for 10 h, after which the pyridine and excess propionic anhydride were removed by distillation. The residue was crystallized from ligroin–benzene (1 : 1) to give 0.5 g (44%) of VI with mp 228° and R_f 0.54. IR spectrum: 1725 (C=O) and 1428 and 1105 cm^{-1} ($Si-C_6H_5$). Found: C 76.1; H 8.1; N 3.4%. $C_{29}H_{35}NO_2Si$. Calculated: C 76.1; H 7.7; N 3.1%. The picrate had mp 224.5-226° (from alcohol–acetone). Found: N 8.0%. $C_{29}H_{35}NO_2Si \cdot C_6H_3N_3O_7$. Calculated: N 8.2%. The hydrochloride had mp 242-243° (from alcohol–acetone). Found: C 70.7; H 7.1; N 3.1; Cl 7.4%. $C_{29}H_{35}NO_2Si \cdot HCl$. Calculated: C 70.5; H 7.3; N 2.8; Cl 7.2%.

LITERATURE CITED

1. N. S. Prostakov and A. V. Varlamov, Khim. Geterotsikl. Soedin., No. 12, 1637 (1970).
2. M. M. A. Hassan and A. F. Casy, Org. Magn. Res., 2, 197 (1970).
3. N. S. Prostakov and N. N. Mikheeva, Usp. Khim., 31, 1191 (1962).
4. I. N. Nazarov, N. S. Prostakov, and N. I. Shvetson, Zh. Obshch. Khim., 26, 2798 (1956).
5. E. Eliel, N. Allinger, S. Angyal, and T. Morrison, Conformational Analysis, Wiley (1965).
6. J. Hajdukovic, J. Regnier, and M. L. C. Martin, Compt. Rend., C, 272, 330 (1971).
7. G. R. Clemo and K. H. Jack, Chem. Ind., 195 (1953).
8. B. L. Lenitz, C. M. Martini, M. Prizner, and P. C. Nachod, J. Amer. Chem. Soc., 74, 5564 (1952).
9. R. Granger, J. P. Chapat, F. Simon, J. P. Lizad, and P. Loycux, Compt. Rend., C, 272, 337 (1971).
10. N. S. Prostakov, B. E. Zaitsev, N. M. Mikhailov, and N. N. Mikheeva, Zh. Obshch. Khim., 34, 463 (1964).

SYNTHESIS OF INDOLIZINES AND PYRIDINIUM YLIDS FROM 4,5-DISUBSTITUTED α-PICOLINES

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New 1,3-diacetylindolizines were obtained from 4-phenyl- and 4-benzyl-2,5-dimethylpyridines; some transformations involving their acetyl groups were realized. The same pyridine bases were used in syntheses of pyridinium ylids. The transformations of the latter to indolizines were studied.

Of the rather large number of synthesized indolizines, there are few that have substituents in the six-membered ring. This is explained, first, by the low degree of accessibility of substituted α-picolines and, second, by the occurrence of electrophilic substitution reactions in the five-membered ring of indolizines. Using our previously obtained 4-phenyl- and 4-benzyl-2,5-dimethylpyridines (I, II) [1, 2] we synthesized new pyridinium ylids and indolizines with substituents in the pyridine ring.

7-Phenyl- and 7-benzyl-6-methyl-1,3-diacetylindolizines (III, IV) were obtained by the Scholtz method [3] from pyridines I and II. Only the carbonyl group attached to C_1 undergoes reaction in the reaction of III and IV with phenylhydrazine, and hydrazones V and VI, respectively, are isolated. When alkali is present, both acetyl groups of indolizine III undergo condensation with benzaldehyde to give 6-methyl-7-phenyl-1,3-dicinnamoylindolizine (VII). However only 6-methyl-7-phenyl-3-acetyl-1-(p-dimethylaminocinnamoyl)indolizine (VIII) was isolated in low yield in the condensation with p-dimethylaminobenzaldehyde under similar conditions. The structure of indolizines III-VIII was confirmed by the spectral data (see the experimental section).

