SYNTHESIS OF N-SUBSTITUTED 1H-INDENO[2,1-b]PYRIDINES

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It was established that N-phenacyl and p-nitrophenacyl bromides and N-methyl-1-azafluorenium iodide, as well as N-phenacyl-7-nitro-1-azafluorenium bromide, are converted to N-substituted 1H-indeno[2,1-b]pyridines rather than to the corresponding yilds or indenoindolizines upon treatment with bases under various conditions. All of the pseudoazulenes of this type were isolated in the form of crystalline black or dark-violet substances. In contrast to pseudoazulenes of the 1H-indeno[1,2-b]- and 2H-indeno[2,1-c]pyridine series, they are stable both in the solid state and in solutions. 1H-1-Methylindeno[2,1-b]pyridine forms a perchlorate and a picrate (retention of the pseudoazulene structure) but is converted to N-methyl-1-azafluorenium chloride by the action of hydrogen chloride. Spectral characteristics are presented for all of the compounds obtained.

In a relatively new area of organic chemistry, viz., the chemistry of pseudoazulenes [1], considerable attention is being directed to the synthesis of stable compounds of this series. The production of polyaryl-substituted pyridines and benzopyridines, which have been found to be stable substances, has been reported [2, 3].

The starting compounds for the synthesis of pseudoazulenes of the NH-indenopyridine type are the as yet difficult-to-obtain azafluorenes. The stabilities of such pseudoazulenes evidently depend on the position of the nitrogen atom in these systems. The pseudoazulenes obtained from mono- and diaryl-substituted 2- and 4-azafluorenes have been found to be labile [3, 4]. Of the pseudoazulenes of this type, only 2H-1,2,3-trimethyl-9-phenylindeno[2,1-c]pyridine has been isolated and characterized [5]. The instability of NH-indenopyridines is explained by the o-quinoid structure of the benzene ring [3, 4]. In connection with the fact that the benzenoid structure of the phenyl ring is retained in the pseudoazulenes that can be obtained from 1- and 3-azafluorenes, one might expect that such NH-indenopyridines would be stable substances. Information regarding N-substituted 1H-indeno[2,1-b]pyridines is available. To synthesize them we used 1-azafluorene (I), which was obtained by dehydrocyclization of 2-methyl-3-phenylpyridine [6], as well as 7-nitro-1-azafluorene (II), which is formed in higher than 70% yield in the nitration of azafluorene I. The 7-nitro-1-azafluorene structure was confirmed by the analytical and spectral data. Its mass spectrum contains an intense molecular-ion peak (M^+) with m/e 212 (86%) and an $[M-NO_2]^+$ ion peak with m/e 166 (100%). The orientation in the nitration of azafluorene I (C_7) is the same as the nitration of fluorene (C_2). This is confirmed by the data from the PMR spectrum of II.

N-Phenacyl- (III) and N-4-nitrophenacyl-1-azafluorenium (IV) bromides, N-phenacyl-7-nitro-1-azafluorenium bromide (V), and N-methyl-1-azafluorenium iodide (VI) were obtained by treatment of azafluorenes I and II with ω-bromoacetophenone, ω-bromo-4-nitroacetophenone, and methyl iodide, respectively.

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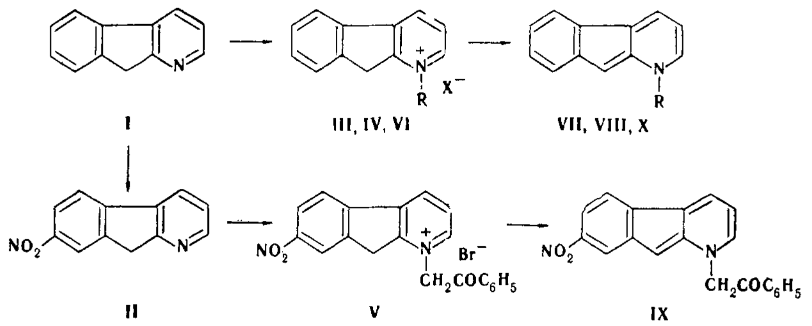

III, VII $R=CH_2COC_6H_5$; IV, VIII $R=CH_2COC_6H_4NO_2\text{-}p$; VI, X $R=CH_3$; III, IV $X=Br$; VI $X=I$

Quaternary salts III-V were treated at 0°C with a solution of sodium acetate or potassium carbonate (the conditions for the conversion of pyridinium salts to ylids) and were also heated with 40% potassium carbonate solution (the method for the preparation of indolizines from the corresponding α-alkyl-substituted pyridinium salts). It was established that neither ylids nor indenoindolizines are formed under these conditions, but pseudoazulenes are isolated in 52-99% yields.

