3,4-Ethylenedioxybenzylidene-p-(n-butyl)aniline. A mixture of 61 mmole of 3,4-ethylenedioxybenzaldehyde and 97 mmole of p-(n-butyl)aniline was dissolved in 65 ml of anhydrous toluene, 9.7 mmole of boron trifluoride etherate was added, and the mixture was refluxed for 25 h with a Dean–Stark trap. The mixture was then worked up as described above, and the reaction product obtained after chromatography and removal of the solvent by distillation was vacuum dried at 70-80° to give 10 g (50%) of a viscous liquid with n_D^{20} 1.1620. UV spectrum, λ_{max}, nm (log ε): 232 (4.32), 283 (3.96), and 317 (3.85) in alcohol. Found: C 77.3; H 7.2; N 4.4%. $C_{19}H_{21}NO_2$. Calculated: C 77.2; H 7.2; N 4.7%.

2-[p-(n-Amyl)phenyl]-6-formylquinoline. A 0.3-g sample of Raney nickel was added to a solution of 1.3 g of IId in 25 ml of moist toluene, after which the mixture was hydrogenated in a long-necked hydrogenation flask. The catalyst was then removed by filtration, and the solvent was evaporated to give 0.35 g (65%) of a product with mp 71-72° (from hexane). IR spectrum: 1710 cm^{-1} (CO). PMR spectrum (CCl_4), δ, ppm: 1.20 t (3H) for CH_3, 1.48-2.17 m (6H) for the CH_2 groups, 2.97 t (2H) for the aromatic ring CH_2 groups, 7.52 d (J = 8 Hz, 2H) for the aromatic protons adjacent to the C_5H_{11} group, 8.05-8.55 m (7H) for the aromatic protons, and 10.35 s (1H) for the CHO groups. Found: C 83.0; H 6.9; N 4.7%. $C_{21}H_{21}NO$. Calculated: C 83.1; H 7.0; N 4.6%.

2-[p-(n-Amylphenyl]quinoline-6-carboxylic Acid. A mixture of 1 g of IId and 50 ml of hydrochloric acid (1 : 1) was refluxed for 30 h, after which it was cooled, and the resulting precipitate was recrystallized from alcohol to give 0.8 g (80%) of a product with mp 245-247°. IR spectrum (in mineral oil): 1700 cm^{-1} (CO). PMR spectrum (CF_3COOH), δ, ppm: 0.77 t (3H) for the CH_3 group, 1.0-1.75 m (6H) for the CH_2 groups, 2.68 t (2H) for the aromatic ring CH_2 groups, and 7.45-9.03 m (9H) for the aromatic protons. Found: C 78.6; H 6.3; N 4.5%. $C_{21}H_{21}NO_2$. Calculated: C 79.0; H 6.6; N 4.4%.

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HETARYLATION OF CYCLOPENTADIENE, INDENE, AND AZULENE

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S. N. Baranov, and N. R. Kal'nitskii

UDC 547.821.831–835

The direct hetarylation of cyclopentadiene, indene, and azulene with several benzopyridines in the presence of acyl halides was studied. It is shown that the most electrophilic N-benzoylisoquinolinium salt is capable of hetarylating CH acids with $pK_a < 21$.

Donetsk State University. Donetsk Physical-Organic Chemistry Branch, Institute of Physical Chemistry, Academy of Sciences of the Ukrainian SSR. Translated from Khimiya Geterotsiklicheskikh Soedinenii, No. 10, pp. 1368-1375, October, 1975. Original article submitted July 17, 1974.

N-Heteroaromatic systems with free α or γ positions in the presence of acyl halides hetarylate such weak CH acids as acetophenone (pK_a 19) and acetone (pK_a 20) without catalysts [1]. It seemed of interest to ascertain the limiting pK_a values of CH acids that are still able to undergo this reaction. For this, we studied the possibility of hetarylation of cyclopentadiene (CPD, pK_a 15), indene (pK_a 18.5), azulene and guaiazulene (pK_a 20-21), and fluorene (pK_a 22.9)* with pyridine, quinoline, and isoquinoline in the presence of acyl halides.

