

PHOTOCHEMICAL REACTIONS OF 7-AMINOCOUMARINS.

5.* [2 + 2]-CYCLOADDUCTS WITH *trans*-STILBENE

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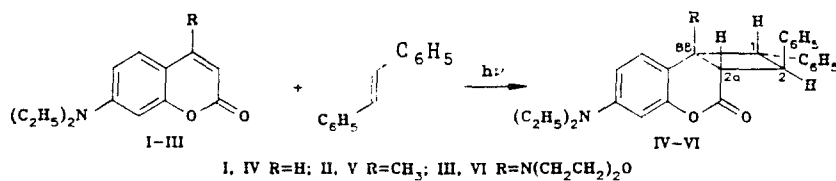
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The photocycloaddition of trans-stilbene to 7-diethylaminocoumarin, 4-methyl-7-diethylaminocoumarin, and 4-(N-morpholino)-7-diethylaminocoumarin was investigated. Adducts involving stereospecific (2 + 2)-cycloaddition at the 3-4 bond were isolated. On the basis of the PMR spectra and an x-ray diffraction study, it was established that the phenyl groups in the cycloadducts occupy 1-endo and 2-exo positions.

In [2] we studied the photocycloaddition of styrene to various 7-aminocoumarins and found that it leads to the regio- and stereospecific formation of [2 + 2]-cycloadducts at the 3-4 bond with *cis* fusion of the rings.

The aim of the present research consisted in an investigation of the stereochemistry of the photoreactions of 7-aminocoumarins with *trans*-stilbene. The interest in the cycloaddition of stilbene was due to the desire to make a more thorough study of the stereoselectivity of the reactions under consideration, since the number of possible stereoisomers in this case (disregarding *cis* or *trans* fusions of the rings) reaches four. It is also known that stilbene is capable of participating in concerted processes with a high degree of stereoselectivity [3] and remains the subject of great attention in theoretical investigations of [2 + 2]-photocycloaddition [4].

To study the photoreactions we selected a number of 7-diethylaminocoumarins with substituents of different sizes in the 4 position: 7-diethylaminocoumarin (I), 4-methyl-7-diethylaminocoumarin (II), and 4-(N-morpholino)-7-diethylaminocoumarin (III). Compounds IV-VI were isolated as the only isomers as a result of the photolysis of 0.05 M solutions of the coumarins for 8-10 h in the presence of excess stilbene. The percentages of the cycloadducts in the reaction mixtures ranged from 80 to 90%; however, because of a tendency for retrodecomposition, the preparative yields did not exceed 65% (Table 1).



On the basis of [2] we adopted *cis* fusion of the cyclobutane and coumarin fragments for all of the cycloadducts. To substantiate the detailed structures of IV-VI we used data from the PMR spectra of adducts of coumarin II and a number of other coumarins with styrene [2], the structures of which were confirmed by x-ray diffraction studies. The chemical shifts of the cyclobutane protons in IV and V are located at 3.3-4.3 ppm (Table 2). In the spectrum of adduct V the signal at 3.70 ppm is a doublet ($^3J_{1,2} = 11.0$ Hz) and was ascribed to the 1-H proton on the basis of the characteristic value of the chemical shift which, for most 1,2-diphenylcyclobutanes, lies at 3.5-4.5 ppm [3, 4]. Furthermore, in the spectrum of adduct V we identified

*For Communication 4, see [1].

