Cycloaddition Reactions of Cyclopropenones. 4. Reaction of Some 2-Aminopyridines with Methylphenylcyclopropenone

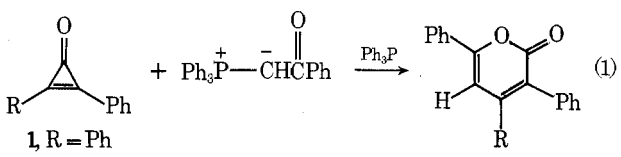
Albert Kascheres,* Concetta Kascheres, J. Augusto R. Rodrigues, and Ana Rita A. Santana

Instituto de Química, Universidade Estadual de Campinas, C.P. 1170, Campinas SP, Brazil 13.100

Received May 12, 1976

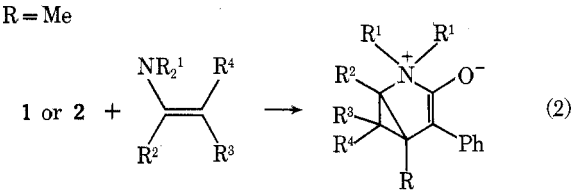
Methylphenylcyclopropenone (**2**) undergoes a cycloaddition reaction across the PhC–CO bond with 2-aminopyridine (**3a**) in ether to produce the insoluble *cis*-3,4-dihydro-3-methyl-4-phenyl-2*H*-pyrido[1,2-*a*]pyrimidin-2-one (**6a**). Rearrangement of **6a** to α-methyl-*trans*-cinnamamide **7a** occurs slowly in refluxing chloroform. 2-Amino-3-methyl- and 2-amino-4-methylpyridine react similarly, while 2-amino-5-methylpyridine eventually affords, in addition, the α-(2-pyridylamino) acid **10a.** 2-Amino-6-methylpyridine reacts very slowly to give **10b** exclusively. A lack of reactivity shown by aniline suggests that both products arise by way of initial nucleophilic attack of the aminopyridine ring nitrogen on the cyclopropenone ring, with steric hindrance at this nitrogen favoring subsequent formation of an intermediate of apparent reaction at the exo nitrogen.

The most recent chemistry of cyclopropenones involves the use of these compounds in cycloaddition reactions with a wide variety of substrates.[1] The cyclopropenone utilized in the vast majority of these investigations has been diphenylcyclopropenone (**1**). The present discussion will be restricted to those reactions which have been postulated to involve initial nucleophilic attack on the electrophilic cyclopropenone ring. In such cases, cycloaddition to **1** has been found to occur across the C–CO bond (eq 1,[2] 2,[3a] 3[4]).

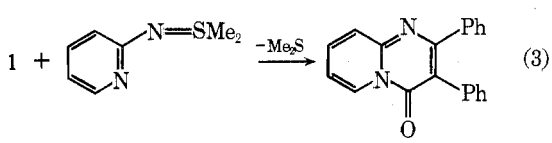


1, R = Ph
2, R = Me

(1)



(2)



(3)

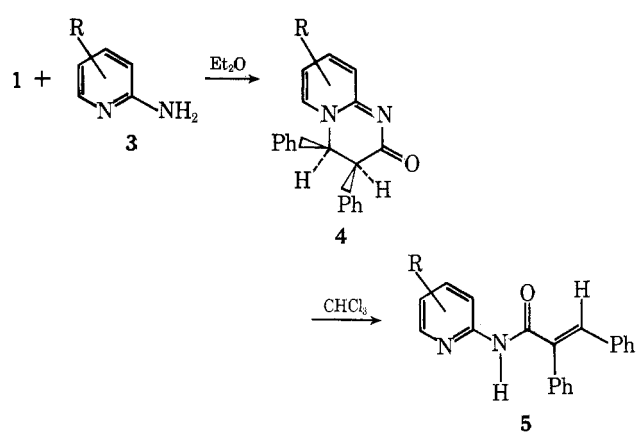
Alkylphenylcyclopropenones, which offer the interesting possibility of comparing the reactivities of two different C–CO bonds, have not been extensively studied.[5] In the only two examples of C–CO cycloaddition available from the literature, reaction of methylphenylcyclopropenone (**2**) has been observed to occur with exclusive cleavage of the MeC–CO bond (eq 1,[2] 2[3b]).

