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Michael Addition, Isomerization and Derivatives of 2-Carboxamido-3,4-trimethylene-1-indenone[1]

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In two recent papers (8,9) we have discussed the synthetic utility of Michael addition of cyanide ion to indenones, and have noted that other Michael reagents add quite well to 2-carboxamido-3-phenylindenone (9). Among these reagents were nitromethane, acetone, malononitrile, bisulfite and hydroxide ion. The addition of cyanide ion to 2-carboxamido-3, 4-trimethyleno-1-indenone (2, Scheme 1), has led to a variety of interesting compounds (5,6,10,11). We wish to report here the results of attempted addition of other Michael reagents to compound 2.

We have shown that β-substituted α-cyanocinnamonitriles can be cyclized in concentrated sulfuric or polyphosphoric acids to indenones, indanones, or mixtures of these, the product depending on the nature of the β-substituents (2,6,7). Cyclization of β-substituted α-cyanocinnamonitriles which do not have a γ-hydrogen atom, such as the β-phenyl or β-*t*-butyl analogs, produce only colored indenones, such as 3-phenyl or 3-*t*-butyl-2-carboxamidoindenones (2,6). Cyclization of ylidenemalononitriles having a γ-hydrogen, as for example 2-cyano-3-isopropylcinnamonitrile, gives a mixture of about one part of colored endocyclic double-bonded indenone, 3-isopropyl-2-carboxamindoindenone, to two parts of white exocyclic double-bonded isomer, 3-isopropylidene-2-carboxamido-1-indanone (6). There is a departure from the above pattern for ylidenemalononitriles with a γ-hydrogen when the β-substituent is part of a fused carbocyclic ring. Cyclization of α-tetrylidenemalononitrile (1a, Scheme 1) yields only the yellow 2-carboxamido-3, 4-trimethyleno-1-indenone (2); whereas 1-benzosuberylidenemalononitrile (1b) gives only the white indanone 3 (7). The formation of only one of two possible double-bond isomers in the cyclization of 1a and 1b is attributed to competing forces: conjugation, which favors the indenone structure, and steric strain, which favors the indanone form.

Discussion

In a continuation of studies of the Michael addition to indenones (9), attempts were made to add acetone to 2-carboxamido-3,4-trimethyleno-1-indenone 2, using various basic catalysts, such as sodium hydroxide, sodium ethoxide or potassium τ-butoxide. Although colorless solutions were obtained, work-up in the usual way resulted in recovered yellow indenone 2. Addition of sodium hydride to an acetone solution of 2, followed by quenching with acid over ice, produced a light beige compound which could be collected and dried. The infrared spectrum of this compound was similar to that of 2, except for a change in relative intensity and wavelength of the two carbonyl bands, indicating conversion to a non-conjugated ketone, and the disappearance of a conjugated olefinic band. Attempts to recrystallize this compound from ethanol or ether produced a yellow solution on warming, from which 2 recrystallized in high yield. When heated in a capillary tube, the compound went through a phase transition with concomitant color change to yellow-orange between 160-170°, and finally melted at 200-202°, as did a sample of 2 heated concurrently. This compound is therefore the previously unknown unsaturated indanone 4, formed by removal of the vinylogously activated γ-hydrogen of 2 by the acetone anion, to give the resonance-stabilized anion of 4, situated between

three trigonal carbon atoms. Quenching this ion in cold acid produces 4, which reverts to the thermodynamically more stable indenone 2 when heated.

To prove the intermediacy of the carbanion of 4, a trapping experiment was conducted by adding methyl iodide to the colorless solution of 2 and sodium hydride in acetone. The product isolated was the expected 2-methyl-2-carboxamido-4,5-dihydroacenaphthen-1-one, 5a. It exhibited a characteristic ultraviolet spectrum of indanone systems of this type (2,7), as well as the expected pmr characteristics.

In view of the ease with which compound 2 was converted to 5a, further studies on the rearrangement and alkylation of 2 were conducted using various alkylating agents in different solvents. The general procedure consisted of treating 2 with sodium hydride in a solvent. After evolution of hydrogen, an excess of a particular alkyl halide was added to the mixture. The products were isolated by diluting the reaction mixture with water and removing the excess alkyl halide on a steam bath. The product precipitated or was collected by chloroform extraction. Unreacted starting material (2) remained in the basic solution.

