REACTIONS OF DICHLOROCARBENE WITH N-(2,2-DIPHENYLVINYLIDENE)-ANILINES. 1,3-DIPOLAR DERIVATIVES OF KETENIMINE-YLIDES

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Ketenimine-ylides $Ph_2C{=}C{-}N^+({=}CCl_2)Ar$, formed by the reaction of N-(2,2-diphenylvinylidene)anilines with dichlorocarbene, generated by heating sodium trichloroacetate in chloroform, undergoes [2 + 3]-cycloaddition with dimethylacetylenedicarboxylate, methyl methacrylate, and dimethyl fumarate to give pyrrole derivatives; in addition, pyridine derivatives are formed in the reaction with dimethyl fumarate. In the absence of a dipolar compound, ketenimines-ylides give N-aryl-N-(2,2-diphenylvinyl)amides of di- and trichloracetic acids.

We have shown [1] that the reaction between dichlorocarbene, generated from chlororform and potassium tert-butoxide, and N-(2,2-diphenylvinylidene)anilines (I) gives an acid chloride or an ester of N-aryl-N-(2,2-diphenylvinyl)carbamic acid. It was proposed that the reaction occurs through an intermediate ketenimine-ylide $Ph_2C{=}C{-}N^+({=}CCl_2)Ar$ (II), which is formed by attack by the unshared electron pair at the ketenimine (I) nitrogen atom on the dichlorocarbene.

In the present work, we have studied the reaction of the N-(2,2-diphenylvinylidene)-anilines (Ia and b) with dichlorocarbene in the presence of 1,3-dipolar copounds [dimethylacetylene dicarboxylate (III), methyl methacrylate (IV), and dimethyl fumarate (V)] in order to confirm the formation of intermediate ketenimine-ylides. Dichlorocarbene was generated by the thermal decomposition of sodium trichloroacetate in chloroform in the presence of the phase transfer catalyst benzyltriethylammonium chloride [2]. Physical constants and elemental analysis data for the reaction products are given in Table 2; structures of the compounds were confirmed by spectral methods (Table 1), and by chemical reactions. The reaction of the ketenimine Ia with dichlorocarbene in the presence of the dipolar compound III gives the lactam VIa. The mass spectrum of compound VIa has a molecular-ion peak with m/z 439. The IR and NMR spectral data confirm that the molecule contains an amide and two methoxycarbonyl groups, while the position of the long-wave maximum (λ 403 nm) in the UV spectrum of compound VIa confirms the presence of a conjugated π-system. The selective reduction of the endocyclic double bond of compound VIa with lithium ethoxyaluminum hydride gives the lactam VIIa. The PMR spectrum of compound VIIa contains doublets at 3.66 and 3.97 ppm from the vicinal methine protons, and the UV spectrum shows a significant hypsochromic shift of the long-wave maximum ($\Delta\lambda$ 130 nm) compared with the spectrum of compound VIa.

The reaction of the ketenimine Ia with dichlorocarbene and methyl methacrylate gave the lactam VIIIa (main product) and the ester IXa. The mass spectrum of compound VIIIa contains a molecular ion peak with m/z 397. The PMR spectrum shows signals from the nonequivalent protons of the methylene group (AB system). In the IR spectrum the stretching vibrations of the ester and amide C=O groups absorb at 1742 and 1712 cm^{-1}, respectively. The ^{13}C NMR spectrum agrees with the structure of compound VIIIa. Reduction of the latter with AlH_3 gave the alcohol Xa, indicating that the product VIIIa is the [2 + 3]-cycloaddition compound of the ketenimine-ylide and methyl methacrylate, and not its regioisomer, methyl 2-benzhydryliden-3-methyl-5-oxo-1-phenylpyrrolidine-3-carboxylate. The mass spectrum of compound Xa contains a molecular ion peak with m/z 355. The PMR spectrum shows singlets at 0.83, 1.33, and 3.02 ppm from the Me, OH, and OCH_2 groups, and also signals (AB system) due to the methylene groups at 2.25 and 2.46 ppm ($C{-}CH_2{-}C$), and at 3.07, 3.44 ppm ($N{-}CH_2{-}C$). In

