.0) of the quaternary carbons attached to the two methyl groups in TACP was very close to value for the corresponding carbon atoms in (2a). A similar correlation may be observed for the chemical shifts (δ 55.3 in TACP) of the methylene carbon atoms in the cyclohexane ring. By means of this spectroscopic analysis the framework of the product was confirmed as (2a). Accordingly, the cyclopropane ring of TACP has been readily cleaved by attack of the nucleophilic pyridine base in the reaction.



(2a)

Solvatochromic Shifts in the Electronic Spectrum.—It is particularly interesting that the absorption maximum at longer wavelengths in the visible region was subject to remarkable blue shifts when more polar solvents were employed in the measurement of the spectrum. The results are summarized in Table 1. The transition energies (E_{ct}) of (2a) measured in various solvents were plotted against Kosower's Z value,[7] and a good linear line was obtained as shown in Figure 1: $E_{ct} = 0.636Z + 29.1$ (n 12, r 0.973). Eicher has reported on the solvatochromic properties of 4-diacetylmethylene-1,4-dihydro-*N*-methyl-2,3,5,6-tetraphenylpyridine (4), a sort of merocyanine dye.[8] The absorption maximum of (4) is *ca.* 100 nm higher than that of (2a) in the same solvent. In other words, less excitation energy is necessary for the merocyanine derivative (4) compared with (2a). However, the susceptibility to the solvent effect is very similar in both systems. In other merocyanine derivatives such as 4-(3,3-diformylallylidene)-1-methyl-1,4-dihydroquinoline, analogous results were reported.[9] The Z value of a solvent corresponds to the transition energy of *N*-ethyl-4-methoxycarbonylpyridinium iodide (3) dissolved in the solvent; also this pyridinium iodide is definitely proved to be a charge transfer complex.[10] Thus, the product (2a) could be regarded as an intramolecular charge transfer complex on the basis of the solvent effect on the electronic spectrum. It may be noted that the solvent effect on the charge transfer band does not depend upon the magnitude of E_{ct}.

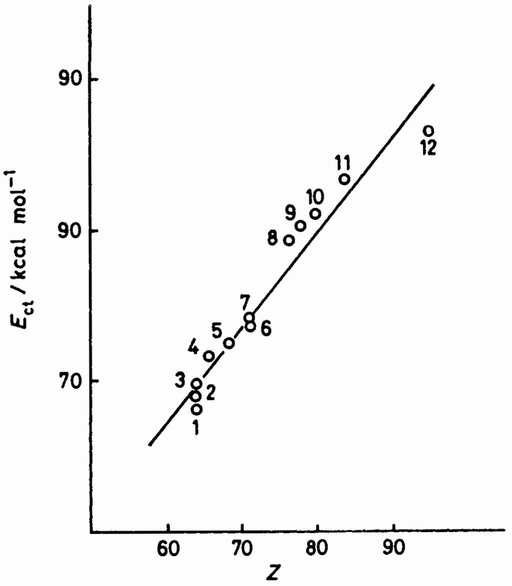
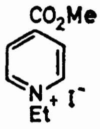
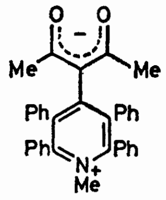


FIGURE 1 Correlation between the transition energy E_{ct} of (2a) and the Z value of the solvents employed in the measurements: 1, C_6H_6; 2, $(CH_2Cl)_2$; 3, CH_2Cl_2; 4, $(CH_3)_2CO$; 5, DMF; 6, CH_3CN; 7, DMSO; 8, Pr^{i}OH; 9, Bu^{n}OH; 10, EtOH; 11, MeOH; 12, H_2O



(3)



(4)

In hydroxylic solvents, there was no linear correlation between the solvatochromic shift and the β-scale of the solvent,[11] but a good linear relationship between E_{ct} and the α-scale was observed as shown in Figure 2: $E_{ct} = 15.7\alpha + 68.9$ (n 6, r 0.968); $Z = 25.4\alpha + 61.3$ (n 6, r 0.848).

Hydrogen bonding to enolate oxygen should stabilize the ground state relative to the electronic excited state and the effect of protic solvents should be hypsochromic. The magnitude of the blue shifts should be expected to increase with increasing hydrogen-bonding ability (α-scale) of protic solvents and acetonitrile. Enhanced shifts are in the order CH_3CN (α 0.29) < Pr^{i}OH (α 0.69) < Bu^{n}OH (α 0.71) < EtOH (α 0.85) < MeOH (α 0.99) < H_2O (α 1.02). These results are in accord with expectation. A similar solvatochromic shift has been ob-