Recently, we reported[6] the reaction of **1** with a variety of 2-aminopyridines (**3**) in ether to produce insoluble *cis*-3,4-dihydro-3,4-diphenyl-2*H*-pyrido[1,2-*a*]pyrimidin-2-ones (**4**). The formation of **4** was suggested to involve initial nucleophilic attack of the aminopyridine ring nitrogen on C-2 of the cyclopropenone, followed by rupture of the C–CO bond. In chloroform solution, **4** readily rearranges to *cis*-2,3-diphenylacrylamides **5.**

In view of the limited data available concerning the reactivity of alkylphenylcyclopropenones, a study of the chemical behavior of **2** toward 2-aminopyridines was considered to be appropriate.

Results and Discussion

While the reaction of diphenylcyclopropenone (**1**) with 2-aminopyridines (**3a–d**) in ether was complete within 17 h

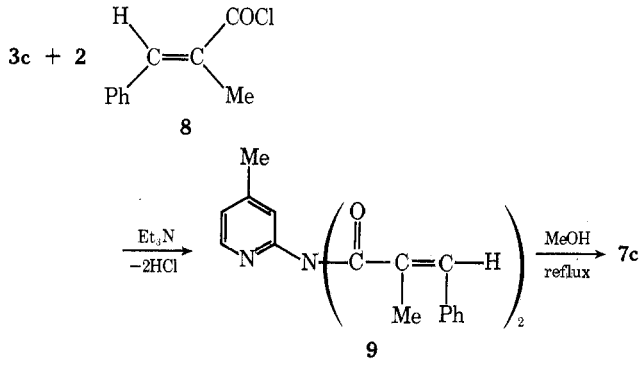


at room temperature,[6] that of methylphenylcyclopropenone (**2**) required reaction times of 7–22 days, even though more concentrated solutions of reagents could be employed owing to the greater solubility of **2** in ether. Thus, solutions (5 ml) containing 4 mmol of **2** and **3a–d** began to deposit crystalline solids after several hours (see Table I). The ether-insoluble material was a 1:1 adduct as indicated by elemental analysis and NMR integration. The uv and ir spectra were comparable to those of **4,** suggesting the presence of a 3,4-dihydro-2*H*-pyrido[1,2-*a*]pyrimidin-2-one nucleus. The NMR spectra ($CDCl_3$) showed a 3 H doublet at δ 1.05 (J = 7 Hz), a 1 H quintuplet at δ 3.25 (J = 7 Hz), and a 1 H doublet at δ 5.25 (J = 7 Hz). A similarity between the chemical shift and coupling constant of this latter absorption and those of H-4 in **4** (δ 5.3, J = 7 Hz) suggested *cis*-3,4-dihydro-3-methyl-4-phenyl-2*H*-pyrido[1,2-*a*]pyrimidin-2-one (**6**) (Table II) as the structure of the product. Although considerably more stable than the diphenyl analogues **4** (the NMR spectrum of **6c,** for example, was unchanged when the sample was allowed to stand in the NMR tube for 5 days), **6a, 6c,** and **6d** were transformed to α-methyl-*trans*-cinnamamides **7**[7] in high yields (80–85%) upon heating in chloroform at reflux for 5 days. The 2-amino-3-methylpyridine derivative **6b** afforded only 30% of **7b,** the remainder being a mixture (by NMR analysis) of **6b** and a substance showing a doublet at δ 5.0 (J = 5.5 Hz). This by-product may be the trans isomer of **6b,** formed as a result of isomerization α to the carbonyl. The mixture was not separable. The NMR spectra of **7a, 7c,** and **7d** (Table III) showed large deshielding shifts for H-3, as observed previously in the case of **5.** The cis methyl–phenyl relationship in **7** was not apparent from the NMR spectra, although hydrolysis (refluxing ethanolic KOH) gave **3** and α-methyl-*trans*-cinnamic acid in quantitative amounts. Since the possibility of isomerization during the process of hydrolysis could not be ruled out,[8] it was considered necessary to