The resulting 1H-1-phenacyl- (VII) and 4-nitrophenacyl-indeno[2,1-b]pyridines (VIII) and 1H-7-nitro-1-phenacylindeno-[2,1-b]pyridine (IX) are stable, colored, crystalline substances. A singlet signal of a proton attached to C_9, which is shifted as compared with the analogous signals of quaternary salts III and V to weak field as a consequence of redistribution of the electron density in the case of the formation of an aromatic pseudoazulene system, is observed in the PMR spectra of pseudoazulenes VII and IX at 5.8-5.9 ppm. The singlet signal of two protons in the same region should be assigned to the methylene protons of the phenacyl group. Molecular-ion peaks (M^+) are observed in the mass spectra of pseudoazulenes VII-IX. The fragmentation of these compounds under electron impact confirms their structure.

1H-1-Methylindeno[2,1-b]pyridine (X) and a stable crystalline dark-cherry-red substance were obtained from quaternary salt VI by treatment with 40% aqueous sodium hydroxide. The one-proton singlet signal in the PMR spectrum at 6.00 ppm is related to the proton attached to the C_9 atom, and this confirms the pseudoazulene structure of this compound. The chemical shift of the three-proton singlet (3.77 ppm) is characteristic for a methyl group attached to a nitrogen atom. A maximally intense M^+ peak with m/e 181 (100%) and a peak of an $[M-CH_3]^+$ fragment with m/e 166 (29%) are observed in the mass spectrum of pseudoazulene X.

The UV spectra of VII-X contain an absorption maximum in the long-wave region (520-580 nm) that is characteristic for pseudoazulene structures [1, 2].

It has been established [7] that N-phenacyl-2,5-dimethyl-4-(4-nitrobenzyl)pyridinium bromide is converted to 2,5-dimethyl-1-phenacyl-4-(4-nitrobenzylidene)-1,4-dihydropyridine on treatment with a solution of potassium carbonate. However, 2,5-dimethyl-4-benzylpyridinium 4-nitrobenzoylmethylid is formed under the same conditions from N-(4-nitrophenacyl)-2,5-dimethyl-4-benzylpyridinium bromide. The introduction of an electron-acceptor substituent in the N-phenacyl group stabilizes the ylid system. In this connection, one might have assumed that quaternary salt IV is converted to 1-azafluorenium 4-nitrobenzoylmethylid on treatment with bases. However, as pointed out above, pseudoazulene VIII is also formed in this case. An intense band of a phenacyl carbonyl group (1702-1716 cm^{-1}), which is absent in the spectra of pyridinium benzoylmethylids [7, 8], is present in the IR spectra of 1H-1 phenacylindeno[2,1-b]pyridines VII-IX. In addition, the bands at ∿ 3500 and ∿ 3390 cm^{-1} that are characteristic for ylids [8] are not observed.

Rapid decolorization of the solution occurs when a colored ether solution of pseudoazulene X is treated with dry hydrogen chloride, and N-methyl-1-azafluorenium chloride XI precipitates. Consequently, under these conditions pseudoazulene X is protonated at the C_9 atom, and the pseudoazulene system is converted to an azafluorene system. However, the pseudoazulene structure is retained on treatment of X with 57% perchloric acid and picric acid in methanol. The UV spectra of alcohol solutions of 1H-1-methylindeno[2,1-b]pyridine perchlorate and picrate obtained in this way contain absorption maxima at 580 and 590 nm, which are characteristic for pseudoazulenes.

