Table II

Substrate	Reaction time, hr.	Product[a]	Mp, °C	Yield, %[b]
1b	48	7	188.5–190	58
1c	48	7		45
1d	48	7		57
5a	20	7a	203–204	57, 62[c]
5b	20	7b	209.5–210.5	24, 39[c]
5c	27	7c	226–227	21, 24[c]
8	20	9	269–270.5	35, 43[c]

[a] Satisfactory analyses (±0.4% for C, H, N) were reported for compounds **7**, **7a–c**, and **9**: Ed. [b] Based upon substrate. [c] Based upon unrecovered substrate.

oped that allowed conversion of **7** to the corresponding 2-amino-4(3*H*)-quinazolinone (**10**) in 86% yield.

Experimental Section

Melting points were taken on a Fisher-Johns melting point apparatus and are uncorrected. Nuclear magnetic resonance spectra were obtained on a Jeol C60HL spectrometer. Infrared spectra were obtained on a Perkin-Elmer Model 257 spectrophotometer. The mass spectrum was obtained with a Hitachi Perkin-Elmer RMU-6E spectrometer. The ultraviolet spectrum was obtained on a Unicam SP-800B spectrophotometer. Microanalyses were performed by Galbraith Laboratories, Knoxville, Tenn. The dimethylformamide (DMF) used as solvent was reagent grade and was stored over 4A molecular sieves (Linde). The benzoylcyanamide[7] was recrystallized from benzene/petroleum ether (30–60) and had a melting point of 139–40° dec (lit.[7] 143°).

Synthesis of 7, 7a–c, and 9. Two millimoles of the amino ester, acid, or amide were dissolved in 10 ml of DMF and benzoylcyanamide (146 mg, 1 mmol) was added. The solution was stirred and heated at 90–95° for 5 hr, then an additional 1 mmol of benzoylcyanamide was added and stirred until this portion had completely reacted (tlc). The solution was then concentrated (*in vacuo*) to a volume of 3–4 ml and poured into 5–10 ml of 95% ethanol, which was then poured into 35 ml of ice water. The mixture was stirred overnight, cooled, filtered, and washed with water. A further washing of the solid material with diethyl ether removed any of the unreacted substrates studied, which could then be recovered. The powdered material remaining was recrystallized from 70% ethanol (Norit). Analytical samples were recrystallized twice. Yields (based upon powdered material) and melting points are listed in Table II.

Hydrolysis of 7. Fifty milligrams of an analytical sample of **7** was heated on a steam bath with 3 ml of 0.5 *N* sodium hydroxide for 15 min. Complete dissolution required approximately 10 min. The solution was filtered hot (Norit), then allowed to cool, and acidified to pH 5.5–6.0 with acetic acid. The fine white powder (86%) was filtered, washed with water and ether, and dried *in vacuo*. Purification was achieved by dissolution in dilute alkali and reprecipitation with acetic acid. The uv spectrum of **10** (95% ethanol) was identical with that reported.[8]

Registry No.—**1b**, 87-25-2; **1c**, 118-92-3; **1d**, 88-68-6; **5a**, 6705-03-9; **5b**, 2941-78-8; **5c**, 4389-45-1; **7**, 52393-73-4; **7a**, 52393-74-5; **7b**, 52393-75-6; **7c**, 52393-76-7; **8**, 52393-72-3; **9**, 52393-77-8; benzoylcyanamide, 15150-25-1.

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(4) Reaction of 3-methoxyanthranilic acid gave an anomalous product whose analysis corresponded to $C_{24}H_{22}N_4O_6$, suggesting the product was derived from 2 equiv of the anthranilic acid and one equivalent of benzoylcyanamide. A complete structure proof has not been accomplished, because of the lack of additional structural evidence.

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Photochemical and Thermal Internal Cycloadditions in *retro*-γ-Ionylidenemalononitrile