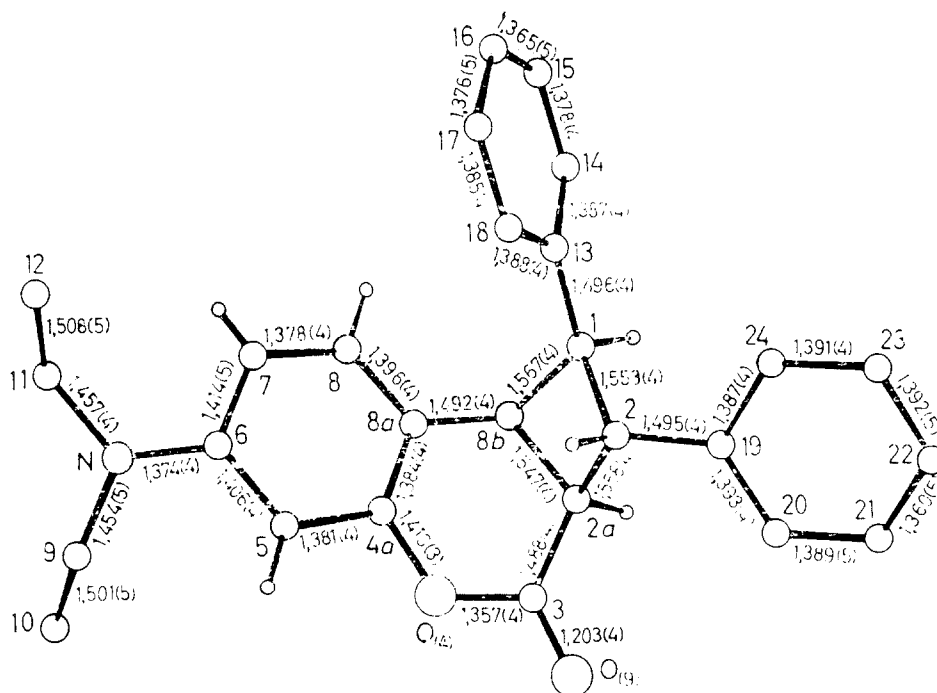


Fig. 1. Structure of the IV molecule in the crystalline state.

TABLE 1. Characteristics of IV-VI

Com- pound	Empirical formula	mp, °C	R_f^*	IR spectrum, cm^{-1}		λ_{max} , nm (log ϵ), in 2 propanol	Yield %	Quantum yield of the photo- reactn.***
				C=O	C=O			
IV	$\text{C}_{27}\text{H}_{27}\text{NO}_2$	145	0.43	1735	1615, 1590, 1545	218 (4,19), 214 (4,40), 284 (4,27), 310 (3,93)	63	0,044
V	$\text{C}_{28}\text{H}_{26}\text{NO}_2$	134	0.43	1757	1638, 1572, 1531	216 (4,74), 246 (4,38), 282 (4,25), 304 (4,06)	59	0,061
VI	$\text{C}_{31}\text{H}_{34}\text{N}_2\text{O}_3$	81	0.32	1755	1625, 1560, 1520	214 (4,58), 252 (4,12), 283 (4,11)	55	0,085

*Determined on Silufol UV-254 plates in a hexane-acetone system (4:1)

**Measured in 1,4-dioxane at coumarin I-III concentrations of 0.08 mole/liter and an olefin concentration of 0.50 mole/liter. The quantum yield of the reaction to form coumarin VII under these conditions is 0.003.

the strong-field signal of a 2a-H proton at 3.31 ppm, which also has a doublet structure ($^3J_{2a,2} = 9.5$ Hz). The weak-field 2-H signal has the form of a distorted triplet with a broad central line and includes close values of the two vicinal constants (Table 2). By means of the $^3J_{2a,2}$ and $^3J_{1,2}$ constants found for adduct V we identified the doublet-doublet signal of the 2-H proton in the spectrum of IV [spin-spin coupling constants (SSCC) 11.0 and 9.8 Hz], as well as the signal of the 1-H proton (SSCC 11.0 and 8.0 Hz). The subsequent assignment of the PMR signals for IV presents no difficulties (Table 2). The cyclobutane protons in adduct VI were also assigned on the basis of an analogy in the vicinal constants. A specific characteristic of VI is equivalence of the coumarin 7-H and 8-H protons, as a result of which the corresponding $^3J_{7,8}$ SSCC does not appear. On the other hand, the methylene protons of the morpholine $\text{N}(\text{CH}_2)_2$ fragment in adduct VI are nonequivalent and show up in the form of a symmetrical multiplet at 2.55 ppm, which constitutes evidence for hindered rotation of this substituent.