The reactions of quaternary pyridinium and benzopyridinium salts with similar CH acids in the presence of alkali metals, which lead to the formation of heterocyclic analogs of sesquifulvalene, are known [3-5]. In these cases, either organometallic compounds with a polar $\overset{\delta-}{\geq C}\curvearrowright Me$, bond or carbanions, either free or in the ion pair state, essentially undergo hetarylation. However, insofar as we know, the hetarylation of cyclopentadiene, indene, fluorene, or azulene in the absence of catalysts has not been studied.†

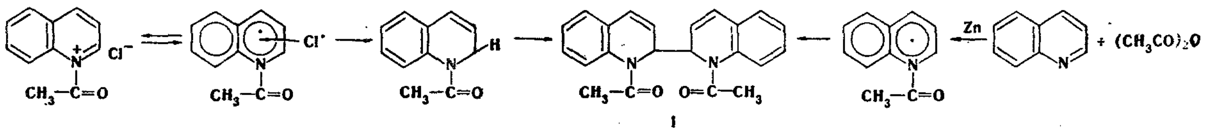
It was found that in the reaction with cyclopentadiene and indene, N-acylpyridinium and benzopyridinium salts behave differently as a function of the electrophilicity of the N-acylheteroaromatic cation and the acidity of the substrate.

Specifically, none of the investigated N-acylpyridinium salts hetarylated cyclopentadiene, indene, and fluorene under various conditions: Only the starting reagents of their polymerization products were isolated in all cases.

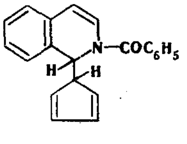
Hetarylation also did not take place in the reaction of N-acetyl salts of isoquinoline and quinoline with cyclopentadiene. In all cases we obtained the same compounds, regardless of the CH acids used in the reaction.

Similar compounds were also obtained by heating N-acetyl salts in the absence of a hetarylateable component. We found that the compounds obtained are 1,1'-diacetyl-1,2,1',2'-tetrahydro-2,2'-diquinolyl (I) and 2,2'-diacetyl-1,2,1',2'-tetrahydro-1,1'-diisoquinolyl, which were subsequently separated to give their stereoisomers, which proved to be identical to the compounds that we obtained by reduction of quinoline and isoquinoline with zinc dust in acetic anhydride.

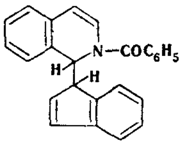
Under the hetarylation conditions, the N-acylcylammonium cations evidently react with the anions to give a charge-transfer complex (CTC), which then undergoes decomposition to radicals, which dimerize via the following scheme:



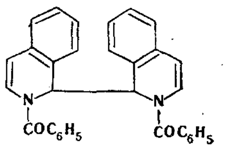
Under standard conditions, the more electrophilic N-benzoylisoquinolinium chloride hetarylated CPD and indene to give adducts II and III (Table 1), but the reaction with fluorene also gave dimer IV, from which we obtained a disisoquinolyl by alkaline hydrolysis, which confirms its structure.



II

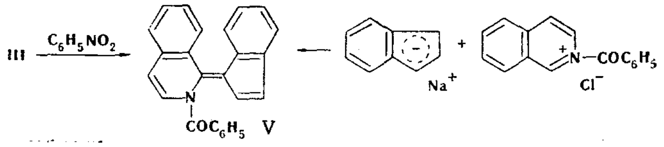


III



IV

Oxidation of colorless II and III with nitrobenzene gives colored heterocyclic analogs of sesquifulvalene of the V type. These same compounds are formed in the reaction of indenylsodium (cyclopentadienylsodium also reacts similarly) with the appropriate salts, for example:



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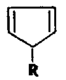
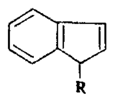
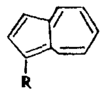
*The pH_a values are presented on the McEwen–Streitwieser–Applequist–Dessy scale (the MSAD scale) [2].
†See [6] for our preliminary communication in this regard.

TABLE 1. Heterocyclic Derivatives of Cyclopentadiene, Indene, and Azulenes

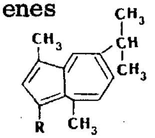




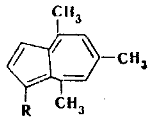
III a-c



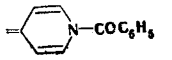
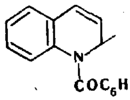
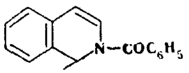
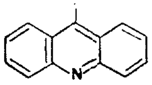
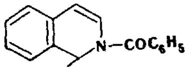
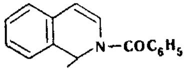
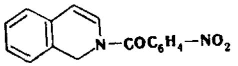
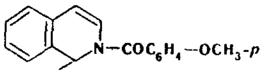
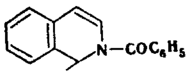
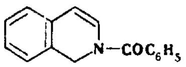
VIII a-d