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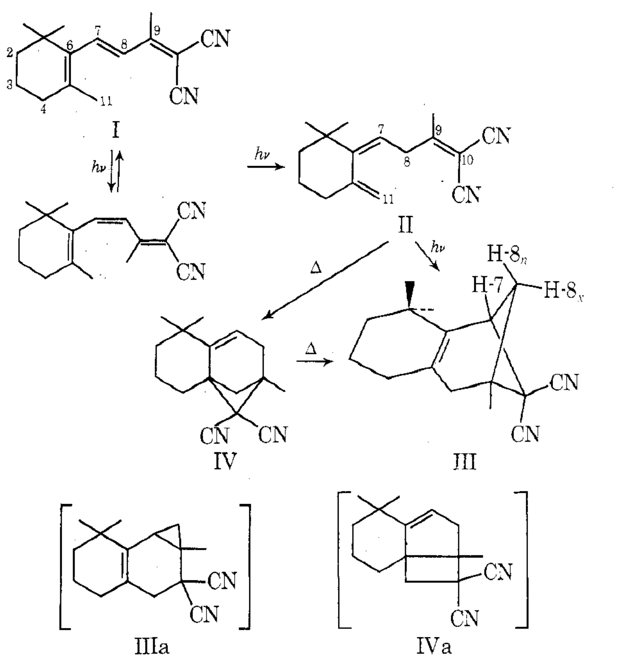
In connection with studies of hindered 7-cis isomers of retinal analogs,[1] we have reinvestigated reactions from direct irradiation of several dienes and trienes in this series. Similar to previous reports,[2] we observed in most cases primarily rapid, reversible geometric isomerization, electrocyclization (trienes), and irreversible 1,5-sigmatropic hydrogen migration products (dienes and trienes). Therefore, with a typical ionylidene derivative during the initial period of irradiation a mixture of 7,8 and 9,10 geometric isomers is produced,[2,3] along with less efficient formation of a cyclohexadiene, all of which eventually disappear to give the final product, a *retro*-γ-ionylidene derivative. However, in one instance we observed an additional secondary photoreaction and unexpected thermal rearrangements. These are described below.

retro-γ-Ionylidenemalononitrile (II) is the principal end product from direct irradiation of a dilute ether solution of β-ionylidenemalononitrile (I) when light of >360 nm (Corning 0-51 filter) is used. Upon further irradiation with light >290 nm (Pyrex filter) a new photoproduct is formed. The spectroscopic properties of the product, after its isolation by column chromatography (silica gel), suggest that it is formally an internal 4 + 2 cycloadduct, III.[4]



The mass spectrum of III shows that it is isomeric to I and II (*m/e* for M^+ 240). The compound is clearly not a cyclohexadiene because of the absence of vinyl hydrogens from its nmr and ir spectra. The pmr spectrum is in fact quite indicative of the structure. The three methyl groups (δ 1.17, 1.19, and 1.35) are now nonequivalent as expected for III. A broad singlet at δ 2.32, attributable to the allylic hydrogens at C-11, overlaps with a quartet (d of d) at 2.38. The latter (H-8_{exo}) is shown by double irradiation to couple with two single H's at 3.19 (d, J = 8.5 Hz, H-7) and 1.51 (d, J = 6.0 Hz, H-8_{endo}). This pattern of coupling is in agreement with compounds of a bicyclo[*n*.1.1] structure in which the bridgehead hydrogens are known to couple only with the exo hydrogen of the methylene bridge (endo hydrogen being orthogonally oriented to the bridgehead hydrogen).[5] The alternative 4 + 2, head-to-head adduct (IIIa), though also not containing any vinyl hydrogens, cannot account for this pattern of coupling of three hydrogens and also the H-11's would appear at a much lower field. Also, consistent with structure III, the ^{13}C nmr spectrum of the photoproduct shows the presence of two quaternary olefinic carbons at δ 140.4 and 129.3, two cyano carbons at δ 115.9 and 112.9, and three aliphatic quaternary carbons at δ 49.0 (C-9), 41.2 (C-1), and 19.2 (C-10) along with other methyl, methylene, and methine carbon signals. Finally, structure III also accounts for the peaks at *m/e* 121 and 62 in its mass spectrum. The cyclopropenyl cation formed by the loss of the cyclobutane ring and an allylic hydrogen probably corresponds to the 121 peak and the associated metastable peak should have a *m/e* 62.

This reaction appears to have some generality because in a similar manner 3,4-dehydro-I gives 3,4-dehydro-III as the only end product: nmr, three methyl singlets at δ 1.08, 1.11, and 1.47, three coupled H's at 1.66 (d, J = 10.0 Hz, H-8_{endo}), 2.58 (d of d, J = 5.0, 10.0 Hz, H-8_{exo}), and 3.44 (d, J = 5.0 Hz, H-7), a broad methylene singlet at 2.56, and a singlet for two vinyl H's at 5.28 ppm.