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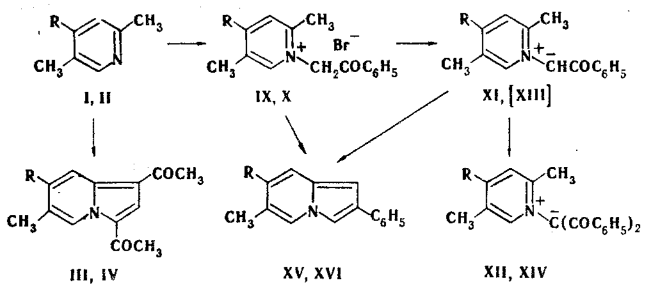

I, III, IX, XI, XII, XV R = C_6H_5; II, IV, X, XIII. XIV, XVI R = $C_6H_5CH_2$

The synthesis of phenacylpyridinium ylids XI and XIII from I and II was accomplished by the method in [4] by treatment of 1-phenacylpyridinium bromides (IX and X) with potassium carbonate solution. Stable dibenzoylmethylids XII and XIV were obtained by benzoylation of ylids XI and XIII.

The PMR spectra of CF_3COOH solutions of ylid XI and quaternary salt IX are practically identical (see Table 1), but the integral intensity of the singlet at 6.25-6.50 ppm in the spectrum of a CF_3COOD solution of XI is reduced from 2H to 1H as compared with the spectrum of a CF_3COOH solution. This constitutes evidence for the presence in ylid molecule XI of a carbanion to which a proton or deuteron is added in acidic media. The PMR spectra of CF_3COOH and CF_3COOD solutions of XII and XIV are completely identical (see Table 1), and it is difficult to draw a conclusion regarding the ylid structure of these compounds on the basis of them. The presence of a diamagnetic shift of the signal of the α proton of the pyridine ring on passing from starting quaternary salts IX and X to dibenzoylmethylids XII and XIV (see Table 1, solvent $CDCl_3$ or CCl_4-CDCl_3), which is in agreement with the corresponding data for diacylpyridinium ylids and their salts [5], is indirect proof in favor of a structure of this sort for them. The presence of a low intensity M^+ peak and a rather intense (~30%) $(M-18)^+$ ion peak is characteristic for the mass spectra of pyridinium ylids XI, XII, and XIV.

TABLE 1. PMR Spectral Data for Substituted Pyridinium Ylids and Indolizines

Compound	Solvent	Chemical shifts, δ, ppm					
		β-CH_3*	α-CH_3*	γ-CH_2-Ph*	N^+-CH_2*-(N^+-CHD-)*	α-H (ylid),* 5-H (indolizine)*	other aromatic protons
IX	CCl_4+CDCl_3	2,34	2,78	—		9,58	6,90—7,60 m 8,16 m†
	CF_3COOH	2,55	2,80	—	6,50	8,67	7,36—8,05 m 8,32 m†
	CF_3COOD	2,55	2,80	—	(6,50)	8,69	7,77—8,07 m 8,28 m†
X	CCl_4+CDCl_3	2,35	2,64	4,09		9,44	6,90—7,50 m 8,15 m†
XI	CF_3COOH	2,58	2,80	—	6,30	8,48	7,40—7,92 m 8,17 m†
	CF_3COOD	2,58	2,80	—	(6,25)	8,45	7,35—7,95 m 8,12 m†
XII	CCl_4+CDCl_3	2,43	2,80	—		8,33	6,85—7,75 m
	CF_3COOH	2,46	2,78	—		8,56	7,17—7,82 m 7,80 s (3-H)
	CF_3COOD	2,47	2,79	—		8,56	7,17—7,82 m 7,80 s (3-H)
XIV	$CDCl_3$	2,34	2,62	4,07		8,21	6,70—7,50 m
	CF_3COOH	2,36	2,60	4,20		8,40	6,83—7,73 m
	CF_3COOD	2,40	2,62	4,25		—	6,91—7,74 m
XV	CF_3COOH	2,52	—	—	5,93	8,79	7,15—8,07 m
	CF_3COOD	2,53	—	—	(5,93)	8,83	7,25—8,03 m
XVI	CCl_4+CDCl_3	1,97	—	3,80	—	—	7,02—7,78 m 6,45 s (3-H) 6,95 s (1-H)
	CF_3COOH	2,52	—	4,23	5,80	8,66	6,93—7,88 m
	CF_3COOD	2,56	—	4,29	(5,83)	8,68	7,26—7,92 m

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*Singlets.