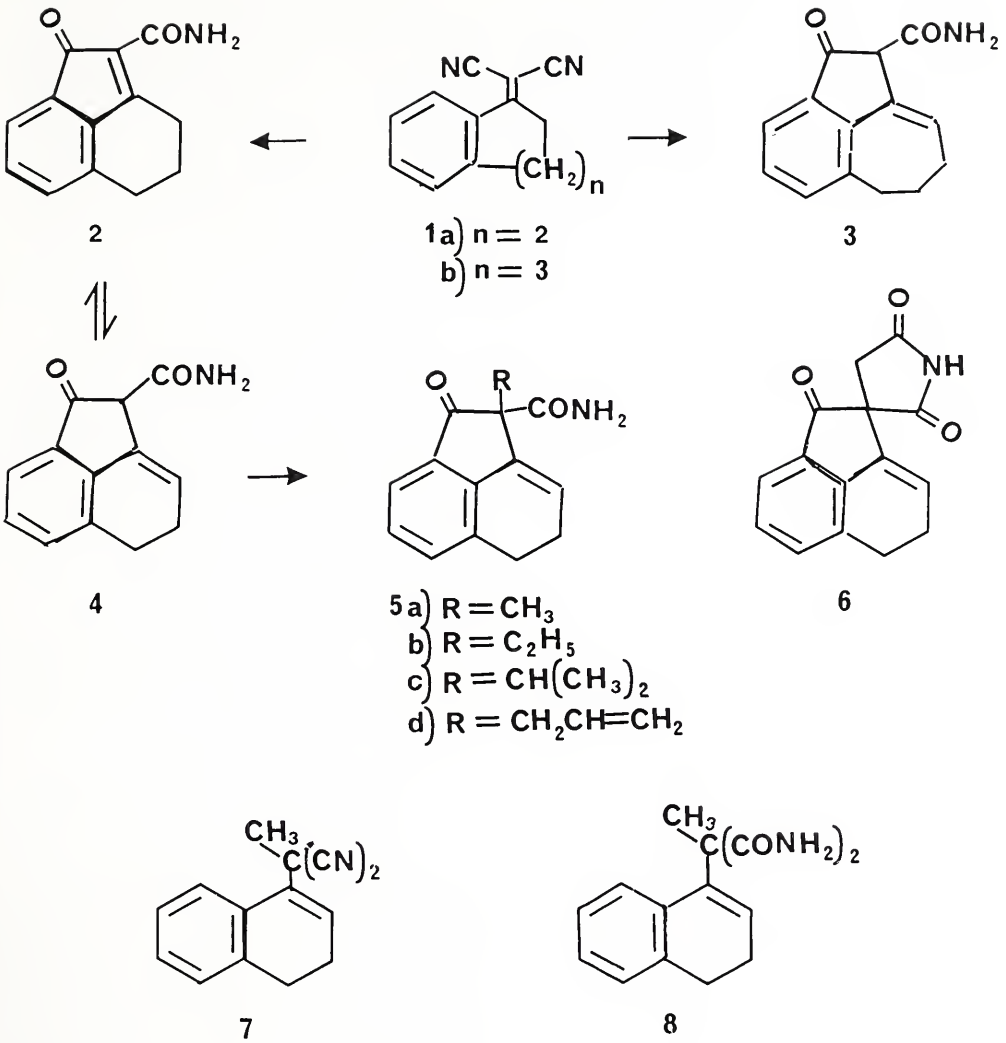
This procedure led to a series of compounds of the general structure 5, except where the alkylating agent was bromoacetate. In this case the product isolated was the spirosuccinimide 6. Compound 6 is formed, following alkylation, by an intramolecular cyclization between the newly introduced carbethoxy group and the carboxamide function. The rearranged alkylated products were characterized by elemental analyses and spectral properties. Certain spectral features are common to all these compounds: 1) the pmr shows a characteristic vinyl triplet (J = 4 cps) between δ 6.4 and 6.0; 2) the infrared spectra exhibit two sharp carbonyl peaks at 5.89 (ketone) and 5.99μ (amide), but 6 shows typical imide absorption at 5.62 and 5.86μ; 3) the ultraviolet spectra have the characteristic unsaturated indanone absorption pattern (2,7) with maxima between 245-248 mμ and shoulders at 255 and 280 mμ.