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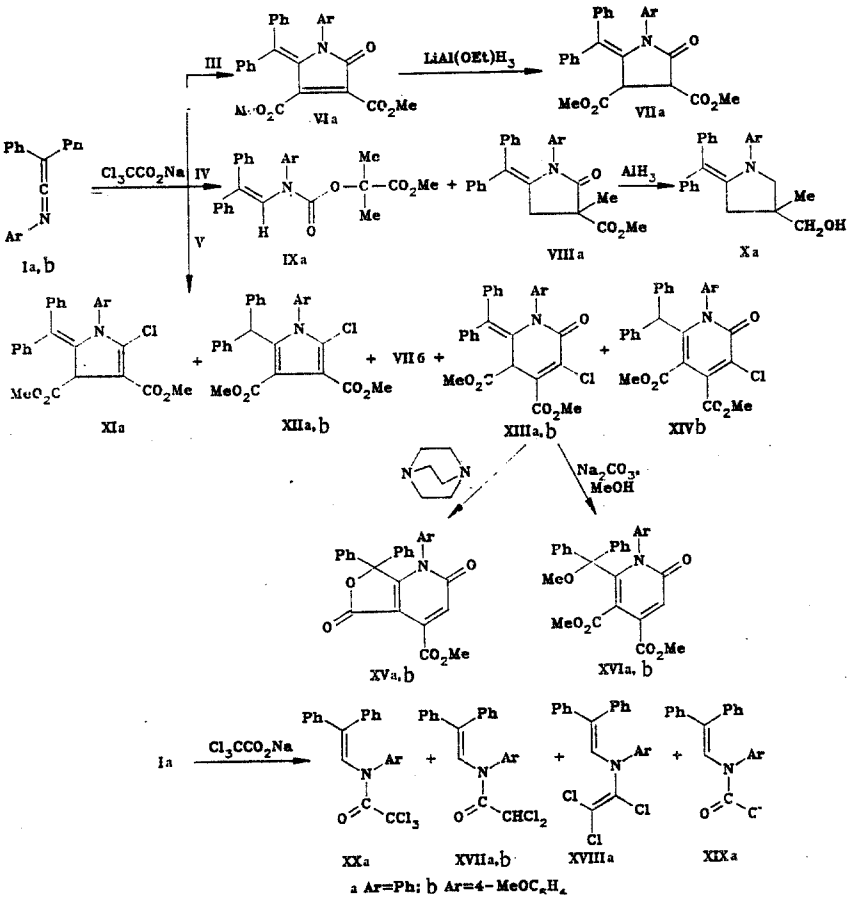
TABLE 1. UV, IR, and NMR Spectra of the New Compounds*