Table I. Formation of *cis*-3,4-Dihydro-2*H*-pyrido[1,2-*a*]pyrimidin-2-one (6) and/or α-(2-Pyridylamino) Acid 10 in Ether

2-Amino-pyridine	Reaction time, days	% yield 6	% yield 10[a]
3a	17 (22)	38 (42)	
3b	7 (14)	73 (76)	
3c	7 (17)	46 (52)	
3d	13 (19)	28 (33)	(30)
3e	40		60

[a] Based upon methyl ester derivative.



prepare an example of this system by an alternative route. Addition of the acid chloride **8** to an equimolar quantity of **3c** in benzene containing triethylamine resulted, surprisingly, in the formation of the 2:1 adduct **9** in 75% isolated yield. The structure containing both acyl moieties on the exo nitrogen was suggested by the presence, in the NMR spectrum, of a six-hydrogen doublet (J = 1.5 Hz) for the vinyl methyl groups. Refluxing of a solution of **9** in methanol for 16 h afforded **7c** and methyl α-methyl-*trans*-cinnamate in equimolar amounts.

When the oily residue formed upon removal of the solvent from the ether-soluble fraction of the reaction of **3d** was allowed to stand for several days, an ether-insoluble, amorphous solid was obtained (see Table I). Analysis of the mass spectrum [m/e 270 (M^+), 226 ($(M - CO_2)^+$)] and the NMR spectrum [δ 3.30, benzylic AB quartet (J = 13.5 Hz)] suggested structure **10a** for this hydrolysis product. The crystalline methyl ester (**11a**) was formed quantitatively upon heating **10a** in methanol containing a trace of sulfuric acid.

The NMR spectrum of the residue immediately after evaporation of the solvent from the ether-soluble fraction contained a 3 H singlet at δ 1.40, a 3 H doublet (J = 2 Hz) at δ 1.80, and a 2 H singlet at δ 3.05. With time these absorptions disappeared, while those corresponding to **10a** increased in intensity. This observation demonstrates the initial existence of an unstable primary product which may best be represented as the imidazo[1,2-*a*]pyridin-3(2*H*)-one **12**. The alkaline hydrolysis of 3,5-dinitro-2-pyridylalanylglycine has been suggested to proceed through an analogous intermediate.[9]

The reaction of **2** with **3e** was extremely slow, with *no* formation of ether-insoluble material. The NMR spectrum of the crude product showed again the absorptions attributable to **12**. Eventually, **10b** was isolated and characterized as the easily recrystallizable methyl ester **11b**, which was obtained in an overall yield of 60%.

Thus, it is apparent that steric hindrance at the pyridine ring nitrogen in **3** affects the rate as well as the pathway of the reaction with methylphenylcyclopropenone (**2**). Also, aniline was found to be totally unreactive toward **2** suggesting that the mechanism of formation of **6** and **10** must involve initial participation of the ring nitrogen of **3**. The pyridopyrimidinones **6** can be pictured as arising by way of nucleophilic attack on C-3 of **2** to produce **13** (Scheme I), with subsequent rearrangement to a ketene or cyclopropanone as proposed previously for the reaction of diphenylcyclopropenone (**1**).[6] As the steric interaction in **13** increases on passing from **3a–c** to **3d** and **3e**, a pathway involving transformation to **14** may become important. This process may involve a transition state wherein appreciable positive charge is placed upon the cy-

Table II. Some *cis*-3,4-Dihydro-3-methyl-4-phenyl-2*H*-pyrido[1,2-*a*]pyrimidin-2-ones (6)

