7-AMINOCOUMARINS (REVIEW)

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The principal methods for the synthesis of 7-amino coumarins and their reactivities are described. The luminescence properties and generation characteristics of this important class of organic dyes are examined.

Coumarin (2H-1-benzopyran-2-one) is a two-ring system that contains condensed benzene and α-pyrone rings.

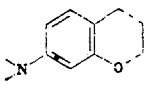
The interest in coumarin derivatives is due primarily to their extensive practical application; moreover, more than a thousand natural coumarins, many of which have high physiological activity, are known. However, not enough attention has been directed to the systematization of data pertaining to the behavior of coumarins in chemical reactions. A review of methods of preparation and reactivities was published in 1954 [1], two reviews dealing with their chemistry were published in almost inaccessible journals [2, 3], and problems involving their reactivities were partially touched upon in [4-15].

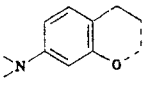
Most of the research of synthetic coumarins is purely pragmatic in character; coumarins are widely used as fluorescent bleaches, dyes, and markers in the textile, polymer, printing, photographic, motion-picture, and other industries. 7-Amino coumarins, which are used as active media in lasers with smooth spectral tuning, have recently generated particular interest; 7-aminocoumarins that have not been described in previously published reviews are therefore the subject of our reivew.

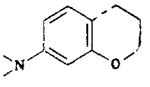
1. METHODS OF SYNTHESIS

1.1. Reduction of 7-Nitrocoumarins

A significant number of coumarins that contain an unsubstituted amino group in the 7 position have been obtained by reduction of the corresponding 7-nitro derivatives with iron and ammonium chloride [16-18] or hydrochloric acid [19]; with iron and acetic acid [20]; with stannous chloride [21]; with tin and hydrochloric acid [22]; with ammonium hydrosulfide [23, 24]; by catalytic hydrogenation [25, 26]. Of course, the problem of the prior synthesis of a pyran ring via one of three possible pathways (types 1-3) is not eliminated in this case.*


type 1


type 2


type 3

1.2. Cyclocondensation of Type 1

Synthesis from Salicylaldehydes. The most widely used method for the synthesis of practically important 7-aminocoumarins containing diverse aryl and hetaryl substituents in the 3 position consists in the reaction of 4-aminosalicylaldehydes with substituted acetic acids and their functional derivatives.

*In only one case a 7-nitrocoumarin derivative, which was then reduced to the corresponding amine, was obtained by the introduction of a nitro group into a ready-made coumarin system [21].

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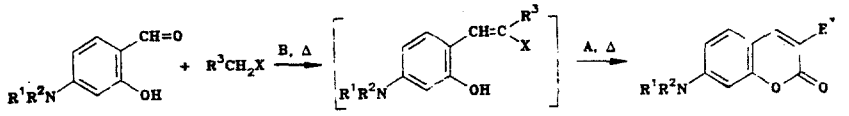
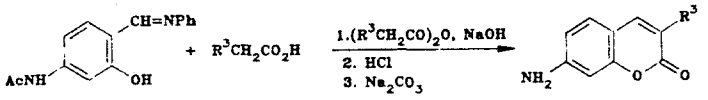
This method for the preparation of 7-aminocoumarins can be represented in the form of a two-step scheme: in the first step crotonic condensation is realized under the influence of bases, and in the second lactonization of the resulting coumarinic acid is realized under the influence of agents with acidic character. In practice, the initial reaction product is usually not isolated, and the coumarin is obtained directly from the reaction mixture.

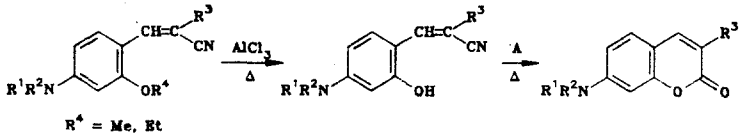


Primarily 4-acetamido, nitro, and disubstituted amino derivatives* are used the starting salicylaldehydes. The condensing agents are alkalis, secondary and tertiary amines, and salts of carboxylic acids; the cyclizing agents are HCl, CH_3COOH, and mixtures of these agents and, less often, H_2SO_4 and H_3PO_4, $ZnCl_2$. and $AlCl_3$.

Several examples of the use of salicyclideneanilines as the starting carbonyl component have been described [28-33]; the first step is usually realized under the conditions of the Perkin condensation.



In the cyclocondensation of 2-alkoxy-4-aminosalicylaldehydes with acetonitriles one usually separates the two reaction steps with isolation of coumarinic acid nitriles. Cyclization in this case is preceded by dealkylation, which proceeds under the influence of acidic agents: $ZnCl_2$, $AlCl_3$, $C_5H_5N \cdot HCl$, and HBr in CH_3COOH.

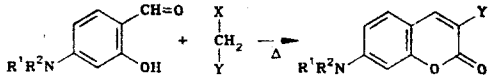


Not only removal of the alkyl group but also the formation of a pyran ring occur in the presence of $AlCl_3$ [34, 35]. When R^4 = $MeOCH_2$ and Me_2NSO_2 [36, 37], dealkylation and lactonization are realized simply by heating in aqueous mineral acids.

It should be noted that the examined scheme was not realized in the case of alkylacetic acids or their functional derivatives; however, the Perkin reaction was realized in the case of 4-nitrosalicylaldehyde with sodium acetate and acetic anhydride and led to 7-nitrocoumarin in 58% yield [19].

Coumarins obtained from salicylaldehydes are presented in Table 1.

In addition to 3-aryl and 3-hetaryl derivatives, 7-aminocoumarins with ethoxycarbonyl [46, 47, 57], carboxy [37], aminocarbonyl, ureido, aminothiocarbonyl, nitrile [47], acyl [72], and alkyl- [47] or arylsulfonyl groups in the 3 position were obtained from 4-aminosalicylaldehydes by Knoevenagel condensation with activated acetic acids and their functional derivatives.† The reactions were readily accomplished by heating, most often in the presence of piperidine.



X=COOAlk, COOH, COONa, CN; Y=ArCO, HetCO, COOH, COOEt, ArN(Alk)CO, CN, RSO_2, $R_2NCONRCO$, H_2NCS

*The preparation of 3-arylcoumarins with a primary amino group in the 7 position has been described [27]; an advantage of the proposed method consists in the direct use of 4-aminosalicylaldehyde instead of its 4-acetamido derivative.
†See also [237-240].

TABLE 1. 3-Aryl- and 3-Hetaryl-7-aminocoumarins Obtained from Salicylaldehydes

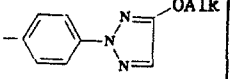
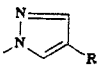
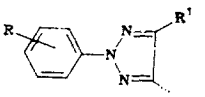
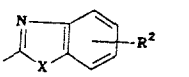
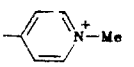
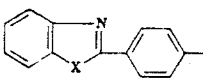
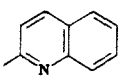
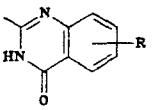
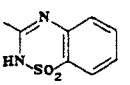
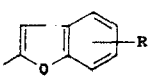
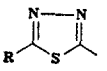
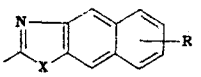
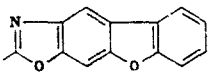
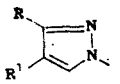
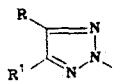
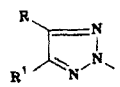
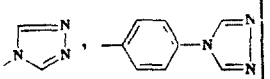
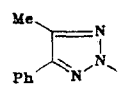
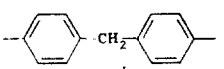
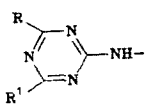
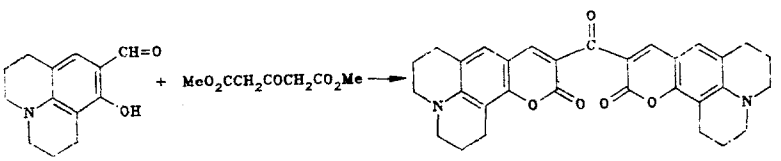
No.	Substituent at C(7)	Substituent at C(3)	Literature source
1	2	3	4
1	NH_2	Ph, substituted Ph	[19, 27—29, 34—41]
2	NH_2	α- and β-Naphthyl	[37]
3	NH_2		[42]
4	NH_2		[36]
5	NH_2		[36]
6	NH_2		[30, 32]
7	NHAc		[31]
8	NHAc		[43]
9	NHAc		[44]
10	R, R^1 = H, Alk, form a heteroring with N	 X = O, S, NH, NAlk	[36, 45—54]
11	NMe_2		[55]
12	NEt_2	 X = O, NH, NMe	[56]
13	NEt_2		[57]
14	NEt_2		[58]
15	NEt_2		[59, 60]
16	$NAlk_2$		[61]

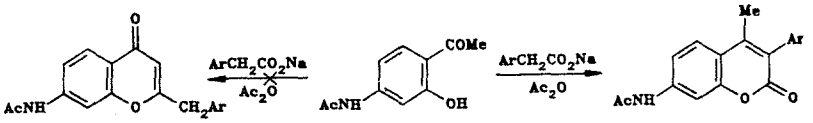
TABLE 1 (continued)...