Compound	UV spectrum, λ, nm (log ε)	IR spectrum, ν, cm^{-1}	PMR spectrum, δ, ppm (J, Hz)
VIa	262 (4,13), 403 (4,26)	1070, 1120, 1210, 1292, 1383, 1450, 1600, 1708 s, 1720 s, 1755, 2960 w, 3077 w	3,23 and 3,83 (3H, s, OMe); 6,8—7,5 (15H, arom.)
VIIa**	237 (3,88), 271 (3,91)	1024, 1175, 1236 s, 1367, 1443, 1497, 1600, 1641, 1734 s, 1743 s, 2858 w, 3060 w	3,54 and 3,73 (3H, s, OMe); 3,66 and 3,97 (1H, d, J=3, CH); 6,7—7,3 (15H, arom.)
VIIb	238 (3,89), 272 (3,92)	1050, 1170, 1259 s, 1355, 1445, 1523, 1651, 1741 s, 2848, 2961, 3070 w	3,59, 3,63, 3,81 (3H, s, OMe); 3,70 and 4,06 (1H, d, J=3, CH)
VIIIa	239 (4,05), 274 (4,23)	1079, 1130, 1244, 1367, 1445, 1497, 1598, 1640, 1712 s, 1742 s, 2962, 3023, 3063 w	1,48 (3H, s, Me); 2,79 and 3,27 (2H, d.d J=15, CH_2); 3,70 (3H, s, OMe); 6,6—7,3 (15H, arom.)
IXa	—	1022, 1140 s, 1177 s, 1269, 1314 s, 1376, 1449, 1494, 1598, 1622, 1711 s, 1742 s, 2955, 3031, 3063 w	1,35 (6H, s, Me); 3,70 (3H, s, OMe); 6,8—7,3 (16H, =CH—, arom.)
Xa	—	1050, 1182, 1230, 1320, 1381, 1442, 1493 s, 1592 s, 1623, 2860, 2920, 3075, 3425 w	0,83 (3H, s, Me); 1,33 (1H, s, OH); 2,25 and 2,46 (2H, d.d. J=14, CCH_2C); 3,02 (2H, s, OCH_2); 3,07 and 3,44 (2H, d.d J=10, NCH_2); 6,5—7,3 (15H, arom.)
XIIa	261 (3,85)	1090, 1173, 1219 s, 1287, 1438, 1515 s, 1600, 1714 s, 1735 s, 2951, 3070 w	3,21 and 3,83 (3H, s, OMe); 5,25 (1H, s, CH); 6,8—7,5 (15H, arom.)
XIIb	249 (4,08)	1065, 1170, 1230 s, 1263 s, 1300 s, 1450, 1521 s, 1615, 1712 s, 1742 s, 2850 w, 2960, 3070 w	3,31, 3,85 and 3,88 (3H, s, OMe); 5,34 (1H, s, CH); 6,7—7,4 (14H, arom.)
XIIIa	248 (4,22), 344 (3,62)	1168, 1212 s, 1251 s, 1370, 1454, 1504, 1608, 1635, 1694 s, 1747 s, 2963, 3081 w	3,93 (6H, s, OMe); 5,08 (1H, s, CH); 6,8—7,6 (15H, arom.)
XIIIb	255 (4,31), 350 (3,67)	1160, 1218 s, 1256 s, 1365, 1443, 1520 s, 1617, 1631, 1690 s, 1746 s, 2963 w, 3075 w	3,88 (3H, s, OMe); 4,05 (6H, s, OMe); 5,18 (1H, s, CH); 6,8—7,8 (14H, arom.)
XIVb	285 (3,75)	1051, 1178, 1259 s, 1306, 1452, 1522 s, 1619, 1700 s, 1752, 2848, 2967, 3040	3,64, 3,77 and 3,81 (3H, s, OMe); 5,38 (1H, s, CH); 6,3—7,5 (14H, arom.)
XVa	267 (4,05), 314 (3,79)	1110, 1275, 1293, 1471, 1505, 1564, 1628, 1695 s, 1752 s, 1780 s, 2963 w, 3070	4,08 (3H, s, OMe); 6,5—7,6 (16H, =CH—, arom.)
XVb	268 (4,13), 314 (3,82)	1104, 1272, 1292, 1467, 1512, 1560, 1621, 1690 s, 1735 s, 1768 s, 2841 w, 2962 w, 3067 w	3,69 (3H, s, OMe); 4,00 (3H, s, OMe); 6,3—7,4 (15H, =CH—, arom.)
XVIa	238 (3,84), 325 (3,78)	967, 1128 s, 1280, 1308, 1461, 1504, 1549, 1600, 1623, 1690 s, 1752 s, 2850, 2960, 3063	3,35 (6H, s, OMe); 4,15 (3H, s, OMe); 6,5—7,7 (16H, =CH—, arom.)
XVIb	239 (4,03), 326 (3,85)	965, 1259 s, 1293 s, 1458, 1520, 1542, 1610, 1621, 1684 s, 1735 s, 2845, 2957, 3074 w	3,15 (6H, s, OMe); 3,64 and 3,91 (3H, s, OMe); 6,4—7,2 (15H, =CH—, arom.)
XVIIa	—	1083 w, 1220, 1352 s, 1450, 1500, 1600, 1638, 1696 s, 3044 w, 3068, 3088 w	5,92 (1H, s, $CHCl_2$), 6,7—7,9 (16H, =CH—, arom.)
XVIIb	—	1042, 1260 s, 1358 s, 1450, 1502, 1520 s, 1600, 1698 s, 2852, 2980, 3032, 3065, 3090	3,76 (3H, s, OMe); 5,98 (1H, s, $CHCl_2$); 6,7—7,8 (15H, =CH—, arom.)
XVIIIb	—	960, 1157, 1246 s, 1265 s, 1452, 1498 s, 1600 s, 1635, 2928, 3026, 3067	6,34 (1H, s, =CH—); 6,9—7,3 (15H, arom.)
XXa	—	1086, 1270 s, 1324 s, 1455, 1504, 1605, 1630, 1710 s, 3043, 3072, 3092	6,9—7,6 (=CH—, arom.)

*^{13}C NMR spectra, δ, ppm: VIa — 52.1 (OMe), 161.4, 163.3 and 164.7 (CO); VIIIa — 20.0 (Me), 41.4 (CH_2), 52.1 (C_3), 52.7 (OMe), 171.7 and 174.3 (CO); XIIa — 49.1 (CH), 51.2 (OMe), 162.5 and 165.1 (CO); XIIIa — 47.7 (CH), 52.7 and 53.2 (OMe), 157.9, 163.9 and 169.0 (CO); XVIIa — 63.4 ($CHCl_2$), 163.8 (CO); XXa — 93.2 (CCl_3), 160.1 (CO).
**PMR spectra were taken with the addition of catalytic amounts of trifluoroacetic acid.

the IR spectrum, the stretching vibrations of the OH group absorb at 3425 cm^{-1}, while there is no absorption in the carbonyl region. The mass spectrum of the ester IXa contains a molecular ion peak with m/z 415. The PMR spectrum shows signals at 1.35 and 3.70 ppm due to

two equivalent methyl groups and a methoxy group. The IR spectrum contains bands due to the ester and carbamate C=O stretching vibrations.