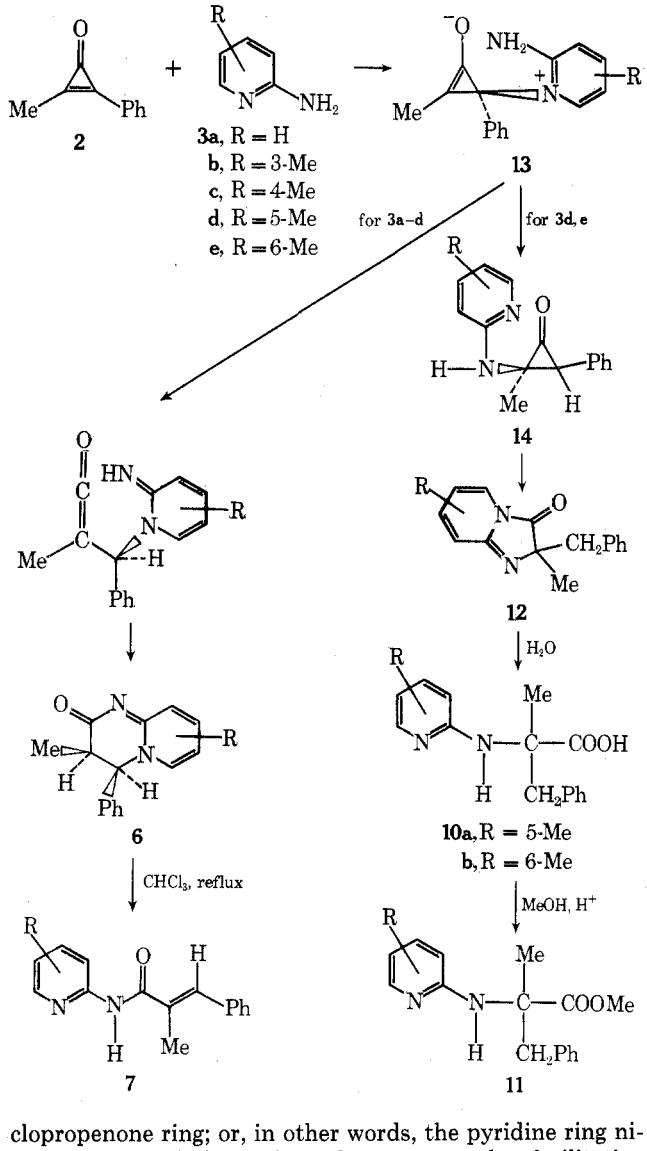
Substituent R	Mp,[a] °C	Formula	Anal.	C	H	N	NMR (CDCl3), δ	Ir (KBr), cm−1	Uv (EtOH), λmax (ε)
H (**6a**)	164–168	$C_{15}H_{14}N_2O$	Calcd	75.61	5.92	11.76	1.05 (3 H, d, J = 7 Hz)	1661 (w)	265 (11 730)
			Found	75.50	5.97	11.80	3.25 (1 H, quint., J = 7 Hz, H-3)	1622	346 (7700)
							5.25 (1 H, d, J = 7 Hz, H-4)	1551	
							6.50 (1 H, dt, J = 7 and 1.8 Hz)	1492	
							7.00 (1 H, dd, J = 8.5 and 1.8 Hz)		
							7.25–7.65 (7 H, m)		
9-Me (**6b**)	146–148	$C_{16}H_{16}N_2O$	Calcd	76.17	6.39	11.10	1.05 (3 H, d, J = 7 Hz)	1650 (w)	
			Found	76.35	6.50	11.21	2.35 (3 H, s)	1620	
							3.25 (1 H, quint., J = 7 Hz, H-3)	1570	
							5.25 (1 H, d, J = 7 Hz, H-4)	1480	
							6.45 (1 H, t, J = 7 Hz)		
							7.25–7.50 (7 H, m)		
8-Me (**6c**)	162–165	$C_{16}H_{16}N_2O$	Calcd	76.17	6.39	11.10	1.05 (3 H, d, J = 7 Hz)	1664 (w)	268 (10 660)
			Found	76.03	6.55	11.29	2.30 (3 H, s)	1629	340 (8150)
							3.22 (1 H, quint., J = 7 Hz, H-3)	1540	
							5.30 (1 H, d, J = 7 Hz, H-4)	1490	
							6.35 (1 H, dd, J = 7 and 1.8 Hz)		
							6.80 (1 H, s)		
							7.20–7.60 (6 H, m)		
7-Me (**6d**)	158–160	$C_{16}H_{16}N_2O$	Calcd	76.17	6.39	11.10	1.05 (3 H, d, J = 7 Hz)	1660 (w)	
			Found	76.33	6.43	11.14	2.10 (3 H, s)	1630	
							3.22 (1 H, quint., J = 7 Hz, H-3)	1555	
							5.30 (1 H, d, J = 7 Hz, H-4)	1500	
							7.00 (1 H, d, J = 9.5 Hz)		
							7.25–7.50 (7 H, m)		