The alkylation of 2 with primary alkyl halides, such as methyl iodide, ethyl bromide or allyl bromide, appeared to be relatively solvent independent, and the anticipated products 5a, 5b and 5d were obtained in roughly equivalent yields using tetrahydrofuran (THF), dimethylsulfoxide (DMSO) or acetone. However, alkylation with the secondary alkyl halide, isopropyl bromide, seemed to be solvent dependent. Thus 5c was formed in good yield in DMSO, but when the reaction was carried out in THF, 5c was obtained in only 2% yield, and acidification of the mother liquor gave starting compound 2 in 75% recovery. In acetone, only starting material was recovered. The anomalous behavior displayed in the alkylation with isopropyl bromide was undoubtedly due to increased steric hindrance to the approach of the carbanion of 4 to the secondary halide site. The success of this alkylation in DMSO can be attributed to the enhanced reactivity exhibited by carbanions in the solvent (12).

One other distinction was observed with the isopropyl derivative 5c. The pmr spectrum showed the methyl groups of the isopropyl group as two sets of doublets (each coupled with CH) at δ 1.00 and 0.80 (J = 7 cps). The magnetic nonequivalence of the methyl groups arises from the fact that they are attached to a carbon atom adjacent to an asymmetric center. Thus even with free rotation the two methyl groups are in dissimilar chemical environments and have different chemical shifts.

As stated above, compound 5a was synthesized by a two-step process from compound 1a, by first cyclization to 2 and then rearrangement and methylation to 5a. An alternate route to 5a was envisoned by reversing this sequence. Treating 1a with sodium hydride in DMSO or THF gave the desired rearranged methylated product 7 in good yield. The structure of 7 was confirmed by its pmr spectrum, which showed a vinyl triplet at δ 6.33 (J = 4 cps) and a methyl singlet at δ 2.01. Attempted cyclization of 7 with either sulfuric or polyphosphoric acid were unsuccessful. In sulfuric acid only water-soluble products, probably sulfonated derivatives of 7, were formed. In polyphosphoric acid,

Scheme 1

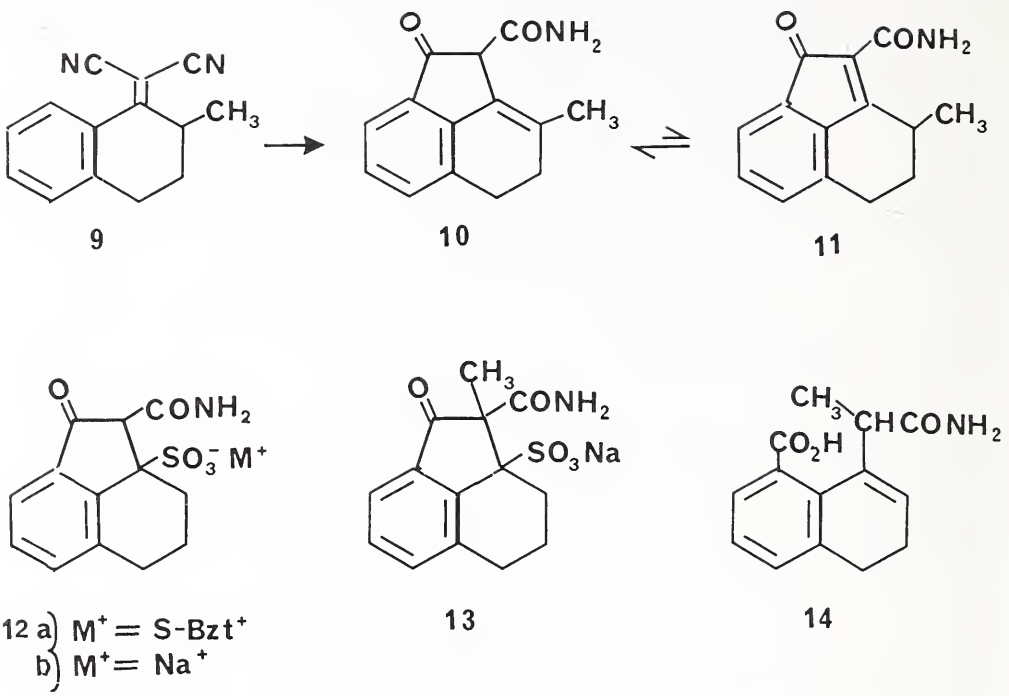


the only product, in low yield, was the diamide 8. The failure of 7 to cyclize under normal cyclizing conditions (7) is analogous to results of Campaigne and Roelofs (4) who were unable to cyclize most saturated malononitrile derivatives. They found that a conjugated double bond system which holds a nitrile group in close proximity to the aromatic ring is required for cyclization.