The reaction of the ketenimine Ia with dichlorocarbene in the presence of a 20-fold excess of dimethyl fumarate gave a mixture of the isomeric compounds XIa and XIIa (in the ratio 1:8) and a small quantity of the lactam XIIIa. On standing in solution, the pyrroline XIa isomerized to the pyrrole XIIa. The PMR spectrum of compound XIIa shows signals from the MeO group (3.21 and 3.83 ppm) and the benzhydryl proton (5.25 ppm). In the PMR spectrum of the mixture of compounds XIa and XIIa, additional signals from the protons of the MeO group and methine proton of the pyrroline XIa, respectively, appear at 3.42, 3.48, and 4.75 ppm. The ^{13}C NMR spectrum of compound XIIa show peaks at 162.5 and 165.1 ppm corresponding to the carbonyl carbon atoms; these values are similar to the values for the corresponding carbon atoms in compound VIa and to the mean value for α, β-unsaturated acid esters (165.8 ppm), but differ from the values for saturated acid esters (171.6 ppm) [3] (see also compound VIIIa). The mass spectrum of the lactam XIIIa contains a molecular ion peak with m/z 487. In the PMR spectrum are signals at 5.08 ppm, corresponding to the methine proton, and at 3.93 ppm corresponding to protons of the MeO group. In the ^{13}C NMR spectrum are signals from the amide carbonyl carbon atoms, and the conjugated and nonconjugated ester groups at 157.9, 163.9, and 169.0 ppm, respectively.

When the reaction was carried out with 1 equivalent of the ketenimine Ia or b and dichlorocarbene in the presence of only 2 equivalents of dimethyl fumarate, a six-membered lactam is one of the main products of the reaction. From the ketenimine Ib and dimethyl fumarate were obtained the substituted pyrrole XIIb, the five-membered lactam VIIb, and the six-membered lactams XIIIb and XIVb. The spectral characteristics of the N-(4-methoxyphenyl)-substituted compounds XIIb, XIIIb, VIIb, and those of the N-phenyl substituted compounds XIIa, XIIIa, VIIa are similar.

The reaction between the 1,4-diazabicyclo[2.2.2]octane and the lactams XIIIa and b gave compounds XVa and b. Treatment of lactams XIIIa and b with sodium carbonate in methanol gives compounds XVIa and b. The difference in the position of the long-wave maxima in the UV spectra of compounds XIIIa, b; XIVb; XVa, b; and XVIa, b (Table 1) confirms that they

TABLE 2. Melting Points and Elemental Analysis Data for New Compounds

Compound	T_{mp}, °C*	M**	Found, %			Empirical formula	Calculated, %		
			C	H	N		C	H	N
VIa	171—173	439	74,1	5,0	2,7	$C_{27}H_{21}NO_5$	73,8	4,8	3,2
VIIa	104—107	—	73,9	5,3	2,7	$C_{27}H_{23}NO_5$	73,5	5,3	3,2
VIIb	—	471	—	—	—	$C_{28}H_{25}NO_5$	—	—	—
VIIIa	111—113	397	78,5	5,9	3,2	$C_{26}H_{23}NO_3$	78,6	5,8	3,5
IXa	106—108	415	75,1	6,1	3,0	$C_{26}H_{25}NO_4$	75,2	6,1	3,4
Xa	108—112	355	84,4	7,1	3,5	$C_{25}H_{25}NO$	84,5	7,1	3,9
XIIa	134—136	—	70,7	4,8	2,5	$C_{27}H_{22}ClNO_4$	70,5	4,8	3,0
XIIb	—	489	—	—	—	$C_{28}H_{24}ClNO_5$	—	—	—
XIIIa	228—232	487	68,8	4,6	2,6	$C_{28}H_{22}ClNO_5$	68,9	4,5	2,9
XIIIb	217—219	517	67,6	4,9	2,9	$C_{29}H_{24}ClNO_6$	67,3	4,7	2,7
XIVb	—	517	—	—	—	$C_{29}H_{24}ClNO_6$	—	—	—
XVa	221—223	437	74,3	4,4	2,9	$C_{27}H_{19}NO_5$	74,1	4,4	3,2
XVb	228,5—229,5	467	72,2	4,5	2,7	$C_{28}H_{21}NO_6$	71,9	4,5	3,0
XVIa	210—212	483	72,1	5,2	2,6	$C_{29}H_{25}NO_6$	72,0	5,2	2,9
XVIb	163,5—165,5	513	69,9	5,3	2,4	$C_{30}H_{27}NO_7$	70,1	5,3	2,7
XVIIa	123—124	381	69,0	4,3	3,4	$C_{22}H_{17}Cl_2NO$	69,1	4,5	3,7
XVIIb	92,5—94	411	67,3	4,6	2,9	$C_{23}H_{19}Cl_2NO_2$	67,0	4,6	3,4
XVIIIa	124—126	—	65,9	4,0	3,2	$C_{22}H_{18}Cl_3N$	65,9	4,0	3,5
XXa	103—105	415	63,2	3,9	3,0	$C_{22}H_{16}Cl_3NO$	63,4	3,9	3,4