[a] Melting points varied somewhat with heating rate.

Table III. Some α-Methyl-*trans*-cinnamamides (7)

Substituent R	Yield, %	Mp, °C	Formula	Anal.	C	H	N	NMR ($CDCl_3$), δ	Ir (KBr), cm^{-1}
H (**7a**)	85	69–70	$C_{15}H_{14}N_2O$	Calcd	75.61	5.92	11.76	2.20 (3 H, d, J = 1.5 Hz)	3180
				Found	75.50	5.95	11.79	6.95 (1 H, m, H-5)	1665
								7.20–7.40 (6 H, m)	1595
								7.65 (1 H, dt, J = 7 and 1.8 Hz, H-4)	1575
								8.10–8.35 (2 H, m, H-3 and H-6)	1510
								8.60 (1 H, braod, D_2O exchangeable)	
3-Me (**7b**)	30	53–55	$C_{16}H_{16}N_2O$	Calcd	76.17	6.39	11.10	2.20 (3 H, d, J = 1.5 Hz)	3200
				Found	76.41	6.31	11.25	2.30 (3 H, s)	1650
								6.95–7.60 (8 H, m)	1585
								8.20 (1 H, dd, J = 5 and 1.8 Hz, H-6)	1515
								8.60 (1 H, broad, D_2O exchangeable)	
4-Me (**7c**)	80	86–87.5	$C_{16}H_{16}N_2O$	Calcd	76.17	6.39	11.10	2.20 (3 H, d, J = 1.5 Hz)	3175
				Found	76.28	6.36	11.02	2.35 (3 H, s)	1665
								6.80 (1 H, d, J = 5 Hz, H-5)	1610
								7.20–7.50 (6 H, m)	1565
								8.05–8.20 (2 H, m, H-3 and H-6)	1515
								8.65 (1 H, broad, D_2O exchangeable)	
5-Me (**7d**)	85	72–73	$C_{16}H_{16}N_2O$	Calcd	76.17	6.39	11.10	2.20 (6 H, m)	3200
				Found	76.11	6.41	10.96	7.20–7.60 (7 H, m)	1660
								8.05 (1 H, s, H-6)	1590
								8.20 (1 H, d, J = 8 Hz, H-3)	1500
								8.65 (1 H, broad, D_2O exchangeable)	

Scheme I



clopropenone ring; or, in other words, the pyridine ring nitrogen serves to polarize the cyclopropenone, thus facilitating reaction at the exo nitrogen.

The difference noted in the behaviors of methylphenylcyclopropenone (**2**) and diphenylcyclopropenone (**1**) in this reaction may be attributed to the less reactive, more selective nature of the former reagent.

Experimental Section[10]

Reaction of Methylphenylcyclopropenone (2) with 2-Aminopyridines (3). A. Isolation of *cis*-3,4-Dihydro-3-methyl-4-phenyl-2*H*-pyrido[1,2-*a*]pyrimidin-2-ones 6. A solution of methylphenylcyclopropenone[5] (0.576 g, 4 mmol) and the selected aminopyridine (4 mmol) in 5 ml of ether (dried over molecular sieve) was allowed to stand at room temperature (a precipitate began to form after several hours). After the determined time, the solvent was separated from the crystalline solid, **6**, which was washed with four 10-ml portions of dry ether.