In order to compare the properties of the 2-methyl derivative 5a with those of its isomer, 2-carboxamido-3-methyl-4,5-dihydroacenaphthen-1-one (10, Scheme 2) we synthesized compound 9, 2-methyl-1-tetrylidenemalononitrile, from 2-methyl-1-tetralone by condensation with malononitrile. As has been noted earlier (3) the usual condensation in refluxing benzene (15) was unsuccessful, but when isopropanol was used as the solvent, this hindered ketone condensed quite well to give 9. There is a distinct difference in the ultraviolet spectra of the two isomers, 7 and 9. Compound 7 shows λ max at 260 mμ ($\epsilon = 6{,}600$) while 9, having the conjugated double-bond system, has λ max at 309 mμ ($\epsilon = 16{,}700$) (2).

Treatment of 9 with concentrated sulfuric acide produced a pale yellow product,

Scheme 2



which did not melt sharply, but had the characteristics of compound 10, as shown by elemental analysis, and the presence of a methyl singlet at δ 1.87 and a methine singlet at δ 4.10 in the pmr spectrum. The isomer, 11, should have a methyl doublet and a split methine proton. The ultraviolet pattern also exhibited the typical indanone pattern quite similar to that of 5a. However, other characteristics indicate that 10 exists in a rapid tautomeric equilibrium at room temperature with a very small percent of 11. The compound is not white, but possesses a slight yellow tinge. Soxhlet extraction of the crude product with diethyl ether, a procedure used to separate yellow indenones from white indanones (2), failed to remove the color. Six recrystallizations from ethanol also failed to decolorize the product, and the melting point range was not narrowed. The compound became deeper yellow as the temperature increased, and melted with decomposition. A thin layer chromatograph of 10 on silica gel gave a yellow band, $R_f = 0.375\text{-}0.50$, eluted with chloroform, but attempted resolution of this band with other solvents was unsuccessful.

Isolation of indanone 10 as the cyclized product from 9 may seem surprising at first glance, since a similar cyclization of 1a (Scheme 1) gives only idenone 2. Although 2 could be converted to the isomeric indanone 4, it was unstable and easily reverted to 2. The change in order of stability between the α, β-unsaturated isomer and the β, γ-unsaturated isomer, produced by the introduction of the γ-methyl group, can be accommodated within the earlier discussion of relative stabilities in the unsaturated 6,6,5-ring system. The greater stability of 2 in comparison to 4 was attributed to the fact that conjugation of the double bond with the ketone and amide carbonyls is of higher energy than steric strain imposed by placing the double bond in the five-membered ring. The introduction of the γ-methyl group brings in a third influence, hyperconjugation of the methyl group with the double bond, which will favor the β, γ-isomer. This is in accord with studies of aliphatic α, β- and β, γ-unsaturated ketones, in which it was found that

introduction of a γ-methyl group into the system shifted the equilibrium toward the β, γ-isomer (13).

Addition of non-carbon nucleophiles to 2 was relatively unsuccessrul. In attempts to add thiocyanate, cyanate, or amines, starting material were recovered in high yield. However, addition of the neutral nucleophile, sodium bisulfite, followed by treatment with S-benzylisothiuronium chloride produced the salt of the corresponding 3-sulfonic acid, 12a (Scheme 2). The corresponding sodium salt (12b) was also obtained by evaporation of a solution of 2 and sodium bisulfite in 50% ethanol. Acidification of a solution of 12b in water led to the isolation of 2, *via* a retro-Michael reaction. In order to prevent the retro-Michael reaction, 12b was converted to the methylated derivative 13 by treating 12b with sodium hybride followed by methyl iodide. However, 13 was also unstable in acid solution, giving 5a.

When indenone 2 was treated with sodium hydroxide in ethanol, followed by methyl iodide, the product obtained after acidification was 2- (8-carboxy-3,4-dihydro-1-naphthyl) propanoamide (14). Indenone 2 had been shown to give 8-carboxy-3,4-dihydro-1-naphthylacetic acid on refluxing aqueous alcholic sodium hydroxide (1) and more recently 3a,4,5,6-tetrahydrosuccinimido [3,4-b) acenaphthen-10-ones substituted at the 10a-position were shown to undergo fascile acid cleavage (8). When a solution of 5a in ethanol was treated with sodium hydroxide at room temperature, it was converted in nearly quantitative yield to 14. This suggests that 5a was an intermediate in the formation of 14 from 2. This may have occurred *via* addition of hydroxide ion to 2, followed by alkylation and elimination of water to form 5a. Indeed, hydroxide has been shown to add to such indenones (9). However, the strong base may have merely deprotonated 2, forming the more stable anion of 4, which was then alkylated and cleaved by excess alkali to give 14.