*Compound VIa was recrystallized from a mixture of CCl_4 and CH_2Cl_2; VIIa, VIIIa, IXa, XIIa, XVIIa and b, and XXa from a mixture of ether and hexane; Xa and XVIIIa from hexane; XIIIa and b, and XVb from a mixture of ether and CH_2Cl_2; XVa and XVIa and b from a mixture of ether, hexane, and CH_2Cl_2.
**Mass spectrometrically, in chlorine containing compounds M for ^{35}Cl.

contain different chromophores, moreover, compounds with benzhydrylidene groups absorb at longer wave lengths.

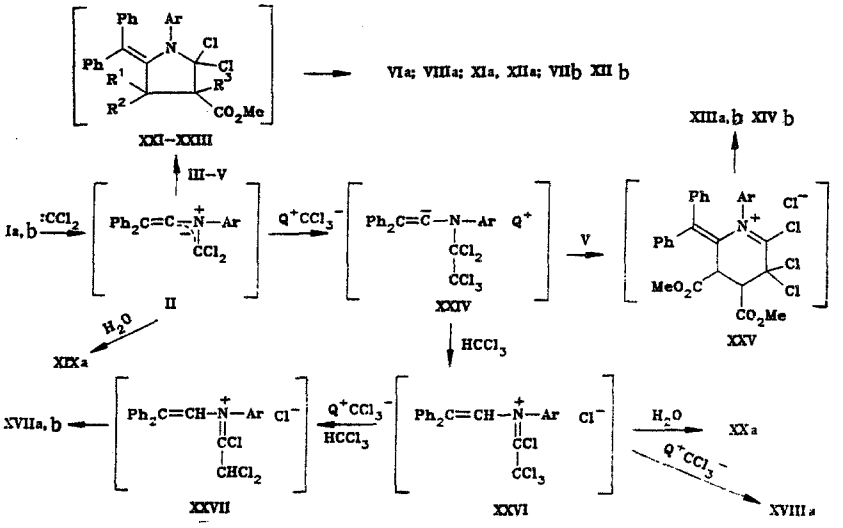
Together with these products, the formation of which involves the dipolar compounds, small amounts of the amides XVIIa and b, the amine XVIIIa, and the carbamoyl chloride XIXa were also isolated; these compounds are the result of the reaction of the ketenimines with dichlorocarbene, its precursor (the trichloromethyl anion), and chloroform. Compounds XVIIa-XIXa are products of the reaction of the ketenimine Ia with excess sodium trichloroacetate in the absence of the dipolar compound; when insufficient sodium trichloroacetate is present, the main product is not the amide XVIIa, but the amide XXa.

The results obtained can be explained by the following series of changes: the reaction of the ketenimines Ia and b with dichlorocarbene give the ketenimine-ylides IIa and b which react with dipolar compounds to give the corresponding unstable five-membered heterocyclic ring compounds (XXI-XXIII). The latter readily lose a molecule of HCl to give the substituted pyrroles XIIa and b, or are hydrolyzed during the reaction work-up to the lactams VIa, VIIIa, and VIIb.

When active dipolar compounds such as dimethylacetylenedicarboxylate, or a large excess of less active compounds such as methyl methacrylate and dimethyl fumarate are employed, the (2 + 3)-cyclo addition compounds of ketenimine-ylides and dipolar compounds are the main product of the reaction. In the presence of a smaller quantity of the less active dimethyl fumarate, the ketenimine-ylides II also react with the trichloromethyl anion to give the anion XXIV; the addition of this compound to dimethyl fumarate, followed by cyclization, gives the compound XXV.

Loss of HCl from the latter and hydrolysis of the reaction mixture leads to the final lactam XIIIa and b, and XIVb. In the absence of the dipolar anion XXIV, a proton is lost from the chloroform used as solvent, to give compound XXVI, which on hydrolysis yields the amide XXa; in the presence of excess sodium trichloroacetate, XXVI undergoes either dehalogenation to give the amine XVIIIa or hydrodehalogenation to give the amines XXVII which then hydrolyze to the amides XVIIa, b. The dehalogenation of perhalogenoalkanes by heating sodium trichloroacetate in glyme is described in the literature [4]. In our case, when chloroform is used as a solvent, this process is hydrodehalogenation. The proposed reaction scheme is

confirmed by replacing chloroform by deuterochloroform, when the amine $Ph_2C{=}CDNPhCCl{=}CCl_2$ (XVIIIa-D_1) and amide $Ph_2C{=}CDNPhC(O)CCl_2D$ (XVIIa-D_2) are obtained.