TABLE 1. Colors of Solutions of Pseudoazulenes VII-X

Compound	Solvent						
	C_6H_{12}	CCl_4	C_6H_6	$(C_2H_5)_2O$	C_2H_5OH	$(CH_3)_2CO$	$CH_3COOC_2H_5$
VII		Pink	Violet	Pink	Pale-violet	Lilac	Lilac
VIII			Pale-pink			Violet	Pink
IX			Yellow-brown			Black-brown	Brown
X	Pink	Crimson	Dark-cherry-red	Dark-pink	Crimson	Bright pink	Dark-pink

Thus N-substituted 1H-indeno[2,1-b]pyridines are stable substances and in this respect differ from the labile 1H-indeno[1,2-b]- and 2H-indeno[2,1-c]pyridine derivatives. They were stored in our laboratory in air and remained unchanged for 6 months. Their solutions in various solvents are also stable. Pseudoazulenes VII-IX also remain unchanged upon prolonged refluxing in 40% potassium carbonate solution and when ether solutions of them are passed through a layer of aluminum oxide.

EXPERIMENTAL

The PMR spectra of the compounds were recorded with Hitachi—Perkin—Elmer R 22 (90 MHz) and Tesla 467-BS (60 MHz) spectrometers with tetramethylsilane as the internal standard. The mass spectra were obtained with an MKh-1303 spectrometer at 70 V. The UV spectra of ethanol solutions were recorded with a Hitachi spectrophotometer. The IR spectra of KBr pellets were recorded with a UR-20 spectrometer.

7-Nitro-1-azafluorene (II). A 10-g (0.06 mole) sample of azafluorene I was added gradually in the course of 4 h with stirring to a cooled (to —5°C) nitrating mixture (65 g of sulfuric acid and 21 g of nitric acid), after which the mixture was maintained at 80°C for 1 h. It was then cooled and poured over ice, and the aqueous mixture was neutralized with sodium carbonate solution. The precipitate was washed with water and crystallized from acetone to give 9.7 g (76%) of II with mp 210-211°C (from acetone). PMR spectrum (in $CDCl_3$): 8.60 (d, J_{23} = 5.0 Hz, 2-H), 8.42 (s, 8-H), 8.31 (d, J_{65} = 7.5 Hz, 6-H), 8.10 (d, J_{43} = 7.5 Hz, 4-H), 7.86 (d, J_{56} = 7.5 Hz, 5-H), 7.35 (q, J_{32} = 7.5, J_{34} = 4.0 Hz, 3-H), and 4-11 ppm (s, 2H, 9-CH_2). IR spectrum, cm^{-1}: 1616 m, 1600 m, 1575 m, 1525 vs, 1460 m, 1395 s, and 1338 vs. Mass spectrum, m/e (%): 212 (86), M^+, 195 (7), $[M-OH]^+$, 182 (8), $[M-NO]^+$; 166 (100), $[M-NO_2]^+$. Found: C 67.5; H 3.9; N 13.6%. $C_{12}H_8N_2O_2$. Calculated: C 67.9; H 3.8; N 13.2%.

Quaternary 1-Azafluorenium Salts (III-VI). A) A mixture of 1.7 g (0.01 mole) of azafluorene I and 2.0 g (0.01 mole) of ω-bromoacetophenone was refluxed for 6 h, and the resulting precipitate was washed with ether to give 2.0 g (55%) of salt III with mp 187-188°C (dec., from ethanol). PMR spectrum (in CF_3COOD): 8.78 (d, J_{23} = 8.0 Hz, 1H, 2-H), 8.58 (d, J_{43} = 6.0 Hz, 1H, 4-H), 7.44-8.20 (m, 12H, aromatic protons), 6.55 (s, 2H, N—CH_2), and 4.35 ppm (s, 2H, 9-CH_2). IR spectrum, cm^{-1}: 1695 vs, 1620 m, 1600 m, 1450 vs, 1390 m, 1345 s, 1315 m, 1235 2, and 1210 m. Found: N 3.6%. $C_{20}H_{15}NO \cdot HBr$. Calculated: N 3.8%. Salt V, with mp 206-208°C (dec., from ethanol), was similarly obtained in 64% yield from azafluorene II and ω-bromoacetophenone. PMR spectrum (in CF_3COOH): 7.49-9.08 (m, 11H, aromatic protons), 6.60 (s, 2H, N—CH_2), and 4.57 ppm (s, 2H, 9-CH_2). IR spectrum, cm^{-1}: 1702 s, 1630 m, 1600 m, 1540 s, 1455 s, 1345 vs, and 1230 m. Found: N 6.8%. $C_{20}H_{14}N_2O_3 \cdot HBr$. Calculated: N 6.8%.