1	2	3	4
17	$NAlk_2$		[62, 63]
18	$NAlk_2$	 X = O, S, NH, NAlk	[47, 49, 52]
19	$NAlk_2$		[49]
20		Ph, substituted Ph	[64, 65]
21		Ph, substituted Ph	[66—68]
22			[69]
23		 (3,3')	[70]
24		Ph, substituted Ph	[71]

Double Knoevenagel condensation made it possible to arive at 3,3'-carbonyl- [72] and m-phenylenedisulfonyl-bis(coumarinyl) derivatives [47]:

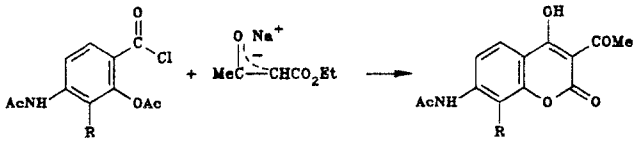


Synthesis from o-Hydroxyaryl Ketones. It is known that the Kostanecki—Robinson reaction, which consists in heating an o-hydroxyaryl ketone, which acts as a methylene component, with anhydride and the sodium salt of a carboxylic acid, is a general method for the synthesis of chromones, which are isomers of coumarins. An exception to this rule, which leads to the formation of primarily coumarins, is the Bargellini condensation, a classical variant of which wa used to obtained 3-aryl-4-methyl-7-acetamidocoumarins.



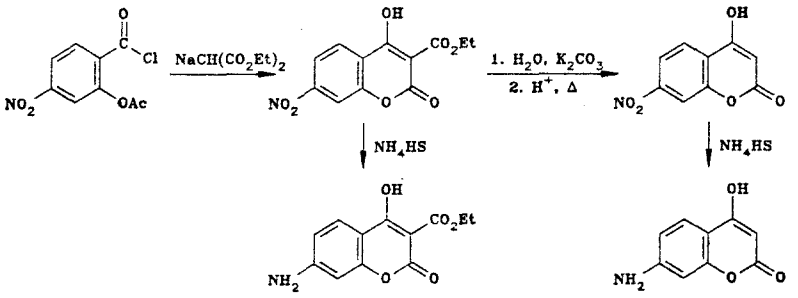
Ar=Ph [19, 73], 2-furyl[74]

Synthesis from Salicyclic Acid Derivatives. Two variants of the classical Anschutz method for the preparation of 4-hydroxycoumarins have been realized. Ishii and co-workers [75, 76] carried out the acylation of sodioacetoacetic ester with 4-acetamidosalicylic acid chlorides to synthesize 3-acetyl-4-hydroxy-7-aminocoumarins.



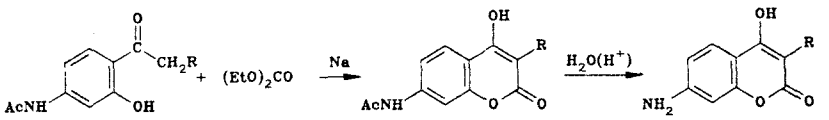
R=H (38% yld), Br (80% yld)

3-Ethoxycarbonyl-4-hydroxy-7-nitrocoumarin and 3-unsubstituted 4-hydroxy-7-nitrocoumarin were obtained in the acylation of sodiomalonic ester with 2-acetoxy-4-nitrosalicylic acid chloride [23, 24].



1.3. Cyclocondensation of Type 2. Synthesis from o-Hydroxyphenyl Ketones (Boyd–Robertson Reaction)

The reaction of o-hydroxyphenyl ketones with diethyl carbonate in the presence of sodium is the best method for the synthesis of 4-hydroxycoumarins. 2-Hydroxyphenyl ketones with a 4-acetamido group are usually used for the synthesis of 7-amino-4-hydroxycoumarins [23, 24, 77-80]. The acetyl protective group is readily removed by the action of hydrochloric acid.



R = H, Me, Et

It is known that 3-aryl-substituted chromones and coumarins coexist in plants, and it has been postulated that they arise from a common genetic precursor. Subba Rao and co-workers [81] have demonstrated this: 3-phenylcoumarin was isolated under the conditions of the Boyd–Robertson reaction of 4-acetamido-2-hydroxydeoxybenzoin with diethyl carbonate, and isoflavone was isolated under the influence of ethyl orthoformate.

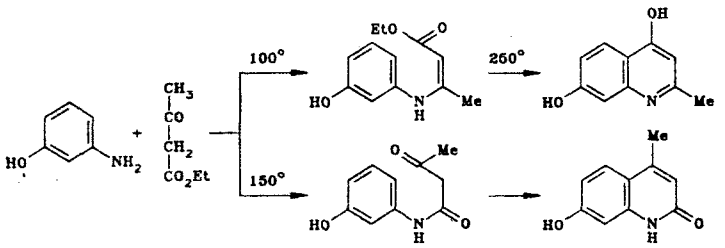
1.4. Cyclocondensation of Type 3. Synthesis from Phenols (Pechmann Reaction)

The most convenient method for the synthesis of coumarins is the condensation of phenols with β-dicarbonyl compounds. The presence of a donor meta substituent in the phenol molecule significantly facilitates the reaction; nevertheless, the scheme under consideration is not the most widely used method for the preparation of the desired unsubstituted and monosubstituted 7-amino derivatives. The fact is that, although the Pechmann condensation is regiospecific with respect to the site of cyclization (the ortho position relative to the reacting functional group and the para position relative to the other), it is unselective with respect to the functional groups, viz., the amino and hydroxy groups.

On the basis of the first studies of Pechmann [82-84] one might have concluded that the amino group in N-unsubstituted and, apparently, N-monosubstituted m-aminophenols is the more

*The possibility of the formation of 4-hydroxyquinoline structures was not considered in any of the subsequent studies of cyclocondensation of type 3.

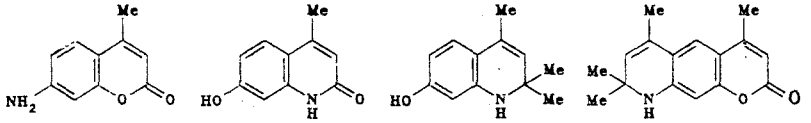
active group in the reaction with acetoacetic ester. Thus only a carbostyril (through the intermediate formation of an anilide) and a 4-hydroxyquinoline* (through the intermediate formation of an anil*) are formed in the thermal reaction of m-aminophenol with acetoacetic ester.



Two groups of researchers confirmed Pechmann's observations: 7-hydroxy-4-methylcarbostyril was isolated in 96% [85] and 60% [86] yields as a result of the thermal condensation of m-aminophenol with acetoacetic ester at 160°C.

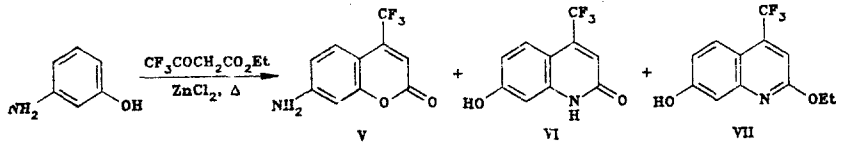
The nature of the β-keto ester has a pronounced effect on the regioselectivity of the reaction: the corresponding 7-aminocoumarins are the principal products when m-aminophenol is heated with 2-methyl- and 4,4,4-trifluoroacetoacetic esters [86].

A mixture of four compounds, viz., 7-aminocoumarin I, 7-hydroxycarbostyril.II, 7-hydroxydehydroquinoline III, and pyranodihydroquinoline IV, once again with preponderance of products of reaction at the amino group, is obtained in the condensation of m-aminophenol with acetoacetic ester in the presence of anhydrous zinc chloride.†



I (14%) II (25%) III (7%) IV (10%)

A detailed investigation of the nature and ratio of the products of the Pechmann condensation in the case of the reaction of m-aminophenol with trifluoroacetoacetic ester in the presence of $ZnCl_2$ was made in 1980 by Bissell and co-workers [89], who showed that three components, viz., coumarin V, carbostyril VI, and quinoline VII, which is alkylated at the oxygen atom of the lactam group, are invariably obtained under all of the tested conditions; the overall yield is 43-83%, and the amount of the coumarin in the mixture ranges from 46% to 72%.



V VI VII

Thus attempts to realize, in practice, the direct reaction of m-aminophenols with primary and secondary amino groups with β-dicarbonyl compounds lead to mixtures of diverse substances, the separation of which is difficult.

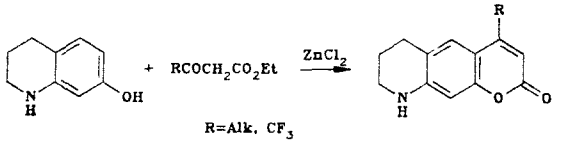
Various protective groups have been investigated in order to exclude the formation of side products. It was found that acetyl and phthalimido protective groups hinder the occurrence of the Pechmann reaction with the use of $ZnCl_2$ and H_2SO_4 as the condensing agents.‡ Thus in the reaction with trifluoroacetoacetic ester ($ZnCl_2$) 3-acetamidophenol gave only 6% of a mixture containing 62% coumarin V, 11% quinoline VI, and 7% ethoxyquinoline VII. 3-Phthalimidophenol did not undergo the reaction at all.

*In 1967 [88] it was shown that such anils undergo thermal arrangement to the corresponding 7-aminocoumarins under the influence of equimolar amounts of diverse anilines.
†It was subsequently established that the formation of coumarins is favored by a number of agents with acidic character, but $ZnCl_2$ remains the agent that is most often used; as noted in [87], the addition of powdered zinc prevents the formation of colored side products.
‡ The use of phosphorus oxychloride in the synthesis of 7-amino-4-methylcoumarin was reported in [90].