†Two ortho hydrogen atoms of the phenyl group relative to the oxo group. The following abbreviations are used: s is singlet and m is multiplet.

6-Methyl-2,7-diphenylindolizine (XV) [7] and 6-methyl-7-benzyl-2-phenylindolizine (XVI) were obtained from salts IX and X under the conditions of the Chichibabin reaction [6]. Indolizine XVI is also formed when a chloroform solution of ylid XIII is passed through a layer of aluminum oxide. However, because of side processes associated with destruction of the ylid [4], indolizine XVI was isolated in low yield. The higher lability of ylid XIII as compared with ylid XI made it impossible to characterize it by spectral and analytical data. The resonance signal of the methylene protons in the PMR spectra of CF_3COOH solutions of indolizines XV and XVI at 5.80-5.93 ppm and the absence of signals at 4.10-4.30 ppm provide evidence for protonation of these indolizines at the C_3 atom rather than at C_1, as was established also by Fraser and co-workers [8].

EXPERIMENTAL METHOD

The UV spectra of ethanol solutions of the compounds were measured with an Hitachi EPS-3T spectrometer. The IR spectra of KBr pellets of the compounds were recorded with a UR-20 spectrometer. The PMR spectra of solutions of III and IV in CCl_4-CDCl_3 were recorded with an HA-100D spectrometer, and the PMR spectra of IX-XVI were recorded with T-60 and BS487C spectrometers (8 MHz); the internal standard for the solutions in $CDCl_3$ or CCl_4-CDCl_3 was hexamethyldisiloxane, whereas the internal standard for solutions in CF_3COOH and CF_3COOD was tetramethylsilane. The mass spectra were obtained with MKh-1303 and LKB-9000 (ylids XII and XIV) spectrometers. Thin-layer chromatography (TLC) of XII and XIV-XVI was carried out on activity II aluminum oxide with elution by chloroform.

Salt IX was obtained in 86% yield by the method in [7] and had mp 209.5-210.5° (from alcohol). IR spectrum, ν, cm^{-1}: 3518, 3380 (OH group of the solvate); 3006, 1701 (C=O); 1642, 1500-1610, and 683-772. UV spectrum, λ_{max}, nm (log ε): 250 (4.36), 282 (4.36), and 430 (3.10). Found: N 3.5%. $C_{21}H_{20}BrNO$. Calculated: N 3.7%.

6-Methyl-7-phenyl-1,3-diacetylindolizine (III). A mixture of 6.6 g (0.04 mole) of pyridine I and 24.5 g (0.24 mole) of acetic anhydride was heated in a sealed ampul at 250-260° for 8 h, after which the mixture was poured over ice, and the aqueous mixture was neutralized with 20% sodium carbonate solution and extracted successively with ether and chloroform. The ether extract was treated in the cold with 10% hydrochloric acid until it was acidic with respect to Congo red, after which it was shaken with sodium carbonate solution, combined with the chloroform extract, and dried with magnesium sulfate. Evaporation of the solvent yielded 1.1 g (20.8% based on converted pyridine I) of indolizine III. Four crystallizations from petroleum ether (with activated charcoal) gave colorless acicular crystals with mp 171.8-172°. IR spectrum, ν, cm^{-1}: group of bands at 2925-3108, 1643, 1578, 1522, 764, and 701. UV spectrum, λ_{max}, nm (log ε): 234 (4.18), 264 (4.44), 294 (4.16), and 352 (4.40). PMR spectrum, δ, ppm: 9.70 s (1H), 8.33 s (1H), 7.70 s (1H), 7.23-7.47 m (5H), 2.50 s (3H), 2.47 s (3H), and 2.23 s (3H). Found: C 78.2; H 6.1; N 4.7%; M 291. $C_{19}H_{17}NO_2$. Calculated: C 78.3; H 5.9; N 4.8%; M 291. The aqueous acidic layer was treated with sodium hydroxide and extracted with ether, from which 3.29 g of starting pyridine I was obtained after drying.