A common peculiarity of the PMR spectra of adducts IV-VI is a shift of ~1.5 ppm to strong field of the signal of the 8-H proton (5.9-6.2 ppm) as compared with the signals of the starting coumarins, as well as the isolation of signals of two o-phenyl protons (7.0-7.1 ppm) from the overall multiplet signal of aromatic protons at 7.2-7.3 ppm. Similar principles are also observed for the adduct of coumarin II with styrene [2], which makes it possible to assume an endo orientation of the 1-phenyl group. Considering the stereospecificity of the reactions under consideration, as well as their occurrence through the

TABLE 2. PMR Spectra of IV-VI

Compound	Chemical shifts, δ , ppm (SSCC, J, Hz)									
	1-H	2-H, dd	2a-H	5-H	7-H	8-H, d	8a-R	NCH ₃ (q, J=7.0)	NCH ₃ -CH ₃ (t, J=7.0)	Phenyl protons
IV	4.11 dd (11.0; 8.0)	1.28 (11.0; 9.0)	3.68 dd (9.8; 8.0)	6.36 d (2.8)	6.11 dd (8.8; 2.8)	5.95 (8.8)	3.96 dd (8.0; 8.0)	3.29	1.14	7.04 and 7.25 (2H, m, and 8H, m 2C ₆ H ₅)
V	3.70 d (11.0)	4.02 (11.0, 9.5)	3.31 d (9.5)	6.32 d (2.7)	6.06 dd (8.9; 2.7)	5.88 (8.9)	1.55 s	3.27	1.12	7.00 and 7.25 (2H, m, and 8H, m 2C ₆ H ₅)
VI	4.12 d (11.0)	3.78 (11.0; 9.5)	3.52 d (9.5)	6.38 dd (1.5; 1.5)	6.15 d (1.5)	6.15 (1.5)	2.55 m 3.70 m	3.35	1.15	7.05 and 7.27 (2H, m, and 8H, m 2C ₆ H ₅)

TABLE 3. Bond Angles in the IV Molecule

Angle	($^\circ$)
C ₍₃₎ O ₍₄₎ C _(4a)	121,5(2)
C _{(6)NC₍₉₎}	121,6(3)
C _{(6)NC₍₁₁₎}	121,4(3)
C _{(5)NC₍₁₁₎}	116,7(3)
C _{(2)C_{(1)C_(8b)}}	87,6(2)
C _{(2)C_{(1)C₍₁₃₎}}	123,0(2)
C _{(8b)C_{(1)C₍₁₃₎}}	121,8(2)
C _{(1)C_{(2)C_(2a)}}	87,0(2)
C _{(1)C_{(2)C₍₁₉₎}}	119,8(2)
C _{(2a)C_{(2)C₍₁₉₎}}	120,8(2)
C _{(2)C_{(2a)C₍₃₎}}	117,0(2)
C _{(2)C_{(2a)C_(8b)}}	88,1(2)
C _{(3)C_{(2a)C_(8b)}}	119,5(2)
O _{(4)C_{(3)O₍₉₎}}	117,3(3)
O _{(4)C_{(3)C_(2a)}}	118,0(3)
O _{(9)C_{(3)C_(2a)}}	124,7(3)
O _{(4)C_{(4a)C₍₅₎}}	112,7(2)
O _{(4)C_{(4a)C_(8a)}}	122,8(2)
C _{(5)C_{(4a)C_(8a)}}	124,4(3)
C _{(4a)C_{(5)C₍₆₎}}	120,2(3)
NC _{(6)C₍₅₎}	121,5(3)
NC _{(6)C₍₇₎}	122,1(3)
C _{(5)C_{(6)C₍₇₎}}	116,5(3)
C _{(6)C_{(7)C₍₈₎}}	121,0(3)
C _{(7)C_{(8)C_(8a)}}	123,2(3)
C _{(4a)C_{(8a)C₍₈₎}}	114,7(3)
C _{(4a)C_{(8a)C_(8b)}}	122,0(2)
C _{(8)C_{(8a)C_(8b)}}	123,2(2)
C _{(1)C_{(8b)C_(2a)}}	87,0(2)
C _{(1)C_{(8b)C_(8a)}}	116,3(2)
C _{(2a)C_{(8b)C_(8a)}}	110,5(2)
NC _{(9)C₍₁₀₎}	114,2(3)
NC _{(11)C₍₁₂₎}	112,4(3)
C _{(1)C_{(13)C₍₁₄₎}}	119,7(2)
C _{(13)C_{(13)C₍₁₈₎}}	122,9(2)
C _{(14)C_{(13)C₍₁₈₎}}	117,4(3)
C _{(13)C_{(14)C₍₁₅₎}}	121,7(3)
C _{(14)C_{(15)C₍₁₆₎}}	120,1(3)
C _{(15)C_{(16)C₍₁₇₎}}	119,5(3)
C _{(16)C_{(17)C₍₁₈₎}}	120,5(3)
C _{(13)C_{(18)C₍₁₇₎}}	120,8(3)
C _{(2)C_{(19)C₍₂₀₎}}	122,1(2)
C _{(2)C_{(19)C₍₂₄₎}}	120,0(2)
C _{(20)C_{(19)C₍₂₄₎}}	117,9(3)
C _{(19)C_{(20)C₍₂₁₎}}	120,6(3)
C _{(20)C_{(21)C₍₂₂₎}}	120,4(3)
C _{(21)C_{(22)C₍₂₃₎}}	120,7(3)
C _{(22)C_{(23)C₍₂₄₎}}	118,5(3)
C _{(19)C_{(24)C₍₂₃₎}}	121,9(3)