In 1961 Pretka [91] unexpectedly observed that an alkoxycarbonyl group not only protects the amino group in m-aminophenol and its derivatives but also has an appreciable activating effect on the reaction: the most diverse β-dicarbonyl compounds gave good yields at 20°C under the influence of aqueous sulfuric acid (d ∿ 1.68) (a carbamoyl protective group did not activate the process, and the yields of coumarins were low). This remarkable fact was confirmed [89] with the use of trifluoroacetoacetic ester as the β-dicarbonyl cyclocomponent and $ZnCl_2$ as the condensing agent. It was established that urethane blocking groups give different results, depending on the nature of the alkoxy group in the urethane. Isobutyl 3-hydroxycarbanilate led to a reaction product (77% yield) containing 53% coumarin V and 23% quinoline VI; 2-alkoxyquinoline VII and a urethane derivative of coumarin V were not detected. The benzyl ester was unsuitable, and ethyl m-hydroxycarbanilate led to the expected urethane derivative of 7-aminocoumarin V, which was free of admixed side products VI and VII, but its yield (37%) was not high enough.

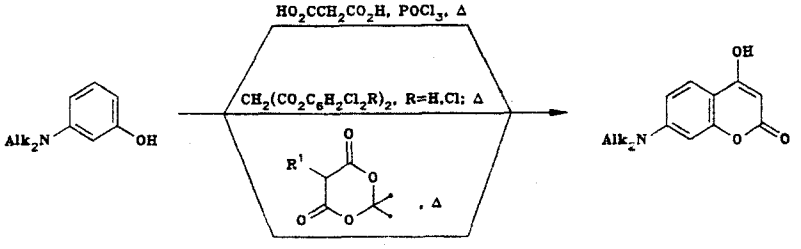
Let us note that, despite the low degree of effectiveness of the use of m-aminophenols with primary and secondary amino groups in the Pechmann condensation [82-84], 7-aminocoumarins (N-unsubstituted and monosubstituted) continue to be obtained by this method [92-108], sometimes with fairly good results.

To prevent the formation of products of condensation at the amino group of aminophenols one can also use another method, viz., protection of the ortho position with respect to it. Appleton [109] was the first to realize this possibility: he obtained 7-methylamino-4,6-dimethylcoumarin in 85% yield as a result of the reaction of 4-methyl-3-methylaminophenol with acetoacetic ester ($ZnCl_2$). Atkins and co-workers [86, 99] and Harnisch [107] used an original variant of blocking the para position relative to the hydroxy group: 7-hydroxy-1,2,3,4-tetrahydroquinoline served as the starting aminophenol for them.



In Pechmann's research [82, 110] he demonstrated that the cyclocondensation that he proposed for the synthesis of coumarins can be successfully used in the case of m-aminophenols with a tertiary amino group. This was subsequently confirmed in a number of studies [85, 87, 98, 100, 102, 104-108, 111-113]. However, a competitive reaction, viz., the formation of isomeric (with respect to coumarins) chromones, which proceeds in the absence of condensing agents (Manzer–Mohl reaction), was also observed in these cases. Thus 2-methyl-7-dimethylaminochromone was obtained as a result of the thermal (200°C) condensation of m-dimethylaminophenol with acetoacetic ester (a coumarin was formed in the presence of $ZnCl_2$) [111].*

The unsuccessful attempt to obtain 4-hydroxy-7-dialkylaminocoumarins by heating m-dialkylaminophenols with diethyl malonate [114] is explainable from the point of view of [111]. 4-Hydroxy-7-dialkylaminocoumarins were isolated as a result of the thermal condensation of m-dialkylaminophenols with the reactive bis(2,4-dichlorophenyl) and bis(2,4,6-trichlorophenyl) malonates (80% yields) [114], as well as with 2,2-dimethyl-4,6-dioxo-1,3-dioxanes (∿40% yields) [100] or by heating m-dialkylaminophenols with malonic acid in the presence of phosphorus oxychloride (∿60% yields) [114].



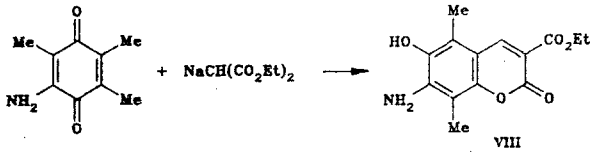
*The results of Woods and co-workers are not in agreement with the results of the cited study: they obtained 7-dimethylamino-4-methylcoumarin in the thermal condensation (150°C) of m-dimethylaminophenol with acetoacetic ester in 65% yield [85]. Coumarins were also isolated when β-keto esters were heated with 4-dimethylaminosalicylic acid [97].

An example of the preparation of an unsubstituted (in the pyran ring) 7-aminocoumarin in 8% yield from m-dimethylaminophenol and malonic acid in the presence of H_2SO_4 has been described [115]. There are several patents on methods for the purification of 7-dialkylamino-4-methylcoumarins — products of the reaction of m-dialkylaminophenols with acetoacetic ester in the presence of $ZnCl_2$ [116-119].

Much is unclear with respect to the β-dicarbonyl component. The most diverse variants are claimed in patents, but examples of the use of only a small set of such components are presented: α-alkylacetoacetic esters [91, 120], alkanoyl [91] and aroylacetic esters [91, 97] 2-ethoxycarbonyl-substituted cyclohexanone and cyclopentanone [91, 98, 121], diethyl acetonedicarboxylate [92, 113, 122], ethyl β-ethoxy-α-ethoxycarbonylacrylate [106], and α-phenylformyl- [88, 94] and α-phenylacetoacetic esters [19, 94]. There is no unified opinion regarding the latter ester. The synthesis of 3-phenyl-4-methyl-7-aminocoumarin from m-aminophenol and α-phenylacetoacetic ester under the influence of $AlCl_3$ was presented in a Dutch patent [94]. This contradicts the observations of Mehendale and Sunthankar [19], all attempts by whom to accomplish the Pechmann condensation between m-diethylaminophenol and α-phenylacetoacetic ester were unsuccessful.

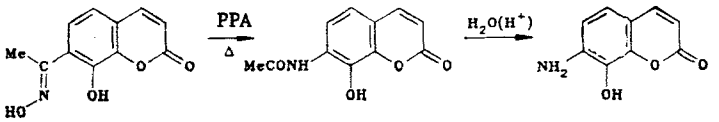
1.5. Other Methods for the Preparation of 7-Aminocoumarins

Synthesis from Quinones. It is known that upon treatment with sodiomalonic ester tetrasubstituted quinones undergo Michael condensation in their enol forms to give dihydrocoumarins, which usually undergo dehydrogenation to coumarins during the reaction. The only similar reaction was realized in the case of amino derivatives of quinone. Coumarin VIII, which was formed as a consequence of attack by the enolate anion of the methyl group in the para position relative to the amine function, was isolated in 97% yield as a result of the reaction of aminotrimethylquinone with sodiomalonic ester [123].



VIII

Rearrangement of 7-Acylcoumarin Oximes. One example of the Beckmann rearrangement of 7-acetyl-8-hydroxycoumarin oxime, which proceeds under the influence of polyphosphoric acid (PPA), has been described [22].



2. REACTIVITIES

The ^1H and ^{13}C NMR spectroscopic data [10, p. 647] provide evidence that the heterocyclic ring of coumarin has aliphatic character; nevertheless, it undergoes electrophilic substitution the typical reaction of aromatic compounds.

The following principles can be formulated through correlation of the data in [1, 10, 124]

In unsubstituted coumarin, which is somewhat less reactive than benzene, electrophilic substitution takes place at the $C_{(6)}$ atom, and the 8 and 3 positions are involved to a certain extent; in the case of the more active 7-hydroxy derivatives the 8 position is the most reactiv but substitution is also realized at the $C_{(6)}$ and $C_{(3)}$ atoms.

Electrophilic reagents such as bromine and mercury salts initially add to the $C_{(3)}=C_{(4)}$ double bond; electrophilic substitution in the benzene ring is realized under more severe conditions.

As in the case of pyrones, the properties of the heterocyclic ring of coumarin depend markedly on the character of the substituents present in this ring. Thus an electron-donor group in the 4 position increases the electron density of the lactone ring to such an extent that the $C_{(3)}$ atom becomes the preferred site of any electrophilic attack.

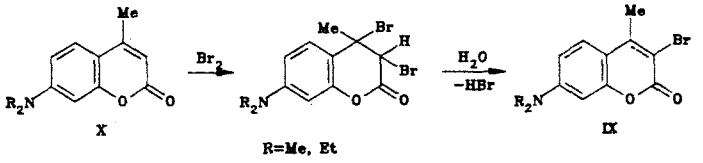
The heterocyclic ring of coumarin is more reactive to attack by nucleophilic than electrophilic particles. Weak nucleophiles attack the 4 position, and strong nucleophiles give products of reaction at the $C_{(2)}$ atom (the presence of a hydroxy group in the 7 position slows down nucleophilic addition appreciably).

Bases have different effects on coumarins, depending on their structures, but opening of the lactone ring and the formation of coumarinic acid salts usually occur.

The principal reactions known for 7-aminocoumarins are presented below. However, it should once again be emphasized that most of the research in this area is pragmatic in character, and systematic studies of the reactivities of 7-aminocoumarins are, in fact, not available.

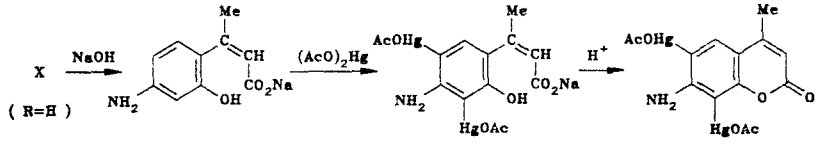
2.1. Reactions Involving the Coumarin Ring

Bromination. The bromination of 7-aminocoumarins was studied in the case of dialkylamino-4-methyl derivatives in [110, 125]. It was established that a dibromo derivative is obtained initially as a consequence of the addition of bromine to the double bond. During storage, as well as upon contact with water, the dibromo derivative undergoes spontaneous dehydrobromination. The use of equimolar amounts of the reagents in aqueous mineral acid leads to 3-bromo-7-di-alkylaminocoumarins IX in 69-84% yields [110].