6-Methyl-7-benzyl-1,3-diacetylindolizine (IV). This compound was obtained by the procedure used to synthesize III. Reaction of 5 g (0.0164 mole) of pyridine II and 25.5 g (0.25 mole) of acetic anhydride yielded 1.98 g of starting II and 0.88 g (19% based on converted pyridine II) of indolizine IV. After purification on aluminum oxide or four crystallizations from ligroin with activated charcoal, indolizine IV was obtained as colorless acicular crystals with mp 159.5-160°. IR spectrum, ν, cm^{-1}: group of bands at 2885-3030, 1645, 1602, 1520, 1492, 730, and 712. UV spectrum, λ_{max}, nm (log ε): 230 (4.20), 260 (4.50), 293 (4.10), and 345 (4.39). PMR spectrum, δ, ppm: 9.50 s (1H), 8.24 s (1H), 7.60 s (1H), 6.96-7.17 m (5H), 3.96 s (2H), 2.44 s (3H), 2.40 s (3H), and 2.13 s (3H). Found: C 78.4; H 6.5; N 4.5%; M 305. $C_{20}H_{19}NO_2$. Calculated: C 78.5; H 6.4; N 4.6%; M 305. The perchlorate of IV had mp 189-190° (from ethyl acetate). Found: N 3.7%. $C_{20}H_{19}NO_2 \cdot HClO_4$. Calculated: N 3.5%.

7-Phenyl- and 7-Benzyl-3-acetyl-6-methyl-1-(α-phenylhydrazylidenethyl)indolizine (V and VI). Solutions of 0.28 g (0.96 mmole) of indolizine III in 1 ml of acetic acid and 0.28 g (2.6 mmole) of phenylhydrazine in 1 ml of acetic acid were mixed, and the mixture was worked up to give 0.06 g (16.4%) of yellow crystals of phenylhydrazone V with mp 211-212° (from ethyl acetate). IR spectrum, ν, cm^{-1}: 3326, 1617, 777, 742, 703, and 692. UV spectrum, λ_{max}, nm (log ε): 225 (4.32), 252 (4.34), 310 (4.24), and 380 (4.16). Found: ~~C 78.7; H 6.3;~~ N 10.9%; M 381. $C_{25}H_{23}N_3O$. Calculated: C 78.7; H 6.0; N 11.0%; M 381.

Hydrazone VI, with mp 203-203.5° [from ethyl acetate–acetic acid (10 : 1)], was similarly obtained as yellow crystals in 73.5% yield from indolizine IV. IR spectrum, ν, cm^{-1}: 3323, 1616, 752, 732, 702, and 693. UV spectrum, λ_{max}, nm (log ε): 242 (4.35), 302 (4.32), 340 (4.32), and 380 (4.26). Found: N 10.5%; M 395. $C_{26}H_{25}N_3O$. Calculated: N 10.6%; M 395.

6-Methyl-7-phenyl-1,3-dicinnamoylindolizine (VII). A mixture of 0.5 g (1.72 mmole) of indolizine III, 0.5 g (12.5 mmole) of sodium hydroxide, and 0.36 g (3.4 mmole) of benzaldehyde in 30 ml of ethanol was refluxed for 2 h, after which it was cooled and filtered. The alcohol was removed from the filtrate by distillation, and the residue was extracted with boiling ligroin, from which 0.21 g (29%) of bright-yellow crystals with mp 225-226° (from alcohol) was isolated. IR spectrum, ν, cm^{-1}: 3034, 1647, 1592, 977, 762, 737, 792, and 682. UV spectrum, λ_{max}, nm (log ε): 226 (4.42), 260 (4.18), 306 (4.54), and 394 (4.62). Found: C 84.6; H 4.9; N 2.9%; M 467. $C_{33}H_{25}NO_2$. Calculated: C 84.8; H 5.3; N 3.0%; M 467.

6-Methyl-7-phenyl-3-acetyl-1-(p-dimethylaminocinnamoyl)indolizine (VIII). A mixture of 0.4 g (1.37 mmole) of indolizine III, 0.44 g (2.96 mmole) of p-dimethylaminobenzaldehyde, and 0.43 g (10.7 mmole) of sodium hydroxide in 25 ml of ethanol was refluxed for 2 h, after which it was cooled and filtered to give 0.11 g of starting indolizine. The alcohol was removed from the filtrate by distillation, and the residue was extracted with boiling ligroin, from which 0.02 g (3.3%) of chalcone VIII was isolated upon cooling. The red-orange crystals had mp 123-125° (from alcohol). IR spectrum (UR-10, mineral oil suspension), ν, cm^{-1}: 1630, 1608, 988, 808, 780, 770, and 700. UV spectrum, λ_{max}, nm (log ε): 226 (3.52), 310 (3.22), 360 (3.44), and 434 (4.82). Found: M 422. $C_{28}H_{26}N_2O_2$. Calculated: M 422.