B) A solution of 4 g (0.024 mole) of azafluorene I and 6.8 g (0.048 mole) of methyl iodide in 15 ml of methanol was refluxed for 4 h, and the resulting precipitate was washed with cold methanol to give 6.7 g (89%) of methiodide VI with mp 210-212°C (dec., from methanol). PMR spectrum (in CF_3COOH): 8.75 (d, J_{23} = 8.0 Hz, 1H, 2-H), 8.5 (d, J_{43} = 6.0 Hz, 1H, 4-H), 7.51-8.10 (m, 5H, aromatic protons), 4.45 (s, 3H, N—CH_3), and 4.40 ppm (s, 2H, 9-CH_2). Found: N 4.4%. $C_{13}H_{11}N \cdot HI$. Calculated: N 4.5%.

N-Substituted 1H-Indeno[2,1-b]pyridines (VII-IX). A) A-10 ml sample of a 40% aquesous solution of potassium carbonate was added to a solution of 0.9 g (2.5 mmole) of salt II in 10 ml of water, and the mixture was refluxed for 5 h. The resulting precipitate was washed with water and dried to give 0.7 g (99%) of pseudoazulene VII as dark-violet crystals with mp 169-172°C (dec., from aqueous dimethylformamide (DMF)) and R_f 0.8 (Al_2O_3, ether). PMR spectrum (in DMSO): 8.28 (d, J_{23} = 7.5 Hz, 1H, 2-H), 6.88-8.13 (m, 10H, aromatic protons), 6.55 (6, J_{32} = J $_{34}$ = 7.5 Hz, 1H, 3-H), 5.96 (s, 2H, $N{-}CH_2$), and 5.91 ppm (s, 1H, 9-H). IR spectrum, cm^{-1}: 1706 s, 1635 m, 1605 m, 1565 vs, 1505 m, 1275 m, 1240 m, 1345 vs, 1225 vs, 1175 s, and 1135 m. UV spectrum, λ_{max} (log ε): 300 (4.28), 346 (3.46) sh, 460 (3.01), 520 nm (3.09). Mass spectrum, m/e (%): 285 (54), M^+; 267 (6), $[M - H_2O]^+$; 257 (11), $[M - CO]^+$; 256 (17), $[M - HCO]^+$; 181 (27); 180 (100), $[M - C_6H_5CO]^+$; 167 (39); 166 (39), $[M - C_6H_5CO\text{-}CH_2]^+$; 154 (42); 105 (33), $[COC_6H_5]^+$; 77 (58),$[C_6H_5]^+$. Found: C 84.5; H 5.4; N 4.6%. $C_{20}H_{15}NO$. Calculated: C 84.2; H 5.3; N 4.9%.

Pseudoazulene VIII was similarly obtained in 54% yield from salt IV as dark-violet crystals with mp 165-166°C (dec., from aqueous acetone). PMR spectrum (in DMSO): 6.74-7.26 (m, aromatic protons), 6.58 (t, J_{32} = J_{34} = 7.0 Hz, 3-H), 6.07 (s, $N{-}CH_3$), and 6.00 ppm (s, 9-H). IR spectrum, cm^{-1}: 1716 s, 1640 m, 1605 m, 1565 vs, 1528 vs, 1471 m, 1440 m, 1350 vs, 1220 vs, 1180 m, and 1140 m. UV spectrum, λ_{max} (log ε): 252 (4.55), 300 (4.00) sh, 480 (3.04), 580 nm (3.16). Mass spectrum, m/e (%): 330 (4), M^+, 313 (23), $[M - OH]^+$, 312 (61), $[M - H_2O]^+$, 282 (17), $[M - H_2O, - NO]^+$, 266 (30), $[M - H_2O, - NO_2]^+$, 181 (74), 167 (100), $[M - CHCOC_6H_4NO_2]^+$, 150 (56), $[COC_6H_4NO_2]^+$. Found: N 8.6%. $C_{20}H_{14}N_2O_3$. Calculated: N 8.5%.