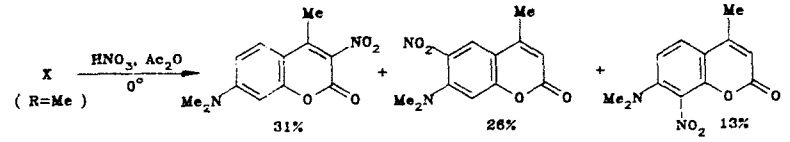


Further bromination of IX (R=Me) in chloroform yielded the isomeric 3,6- and 3,8-dibromo derivatives, as well as the 3,6,8-tribromo derivative [110], which are also obtained under the influence of bromine at 140°C in carbon disulfide or at 170°C in the presence of iodine [1, p. 150]. Treatment of aminocoumarin X (R=Et) with bromine in hydrochloric acid led to 3,6,8-tribromo-7-diethylamino-4-methylcoumarin [110].

Mercuration. Mercuration has been studied only in the case of 7-amino-4-methylcoumarin [126]. It was noted that the reaction does not occur in a neutral medium and that the presence of a solution of alkali is necessary for its realization. Addition to the $C_{(3)}=C_{(4)}$ double bond was not noted (see also [1, p. 152].



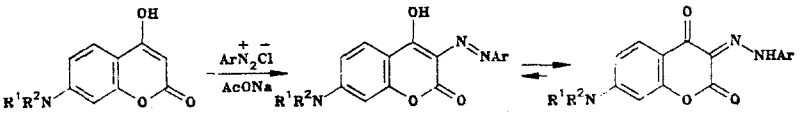
Nitration. The nitration of 7-dimethylamino-5-methylcoumarin (with dilute nitric acid in acetic acid) was first examined by Pechmann and Shaal [110]; however, the positions of the nitro groups in the two isolated products of mono- and dinitration were not established. The reaction was later investigated by Machida and co-workers [127], who limited themselves to the isolation and determination of the structures (by means of PMR spectroscopy) of only the mononitro derivatives. It was established that a mixture of three mononitro compounds is formed in the reaction of aminocoumarin X (R=Me) with nitric acid (d = 1.42) in acetic anhydride (see also [1, p. 144]).



Only one mononitro derivative with a nitro group in the 3 position was isolated in the nitration of 7-acetamido-4-hydroxycoumarin with concentrated nitric acid in glacial acetic acid; this was associated with the activating effect of the 4-hydroxy group [77, 78, 128].

Formylation. The introduction of a formyl group into 7-dialkylaminocoumarins was accomplished in three patents: 3-formyl derivatives were obtained in good yields under the influence of the Vilsmeier reagent.

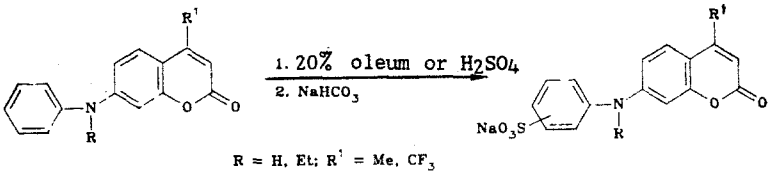
Diazo Coupling. Arenediazonium salts couple with 7-acetamido- and 7-dimethylamino-4-hydroxycoumarins XI in the 3 position, as a result of which arylazocoumarins, which exist preferably in the tautomeric arylhydrazone form, are formed [77, 79, 100].



XI

Arylation. Meerwein arylation, which takes place in the 3 position by the action on 7-aminocoumarins of diverse arenediazonium salts in the presence of mono- and divalent copper salts, is one of the most widely used reactions in the aminocoumarin series [19, 42, 95, 131, 132]. It is surprising that competitive diazo coupling reactions, as specially noted in one of the patents [131], are virtually not observed in the case of amino derivatives of coumarin.

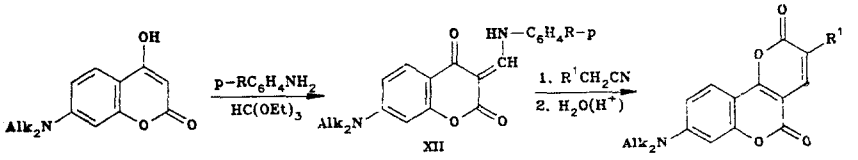
Sulfonation. The sulfonation of only those 7-amino-coumarins that contain an additional benzene or benzimidazole ring in their molecules has been described [103, 133-136]. It was recently shown that 7-benzylamino-4-methyl- and 4-trifluoromethylcoumarins react with 20% oleum to give products of sulfonation of the benzene ring of the amino substituent; the coumarin ring is not affected [103] (see also [1, p. 146]). These results make it possible to assume that the sulfonation of 7-benzylaminocoumarins, which was described in patents in the 1950s without any proof of the structures of the sulfo products obtained [133-135], was also similarly realized.



R = H, Et; R' = Me, CF_3

In the case of 3-(2-benzimidazolyl)-7-diethylaminocoumarin the location of the sulfo group introduced by the action of 10% oleum was not established [136].

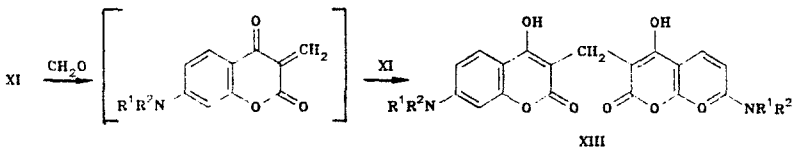
Aminomethylation. Heating 4-hydroxy-7-dialkylaminocoumarin with substituted anilines and ethyl orthoformate in glacial acetic acid leads to the formation of 3-(anilinomethylene) derivatives XII in good yields in the form of mixtures of Z/E isomers [100, 114]. Of the two tautomeric structures, the enamine structure is preferred [114]. The corresponding pyrones are obtained by the reaction of the 3-anilinomethylene 2,4-diones with equimolar amounts of nitriles in the presence of a strong base and subsequent acidification [114].



XII

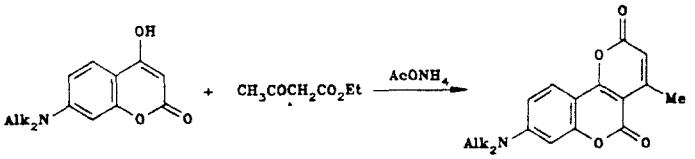
R=H, Cl, NO_2; R'=Ph, Het, $PO(OEt)_2$, CO_2Et, CN, SO_2Ph

Condensation with Formaldehyde. 4-Hydroxy-7-aminocoumarins readily undergo condensation with formaldehyde to give bis(coumarins) XIII [23, 100] (see also [1, p. 146]). The initial product is evidently a 3-methylene-2,4-dioxochromene, which then adds 4-hydroxycoumarin via the scheme of the Michael reaction.

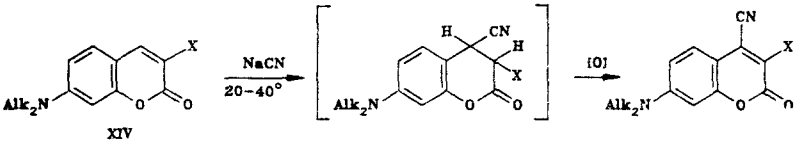


XIII

Condensation with Acetoacetic Ester. A modified Pechmann reaction, which proceeds under the influence of acetoacetic ester in the presence of ammonium acetate and leads to 7-dialkylamino-4-methyl-2H,5H-pyrano[3,2-c]benzopyran-2,5-diones, has been described for 4-hydroxy-7-dialkylaminocoumarins [114].

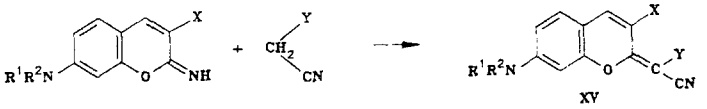


Reaction with Sodium Cyanide. Examples of nucleophilic addition to the double bond of the heterocyclic ring of 7-aminocoumarins have been described: 4-cyanocoumarins are obtained as a result of the reaction of aminocoumarins XIV with sodium cyanide and subsequent oxidation of the intermediate addition products with bromine or lead tetraacetate [137-139] (see also [1, p. 152]). The presence of an electron-acceptor activating X group in the 3 position is necessary for a smooth reaction.



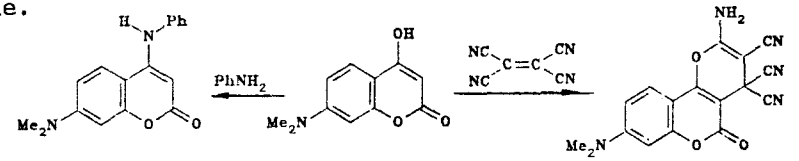
XIV

Condensation with Malonic Acid Derivatives. Imines of 7-amino-3-aryl(hetaryl)coumarins with a tertiary amino group act as carbonyl components in condensation with functional derivatives of malonic acid; 2-alkylidenebenzopyrans XV are obtained as a result [140].