B. Isolation and Characterization of α-(2-Pyridylamino) Acids 10. 1. From the Reaction of 2-Amino-5-methylpyridine (3d). The residue obtained upon evaporation of the solvent from the ether-soluble fraction was allowed to stand for 7 days. After this time, 25 ml of dry ether was added, leaving **10a** as an insoluble, amorphous solid (0.30 g, 30% yield): mp 160–165 °C; mass spectrum *m/e* (% base peak) 270 (0.1, M^+), 252 [2.6, $(M - H_2O)^+$], 226 [3.1, $(M - CO_2)^+$], 179 [26.2, $(M - PhCH_2\cdot)^+$], 161 [87.9, $(M - H_2O, PhCH_2\cdot)^+$], 133 [100, $(M - H_2O, CO, PhCH_2\cdot)^+$]; ir (KBr) 3250, 1680, 1620 cm^{-1}; NMR ($CDCl_3/CD_3OD$) δ 1.60 (3 H singlet), 2.20 (3 H singlet), 3.30 [2 H, AB quartet (J = 13.5 Hz)], 6.70 (1 H doublet, J = 9 Hz), 7.05 (5 H singlet), 7.55 (1 H doublet of doublets, J = 9 and 2 Hz), 7.90 (1 H broadened singlet) (the exchangeable hydrogens were not observed).

The methyl ester, **11a**, was obtained quantitatively upon treatment of **10a** with methanol containing a trace of sulfuric acid (reflux during 16 h): mp 96–96.5 °C (pentane); mass spectrum *m/e* (% base peak) 284 (3.2, M^+), 193 [100, $(M - PhCH_2\cdot)^+$], 161 [18.3, $(M - MeOH, PhCH_2\cdot)^+$], 133 [46.4, $(M - MeOH, CO, PhCH_2\cdot)^+$]; ir (KBr) 3375 (s), 1725 (s), 1610, 1585 cm^{-1}; NMR ($CDCl_3$) δ 1.50 (3 H singlet), 2.20 (3 H singlet), 3.40 [2 H, AB quartet (J = 13 Hz)], 3.70 (3 H singlet), 4.50 (1 H, broad, disappears upon D_2O exchange), 6.20 (1 H doublet, J = 8 Hz), 6.90–7.40 (6 H multiplet), 7.90 (1 H broadened singlet).

Anal. Calcd for $C_{17}H_{20}N_2O_2$: C, 71.81; H, 7.09; N, 9.85. Found: C, 71.73; H, 7.01; N, 9.82.

2. From the Reaction of 2-Amino-6-methylpyridine (3e). Evaporation of the ester afforded an oily residue, which was allowed to stand for 7 days. After this time, extraction with 40 ml of 12% Na_2CO_3 solution, followed by neutralization with concentrated HCl, gave **10b** as an amorphous solid (0.60 g, 60% yield): mp 80–85 °C; ir (KBr) 3250, 1675, 1625, 1605 cm^{-1}; NMR ($CDCl_3$) δ 1.60 (3 H singlet), 2.60 (3 H singlet), 3.30 [2 H, AB quartet (J = 13.5 Hz)], 6.45 (2 H multiplet), 7.05 (5 H singlet), 7.45 (1 H multiplet), 9.40 (2 H, broad).

The methyl ester, **11b**, was obtained quantitatively upon treatment of **10b** with methanol containing a trace of sulfuric acid (reflux during 16 h): mp 76–78 °C (pentane); ir (KBr) 3370 (s), 1725 (s), 1605, 1580 cm^{-1}; NMR ($CDCl_3$) δ 1.50 (3 H singlet), 2.35 (3 H singlet), 3.40 [2 H, AB quartet (J = 13 Hz)], 3.70 (3 H singlet), 4.60 (1 H, broad, disappears upon D_2O exchange), 6.20 (1 H doublet, J = 8 Hz), 6.45 (1 H doublet, J = 7 Hz), 6.90–7.45 (6 H multiplet).