B) A 10-ml sample of 1 N sodium acetate solution was added with stirring at 0°C to a solution of 1 g (2.5 mmole) of salt V in 10 ml of DMF, and the mixture was stirred at this temperature for 2 h. Water (100 ml) was then added, and the precipitate was washed with water, dried over phosphorus pentoxide, and crystallized from acetone to give 0.38 g (52%) of pseudoazulene IX as black crystals with mp 190-192°C (dec.) and R_f 0.8 [Al_2O_3, ether—ethanol (40:1)]. PMR spectrum (in DMSO): 7.07-8.27 (m, 10H, aromatic protons), 6.38 (t, J_{32} = J_{34} = 8.0 Hz, 1H, 3-H), 5.83 (s, 1H, 9-H), and 5.71 ppm (s, 2H, $N{-}CH_2$). IR spectrum, cm^{-1}: 1700 s, 1645 m, 1600 m, 1560 s, 1518 s, 1455 m, 1430 s, 1330 vs, 1230 m, 1207 s, and 1180 s. UV spectrum (in DMF), λ_{max} (log ε): 524 nm (3.20). Mass spectrum, m/e (%): 330 (5), M^+, 253 (20) $[M - C_6H_5]^+$, 252 (100), $[M - C_6H_6]^+$, 222 (16), $[M - C_6H_6 - NO]^+$, 207 (18), $[M - C_6H_5, - NO_2]^+$, 206 (52), $[M - C_6H_6, - NO_2]^+$, 191 (40). Found: C 72.2, H 4.1, N 8.4%. $C_{20}H_{14}N_2O_3$. Calculated: C 72.7, H 4.2, N 8.5%.

Pseudoazulenes VII and VIII were also obtained by this method.

1H-1-Methylindeno[2,1-b]pyridine (X). A 10-ml sample of 40% potassium carbonate solution was added with stirring at room temperature to a solution of 8.5 g (0.027 mole) of salt VI in 100 ml of water, and the mixture was stirred for 30 min. The precipitate was washed with water and crystallized from aqueous acetone to give 3.3 g (68%) of pseudoazulene X as dark-cherry-red crystals with mp 103-104°C (dec.). PMR spectrum (in $CDCl_3$): 8.03 (d, J_{23} = 7.5 Hz, 1H, 2-H), 8.03 (d, J_{43} = 7.5 Hz, 1H, 4-H), 6.96-7.63 (m, 4H, aromatic protons), 6.30 (t, J_{32} = J_{34} = 7.5 Hz, 1H, 3-H), 6.00 (s, 1H, 9-H), and 3.77 ppm (s, 3H, $N{-}CH_3$). IR spectrum, cm^{-1}: 1640 s, 1605 m, 1565 vs, 1505 m, 1435 s, 1335 s, 1212 s, 1177 m, and 1135 m. UV spectrum, λ_{max} (log ε): 304 (4.50), 326 (4.12) sh, 455 (3.46) sh, 580 nm (3.78). Mass spectrum, m/e (%): 181 (100), M^+, 166 (27), $[M - CH_3]^+$, 139 (18), 90.5 (18), M^{++}. Found: 7.2%, M^+ 181. $C_{13}H_{11}N$. Calculated: N 7.7%, M 181. Dry hydrogen chloride was passed through a dark-crimson ether solution of 0.5 g (2.7 mmole) of pseudoazulene X at 0°C until it became colorless. The precipitate was crystallized from methanol to give 0.54 g (92%) of salt XI with mp 215-216°C (dec.). PMR spectrum (in CD_3OD): 8.76 (d, J_{23} = 8.0 Hz, 1H, 2-H), 8.62 (d, J_{43} = 6.0 Hz, 1H, 4-H), 7.36-7.98 (m, 5H, aromatic protons), 4.64 (s, 3H, $N{-}CH_3$), and 4.36 ppm (s, 2H, 9-CH_2). Found: N 6.3%. $C_{13}H_{11}N \cdot HCl$. Calculated: N 6.4%.

A 1-ml sample of 56% perchloric acid was added to a solution of 0.1 g (0.55 mmole) of X in 15 ml of methanol, and the mixture was maintained at room temperature for 1 h. The resulting precipitate was crystallized from ethanol to give 0.06 g (39%) of the perchlorate of pseudoazulene X with mp 158-159°C. UV spectrum, λ_{max} (log ε): 234 (4.34), 280 (4.36), 300 (4.40), 330 (4.05) sh 345 (3.80) sh 470 (2.94) br, 580 nm (3.48). Found: N 4.6%. $C_{13}H_{11}N \cdot HClO_4$. Calculated: N 5.0%.