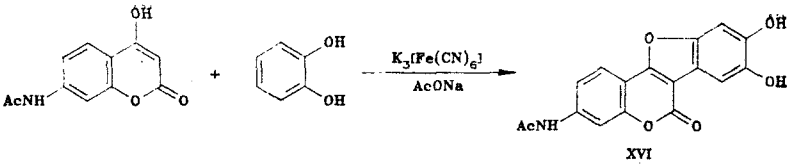


X = Ar, Het; Y = CN, $CONH_2$, CCOAlk

Other Reactions. Wolfbeis [100] accomplished the reaction of 7-dimethylamino-4-hydroxycoumarin with tetracyanoethylene; however, he did not present rigorous proof for the structure obtained. An imine, which actually axists in the enamine tautomeric form, was isolated in the reaction with aniline.



The oxidative reaction of 4-hydroxy-7-acetamidocoumarin with pyrocatechol leads to the creation of coumestan system XVI [80].

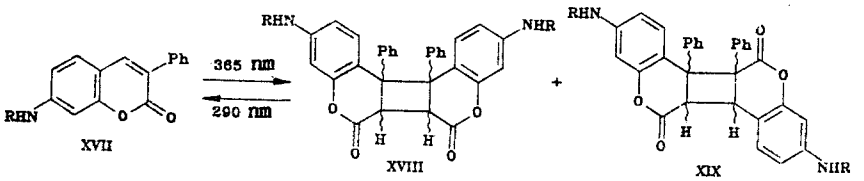


XVI

Photodimerization. Photodimerization is a well-known reaction of coumarins. It is a [2+2]-cycloaddition reaction, the result of which is the formation of four cyclobutane derivatives [10].

The photochemical behavior of one representative of 7-aminocoumarins has been studied in quite some detail by Leaver and co-workers [18]. The irradiation of 7-[4,6-bis(butylamino)-sym-triazin-2-ylamino]-3-phenylcoumarin (XVII) in polymeric films with light with a wavelength of 365 nm leads to a mixture of photodimers, which are the syn and anti isomers

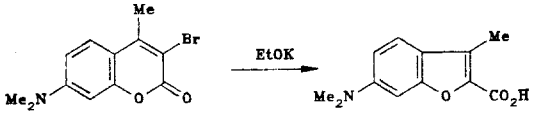
of the "head-to-head" (XVIII) and "head-to-tail" (XIX) [2+2]-cycloadducts. The process can be reversed by irradiating the resulting mixture with light with a shorter wavelength (∿290 nm – the region of absorption of the photodimers); at least 95% of the starting aminocoumarin XVII is rapidly regenerated in this case.



R= 4,6-bis(butylamino)-1,3,5-triazin-2-yl

An equilibrium mixture of coumarin XVII and its photodimers XVIII and XIX is formed under the influence of sunlight (a polychromatic source); the position of the equilibrium depends very markedly on the spectral distribution of the light. Thus a considerably smaller amount of coumarin XVII as compared with the results of direct solar exposure is contained in the equilibrium state when ordinary glass, which cuts out short-wave radiation, is used as the light filters.

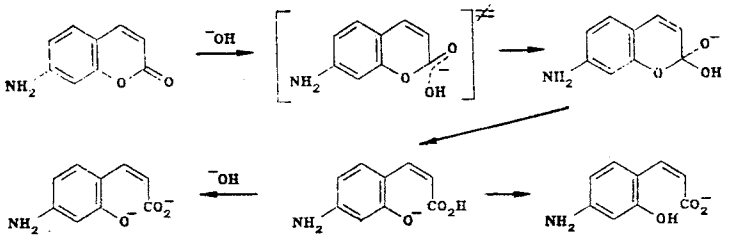
Disruption of the Pyrone Ring of Coumarins. Alkali affects coumarins in different ways, depending on their structures [1, pp. 157-161]. Perhaps one reaction is general in character: the reaction of 3-halocoumarins with alkalis leads to coumarilic acids. This reaction has also been realized with 7-amino derivatives of coumarins by the action of potassium ethoxide [111].



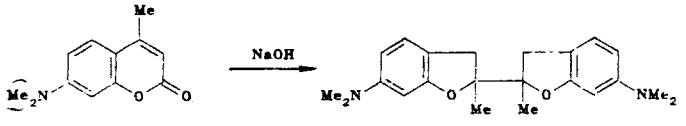
Let us also emphasize a second common feature: the initial action of alkali consists in opening of the pyrone ring and the formation of coumarinic acid salts. Any attempts to isolate the free acid by acidification lead to rapid spontaneous conversion of it to the starting coumarin. Inversion of the cis-coumarinic acid to the trans-coumaric acid occurs in the case of prolonged action of alkali. Electron-donor substituents in the benzene ring give rise to slowing down of alkaline opening of the lactone ring. The introduction of electron-acceptor substituents leads to opposite effects [141, 142].

The mechanism of the process under consideration consists in the rate-determining attack on the coumarinic carbonyl group by the hydroxide anion, which is followed by rapid cleavage of the endocyclic oxygen–carbon bond.

Coumarin gives ethyl coumarate when it is heated with sodium ethoxide; under these conditions 7-dimethylamino-4-methylcoumarin (like 4-methylumbelliferone) forms only coumarinic acid salts [1, p. 158].

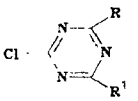
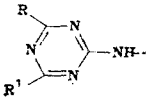
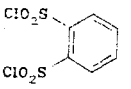
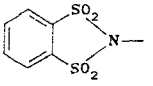
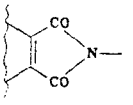
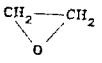
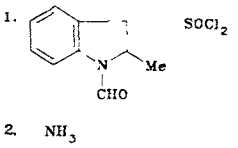
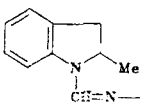
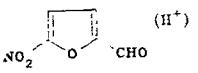
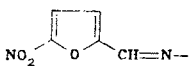


A substance, to which a dicoumarone structure was tentatively assigned, is formed as the chief product when 7-dimethylamino-4-methylcoumarin is fused with alkali [110].



Opening of the pyrone ring and decarboxylation with the formation of 4-amino-2-hydroxypropiophenone were observed in the case of prolonged refluxing in hydrochloric acid (1:1) of

TABLE 2. Reactions Occurring at the Amino Group of 7-Aminocoumarin Derivatives

Starting 7-amino group	Reagent	Final 7-amino substituent	Literature source
NH_2			[18, 147, 149—160, 238]
NH_2	MeI	MeNH traces, Me_2N traces, $Me_3\overset{+}{N}$ quantitative yield	[83]
NMe_2	MeI	$Me_3\overset{+}{N}$	[161]
NH_2	$ClCH_2CO_2Na$	NaO_2CCH_2NH	[161]
NH_2	$BrCH_2CH_2SO_3Na$	$NaO_3SCH_2CH_2NH$	[163]
NH_2	$COCl_2$	O=C=N	[34]
NH_2	1. $COCl_2$; 2. ROH	ROCONH	[34]
NH_2	1. $COCl_2$; 2. RR^1NH	RR^1NCONH	[35, 38]
RNH (R=H, Me)	1. $CSCl_2$; 2. R^1R^2NH	$R^1R^2NHCSNR$	[164]
NH_2	$ClCO_2R$	ROCONH	[34, 165]
NH_2	$ClCH_2COCl$	$ClCH_2CONH$	[166]
NHR (R=Alk, H)		$HO_3SCH_2CH_2CH_2CH_2NR$	[167]
NH_2	PhCOCl	PhCONH	[19, 83]
NH_2	Ac_2O	AcNH	[17, 19, 23, 26, 83, 123]
NH_2	$ClSO_3H$	HO_3SNH	[168]
NH_2	$ClSO_3R$	RSO_3NH	[135]
NH_2			[169]
NH_2			[170]
NH_2	KCNO (AcOH)	H_2NCONH	[35, 165]
NH_2		$[HOCH_2CH_2(OCH_2CH_2)_x]_2N$	[163]
NH_2			[167, 171]
NH_2	$HCONBuCH_2CH_2Ph$, $SOCl_2$	$PhCH_2CH_2NBuCH{=}N$	[172]
NH_2			[26]
NHR (R=H, Alk)	$R^1R^2C{=}O+NaHSO_3$	$NaO_3SCR^1R^2NR$	[135, 173—176]
NH_2	$CH_2O+HSCH_2CO_2H$	$HO_2CCH_2SCH_2NH$	[163]
NHMe	$NaNO_2$, H_2SO_4	O=NNMe	[83]

4-hydroxy-7-acetamido-3-methylcoumarin, which is the enol form of a β-keto lactone [23] (see also [1, p. 160]).

2.2. Reactions Involving the Amino Group

The amino groups in 7-aminocoumarins are capable of undergoing all of the reactions of aromatic amines. They give isocyanates and isothiocyanates upon reaction with phosgene and

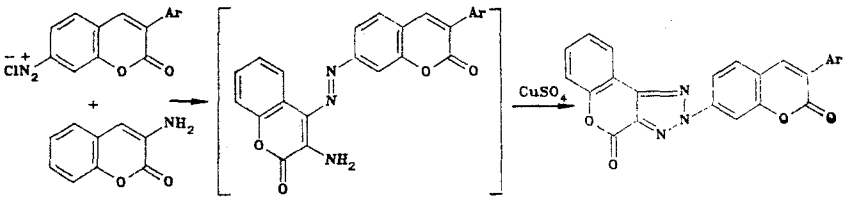
thiophosgene, react with functional derivatives of carboxylic acids and halogen-containing and carbonyl compounds, and form ammonium and diazonium salts. The types of these reactions are presented in Table 2.