XXI $R^1{=}CO_2Me$, $R^3{+}R^2{=}$bond.; XXII $R^1{=}R^2{=}H$, $R^3{=}Me$; XXIII $R^1{=}R^3{=}H$, $R^2{=}CO_2Me$; $Q^+{=}PhCH_2\overset{+}{N}Et_3$

EXPERIMENTAL

UV spectra were taken on a Perkin-Elmer M-402; compounds VIIa and b, and XIIa and b were dissolved in ethanol and the remaining compounds in methanol. IR spectra were recorded on a UR-20; compounds VIIa, XIIb, and XIVb were prepared as 2% solutions in CCl_4, the remaining compounds as KBr pellets. PMR spectra were recorded in Tesla BS-497 (100 MHz) and Varian EM-360 (60 MHz) instruments; compound Xa was prepared as a 5% solution in C_6D_6, and all other compounds as 10% solutions in $CDCl_3$. ^{13}C NMR spectra were obtained on a CFT-20 (20 MHz) for 30% solutions in $CDCl_3$. Silica gel (5-40 μm) was used for the chromatographic separation of the mixtures. Ketenimines Ia, b were obtained by the method described in [5]. Data for new compounds are presented in Tables 1 and 2.

Dimethyl 2-Benzhydryliden-5-oxo-1-phenyl-2,5-dihydropyrrole-3,4-dicarboxylate (VIa). A solution of 0.74 g (2.75 mmole) of ketenimine Ia, 0.5 g (3.5 mmole) of ester III, and 0.09 g (0.4 mmole) of benzyltriethylammonium chloride in 50 ml of $CHCl_3$ was stirred in a current of argon at 60°C and 1.8 g (9.7 mmole) of sodium trichloroacetate then slowly added over a period of 2 h 30 min. The mixture was stirred for a further 30 min, cooled, washed with water, and dried over $MgSO_4$. The solvent was evaporated and separated by column chromatography (eluent hexane and diethyl ether, 4:1) to give 0.8 g of an oil, which was crystallized from a hexane–CCl_4–CH_2Cl_2 mixture to yield 0.45 g (37%) of the lactam VIa.

Dimethyl 2-Benzhydryliden-5-oxo-1-phenylpyrrolidine-3,4-dicarboxylate (VIIa). A solution of $LiAl(OEt)H_3$ in ether was added dropwise to a stirred solution of 0.15 g (0.34 mmole) of the lactam VIa and in 40 ml of absolute ether at 20° until all the starting material had reacted (checked by TLC). The reaction mixture was shaken with water, and the organic layer separated and dried over $MgSO_4$. Separation by TLC (eluent CH_2Cl_2–hexane–ether, 1:3:0.2) gave 0.11 g (73%) of compound VIIa.

Reaction of the Ketenimine Ia with Dichlorocarbene in the Presence of Methyl Methacrylate. A solution of 1.5 g (5.6 mmole) of ketenimine Ia, 0.08 g (0.43 mmole) of benzyltriethylammonium chloride and 7.5 g (75 mmole) of methyl methacrylate in 100 ml of chloroform was stirred in a current of argon at 60°C, and 4.5 g (24 mmole) of sodium trichloroacetate slowly added over a period of 4 h 30 min. When cool, the mixture was filtered, the solvent and excess methyl methacrylate evaporated under vacuum, and the residue separated by column chromatography (eluent hexane–$CHCl_3$–ether, 3:1:0.2). Recrystallization gave 0.55 g (25%) of methyl 5-benzhydryliden-3-methyl-2-oxo-1-phenylpyrrolidine-3-carboxylate (VIIIa), 0.18 g (9%) of methyl 2-[N-(2,2-diphenylvinyl)-N-phenylcarbamoyloxy]-2-methylpropionate (IXa), 0.26 g (14%) N-(2,2-diphenylvinyl)-N-phenylamide dichloroacetic acid (XVIIa), and 0.04 g (2%) of N-(2,2-diphenylvinyl)-N-(trichlorovinyl)aniline (XVIIIa).