Upon heating to 100°, II rearranges to three products: I (5%), III (35%), and a new isomeric compound, IV (60%). The formation of I is in line with other *retro*-γ-ionylidene compounds.[6] The nmr spectrum of the major product shows the presence of methyl singlets at δ 1.17, 1.19, and 1.35, a complex group of signals for 6 H's between δ 1.4 and 2.0. Most indicative of the structure is the presence of a vinyl hydrogen (t, δ 5.74, J = 3.0 Hz) coupled with two H's at δ 2.42 and two coupled hydrogens at 1.61 (d, J = 9.0 Hz) and 1.91 (d). These features are only consistent with a structure from 2 + 2 internal cycloaddition of II. Of the two possible structures (IV and IVa) we favor the head-to-tail adduct IV because of the chemical shifts of coupled methylene hydrogens being too high for hydrogens adjacent to a dicyanomethylene group and more importantly upon heating to 180°, IV undergoes further rearrangement to III. From structure IV, 1,3 migration of the dicyanomethylene group gives III, while from IVa, there is no direct pathway to III.

The unusual photo and thermal chemical properties of II are probably associated with the dicyano group. That electrocyclic products are not formed in direct irradiation reaction must be due to the absence of a di-s-cis conformer necessary for cyclization due to unfavorable steric interaction.[3] The internal cycloadditions are probably associated with the electron deficient property of the 9,10 double bond. It is interesting to note that the directions of addition (4 + 2 or 2 + 2) for the major products in thermal and photochemical reactions are opposite to those normally encountered in cycloaddition reactions. At this time it is not clear whether these cycloadditions are from concerted or stepwise processes. If concerted, the photochemical and thermal reactions must have proceeded by way of $_{\pi}4_s + {}_{\pi}2_a$ ($_{\pi}4_a + {}_{\pi}2_s$) and $_{\pi}2_s + {}_{\pi}2_a$ additions.[7] Such mechanistic and stereochemical questions can be answered with compounds of defined stereochemistry at C-9 and C-10.

Experimental Section

All pmr spectra were recorded on a Varian HA-100 spectrometer and cmr spectra on a Varian XL-100 spectrometer. Deuterated chloroform was used as solvent and TMS as internal standard.

***retro*-γ-Ionylidenemalononitrile (II).** A 10% ether or chloroform solution of β-ionylidenemalononitrile (I)[1b] was sealed in a Pyrex test tube and irradiated with a 200-W Hanovia medium pressure mercury lamp equipped with a Corning 0-51 filter. Progress of reaction was followed by nmr. After 2 days the reaction was complete. The major product was identified as the *retro*-γ-triene II by its nmr spectrum: 1 H (t, J = 7.0 Hz) at 4.90 ppm coupled with 2 H's at 3.19; two additional vinyl hydrogens at 4.48 and 4.98 ppm. Another minor product was also present in the irradiation mixture. The compound, however, was not isolated nor identified. Conditions of photochemical and thermal reactions of II are described in the text.

3,4-Dehydro-β-ionylidenemalononitrile. In 200 ml of CCl_4, 24 g of I was allowed to react with 17.8 g of NBS with 0.5 g of benzoyl peroxide. The nmr spectrum of the product agreed with that of 4-bromo-β-ionylidenemalononitrile. The crude product was allowed to react with a mixture of *N,N*-dimethylaniline (70 ml) and pyridine (30 ml) at 95°. After the usual work-up, the crude product was purified by column chromatography (silica gel with benzene as solvent). The overall yield of 3,4-dehydro-β-ionylidenemalononitrile is 50%: ir (film) 2220, 970, and 730 cm^{-1}; nmr δ 1.12 (s, 6 H), 1.96 (s, 3 H), 2.32 (s, 3 H), 5.92 (s, 2 H), 6.90 (d, J = 16 Hz, 1 H), 7.14 (d, 1 H).

Conditions for photochemical reactions of the tetraenenitrile are similar to those described for I.

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Registry No.—I, 52699-42-0; 3,4-dehydro-I, 52665-36-8; II, 52665-37-9; III, 52665-38-0; 3,4-dehydro-III, 52665-39-1; IV, 52665-40-4; 4-bromo-β-ionylidenemalononitrile, 52665-41-5.

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Biological Probes. II. Ring Labeled Nicotinamide

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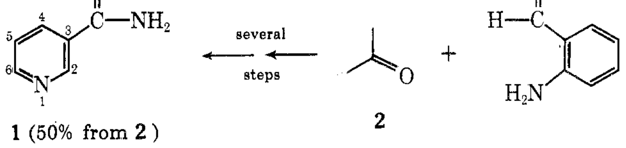
A growing interest in nonradioactive labels for use as general biological probes has led us to the development of efficient methods for the preparation of ring labeled nicotinamide (1). Previously we had described a high yield, six-step synthesis of $^{13}C_6$-amide 1 starting with carbon-13 labeled acetone.[1] We now wish to report a versatile labeling



1 (50% from 2)

2