DIAZONIUM SALTS BASED ON 7-AMINOCOUMARINS

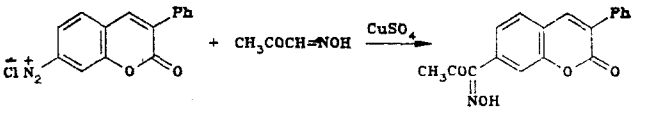
Reduction. The conversion of an amino group to a hydrazino group is of practical importance. It is achieved by diazotization of 7-aminocoumarins and reduction of the resulting diazonium salts with stannous chloride [30, 31, 132, 143, 235, 236].

Sandmeyer Reaction. The replacement of 7-diazo groups by halogen in the presence of copper salts, which is a reaction that is typical for aromatic diazonium salts, has been investigated quite extensively [73, 80, 90, 123]. The preparation of 7-hydroxy- [83] and 7-mercaptocoumarin from coumarindiazonium salts has also been described. In the case of 7-mercaptocoumarin replacement of a diazo group by a thiocyano group is realized initially under the influence of potassium thiocyanate; subsequent hydrolysis in the presence of iron (II) sulfate leads to 7-coumarinyl mercaptan [237].

Diazo Coupling. Several examples of diazo coupling of coumarin-7-diazonium salts with β-naphthylamine [19], 3-aminocoumarin [177], diverse vinyl amines [178], and 1,2-oxazol-5-ones [179] have been presented. 7-(1,2,3-Triazol-2-yl)coumarins are obtained as a result of all of these reactions:



Meerwein Reaction. An original variant of arylation by means of a coumarindiazonium salt was demonstrated by Kirchmayr and Rody [180], who introduced a 3-phenylcoumarin-7-yl group into isonitroazoacetone.



2.3. Peptide Derivatives of 7-Aminocoumarins

Diverse peptide derivatives of 7-amino-4-methyl(or trifluoromethyl)coumarin, which serve as fluorogenic substrates for the identification and quantitative determination of enzymes and for the kinetic analysis of enzyme reactions, attracted a great deal of attention at the end of the 1970s [181-186]. A method developed for the diagnosis of the most important enzymes, which was based on the fluorometric determination of 7-amino-4-methyl(trifluoromethyl)-coumarin liberated as a result of the enzymatic hydrolysis of peptide derivatives, has very high sensitivity.

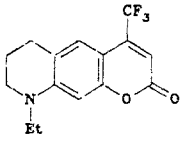
3. PHYSICAL PROPERTIES

3.1. 7-Aminocoumarins as Optical Media for Lasers (Electronic Absorption and Emission Spectra)

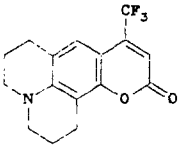
Coumarin derivatives that have an amino group in the 7 position are currently the most effective dyes that generate laser emission in the blue-green region of the spectrum [187-191]. Among all of the known "laser" coumarins, the 7-amino derivatives constitute the most significant part. There are more than 70 different comopunds of this type that generate over the spectral range from 420 nm (7-aminocoumarin — coumarin 120) to 584 nm [7-diethylamino-3-(2-benzothiazolyl)coumarin — coumarin 6] [192]. Laser generation of 7-aminocoumarins has been obtained in the use of virtually all excitation sources known for dyes.

A study of the effect of the molecular structure on the generation efficiency of various derivatives of coumarin compounds in ethanol in the case of laser and lamp excitation showed

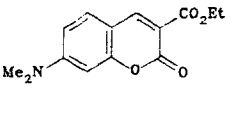
that the generation efficiencies of the very same compounds depend substantially on the type of excitation [190]. In lasers with lamp excitation 7-amino derivatives of coumarin dyes have an important advantage over dyes of other classes, which consists in the existence of strong absorption in the range of wavelengths shorter than 300 nm, i.e., in those regions in which one finds the bulk of the radiation of excitation lamps. It was established that under lamp-excitation conditions coumarins 120, 2, 1, 102, 30, and 6* (the numbering and structures are presented below), which have an amino group in the 7 position, generate emission very efficiently [188, 193-196]; an energy of more than 10 J at a generation efficiency exceeding 1% was obtained with individual 7-aminocoumarins in the case of excitation with a specially designed coaxial lamp [195]. In another communication [197] there is a discussion of the emission of a laser based on coumarin 504 of pulses with energies of 0.4 J at 500 Hz and 2 J at 100 Hz, with an average power of 200 W in both cases, and of the possibility of increasing the generation efficiency of this laser to 1.25%. The development of such lasers based on 7-aminocoumarins makes it possible for them to find extensive application in the solution of not only research problems but also a number of practical problems. Increasing their generation efficiencies can be associated with various factors. Reynolds and Drexhage [187] link an increase in laser efficiency with the creation of molecules that have rigid structures. This is explained by the fact that the π-electron density between the amino group and the benzene ring decreases in the excited state, and mobility of the amino group consequently increases nonradiating transition to the ground state. Thus an amino group with a rigid structure should prevent a decrease in the fluorescence efficiency in polar solvents. This sort of effect was actually demonstrated for coumarin 102, an ethanol solution of which was more efficient in a laser than a solution of coumarin 1 in ethanol. In addition, in contrast to coumarin 1, continuous generation was obtained in an aqueous solution of coumarin 102 [198]. Increasing the rigidity of the amino group by means of one or two six-membered rings, as, for example, in coumarins 153 and 314, as compared with coumarins 355 and 14 also leads to an increase in the fluoresence quantum yield and the laser efficiency [187].



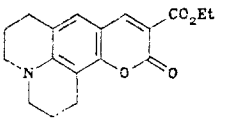
Coumarin 355



Coumarin 153



Coumarin 14



Coumarin 314

An increase in the generation intensity for some 7-aminocoumarins is associated with the removal of oxygen from solutions. Thus for coumarins 1, 102, LD490, and C8F in ethanol it was shown [199] that displacement of oxygen by argon leads to an increase in the fluorescence quantum yield and an improvement in the generation properties. Another way to increase the generation efficiencies of 7-aminocoumarins is the use of transfer of the excitation energy from one dye to another in a mixture of these dyes. For examples, it is noted in [196] that an active medium that is twice as efficient as coumarin 314 is obtained when a mixture of coumarin 1, which is an energy donor, and coumarin 314, which is an energy acceptor, is used in a laser.

7-Aminocoumarins are highly efficient laser media also in laser excitation. In [190] it is noted that, of the investigated coumarins of various types, amino- and alkylaminocoumarins have the best generation parameters in laser excitation.

Various sources of coherent emission – lasers based on molecular nitrogen (λ_{gen} 337 nm), excimer lasers (λ_{gen} 308 nm), and a ruby laser (second harmonic, λ_{gen} – 347 nm) – have been used for the excitation of 7-aminocoumarins. A substantial expansion of the range of generation of coumarins owing to the possibility of obtaining laser emission with nine new coumarin derivatives in the case of excitation by the emission of the second harmonic of a ruby laser has been reported [200]. On the basis of a study of the generation characteristics of 15 coumarins with substituents in the 3, 4, 5, 6, and 7 positions of the coumarin ring in the case of excitation with the second harmonic of a ruby laser Dzyubenko and co-workers [201] established that compounds that contain an electron-donor substituent, viz., an amino group, in the 7 position have the highest efficiencies; 7-diethylamino-4-methyl-3-ethylcoumarin is the most efficient.

*These names are widely accepted in laser technology.

Generation under continuous conditions was obtained in the case of excitation of 7-aminocoumarin dyes with the emission of an argon laser. The production of laser emission under continuous conditions with eight coumarins, seven of which are 7-amino derivatives, over the spectral range 420-585 nm with an output power from 150 to 600 MW was reported in [198, 202]. Coumarins 120, 2, 7, 102, 30, 6, and 10 in aqueous solutions generated under these conditions.

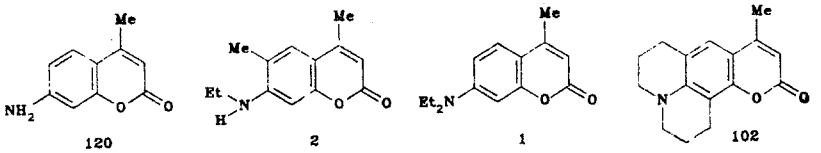
Generation with 7-aminocoumarins was obtained when they were used as active media not only in liquid solutions but also in the gas phase. Laser generation over the spectral range 470-540 nm in vapors of coumarin 153, 7-diethylamino-3-(2-benzoxazolyl)coumarin, and coumarins 7 and 6 was obtained for the first time in [203, 204]. The active medium in this case consisted of a mixture of vapors of coumarins with buffer gases at a pressure of 35 atm and was excited by the third harmonic of a neodymium laser (λ_{gen} 355 nm). It was shown that the generation efficiencies of the coumarins in the vapor phase in the 500 nm range exceed 6% [204]. The creation of a laser based on the dye vapors with lamp excitation, which generates radiation with λ_{gen} 527 nm, was reported for coumarin 6 [7-diethylamino-3-(2-benzothiazolyl)-coumarin] [205, 206].