TABLE 1

The u.v.–visible spectrum of the zwitterion (2a) in various solvents

Solvent	CH_3CN	DMSO	DMF	Acetone	Benzene	$(CH_2Cl)_2$	CH_2Cl_2	Pr^{i}OH	Bu^{n}OH	EtOH	MeOH	H_2O
Z value [a]	71.3	71.1	68.5	65.7	64.0	63.9	64.2	76.3	77.7	79.6	83.6	94.6
α-scale [b]	0.29							0.687	0.710	0.850	0.990	1.017
β-scale [b]		0.752	0.710	0.499				0.92	0.85	0.77	0.62	0.14
$\lambda_{max.}$/nm	388	385	393	399	420	418	404	360	356	353	343	330
E_{ct}/kcal mol^{-1} [c]	73.7	74.3	72.7	71.7	68.1	68.4	69.9	79.4	80.3	81.0	83.4	86.6
log ε	3.0	3.0	3.0	3.0	3.0	3.0	3.0	3.0	3.0	3.0	2.9	3.1
$\lambda_{max.}$/nm	289	291	290		289	287	287			286	285	288
log ε	4.1	4.1	4.1		4.2	4.2	4.2			4.2	4.1	4.2

[a] Ref. 7. [b] Ref. 11. [c] $E_{ct} = hcN_A/\lambda_{max.} = 2.859 \times 10^4/\lambda_{max.}$.

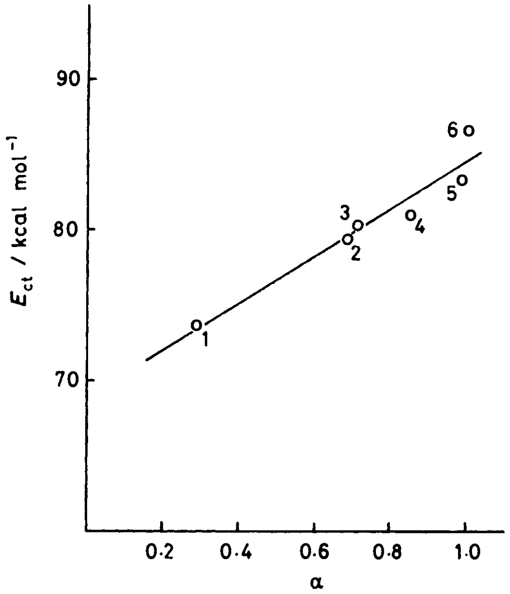


FIGURE 2 Correlation between the transition energy (E_{ct}) of charge transfer band for (2a) and the α-scale of the solvents employed in the measurements: 1, CH_3CN; 2, Pr^iOH; 3, Bu^nOH; 4, EtOH; 5, MeOH; 6, H_2O

served for Kosower's Z value.[7,11] The difference in coefficient for the α-scale in these relationships reflects the different degree of hydrogen bonding toward the counteranion. Accordingly, the hydrogen bond for the β-keto-enolate of this zwitterion seems to be slightly weaker than that for the iodide ion of (3).

Substituent Effect on Charge Transfer Absorption Band of TACP–Pyridine Derivatives (2a—g).—By a similar procedure some 3- and 4-substituted pyridines also reacted with TACP (1) to afford the analogous zwitterion (2a—g). The results are summarized in Table 2. It was also noted in the electronic spectra of these products that the absorption maximum for the zwitterion shifted toward longer wavelengths as the electron-withdrawing property of a substituent on the pyridine ring becomes more powerful. The Hammett plot for the transition energies of (2a—g) measured in acetonitrile was linear as shown in Figure 3: $10^3(E_{ct}^X - E_{ct}^H)/2.303RT = -16.8\sigma - 0.895$ (n 6, r 0.997). This ρ value may be essentially the same as that (ρ −13.4) obtained for N-ethyl-substituted pyridinium iodides.[12] A quite similar correlation was also obtained in ethanol or tetrahydrofuran as solvent. The results again support the charge transfer interaction of both ions in the products (2a—g).

TABLE 2

Substituent effects of the pyridinium ring on the absorption maximum of the charge transfer band measured in different solvents at 25 °C

Compound	(2b)	(2c)	(2d)	(2a)	(2g)	(2f)	(2e)
Substituent	4-Me	4-Et	3-Me	H	4-$CONH_2$	4-CO_2Me	4-CN
[a]	−0.17	−0.15	−0.07	0		0.45	0.66
E_{ct} in EtOH [b]	81.0		79.4	81.0	72.6	68.6	65.0
E_{ct} in CH_3CN [b]	76.2	75.4	73.9	73.7		61.6	57.6
E_{ct} in THF [b]	71.1		69.9	69.7	64.8	57.4	54.1

[a] Hammett's σ value. [b] E_{ct} kcal mol^{-1} = $h\nu N_A/\lambda_{max.} = 2.859 \times 10^4/\lambda_{max.}$.