TABLE 4. Coordinates ($\cdot 10^4$; $\cdot 10^3$ for H) of the Atoms in the IV Molecule

Atom	x	y	z
O ₍₄₎	11226(2)	3003(2)	8766(2)
O ₍₉₎	13331(2)	3274(3)	7845(2)
N	6800(3)	2659(3)	10984(2)
C ₍₁₎	10227(3)	1225(3)	6539(2)
C ₍₂₎	11020(2)	2675(3)	6222(2)
C _(2a)	11800(3)	1873(3)	7310(2)
C ₍₃₎	12205(3)	2744(3)	7978(3)
C _(4a)	9906(3)	2335(3)	9055(2)
C ₍₅₎	9033(3)	2802(3)	9819(2)
C ₍₆₎	7690(3)	2216(3)	10224(2)
C ₍₇₎	7319(3)	1132(3)	9826(3)
C ₍₈₎	8235(3)	694(3)	9075(3)
C _(8a)	9561(3)	1286(3)	8646(2)
C _(8b)	10560(3)	801(3)	7842(2)
C ₍₉₎	7215(3)	3726(3)	11430(3)
C ₍₁₀₎	7996(4)	3113(4)	12480(3)
C ₍₁₁₎	5447(3)	1973(4)	11477(3)
C ₍₁₂₎	4364(4)	2652(5)	10677(4)
C ₍₁₃₎	8789(3)	1154(3)	6273(2)
C ₍₁₄₎	8351(3)	-49(3)	6092(3)
C ₍₁₅₎	7026(3)	-179(3)	5873(3)
C ₍₁₆₎	6105(3)	893(4)	5829(3)
C ₍₁₇₎	6508(3)	2099(3)	6007(3)
C ₍₁₈₎	7840(3)	2233(3)	6224(3)
C ₍₁₉₎	11793(3)	3395(3)	5007(2)
C ₍₂₀₎	13189(3)	3759(3)	4838(3)
C ₍₂₁₎	13875(3)	4426(3)	3678(3)
C ₍₂₂₎	13193(4)	4729(3)	2725(3)
C ₍₂₃₎	11800(4)	4379(3)	2867(3)
C ₍₂₄₎	11121(3)	3712(3)	4013(3)
H ₍₁₎	1082(2)	66(2)	617(2)
H ₍₂₎	1044(2)	335(2)	644(2)
H _(2a)	1264(2)	146(3)	702(2)
H ₍₅₎	936(3)	356(3)	1005(2)
H ₍₇₎	647(3)	69(3)	1008(2)
H ₍₈₎	794(2)	-7(3)	882(2)
H _(8b)	1078(2)	-22(3)	823(2)
H _(9,1)	637(3)	416(3)	1162(2)
H _(9,2)	771(3)	449(3)	1076(2)
H _(10,1)	822(3)	394(3)	1276(3)
H _(10,2)	740(3)	247(3)	1305(3)
H _(10,3)	889(3)	292(3)	1220(3)
H _(11,1)	523(3)	207(3)	1230(3)
H _(11,2)	546(3)	90(3)	1171(2)
H _(12,1)	456(3)	246(3)	991(3)
H _(12,2)	433(4)	394(4)	1029(4)
H _(12,3)	369(3)	222(3)	1100(3)
H ₍₁₄₎	869(2)	-73(3)	615(2)
H ₍₁₅₎	677(3)	-102(3)	577(2)
H ₍₁₆₎	521(3)	80(3)	563(3)
H ₍₁₇₎	582(3)	288(3)	593(3)
H ₍₁₈₎	806(3)	302(3)	640(2)
H ₍₂₀₎	1368(2)	356(3)	551(2)
H ₍₂₁₎	1485(3)	462(3)	364(3)
H ₍₂₂₎	1360(3)	524(3)	193(3)
H ₍₂₃₎	1124(3)	467(3)	207(3)
H ₍₂₄₎	1026(2)	351(2)	410(2)