7-Amino derivatives of coumarin dyes have attracted attention with respect to the possibility of obtaining generation emission with different durations, viz., from several tens of microseconds [207, 208] to several picoseconds [209-211]. Generation emission over the range 440-490 nm with a duration of 52 μsec in a laser with lamp excitation [an ethanol solution of 7-diethylamino-4-methylcoumarin (coumarin 1) with the addition of 1,3-cyclooctadiene (as a quencher of the triplet state) was used as the active medium] was reported in [207]. Mialocg and Goujon [209], using solutions of coumarin 1 and coumarin 10 in a laser with lamp excitation, obtained generation pulses shorter than 10 psec in the case of passive modulation of the quality factor of the cell resonator with a solution of 3,3-dihexylococarboxyanine iodide. Emission with a duration of 5 psec with a power of 1 MW [210] and with a duration of 4 psec with a power of 3 MW for coumarin 6 [211] was recorded in experiments on mode synchronization conducted with lasers using 7-aminocoumarins, viz., coumarins 1, 102, LD466, LD473, and LD490 as the active media.

A distinctive feature of coumarins that have an amino group in the 7 position is the substantial increase in the basicities of these compounds in the case of optical excitation and the shift of the fluorescence and, correspondingly, generation spectra to longer wavelengths. This property is used to expand the range of frequency tuning in a dye laser. As noted in [188], the change in the basicities of these compounds is associated with the different mesomeric forms in the ground (A) and excited (B) states.

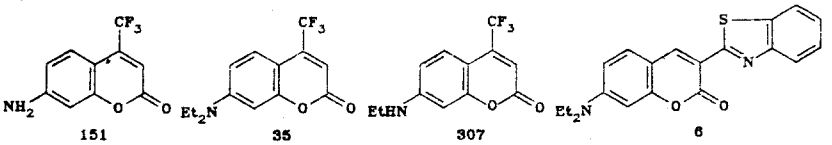
A B

Stabilization of the positive charge on the nitrogen atom is increased when electron-donor alkyl groups are present. In this connection, a successive long-wave shift of the absorption, fluorescence, and generation spectra occurs in the following order: coumarin 120, coumarin 2, coumarin 1, coumarin 102 [188].



120 2 1 102

In addition, a laser shift to the red region is observed when substituents with heterocyclic rings and a trifluoromethyl group are included in the 7-aminocoumarin molecule; this is confirmed by the results of measurements of the spectra of coumarins 151, 307, 35, 153, and 6 and by comparison of them, respectively, with the spectra of coumarins 120, 2, 1, and 102 in ethanol (see Table 3).



151 35 307 6

TABLE 3. Wavelengths of the Absorption,* Fluorescence, and Generation Maxima of Various Coumarins in Ethanol

Coumarin	Wavelengths, nm			Coumarin	Wavelengths, nm		
	absorption	fluorescence	generation		absorption	fluorescence	generation
120	354	430	442	35	402	510	520
151	382	480	490	102	390	465	480
2	366	435	454	153	423	530	540
307	395	490	502	6	458	505	537
1	373	445	460				

*The UV spectra of coumarins were examined in detail in a previous review [13].

The widening of the spectral region of active medium laser radiation takes place on the basis of 7-aminocoumarins, not only by means of structural change of the coumarin molecule, but also as the result of application in the role of active media of coumarin solution mixtures. For the mixtures of coumarin 120 solutions with coumarin 1 the obtained generation is in the 436-472 nm region in the laser with lamp excitation [194]. For mixtures consisting of four coumarins, i.e., coumarin 120, sodium salt 7-sulfomethylamino-4-methylaminocoumarin, 7-diethylamino-3-4-dimethylcoumarin, and 7-diethylamino-4-methyl-3-phenylcoumarin, the obtained generation is in the 462-497 region in the same laser with lamp excitation [194]. However, during laser excitation the same mixture made from the four dyes generated in the 440-500 nm region [212].

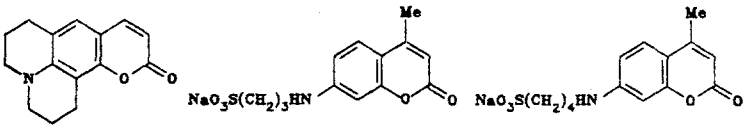
The spectral range of laser tuning on the 7-aminocoumarin solutions may be widened and a corresponding choice of solvents may be made [213].

Spectral absorption and fluorescence maxima for 7-aminocoumarins very strongly depend on the solvent polarity derived from the presence of the two mesomeric forms mentioned above in the ground and excited states, for which this dependence appears stronger, than for xanthene and oxazine dyes [189]. If the addition of the bases in small quantities to the solutions of 7-aminocoumarins does not change spectral positions, then addition of strong acids leads to varied effects. In coumarin 1 aminogroup protonation leads to loss of absorption in the 373 nm region; in coumarin 102 protonation, evidently, this loss takes place with difficulty as the result of much more rigid structure. Protonized forms of coumarins are brought about, accompanied by the appearance of fluorescence in the new spectral regions. In coumari 1 solutions in the protonic solvents, and likewise in the aprotonic solvents, with addition of donor protons in the ground and excited states, the formation of complexes with a hydrogen bond in the carbonyl group may occur.

Although the fluorescence quantum yield of coumarin 1 in the protonic solvents is small, as a rule, compared to the aprotonic, its laser efficiency is higher and its spectral range of laser radiation is substantially wider, so that it may be linked with change of the mutual position of fluorescence spectra and either triplet – triplet or singlet – singlet absorption [214].

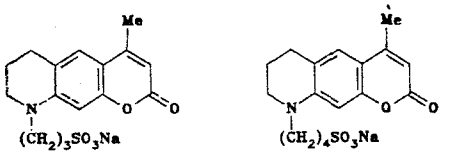
In noting the effect of the solvent on the efficiency and spectral range of generation of 7-aminocoumarins one should especially note research on the use of water as the ideal solvent with respect to its thermooptical properties. For the use of aqueous solutions of coumarins one either utilizes certain additives that increase their solubilities or one synthesizes specially water-soluble coumarins. In [198, 202] it is proposed that N,N-dipropylacetamide or hexafluoro-2-propanol be added as solubilizing agents in small concentrations that do not change the thermooptical properties of water. In [215] nine new dyes, viz., derivatives of coumarin C6H (LD490) that have different functional groups in the 3 position, were investigated in aqueous ethanol solutions.

Drexhage and co-workers [216] have reported the synthesis of 7-aminocoumarins that are soluble in water and generate efficiently under lamp excitation in the spectral range 450-520 nm. It was also shown that replacement of a hydrogen atom in the amino group of coumarin 120 by a $(CH_2)_3SO_3Na$ or $(CH_2)_4SO_3Na$ radical makes it possible to create dyes, viz., coumarin 378 and coumarin 380, with higher energy parameters and lower generation thresholds.



C6H (LD 490) 378 380

In exactly the same way, the generation characteristics of coumarins 386 and 388 are appreciably better than for coumarins with an NH group.



386 388

However, replacement of hydrogen atoms in the amino group by CH_2SO_3Na or CH_2CH_2OH does not improve the generation characteristics of coumarins. Just as in coumarins with a closed amino group in the 7 position of the coumarin 102 type, the introduction of hydroxyethyl or carboxy groups in the 3 or 4 position also creates water-soluble molecules but it does not improve the generation properties.

The chemical and photochemical instability of dyes is the chief problem for their use in lasers, since the energy stability of the laser and its operating life are associated with this. Dyes are most unstable in lasers with lamp excitation, in which the laser medium is subject to the action of emission with a broad spectral range, and the bulk of the emission lies in the UV range of the spectrum. Although the presence of a system of pumping of the active medium in the laser increases its operating life, the generation stability of such lasers still remains low, and the search for laser media that are resistant to the action of the excitation emitter is one of the most pressing problems to this day. The fact that the decrease in the generation stability of 7-aminocoumarins is the result of photochemical processes that occur with the participation of the excited state of the dye and lead to the formation of photoproducts that absorb over the range of the laser emission is generally accepted [216-219]. On the basis of a study of 30 different coumarin and quinolone dyes in [218] it was concluded that the decrease in the laser yield is associated not so much with photodecolorization of the dye as with the formation of photoproducts that increase the absorption in the generation range by a small value, viz., 5-10%; the formation of these products depends on both the solvent and the gas in the atmosphere of which excitation of the dye occurs. This fact was also confirmed in [219], in which on the basis of the change in the absorption of a solution of coumarins during excitation with a xenon lamp it was found that the rate of decolorization depends on the overall "contributed" energy and is directly proportional to the dye concentration. The latter indicates the possibility of the occurrence of a first-order reaction between the dye and the solvent in the excited state with the formation of a photoproduct that absorbs in the laser region.

A detailed investigation of the processes involved in the photodecomposition of ethanol solutions of coumarin 1 in a laser with lamp excitation enabled Winters and co-workers [220] to propose the existence of two photochemical processes that occur under the influence of the excitation emission, viz., dealkylation of the amino substituent and oxidation of the methyl group in the 4 position by air. Five of the resulting photochemical products were isolated and identified. It was also shown that only one of them, viz., 7-diethylamino-4-carboxycoumarin, absorbs in the laser region and decreases the laser yield. The following conclusions were drawn from the results of this research: first, one must replace oxygen by some other quencher of the triplets of coumarin that is not an oxidizing agent; second, one must replace the CH_3 group in the 4 position by a less reactive group such as CF_3; third, one must remove the photochemical products that impair generation by, for example, filtration.