2-Benzhydryliden-4-(hydroxymethyl)-4-methyl-1-phenylpyrrolidine (Xa). A mixture of 0.05 g (1.3 mmole) of lithium aluminum hydride and 0.06 g (0.45 mmole) of aluminum chloride in 10 ml of absolute ether was stirred in a current of argon at 20°C for 30 min, then heated to boiling and a solution of 0.1 g (0.25 mmole) of the lactam VIIIa in 5 ml of ether gradually added over a period of 1 h. The reaction mixture was cooled, 5 ml of water added, the precipitated material filtered off, the organic layer washed with water and dried over $CaCl_2$. Evaporation of the solvent gave 0.088 g (99%) of compound Xa.

Reaction of Ketenimines Ia, b with Dichlorocarbene in the Presence of Dimethyl Fumarate. A. To a stirred solution of 0.74 g (2.75 mmole) of ketenimine Ia, 0.64 g (6.9 mmole) of dimethylfumarate, and 0.09 g (0.4 mmole) of benzyltriethylammonium chloride in 50 ml of chloroform in a current of argon at 60°C was slowly added 2 g (10.8 mmole) of sodium trichloroacetate over a period of 5 h. The mixture was stirred for a further 4 h, cooled, washed with water and dried over $MgSO_4$. After evaporation of the solvent, the excess dimethyl fumarate was removed by distillation under vacuum, and the residue separated by column chromatography (eluent benzene–diethyl ether). Recrystallization gave 0.37 g (28%) of the dimethyl 2-benzhydryliden-6-oxo-1-phenyl-5-chloro-1,2,3,6-tetrahydropyridine-3,4-dicarboxylate (XIIIa), 0.27 g (21%) of dimethyl 2-benzhydryl-1-phenyl-5-chloropyrrole-3,4-dicarboxylate (XIIa), 0.084 g (8%) of the amide XVIIa, 0.047 g (5%) of N-(2,2-diphenylvinyl)-N-phenylcarbamoyl-chloride (XIXa), 0.035 g (3%) of methyl 2,5-dioxo-1,7,7-triphenyl-1,2,5,7-tetrahydrofuro-[3,4-b]pyridine-4-carboxylate (XVa).

Using the same method, but eluting the product with hexane–$CHCl_3$–diethyl ether (3:1:0.2), 0.82 g (2.65 mmole) of the ketenimine Ib gave 0.26 g (25%) of N-(2,2-diphenylvinyl)-N-(4-methoxyphenyl)amide dichloroacetic acid (XVIIb), 0.27 g (22%) of dimethyl 2-benzhydryliden-1-(4-methoxyphenyl)-5-oxopyrrolidine-3,4-dicarboxylate (VIIb), 0.25 g (18%) of dimethyl 2-benzhydryliden-1-(4-methoxyphenyl)-6-oxo-5-chloro-1,2,3,6-tetrahydropyridine-3,4-dicarboxylate (XIIIb), 0.10 g (8%) of dimethyl 2-benzhydryl-1-(4-methoxyphenyl)-6-oxo-5-chloro-1,6-dihydropyridine-3,4-dicarboxylate (XIVb) and 0.035 g (3%) of dimethyl 2-benzhydryl-1-(4-methoxyphenyl)-5-chloropyrrole-3,4-dicarboxylate (XIIb).

B. Using the method described above, 0.81 g (3 mmole) of the ketenimine Ia, 8.64 g (60 mmole) of dimethyl fumarate, 0.09 g (0.4 mmole) of benzyltriethylammonium chloride in 180 ml of chloroform and 2 g (10.8 mmole) of sodium trichloroacetate gave 0.07 g (5%) of the lactam XIIIa and 0.47 g (34%) of the substituted pyrrole XIIa.

Methyl Esters of 1-Aryl-2,5-dioxo-7,7-diphenyl-1,2,5,7-tetrahydrofuro[3,4-b]pyridine-4-carboxylic Acids (XVa and b). A solution of 0.2 mmole of compound XIIIa, b and 0.11 mmole of 1,4-diazabicyclo[2.2.2]octane in 10 ml of anhydrous CH_2Cl_2 was kept for 20 h at 20°C, filtered through 1 g of silica gel, and the solvent distilled off. Recrystallization of the residue gave the ethers XVa and b in 75 and 74% yields, respectively.

Dimethyl Esters of 1-Aryl-2-(α-methoxybenzhydryl)-6-oxo-1,6-dihydropyridine-3,4-dicarboxylic Acids (XVIa and b). A mixture of 0.2 mmole of compound XIIIa, b, 20 mg of anhydrous Na_2CO_3 in 30 ml of anhydrous methanol was refluxed for 1 h 30 min, the methanol removed under vacuum. To the residue was added ether, the mixture filtered, and the solvent evaporated. Recrystallization gave XVIa and b in yields of 76 and 71%, respectively.