4-Benzyl-2,5-dimethyl-1-phenacylpyridinium Bromide (X). A mixture of 10 g (5.1 mmole) of pyridine II and 9.2 g (4.6 mmole) of ω-bromoacetophenone in 50 ml of acetone was heated for 2 h, and the precipitated crystals were removed by filtration and washed successively with acetone and absolute ether to give 17 g (93%) of salt X with mp 216-216.5° (from alcohol). IR spectrum, ν, cm^{-1}: 3022, 2927, 2865, 1695, 1644, 1500-1610, 752, 742, 701, and 675. UV spectrum, λ_{max}, nm (log ε): 250 (4.28) and 420 (2.78). Found: C 66.4; H 5.4; N 3.2%. $C_{22}H_{22}BrNO$. Calculated: C 66.7; H 5.5; N 3.5%.

2,5-Dimethyl-4-phenylpyridinium Phenacylid (XI) and 2,5-Dimethyl-4-phenylpyridinium Dibenzoylmethylid (XII). A total of 11 ml of a 40% potassium carbonate solution [4.2 g (31.5 mmole)] was added in portions with shaking to a suspension of 4 g (10.5 mmole) of salt IX in 20 ml of water, and the resulting bright-orange crystals were extracted with 30 ml of chloroform. Ylid XI was separated from admixed salt IX by passing the chloroform solution through a column (8 by 2.5 cm) filled with activity II aluminum oxide with elution by chloroform. A total of 78 ml of an orange-red solution was collected.

The chloroform was removed in vacuo without heating from 52 ml of the solution (the theoretical ylid XI content was 2.1 g). The residue was triturated with absolute ether to give 1.63 g (77.6%) of ylid XI as red-orange powder with mp 142-143° (the melting point became lower on storage). IR spectrum, ν, cm^{-1}: 3013, 1644, 1585, 1488-1543, 1296, 1213, 722, and 696. UV spectrum, λ_{max}, nm (log ε): 252 (4.16), 282 (4.21), and 434 (3.46). Found: N 4.8%; M 283. $C_{21}H_{19}NO$. Calculated: N 4.6%; M 301.

A solution of 0.55 g (3.9 mmole) of benzoyl chloride in 5 ml of chloroform and 10 ml of a 20% potassium carbonate solution were added to 26 ml of the chloroform solution [the theoretical ylid XI content was 1.05 g (3.3 mmole)], and the mixture was stirred vigorously for 15 min. The chloroform solution was separated, dried with sodium sulfate, evaporated to a small volume, and passed through a column filled with aluminum oxide (elution with chloroform). The chloroform was evaporated from the eluate, and the residue was triturated with absolute benzene to give 0.55 g (40%) of ylid XII as a bright yellow powder with mp 208-208.5° (from benzene) and R_f 0.37. IR spectrum, ν, cm^{-1}: 3407, 3068, 1643, 1518, 1448, 1383, 913, 883, and 702. UV spectrum, λ_{max}, nm (log ε): 284 (4.33) and 320 (4.10). Found: C 83.2; H 5.8; N 3.3%; M 405. $C_{28}H_{23}NO_2$. Calculated: C 83.0; H 5.7; N 3.5%; M 405.

2,5-Dimethyl-4-benzylpyridinium Dibenzoylmethylid (XIV). This compound was obtained as in the preceding experiment in 34.5% yield as pale-yellow plates with mp 183.5-184.5° (from benzene) and R_f 0.30. IR spectrum, ν, cm^{-1}: 3068, 3060, 1642, 1504, 1460, 1395, 888, 735, 723, 702, and 698. UV spectrum, λ_{max}, nm (log ε): 280 (3.92) and 318 (4.02). Found: C 83.2; H 6.3; N 3.2%; M 419. $C_{29}H_{25}NO_2$. Calculated: C 83.0; H 6.0; N 3.3%; M 419.