IX



X

Compound	R	mp, °C	R_f	Empirical formula	Found, %			Calculated, %			Yield, %
					C	H	N	C	H	N	
VIIIa		195—196[a]	0,50	$C_{22}H_{17}NO$	84.4	5,7	4,4	84,4	5,5	4,5	40
VIIIb[b]		105—106[a]	0,46	$C_{29}H_{19}NO$	86,3	5,3	3,8	86,4	5,3	3,9	40
VIIIc		235—236[a]	0,82	$C_{29}H_{19}NO$	86,2	5,0	3,7	86,4	5,3	3,9	55
VIIId		188—189[a]	0,55	$C_{23}H_{15}N$	90,3	4,7	4,6	90,5	4,9	4,6	50
II		142—143[c]	0,15	$C_{21}H_{17}NO$	83,9	6,0	4,5	84,3	5,7	4,6	93
IIIa[d]		116—117[e]	0.14	$C_{25}H_{19}NO$	85,1	5,7	3,9	85,9	5,5	4,0	83
IIIb		121—123[c]	0,16	$C_{25}H_{18}N_2O_3$	76,2	4,9	7,3	76,1	4,6	7,1	20
IIIc		120—121[c]	0,17	$C_{26}H_{21}NO_2$	81,9	5,7	4,0	82,3	5,5	3,8	37
IX		178—179[a]	0,26	$C_{31}H_{29}NO$	86,1	6,5	3,3	86,3	6,7	3,2	51
X		198—199[a] (dec.)	0,35	$C_{29}H_{25}NO$	86,2	6,1	3,6	86,3	6,2	3,5	35

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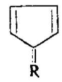
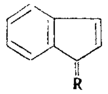
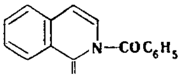
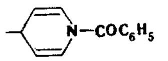
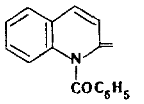
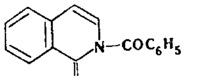
[a] From benzene—hexane (1 : 1). [b] Found: M 363.6 (by the Rast method). Calculated: M 361.4. [c] From butanol. [d] Found: M 376.3 (by the Rast method). Calculated: M 349.0. [e] From benzene.

TABLE 2. Heterocyclic Fulvalenes (V)   Vd

Compound	R	mp, °C*	R_f	μ	Empirical formula	Found, %			Calc., %			Yield, %
						C	H	N	C	H	N	
Va		162—163	0,11	3,1	$C_{21}H_{15}NO$	84,4	5,0	4,2	84,8	5,1	4,3	45
Vb		114—115	0,12	3,0	$C_{17}H_{13}NO$	82,9	5,4	5,7	82,6	5,3	5,7	35
Vc		172—173	0,23	3,4	$C_{21}H_{15}NO$	84,6	4,9	4,2	84,9	5,1	4,3	47
Vd		183—184	0,74	3,1	$C_{25}H_{17}NO$	86.0	5.0	3,8	86,1	4,9	4,0	50

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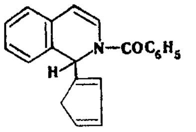
* From benzene—hexane (1 : 1).

The characteristic absorption bands of the N-benzoyl-1,2-dihydroisoquinoline fragment ($\nu_{C=O}$ 1650-1680 cm^{-1}; $\nu_{C=C}$ 1610 cm^{-1}) are observed in the IR spectra of II and III. Under the influence of acids these substances undergo cleavage to give all three components (dicyclopentadienyl or indene, isoquinoline, and benzoic acid) in theoretical yields.

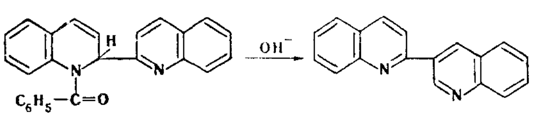
The facile dehydrogenation of II and III to derivatives of the V type constitutes evidence in favor of our proposed structure for these compounds rather than to the structure of the nonisomeric compounds of the VI type, although it seems premature to us to exclude the possibility of the formation of the latter (unfortunately, the PMR spectral data for such compounds could not be interpreted unambiguously).



VI

The relatively small dipole moments of the compounds (Table 2) constitute evidence for the insignificant contribution of the ylid structure corresponding to electron transfer from the heterorings to the five-membered ring. The fact that hetarylfulvalenes V split out acyl residues with great difficulty, while the ylid form would, like other N-acylcyclammonium salts, undergo hydrolysis very readily, is evidence for the absence of any appreciable percentage of the ylid structure.

Quinoline in the presence of benzoyl chloride under standard conditions readily hetarylated azulene and quaiazulene (Table 1), but did not undergo hetarylation with either CPD or indene. Under these conditions, 1-benzoyl-2-(3'-quinolinyl)-1,2-dihydroquinoline (VII) was formed.