In another study [217] dealing with chemical stabilization of the processes involved in the formation of photoproducts in coumarin 1 and coumarin 311 (7-dimethylamino-4-methylcoumarin), which are formed under the influence of the emission of a nitrogen laser, it is concluded that the mechanism of the excitation of coumarins is a bimolecular process that proceeds with the formation of intermediate radicals via transfer of a hydrogen atom from the N-methyl or C-methyl group of one coumarin to the carbonyl oxygen atom of another coumarin. Substances that absorb in a longer-wave region than the starting coumarins can then be formed from the resulting radicals. Von Trebra and Koch [217] suggest that the formation of radicals

be inhibited by the introduction of various additives into solutions of the dyes. They showed that the introduction of small amounts of cysteine hydrochloride to a solution of coumarin 1 increases the emission power of a dye laser by 10% and the continuous operation time to 12 h, while the addition to coumarin 311 of divalent sulfur compounds, viz., ethyl mercaptan (C_2H_5SH) and ethyl disulfide, increases the emission power by 20%, but the oeprating life of the working volume of the dye solution does not change. It should be noted that in [217] it is concluded that it is impossible to stabilize a dye by the introduction into it of the additives mentioned above in lasers with lamp excitation because of the fact that much lower concentrations of the dyes are used in this case, and the excitation mechanism may be different. As in [220], it is concluded that stabilization of the dyes in lasers with lamp excitation should be accomplished by removal of oxygen from the solution and replacing it with a triplet quencher, viz., cyclooctatetraene, and by the synthesis of less reactive coumarin derivatives. In [221] it is asserted that the presence of NH_2 group in the 7 position in coumarin dyes always gives a molecule with weak photostability regardless of the functional group in the 4 position. However, replacement of even one hydrogen atom in the amino group leads to an increase in the stability, and the presence at the nitrogen atom of one or more rings and a CF_3 substituent in the 4 position gives the most photostable coumarins. High photochemical stability was also noted for coumarin 6, which has a diethylamino group in the 7 position and a heterocyclic substituent, viz., a 2-benzothiazolyl group, in the 3 position [188]. The synthesis and investigation of the laser characteristics of a number of new coumarin dyes on the basis of 7-amino derivatives with increased photochemical stability were reported in [222-224]. A CF_3 group was introduced into the 4 position of the coumarin ring in these dyes. In [222] it is noted that the generation efficiency of the synthesized 7-diethylamino-4-trifluoromethylcoumarin is close to the efficiencies of known coumarin compounds, whereas its photochemical stability significantly exceeds theirs. The properties of a number of fluorinated 7-aminocoumarins were described in [223, 225], and it was shown that the photochemical stabilities of some of them significantly exceed that of Rhodamine 6Zh, one of the most efficient and stable dyes. The increase in the operating life of dyes in lasers in [224] is associated with a decrease in the translucidation constants of their solutions, which depend on the solvent used, the purity of the dye, and the presence of UV filtration.

A method, proposed in [226], for increasing the stabilities and operating times in lasers of some 7-aminocoumarin dyes, viz., coumarins 1, 120, 311, and 314, seems of interest. A 0.01-mole sample of 1,4-diazabicyclo[2.2.2]octane (DABCO) was added to solutions of these dyes, used as active media in lasers with excitation with an N_2 laser and with lamp excitation; this increases the photostabilities by a factor of three. The presence of DABCO in the solution does not decrease the average output power, the pulse duration, and the spectral line width; this favorably distinguishes this additive from other means that have been proposed to increase the operating lives but which have also decreased the energy parameters of solutions of coumarins. 1,4-Diazabicyclo[2.2.2]octane (DABCO) is more effective in the stabilization of solutions of coumarins with oxygen than in the stabilization of the same solutions without oxygen. A detailed study of the effect of DABCO on the operating lives of coumarins enabled Von Trebra and Koch [226] to propose that the stabilization of solutions of coumarins is realized via a combined pathway, viz., by quenching of the triplet state of the dyes and by quenching of the singlet oxygen that is formed as a result of interaction of oxygen with the triplet state of the dye.

The above-examined questions regarding the use of 7-aminocoumarins as active laser media make it possible to conclude that the search for highly efficient laser media on the basis of the purposeful synthesis and investigation of 7-amino derivatives of coumarin remains an extremely urgent task, since only the establishment of the precise relationships between the structures of coumarin molecules and their spectral-luminescence and generation properties will make it possible to create dyes that most fully meet practical needs.

3.2. X-Ray Diffraction Analysis

The crystal structure of only 7-diethylamino-4-methylcoumarin has been investigated [227]. The crystals are monoclinic with space group $P2_1$, a = 9.82, b = 6.99, c = 9.28 Å, β = 91.85°, and Z = 2.

3.3. Mass Spectrometry

Mass-spectrometric studies of a number of 7-aminocoumarins were made in [228, 229]. From these studies it may be concluded that the introduction of an unsubstituted amino group

TABLE 4. Chemical Shifts of 7-Diethylamino-4-methylcoumarin

Solvent	^{13}C chemical shifts ($^{1}J_{CH}$), δ, ppm (TMS)											
	$C_{(2)}$	$C_{(3)}$	$C_{(4)}$	$C_{(5)}$	$C_{(6)}$	$C_{(7)}$	$C_{(8)}$	$C_{(9)}$	$C_{(10)}$	4-CH_3	$-CH_2-$	$-CH_3$
96% H_2SO_4	170,4	110,5 (169)	171,1	130,0 (172)	121,8 (169)	150,9	112,7 (172)	141,9	122,5	19,5	55,6	9,6
$CHCl_3$	161,6	108,0 (173)	152,5	125,0 (159)	108,0 (159)	150,1	97,1 (159)	155,5	108,4	18,1	43,8	12,3

into the 7 position and a phenyl group into the 3 position does not cause changes in the character of the fragmentation of the molecular ion: the pathways of the dissociative ionization of 3-phenyl-7-aminocoumarin are similar to those of unsubstituted coumarin and involve the successive ejection of two molecules of CO (or CO and COH). The disruption of the coumarin skeleton may also be realized in more advanced stages of the fragmentation, depending on the character of the substitutents attached to the amino nitrogen atom. For 7-diethylamino derivatives fragmentations of the coumarin type commences from the $[M-CH_3]^+$ ion after splitting out of an ethyl group at the β bond; in the case of 7-triazinylaminocoumarins fragmentation of the molecular ion is due primarily to cleavage of the triazine ring or substituting diethylamino groups. The latter involves the ejection of an ethyl radical, which is uncharacteristic for aliphatic amines:

$$(M-CH_3)^+ = R-\overset{+}{N}(=CH_2)-C_2H_5 \xrightarrow{-C_2H_5^{\cdot}} R-N=CH_2^{+}$$

For compounds that contain a pyrazolyl substituent in the 7 position the elimination of CO is accompanied by the ejection of HCN and CH_3CN molecules; for compounds that contain triazolyl substituents initial splitting out of the latter at the two N–N bonds with the retention of one nitrogen atom in the composition of the charged fragment is characteristic.

3.4. Acidities

The pK_a value of only 7-dimethylamino-4-hydroxycoumarin has been determined: pK_a (EtOH) 6.50 ± 0.11 (by potentiometry), 6.7 (H_2O + 5% EtOH; by spectrophotometry), and 6.0 (H_2O + 5% EtOH; by fluorometry) [230].

3.5. IR Spectra

No special spectral studies of the IR spectra of 7-aminocoumarins have been made. Individual bands of the IR spectra have been presented in a number of synthetic studies [79, 89, 97, 114, 127]. The band of the lactone CO group absorbs at 1680 to 1750 cm^{-1} and usually at ~1710 cm^{-1}; the introduction of strong electron-acceptor substituents into any of the rings increases it, whereas the introduction of electron-donor substituents decreases it.

3.6. NMR Spectra

The PMR spectra of aminocoumarins have been used for identification in a number of synthetic studies [89, 97, 105, 231-233]. Correlations of the 3-H and 4-H chemical shifts (CS) of 6- and 7-substituted coumarins with the Hammett constants were examined in [233]. The ^{13}C NMR spectra for coumarins were presented in general in a previous review [14]. Gottlieb and co-workers [234] studied the ^{13}C NMR spectra of coumarin and a number of its 6- and 7-substituted derivatives and correlated the CS of the α, β-unsaturated lactone system with the Hammett constants: it was observed that the CS of the $C_{(3)}$ atom is in good agreement with σ^+ and that the CS of the $C_{(2)}$ and $C_{(4)}$ atoms are in good agreement with σ. Satisfactory agreement was observed for the two bridge carbon atoms with σ_p^+ rather than with σ_m or σ_m^+. They presented the following CS [δ, ppm, $CDCl_3$–CH_3OH (2:1), tetramethylsilane (TMS) as the internal standard] for 7-aminocoumarin: $C_{(2)}$ (164), $C_{(3)}$ (110), $C_{(4)}$ (145), $C_{(5)}$ (130), $C_{(6)}$ (113), $C_{(7)}$ (153), $C_{(8)}$ (101), $C_{(9)}$ (157), and $C_{(10)}$ (110). Sojka [231] showed by means of the ^{13}C NMR spectra that in 96% H_2SO_4 protonation of 7-diethylamino-4-methylcoumarin is realized at both the oxygen atom of the carbonyl group and at the nitrogen atom (see Table 4).

A paper [232] dealing with the ^{13}C NMR and PMR spectra of 7-aminocoumarins was published only in 1985; the effect of substituents on the ^{13}C and ^{1}H CS was evaluated, and increments of the substituents, as well as the $J(^{13}C-H)$ values, were presented in this paper.

Thus the goal of our review was to familiarize the reader with the method of preparation and properties of 7-aminocoumarins, which have found extensive application in the creation of dye lasers. The authors did not set out especially to exhaustively examine all of the available literature in this area; however, they did strive to fully encompass all of the qualitatively different aspects in the chemistry of 7-aminocoumarins, to isolate the basic principles, and thus to stimulate the further investigation of this narrow but important class of organic compounds.

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