Several intramolecular charge transfer pyridinium salts have been reported,[13] but this is the first example in which the β-keto-enolate anion is separated from the pyridinium part by two saturated carbon atoms or the anionic part interacts with the cationic part without direct conjugation in the same molecule.[14] For the conformation of (2) in solution, there are two possibilities. If charge transfer interaction takes place through space, conformation (5) is preferred. The interaction

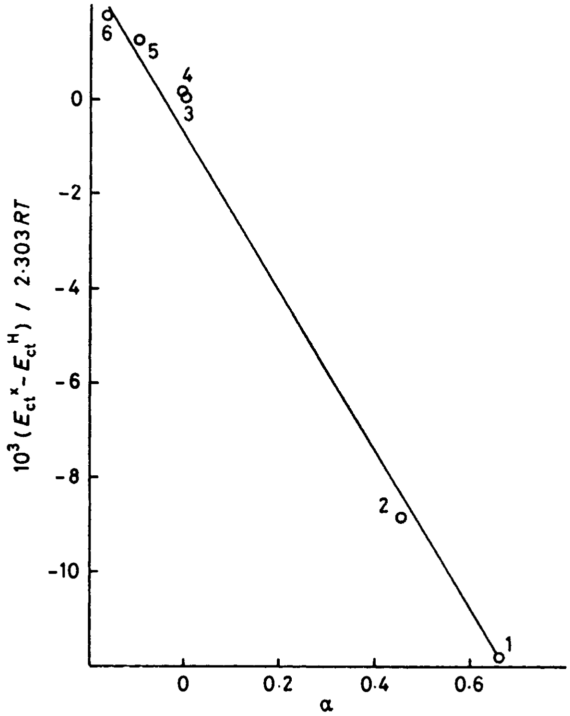
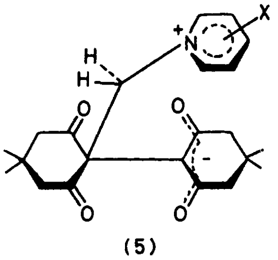


FIGURE 3 Hammett plot for transition energy E_{ct} of the charge transfer band for (2a—g) in acetonitrile as the solvent against σ values of the substituent on the pyridinium ring: 1, 4-CN; 2, 4-CO_2Me; 3, H; 4, 3-Me; 5, 4-Et; 6, 4-Me



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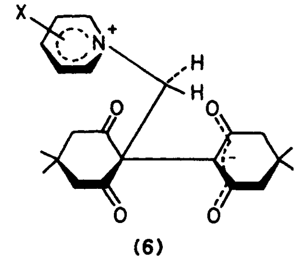

(6)

TABLE 3

Spectral data for pyridinium-β-keto-enolate zwitterions (2a—g)

Compound	M.p. (°C)	$\nu_{max.}$ (Nujol) cm^{-1}	$\lambda_{max.}$ (CH_3CN)/ nm (log ϵ)	Solvent	^1H Chemical shift (δ)				
					CH_3	CH_2 of ring	CH_2	Pyridinium [b]	Other
(2a) [a]	181—182	1 625 1 680 1 715	289(4.1), 388(3.0)	$CDCl_3$	0.80 (s, 3 H) 1.03 (s, 3 H) 1.09 (s, 6 H)	1.95 (s, 4 H) 2.17, 2.94 (ABq, *J* 12 Hz, 4 H)	5.13 (s, 2 H)	7.88 (m, 2 H) 8.32 (m, 1 H) 8.85 (m, 2 H)	
(2b)	194—195	1 640 1 680 1 715	289(4.1), 375(3.1)	$CDCl_3$	6.80 (s, 3 H) 1.10 (s, 9 H)	1.92 (s, 4 H) 2.13, 2.98 (ABq, *J* 12 Hz, 4 H)	5.03 (s, 2 H)	7.45 (d, 2 H) 8.58 (d, 2 H)	2.60 (s, 3 H)
(2c)	195—196	1 640 1 680 1 720	288(4.1), 377(3.0)	$CDCl_3$	0.80 (s, 3 H) 1.10 (s, 9 H)	1.90 (s, 4 H) 2.13, 2.98 (ABq, *J* 12 Hz, 4 H)	5.07 (s, 2 H)	7.50 (d, 2 H) 8.62 (d, 2 H)	1.33 (t, 3 H) 2.76 (q, 2 H)
(2d)	182—183	1 580 1 685 1 720	288(4.1), 388(3.0)	$CDCl_3$	0.78 (s, 3 H) 1.08 (s, 9 H)	1.90 (s, 4 H) 2.13, 2.83 (ABq, *J* 12 Hz, 4 H)	5.03 (s, 3 H)	7.55 (s, 1 H) 8.00 (d, 1 H) 8.47 (d, 2 H)	2.50 (s, 3 H)
(2e)	162—163	1 630 1 680	280(4.1), 495(3.0)	[$^2H_6$]DMSO	0.67 (s, 3 H) 1.00 (s, 9 H)	1.77 (s, 4 H) 1.80, 2.80 (ABq, *J* 12 Hz, 4 H)	4.86 (s, 2 H)	8.35 (d, 2 H) 8.82 (d, 2 H)	
(2f)	161—162	1 640 1 680 1 720	283(4.2), 464(3.0)	$CDCl_3$	0.81 (s, 3 H) 1.10 (s, 9 H)	1.80 (s, 4 H) 2.20, 2.97 (ABq, *J* 12 Hz, 4 H)	5.18 (s, 2 H)	8.23 (d, 2 H) 9.20 (d, 2 H)	4.07 (s, 3 H)
(2g)	250 (decomp.)	1 620 1 680 1 720 2 300 3 100	284(4.2),[c] 393(2.9)[c]	[$^2H_6$]DMSO	0.73 (s, 3 H) 1.00 (s, 9 H)	1.90 (s, 4 H) 2.03, 2.87 (ABq, *J* 12 Hz, 4 H)	4.90 (s, 2 H)	7.80 (d, 2 H) 8.20 (d, 2 H)	8.80 (bs, 2 H)