VII

The structure of VII is confirmed by its mass spectrum (M 362.4), IR spectrum (ν_{CO} 1655 cm^{-1}, $\nu_{C=C}$ 1620 cm^{-1}), and chemical properties (formation of a picrate and conversion to 2,3-diquinolyl as a result of alkaline hydrolysis, and the presence of a double bond). The pathways of formation of VII are as yet unclear.

Attempts to hetarylate fluorene with any N-acyl pyridinium and benzopyridinium salts were unsuccessful.

Thus, in the absence of catalysts, we were able to carry out the hetarylation of compounds pK_a values up to 21 only with the most active N-benzoylisoquinolinium salts. The less reactive quinolinium and pyridinium salts are capable of hetarylation of CH acids with somewhat lower pK_a values (18-19).

EXPERIMENTAL

The IR spectra of chloroform solutions or KBr pellets of the compounds were obtained with a UR-20 spectrometer. Activity II aluminum oxide was used for thin-layer chromatography (TLC); the compounds were eluted with benzene–hexane–chloroform (60 : 1 : 30), and the chromatograms were developed with iodine vapors and in UV light. The dipole moments of benzene solutions of the compounds were measured [7]. Cryoscopic-grade benzene was dried and distilled over sodium metal, after which it was again distilled over phosphorus pentoxide and freshly calcined potassium carbonate. The middle fraction with the following physical constants was selected in the distillation over potassium carbonate: bp 79.8 (740 mm), d_4^{25} 0.8738, n^{25} 1.4979, and ε 2.2725.

The dielectric permeabilities were measured with an E-12-1 apparatus with an oscillographic indicator at 25 ± 0.05°. The densities were determined pycnometrically at 25 ± 0.05°. The dipole moments were calculated from the formula $\mu = 0.221\sqrt{P_\infty - P_{el}}$, where P_∞ is the polarization at infinite dilution and P_{el} is the molecular refraction. The molecular refraction was calculated as the sum of the atomic refractions [8], and P_∞ was obtained from the Hedestrand equation [9]. The dipole moments obtained are presented in Table 2.

Hetarylation of Cyclopentadiene, Indene, and Azulene (typical method). A solution of 0.1 mole of dry six-membered nitrogen base and 0.05 mole of freshly distilled acetyl chloride in absolute benzene was heated at 80-90° for 1 h, after which 0.05 mole of the appropriate CH acid was added, and the mixture was heated at 90-100° until the reaction mixture solidified (2-10 h). In the case of CPD, the mixture of isoquinoline and benzoyl chloride was heated at 80-90° for 1 h, after which it was cooled to 10-12°, freshly distilled CPD (30% excess) was added dropwise, and the reaction, which was exothermic, was carried out at no higher than 30° for 1.5-2 h until the mixture solidified. It was then steam-distilled until the odor of the nitrogen base vanished in the distillate, or the precipitate formed in the reaction mixture was removed by filtration and washed with a suitable solvent or purified by means of preparative chromatography on aluminum oxide. The yields, physical characteristics, and results of elementary analysis of the heterocyclic derivatives of indene, cyclopentadiene, and azulene and its derivatives obtained by this method are presented in Table 1.

2,2'-Dibenzoyl-1,2,1',2'-tetrahydro-1,1'-diisoquinoline (IV). This compound, with mp 190-191° (from butanol) and R_f 0.22, was obtained in the reaction with fluorene, as described above, and was identified by comparison with a sample obtained by heating isoquinoline with benzoyl chloride. IR spectrum (KBr pellets): $\nu_{C_3=C_4}$ 1630 and ν_{CO} 1690 cm^{-1}. Found: C 82.3; H 5.3; N 6.2%; M 493 (Rast method). $C_{32}H_{24}N_2O_2$. Calculated: C 82.0; H 5.2; N 6.0%; M 468.6.

This same isomer was obtained in the reaction of isoquinoline with benzoic anhydride in the presence of zinc dust by the method in [10] and had mp 191-192° (from butanol) and R_f 0.20. Alkaline hydrolysis of IV in an alcohol solution of sodium hydroxide at 90-100° for 10 h gave 1,1'-disisoquinolyl with mp 160-161° and R_f 0.15 (mp 162-163° [10]). The IR spectrum proved to be identical to the spectrum of the sample obtained by the method in [10].