6-Methyl-7-benzyl-2-phenylindolizine (XVI). A) A mixture of 1.5 g (3.7 mmole) of salt X, 7.5 ml of 20% potassium carbonate solution, and 10 ml of chloroform was shaken for 15 min, after which the chloroform solution was passed through a chromatographic column (52 by 1.8 cm) filled with 52 g of activity II aluminum oxide (elution with chloroform). A total of 500 ml of eluate was collected; workup gave 0.11 g (10%) of indolizine XVI as greenish-gray plates with mp 153-155° (from ligroin) and R_f 0.90. IR spectrum, ν, cm^{-1}: 3085, 3063, 3033, 2978, 2953, 2923, 1605, 1495, 1453, 1343, 883, 843, 758, 728, and 695. UV spectrum, λ_{max}, nm (log ε): 264 (4.60) and 350 (3.46). Found: C 88.82; H 6.29; N 4.75%; M 297. $C_{22}H_{19}N$. Calculated: C 88.9; H 6.4; N 4.7%; M 297.

B) A mixture of 1 g (2.5 mmole) of salt X and 8 ml of a 40% K_2CO_3 solution was refluxed for 4 h, after which it was cooled, and the precipitate was removed by filtration, washed with water, and dried to give 0.56 g (74.7%) of shiny pale-yellow plates with mp 155-156° (from ligroin). The product was identical to the product obtained by method A.

LITERATURE CITED

1. N. S. Prostakov and L. A. Gaivoronskaya, Zh. Obshch. Khim., 32, 76 (1962).
2. N. S. Prostakov, L. A. Gaivoronskaya, N. M. Mikhailova, and L. M. Kirillova, Zh. Obshch. Khim., 33, 2573 (1963).
3. M. Scholtz, Ber., 45, 734 (1912).
4. F. Krohnke, Ber., 68, 1177 (1935).
5. C. A. Henrick, E. Ritchie, and W. C. Taylor, Austral. J. Chem., 20, 2467 (1967).
6. A. E. Chichibabin, Zh. Russk. Fiz. Khim. Obshchestva, 59, 477 (1927).
7. N. S. Prostakov and O. B. Baktibaev, Khim. Geterotsikl. Soedin., 1395 (1971).
8. M. Fraser, S. McKenzie, and D. H. Reid, J. Chem. Soc., B, 44 (1966).

CONFORMATIONAL STUDY OF CHIRAL CISOID ENAMINO KETONES*

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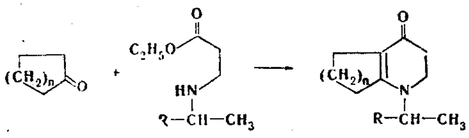
A study of a number of chiral cisoid cyclic enamino ketones by the circular dichroism method showed that they contain an inner disymmetric chromophore. The presence of homoconjugation of the phenyl and enamino ketone chromophores as a result of the drawing together of their π orbitals in space was also established.

In an investigation of chiral cisoid cyclic enamino ketones by the optical rotatory dispersion method in the case of III and IV we established [2] that the character of the rotatory dispersion curves reflects the nature of the cis-enamino ketone chromophore. To obtain further information regarding the three-dimensional structures of the enamino ketones we synthesized a series of compounds (III-VIII) and investigated them by the circular dichroism (CD) method. The enamino ketones necessary for the study were obtained by condensation of cycloalkenones with optically active β-aminopropionic acid esters in the presence of catalytic amounts of trifluoroacetic acid:



n = 1, 2, 3 I, II III-VIII

I R=C_6H_5; II R=$CH_2C_6H_5$; III n=1, R=C_6H_5; IV n=2, R=C_6H_5; V n=3, R=C_6H_5; VI n=1, R=$CH_2C_6H_5$; VII n=2, R=$CH_2C_6H_5$; VIII n=3, R=$CH_2C_6H_5$

The UV spectroscopic data indicate the presence in the products of an enamino ketone chromophore, the absorption maximum of which in all cases is found at 310-330 nm. A bathochromic shift as the polarity of the solvent increases and a large extinction coefficient (log $\varepsilon > 4$) are observed for this absorption band, and this

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