Reaction of Ketenimine Ia with Sodium Trichloroacetate in Chloroform. A. To a stirred solution of 1.3 g (4.8 mmole) of ketenimine Ia and 0.1 g (0.4 mmole) of benzyltriethylammonium chloride in 300 ml of chloroform in a current of argon at 60°C was slowly added over a period of 7 h, 2 g (11 mmole) of sodium trichloroacetate. The mixture was cooled, washed with water, and dried over $MgSO_4$. The solvent was removed, and the residue separated by column chromatography (eluent benzene–hexane) and recrystallized to give 0.81 g of N-(2,2-diphenylvinyl)-N-phenylamide trichloroacetic acid (XXa), 0.12 g of the amide XVIIa, 0.09 g of carbamoyl chloride XIXa, 0.02 g of the amine XVIIIa, and 0.04 g of the N-phenylamide of diphenylacetic acid; the hydrolysis product did not react with the ketenimine Ia. Yields, based on the reacted ketenimine, were 57, 9, 8, and 2%, respectively.

B. To a stirred solution of 0.74 g (2.75 mmole) of the ketenimine Ia and 0.09 g (0.4 mmole) of benzyltriethylammonium chloride in 20 ml of chloroform in a current of argon at 60°C was slowly added 3.8 g (20 mmole) of sodium trichloroacetate. Mixing was continued for a further 2 h and the reaction mixture then worked up as before, to give 0.45 g (43%) of the amide XVIIa, 0.04 g (4%) of the amide XXa, and 0.02 g (2%) of the amine XVIIIa.

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N-ACETYLINDOXYL IN THE SYNTHESIS OF NEW CONDENSED HETEROCYCLES

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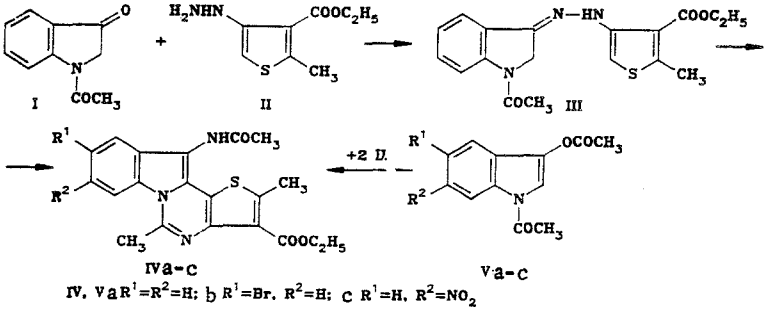
Derivatives of a new heterocyclic system thieno[2',3':5,6]pyrimido[3,4-a]indole, were obtained by the reaction of substituted N,O-diacetylindoxyls with excess N-(2-methyl-3-ethoxycarbonyl-4-thienyl)hydrazine. The reaction of N-acetylindoxyl and 4-hydrazinouracil forms 12-amino-1,3-dioxo-2,4,6-trimethylpyrimido[5',4':5,6]pyrimido[3,4-a]indole.

The reaction of N-acetylindoxyl with arylhydrazines forms arylhydrazones, which when heated in acetic acid in the presence of acetic anhydride undergo rearrangement and cyclocondensation to derivatives of 12-acetylaminoindolo[1,2-c]quinazoline [1]. In the present work the heterocyclization of hydrazines by this reaction has been studied.

The reaction of N-acetylindoxyl (I) with N-(2-methyl-3-ethoxycarbonyl-4-thienyl)hydrazine (II) gives the N-(2-methyl-3-ethoxycarbonyl-4-thienyl)hydrazone of N-acetylindoxyl (III). When the last-named is treated with a mixture of acetic anhydride and acetic acid it is converted by the scheme previously proposed [1, 2] to 11-acetylamino-2,5-dimethyl-3-ethoxycarbonylthieno[2',3':5,6]pyrimido[3,4-a]indole (IVa) in 66% yield. Compound IVa and other derivatives of thieno[2',3':5,6]pyrimido[3,4-a]indole (IVb, c) are also obtained by the reaction of a twofold excess of thienylhydrazine II with N,O-diacetylindoxyl (V) under conditions analogous to the synthesis of 12-acetylaminoindolo[1,2-c]quinazolines [1].



IV, V a $R^1=R^2=H$; b $R^1=Br$, $R^2=H$; c $R^1=H$, $R^2=NO_2$

A derivative of a new heterocyclic system, 12-amino-1,3-dioxo-2,4,6-trimethylpyrimido-[5',4':5,6]pyrimido[3,4-a]indole (VI) is formed by the prolonged heating of N-acetylindoxyl with 4-hydrazinouracil VII in alcohol.

We were unable to isolate the corresponding hydrazone.

*Deceased.

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