Reaction of Isoquinoline with Cyclopentadiene, Indene, or Fluorene in the Presence of Acetyl Chloride. A mixture of 12.9 g (0.1 mole) of isoquinoline, 3.9 g (0.05 mole) of acetyl chloride, and 0.05 mole of indene, cyclopentadiene, or fluorene in 20 ml of absolute benzene was held at room temperature for 24 h or at 80° for 10 h, after which it was steam-distilled, and the solid formed in the distillation flask was separated. In some cases it was better to dissolve the reaction mixture in chloroform; the resulting solution was then washed successively with water, twice with dilute hydrochloric acid (1 : 1), and again with water to neutrality, after which the chloroform extracts were separated, dried, and treated with diethyl ether. The higher-melting meso-diacetyl-1,1',2,2'-tetrahydroisoquinoline isomer, with mp 250-251° (from hexyl alcohol), was precipitated with ether. Found: C 76.5; H 5.8; N 8.1%; M 365 (Rast method). $C_{22}H_{20}N_2O_2$. Calculated: C 76.7; H 5.8; N 8.1%; M 344.4.

A second isomer – dl-N,N-diacetyl-1,1',2,2'-tetrahydroisoquinoline – with mp 187-188° (from butanol) was precipitated from the filtrate by the addition of hexane. Calculated: C 76.7; H 5.8; N 8.1%; M 353 (Rast method). $C_{22}H_{20}N_2O_2$. Found: C 76.5; H 5.7; N 8.1%; M 344.4. The yield of isomers in a ratio of 3 : 2, respectively, was 6 g (69%). These isomers were obtained in a ratio of 1 : 1 in the reaction of isoquinoline with acetic anhydride under the conditions of the Dimroth reaction in the presence of zinc dust [10].

Reaction of Quinoline with Indene and Cyclopentadiene in the Presence of Benzoyl Chloride. A mixture of 12.9 g (0.1 mole) of quinoline, 7 g (0.05 mole) of benzoyl chloride, and 5.8 g (0.05 mole) of indene was held at 130° for 10 h, after which it was steam-distilled, and the residue in the distillation flask was separated, dried, and recrystallized from butanol to give 3.9 g (44%) of white crystals of 1-benzoyl-2-(3'-quinolinyl)-1,2-dihydroquinoline VII with mp 192-193° and R_f 0.24. IR spectrum (KBr pellets); $\nu_{C_3=C_4}$ 1610 and $\nu_{C=O}$ 1642 cm^{-1}. Found: C 83.0; H 5.0; N 8.2%; M 362.4 (mass spectroscopically). $C_{25}H_{18}N_2O$. Calculated: C 82.9; H 4.9; N 8.0%; M 362.4. The product gave a positive qualitative reaction for a double bond. The picrate had mp 228-230° (from glacial acetic acid). Found: N 12.0%. $C_{31}H_{21}N_5O_8$. Calculated: N 11.8%.

In the reaction with cyclopentadiene, the reaction mixture was held at room temperature for 2-3 days; workup gave a substance that, with respect to the IR spectral and chromatographic data, was identical to VII obtained above.

2,3-Diquinolyl with mp 174-175° (mp 175-176° [11]) and R_f 0.38, was obtained in 85% yield by refluxing N-benzoyl-2-(3'-quinolinyl)-1,2-dihydroquinoline VII in an alcohol solution of sodium hydroxide for 5 h. Found: C 84.4; H 4.7; N 10.8%. $C_{18}H_{12}N_2$. Calculated: C 84.3; H 4.5; N 10.9%.

Synthesis of Hetarylfulvalenes (typical method, Table 2). A 139.4-g (1.2 mole) sample of indene or 79.3 g of cyclopentadiene was added with vigorous stirring to a dispersion of 23 g (1 g-atom) of sodium in toluene, after which the temperature was maintained at 40-50° for 1.5 h. The resulting solution of indenyl-(cyclopentadienyl)sodium was then cooled to 18-20° and added in portions to a previously prepared mixture of 1 mole of the six-membered nitrogen base and 1 mole of benzoyl chloride in 250 ml of toluene, and the mixture was stirred vigorously at 5-10° for 2 h. After all of the indenyl(cyclopentadienyl)sodium had been added, the contents of the flask were stirred at room temperature for another hour. The precipitated NaCl was then removed by filtration, the solvent was removed from the filtrate by distillation, and the resulting resin was crystallized from a suitable solvent or purified by means of preparative chromatography on aluminum oxide.

Oxidation of (2-Benzoyl-1,2-dihydroisoquinolin-1-yl)-1-indene. A 1-g sample of III was refluxed in 20 ml of nitrobenzene for 8 h, after which the mixture was steam distilled, and the resulting solid was crystallized from benzene–hexane (1 : 1) to give a product with mp 181-182° and R_f 0.74. According to the IR spectra and melting points, the product was identical to V.

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