The picrate of X was obtained in 85% yield and melted with decomposition above 295°C. UV spectrum, λ_{max} (log ε): 232 (4.60), 283 (4.45) sh, 302 (4.53), 330 (4.34), 360 (4.37), 375 (4.36), 510 (3.92) sh, 590 nm (4.24). Found: N 13.5%. $C_{13}H_{12}N \cdot C_6H_3N_3O_7$. Calculated: N 13.7%.

Tests of the biological properties of the 1-azafluorene derivatives (on chlorella and sugar beet cells) demonstrated that quaternary salts III and VI have herbicidal and fungicidal activity. Pseudoazulene X displayed herbicidal activity. The toxicity of this compound in mice is relatively high, viz., LD_{50} = 50 mg/kg.

LITERATURE CITED

1. H. J. Timpe and A. V. Elcov, Z. Chem., 15, 172 (1975).
2. A. V. El'tsov, G. I. Timpe, and N. I. Rtishchev, Zh. Org. Khim., 11, 398 (1975).
3. G. V. Boyd, J. Chem. Soc., No. 1, 55 (1959).
4. W. Treibs and J. Beger, Lieb. Ann., 652, 192 (1962).
5. W. Treibs and J. Beger, Lieb. Ann., 652, 212 (1962).
6. N. S. Prostakov, A. T. Soldatenkov, and V. O. Fedorov, Khim. Geterotsikl. Soedin., No. 8, 1101 (1979).
7. N. S. Prostakov, A. N. Krapivko, A. T. Soldatenkov, A. A. Savina, and I. Romero, Khim. Geterotsikl. Soedin., No. 3, 384 (1979).
8. I. Surpateanu, J. P. Catteau, P. Karafiloglu, and A. Lablache-Combier, Tetrahedron, 32, 2647 (1976).

SYNTHESIS OF 3-AZAFLUORENE AND 2H-2-METHYLINDENO[1,2-c]PYRIDINE

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4-Methyl-3-phenylpyridine was isolated from the mixture of four isomeric methylphenylpyridines formed in the condensation of crotonaldehyde with phenylacetaldehyde (β-phenylethanol or phenylacetylene) with ammonia in the presence of a cadmium-calcium phosphate catalyst. 4-Methyl-3-phenylpyridine was converted to 3-azafluorene by catalytic dehydrocyclization. A representative of a new series of pseudoazulenes, viz., 2H-2-methylindeno[1,2-c]-pyridine, was obtained by treatment of 3-azafluorene methiodide with sodium hydroxide solution; the product was a crystalline black substance that remained unchanged during storage in air for 1 month.

In a previous communication [1] we presented the results of research on the synthesis and study of some transformations of N-substituted 1H-indeno[2,1-b]pyridines. These pseudoazulenes, in which the phenylene ring has a benzenoid structure, were isolated in the form of deeply colored, stable (under ordinary storage conditions), crystalline substances. With respect to their stabilities, they differ from their 1H-indeno[1,2-b]- and 2H-indeno[2,1-c] pyridine analogs, which are unstable and undergo changes in air even at room temperature [2, 3]. The assumption that the instability of these pseudoazulenes is due to the quinoid structure of their phenylene ring is evidently substantiated. Considering this, one might have assumed that N-substituted 2H-indeno[1,2-c]-pyridines would also be stable, since their phenylene ring also has a benzenoid structure.

The most suitable starting compounds for the synthesis of pseudoazulenes of this type are 3-azafluorene and substituted 3-azafluorenes. A relatively simple method for the production of isomeric (with respect to the position of the nitrogen atom) azafluorenes is the catalytic dehydrocyclization of the correspondingly substituted methylarylpyridines. In particular, 4-methyl-3-phenylpyridine (I) can be converted to 3-azafluorene by this method. To synthesize this pyridine base we used the Chichibabin method [4, 5], viz., cyclocondensation of aldehydes with ammonia. The condensation of crotonaldehyde and phenylacetaldehyde with ammonia was carried out in the vapor phase. Instead of aluminum oxide, which was previously used in reactions of this type, we used a cadmium-calcium phosphate catalyst.

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