Anal. Calcd for $C_{17}H_{20}N_2O_2$: C, 71.81; H, 7.09; N, 9.85. Found: C, 71.76; H, 6.99; N, 9.78.

Ring Opening of 6 in Chloroform. A solution of **6** (200 mg) in 20 ml of chloroform was heated under reflux for 5 days. The solvent was then evaporated and the crude residue extracted with three 25-ml portions of boiling petroleum ether (bp 30–60 °C). The combined extracts were concentrated to a volume of 15 ml and stored at −20 °C for 24 h, whereupon **7** precipitated as colorless crystals.

Reaction of α-Methyl-*trans*-cinnamoyl Chloride (8) with 2-Amino-4-methylpyridine (3c). To a solution of 2-amino-4-methylpyridine (0.432 g, 4 mmol) in 18 ml of benzene containing triethylamine (0.8 ml, 5.6 mmol) there was added a solution of α-methyl-*trans*-cinnamoyl chloride (0.724 g, 4 mmol) in 10 ml of benzene. After 1 h at room temperature, the precipitated triethylammonium chloride (0.53 g) was separated by filtration. Evaporation of the filtrate gave an oil (1.05 g), which by NMR analysis was a 1:1 mixture of **3c** and **9**. This crude material was dissolved in methylene chloride (100 ml), and extracted with two 50-ml portions of 0.25 N HCl, followed by two 60-ml portions of water. The organic layer was dried over $MgSO_4$, and concentrated to a volume of 15 ml, whereupon addition of pentane (50 ml) resulted in precipitation of **9** as a white solid (0.60 g, 75%): mp 123–123.5 °C; ir (KBr) 1705, 1650 (s), 1610 cm^{-1}; NMR ($CDCl_3$) δ 2.10 [6 H doublet (J = 1.5 Hz)], 2.40 (3 H singlet), 6.90–7.40 (14 H multiplet), 8.35 [1 H doublet (J = 5 Hz)].

Anal. Calcd for $C_{26}H_{24}N_2O_2$: C, 78.76; H, 6.10; N, 7.07. Found: C, 78.92; H, 6.27; N, 7.09.

Methanolysis of 9. A solution of **9** (0.140 g, 0.35 mmol) in 30 ml of methanol was heated under reflux for 16 h. After this time, evaporation of the solvent gave an oil, which by NMR analysis was a 1:1 mixture of **7c** and methyl α-methyl-*trans*-cinnamate. The crude product was taken up in 20 ml of boiling petroleum ether and stored at −20 °C for 24 h. The colorless crystals which precipitated (0.085 g, 97%, mp 85–87 °C) furnished an ir spectrum identical with that of **7c**. The soluble fraction afforded 0.060 g (100%) of the sweet-smelling methyl ester, identical with an authentic sample.

Acknowledgment. The authors acknowledge the financial assistance of FINEP (Financiadora de Estudos e Projetos).

Registry No.—**2**, 26307-30-2; **3a**, 504-29-0; **3b**, 1603-40-3; **3c**, 695-34-1; **3d**, 1603-41-4; **3e**, 1824-81-3; **6a**, 59938-68-0; **6b**, 59938-69-1; **6c**, 59938-70-4; **6d**, 59938-71-5; **7a**, 59938-72-6; **7b**, 59938-73-7; **7c**, 59938-74-8; **7d**, 59938-75-9; **8**, 38449-13-7; **9**, 59938-76-0; **10a**, 59938-77-1; **10b**, 59938-78-2; **11a**, 59938-79-3; **11b**, 59938-80-6.