excited singlet state of the aminocoumarin [2], a concerted mechanism with retention of the trans configuration of the phenyl groups in the adducts is most likely for the [2 + 2]-cycloaddition. In this case the 2-phenyl group should occupy an exo position. This is confirmed by the similarity between the $^3J_{1,2}$ SSCC in the spectra of IV-VI and the analogous constant in the spectrum of the adduct of [2 + 2]-cycloaddition of trans-stilbene to indolizine [3], for which a trans orientation of the phenyl groups is proposed. In the case of an endo,exo orientation of the 1,2-phenyl groups certain other details in the PMR spectra of the investigated compounds, in particular, the broad signals of the 2-H and 8b-H protons in the spectrum of IV ($\Delta h_{1,2} \sim 2$ Hz), which attest to the development of a $^4J_{2,8}$ SSCC, and the absence of $^4J_{1,2a}$ SSCC in all cases, also become explainable. In any case, the PMR spectra of adducts IV-VI are similar and provide evidence for the monotypic structures of the synthesized compounds.

For the unambiguous determination of the orientation of the substituents in the cyclobutane ring we carried out an x-ray diffraction study of IV (see Table 3).

In the cyclobutane fragment of the IV molecule (Fig. 1) the phenyl ring attached to the C₍₁₎ atom is endo-oriented. This orientation of the substituents in the four-membered ring is similar to that found previously [2] in the adduct (VII) of 4-methyl-7-diethylaminocoumarin with styrene. The geometrical parameters of the tricyclic systems of the molecules of IV and VII actually coincide completely, and the differences that do exist are due to replacement of the substituents at the C₍₂₎ and C_(8b) atoms. The lengths of the C₍₁₎-C₍₂₎ [1.553(4) Å] and C₍₂₎-C_(2a) [1.558(4) Å] bonds and the C₍₂₎-C₍₁₎-C₍₁₃₎ bond angle [123.0(2)°] are somewhat increased in the IV molecule as compared with the VII molecule (1.537 Å, 1.540 Å, and 121.7°, respectively, in the VII molecule); this is evidently caused by the introduction of a bulky phenyl group in the 2 position. The small increase (to 34.1° as compared with 32.3° in VII) in the angle of bending of the four-membered ring along the C₍₁₎ ... C_(2a) line and (to 34.3° as compared with 32.8° for VII) along the C₍₂₎ ... C_(8b) line is probably associated with the same thing. The certain degree of increase in the C₍₁₎-C_(8b)-C_(8a) and C_(2a)-C_(8b)-C_(8a) bond angles is due to the absence in adduct IV, in contrast to VII, of a methyl group attached to the C_(8b) atom. Short intramolecular C₍₁₃₎...C_(8a) [3.149(4) Å] and C₍₁₃₎ ... C₍₈₎ [3.260(4) Å] contacts are retained in the IV molecule; however, as a consequence of the great degree of puckered character of the four-membered ring, they exceed the values found in VII by ~0.05 Å. In the heterocyclic part of the IV molecule (Table 4) the C_(2a) and C₍₃₎ atoms deviated from the plane of the remaining four atoms by 0.386(4) Å and 0.048(3) Å, respectively; thus, the conformation of the heteroring (a distorted sofa) is similar to that found in adduct VII.