[a] δ_C ($CDCl_3$) 25.48, 26.80, 30.97, 31.24, 31.34, 31.54, 49.54, 52.67, 59.63, 72.25, 109.04, 125.41, 143.86, 147.21, 189.62, and 204.13 p.p.m. [b] Coupling constant for pyridinium ring was 7 Hz. [c] In EtOH.

overcomes the unfavourable eclipse strain in this conformation. In the other conformation (6), the charge transfer interaction occurs through the bonds between the charges. The present data do not establish which form is preferred. Verhoeven *et al.* reported that the through-bond charge transfer interaction is significant in *N*-(*p*-methoxyphenyl)pyridinium.[14]

EXPERIMENTAL

I.r. spectra were recorded on a Hitachi-215 spectrophotometer. The ^1H n.m.r. spectra were determined with a Varian T-60 instrument using tetramethylsilane as internal reference. Electronic spectra were measured on a Hitachi-124 spectrophotometer. We are indepted to Dr. S. Sato Nichiden Varian Inc., Tokyo, for the measurement of ^{13}C n.m.r. spectra.

Purification of Solvents.—Methanol was dried with magnesium and redistilled. 95% Ethanol was dried (CaO), then with magnesium, and redistilled. Propan-2-ol and n-butanol were dried over molecular sieves and redistilled. Acetonitrile was dried (P_2O_5) and redistilled. Dimethyl sulphoxide and dimethylformamide were dried (CaH_2) and redistilled. Acetone was dried with potassium carbonate. Chloroform, dichloromethane, and 1,2-dichloroethane were treated with concentrated sulphuric acid and then neutralized with 5% aqueous sodium hydroxide, followed by distillation after drying (P_2O_5). Benzene was washed with concentrated sulphuric acid, then distilled after drying ($CaCl_2$) and finally dried over sodium. Water was purified by distillation of demineralized water.

Reaction of 3,3,10,10-*Tetramethyldispiro*[5.0.5.1]*trideca*-1,5,8,12-*tetraone* (1) (TACP)[6] *with Pyridines.—General method.* To a solution of TACP (1) (290 mg, 1 mmol) in chloroform (10 ml) was added pyridine (320 mg, 4 mmol) at room temperature and the mixture was stirred for 4 days at the same temperature. After the removal of solvent under reduced pressure at room temperature, the crystalline product was filtered off and was washed with a small amount of chloroform. Recrystallization from chloroform gave rise to a pure sample of 1-(4,4-*dimethyl*-2,6-*dioxo*-1-*pyridiniomethylcyclohexyl*)-4,4-*dimethyl*-2,6-*dioxocyclohexanide* (2a) (340 mg), m.p. 181—182 °C, in 92% yield. The other pyridinium–TACP derivatives (2b—f) were obtained by the same method.

The reaction of isonicotinamide with (1) was done in acetonitrile solution instead of chloroform to overcome solubility problems. A solution of (1) (100 mg, 0.35 mmol) of acetonitrile (5 ml) was treated with isonicotinamide (135 mg, 1.1 mmol) for 4 days at room temperature. After filtration and recrystallization from acetonitrile, yellowish crystals (70 mg) of (2g) were obtained in 47% yield. It decomposed at *ca.* 250 °C.

Physical properties of compounds (2) are summarized in Table 3. Elemental analyses for (2a—c and g) confirmed the structures. Satisfactory elemental analyses for (2d——f) were not obtained owing to their hygroscopic properties.

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