References and Notes

(1) For recent reviews of cyclopropenone chemistry, see K. T. Potts and J. S. Baum, *Chem. Rev.*, **74**, 189 (1974); T. Eicher and J. L. Weber, *Top. Curr. Chem.*, **57**, 1 (1975).
(2) T. Eicher, E. v. Angerer, and A. Hansen, *Justus Liebigs Ann. Chem.*, **746**, 102 (1971).
(3) (a) T. Eicher and S. Böhm, *Chem. Ber.*, **107**, 2186 (1974); (b) *Ibid.*, **107**, 2215 (1974).
(4) T. L. Gilchrist, C. J. Harris, C. J. Moody, and C. W. Rees, *J. Chem. Soc., Perkin Trans. 1*, 1969 (1975).
(5) Methylphenylcyclopropenone (**2**) is as readily available synthetically as diphenylcyclopropenone (**1**) by the method of preparation of the latter: R. Breslow, T. Eicher, A. Krebs, R. A. Peterson, and J. Posner, *J. Am. Chem. Soc.*, **87**, 1320 (1965). Physical properties have been described: A. Krebs and J. Breckwoldt, *Tetrahedron Lett.*, 3797 (1969).
(6) A. Kascheres and J. A. R. Rodrigues, *J. Org. Chem.*, **40**, 1440 (1975).
(7) This product was also observed in the NMR spectra of the ether-soluble material from the reactions, but was not isolated from this source in the present study.
(8) The α-methyl-*trans*-cinnamic acid is, in fact, the stable form available commercially.
(9) A. Signor, L. Biondi, and E. Bordignon, *J. Org. Chem.*, **31**, 1403 (1966).
(10) All melting points were obtained on a Mettler FP 52 melting point apparatus and are uncorrected. Infrared spectra were taken on a Perkin-Elmer 337 spectrophotometer. NMR spectra were recorded with a Varian T-60 spectrometer using tetramethylsilane as an internal standard. Mass spectra were recorded on a Finnigan 1015 S/L quadrupole instrument. The elemental analyses were performed by Alfred Bernhardt Laboratories, West Germany.

Imidazo[1,2-a]pyridines—Novel Substitution Reactions

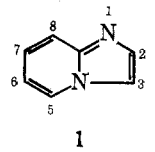
Elli S. Hand and William W. Paudler*

Department of Chemistry, The University of Alabama, University, Alabama 35486

Received April 27, 1976

Treatment of imidazo[1,2-a]pyridines (1) with electrophilic reagents leads to substitution at either C_2 or C_3. While superficially both substitutions could occur via electrophilic attack, substitution at C_2 is interpreted to proceed via nucleophilic attack on an imidazo[1,2-a]pyridinium ion. Oxidation of 2-methyl-3-bromoimidazo[1,2-a]pyridine to its 2-carboxaldehyde is also described.

We have been interested in the chemistry of imidazo[1,2-a]pyridine[1-4] (1) for some time and wish to report here some results obtained when these compounds are subjected to electrophilic reagents. It is known that electrophilic substitution, such as bromination, nitrosation, and nitration,[3-5] takes place at position 3, in accord with frontier π-electron density calculations.[4] Such calculations show the highest π-electron density of the HOMO to be at position 1, followed



1

by position 3 and 5, and a node at the 2 position. One would predict, therefore, that electrophilic attack should occur preferentially at these positions in the order 1 > 3 > 5, and not at position 2. Indeed, no examples of electrophilic reaction at position 2 have been reported. One example of electrophilic substitution at position 5 is known: when the 3 position is blocked by a methyl group, bromination leads to the formation of 5-bromo-3-methylimidazo[1,2-a]pyridine.[5]

However, when the 3-substituted compound, 3-bromo-7-methylimidazo[1,2-a]pyridine (**2a**), was treated with selenium dioxide, neither the expected oxidation of the methyl group to the aldehyde, nor electrophilic substitution at position 5, occurred. Rather, displacement of bromine took place and the diarylselenide **3** was formed.[2] Furthermore, this reaction is reversible, as shown by the formation of **2a** when the diarylselenide **3** was treated with bromine.[2] Again, the expected reaction, formation of diaryldibromoselenide,[6,7] was not observed (see Scheme I).

These unexpected transformations implied a very high susceptibility of the 3 position in this ring system toward electrophilic attack. Some transformations which confirm this