The stereospecific formation of adducts IV-VI, which have a 1-endo-phenyl group, makes it possible to assume, as in the case of the cycloaddition of styrene [2], specific secondary reactions between the attacking molecule of stilbene and the coumarin fragment in the transition state. A different explanation, which is based on the existence of biradical intermediates, was set forth by Kaupp and coworkers [5] from the point of view of the cis effect. In order to evaluate the effectiveness of the cycloaddition of stilbene we measured the quantum yields of the examined reactions (Table 1). It was found that, as compared with the cycloaddition of styrene to coumarin II, the addition of stilbene takes place substantially faster; the presence of an electron-donor substituent in the 4 position accelerates the process appreciably (compare IV and V and VI). A possible explanation for this fact consists in the formation of a reactive exciplex with the participation of the ground state (S₀) of trans-stilbene, which acts as an acceptor, and the excited singlet state (S₁) of 7-aminocoumarin, which acts as an electron-donor component [6]. The photoreactions under consideration proceed through the excited singlet states of the 7-aminocoumarins; this is confirmed by our observed quenching of cycloaddition in the presence of triplet sensitizers (naphthalene, benzophenone, acetophenone, etc.), as well as added compounds that contain heavy atoms (CBr₄, CHBr₃). Similar principles are also valid for other similar [2 + 2]-cycloaddition reactions [7, 8], including the photoreactions of 7-aminocoumarins that we previously studied [9].

EXPERIMENTAL

The IR spectra of KBr pellets of the compounds were recorded with a Perkin-Elmer 577 spectrometer. The UV spectra of solutions in 2-propanol were obtained with a Hitachi EPS-3T spectrophotometer. The PMR spectra of solutions in CDCl₃ were obtained with a Bruker WM spectrometer (250 MHz) with hexamethyldisiloxane (HMDS) as the internal standard.

The syntheses of the adducts were carried out in 100-ml Pyrex reactors; the source of irradiation was a PRK-2 medium-pressure mercury lamp. The reaction mixtures were stirred with a stream of nitrogen and by means of a magnetic stirrer. Monitoring of the compositions of the reaction mixtures and the purity of the synthesized substances was accomplished by means of TLC on Silufol UV-254 plates by elution with hexane-acetone with development by UV light and iodine. The products were isolated by means of column chromatography with columns (35 × 2.5 cm) packed with Silpearl UV silica gel by elution with hexane-acetone.

The differential quantum yields of the photochemical reactions were calculated in accordance with [10] and were determined for solutions of 7-aminocoumarins (80 mmoles/liter) and trans-stilbene (500 mmoles/liter) (or styrene for adduct VII) in 1,4-dioxane. The rate of accumulation of the products was determined by means of liquid chromatography with a Du Pont chromatograph and was simultaneously monitored with a Shimadzu CS-930 densitometer. In the determination of the quantum yields we used light with a wavelength of 370 nm obtained by means of a Shimadzu NGF-16 monochromator. The intensity of the source was determined by the method in [11] and was found to be I₀ = 5.62 · 10⁻¹⁰ ergs/sec.

The crystals for the x-ray diffraction study of IV were grown by slow evaporation of a solution of this compound in hexane-acetone. The transparent prismatic crystals of adduct IV (C₂₇H₂₇NO₂) were triclinic and had the following parameters at 20°C: a = 9.794(1), b = 9.956(1), c = 12.242(1) Å, α = 68.01(1)°, β = 82.39(1), γ = 88.15(1), Z = 2, space group P $\bar{1}$. The cell parameters and the intensities of 3660 independent reflections, 3384 of which, with I ≥ 2σ(I), were used in decoding and

refining the structure, were measured with a Hilger-Watts four-circle diffractometer ($\lambda_{\text{Mo K}\alpha}$, graphite monochromator, $\theta/2\theta$ scanning, $\theta \leq 28^\circ$). The structure was decoded by the direct method and was refined by the total-matrix method of least squares within the anisotropic approximation for all of the nonhydrogen atoms. All of the hydrogen atoms were revealed from the differential series and were then refined isotropically. The final divergence factors $R = 0.055$ and $R_w = 0.060$. All of the calculations were made with an eclipse S/200 computer by means of INEXTL programs [12].

General Method for Obtaining Adducts IV-VI. A mixture of 5 mmoles of the corresponding 7-aminocoumarin and 50 mmoles of trans-stilbene in 100 ml of 1,4-dioxane was irradiated for 8-10 h until the starting coumarin had disappeared virtually completely. The dioxane was evaporated in vacuo, and the residue was chromatographed. The fractions that contained the desired product were evaporated slowly at reduced pressure while avoiding pronounced overheating of the solution. The precipitated crystals were removed by filtration and, when necessary, recrystallized from hexane-acetone.

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