Experimental

All melting points were determined in open capillary tubes with a Mel-Temp heating block and are corrected. Microanalyses were performed by Midwest Microlab, Inc., Indianapolis, IN. Infrared spectra were determined in potassium bromide disks with a Perkin-Elmer Model 137 Infracord, and were calibrated with polystyrene. Ultraviolet spectra were determined in 95% ethanol with a Bausch and Lomb Spectronic 505 Recording Spectrophotometer. Nuclear magnetic resonance spectra were obtained with a Varian A-60 spectrometer in indicated solvents using tetramethylsilane as an internal standard.

2-Carboxamido-4,5-dihydroacenaphthen-1-one (4).

To a mixture of compound 2 (2) (1.95 g, 9.1 mmoles) in acetone (150 mL) was added sodium hydride (0.55 g of 53.7% NaH in mineral oil, 12.5 mmoles) and the mixture was stirred at room temperature for 30 min. The solution was poured onto 500 mL of cracked ice and the resulting clear solution was acidified with 20% sulfuric acid. The resulting light beige compound was collected by filtration to give 1.80 g (92.5%) of 4. Attempted recrystallization of this compound from 95% ethanol led to the isolation of indenone 2 as shown by color (yellow-orange), melting point and congruent infrared spectrum. When a sample of 4 was heated in a capillary tube, the compound underwent a phase transition between 160-170° with concomitant color change to yellow-orange. At this point this sample could not be differentiated from a sample of 2 heated at the same time; both compounds melted at 201-203°. The infrared spectrum of 4 shows peaks at 2.90, 3.00 and 3.10 (NH), 3.40 (CH), 5.90 (C=O) and 6.00 μ ($CONH_2$). Compound 4 lacks a strong band at 14.4μ which is present in the spectrum of 2. Also in 4, the amide carbonyl is more intense than the ketone carbonyl. The reverse is observed in 2.

2-Carboxamido-2-methyl-4,5-dihydroacenaphthen-1-one (5a).

Sodium hydride (1.5 g of 53.7% NaH in mineral oil, 33.5 mmoles) was slowly added to a mixture of compound 2 (4.0 g, 18.7 mmoles) in acetone (100mL) in an Erlenmeyer flask fitted with a drying tube (Drierite). This addition was followed by rapid evolution of hydrogen. The suspension was stirred at room temperature for 1 hr and then treated with methyl iodide (10 mL). The solution became clear after 30 min and after 18 hr contained a white precipitate. The mixture was then diluted with water (250 mL) and the excess alkyl halide and acetone were removed on a steam bath. The solution was cooled and the precipitate was collected by filtration to give 4.4 g (100%) of crude product, melting at 181-188°. Recrystallization from 95% ethanol, after treatment with activated charcoal, yielded white crystals: mp 200-202°; ir 2,90 and 3.14 (NH), 3.40 (CH), 5.89 (CO), 5.99 ($CONH_2$), and 6.29 μ (phenyl); uv (λ max) 245 (ϵ 21,900), 255-260 (shoulder, ϵ 17,100), and 280 mμ (shoulder, ϵ 6,820); pmr (DMSO-d_6) δ 7.45 (3H, multiplet, aromatic), 7.1 (2H, broad singlet, $CONH_2$), 6.01 (1H, triplet, J = 4 cps, vinyl), 3.00-2.50 (4H, multiplet, methylene), and 1.48 (3H, singlet, methyl).

Anal. Calcd for $C_{14}H_{13}NO_2$: C, 74.01; H, 5.73; N, 6.26. Found: C, 73.94; H, 5.85; N, 6.16.

Compound 5a was also prepared using THF as solvent. After evaporation of the excess alkyl halide and THF, the desired product precipitated on cooling the solution, and was collected by filtration to give 62.4% of material melting at 190-194°, with an infrared spectrum identical with that of 5a above.

Compound 5a was also prepared using η-butyl lithium (1.6 M in hexane, Foote) as the base and dry dioxane as the solvent. Isolation of the product as above gave 77% of material, melting at 191-194°, with an infrared spectrum identical to compound 5a.

2-Carboxamido-2-isopropyl-4,5-dihydroacenaphthen-1-one (5c).

Sodium hydride (0.75 g of 53.7% NaH in mineral oil, 17.2 mmoles) was added to a suspension of compound 2 (2.13 g, 10 mmoles) in DMSO (50 mL). The solution was stirred at room temperature until evolution of hydrogen ceased. After 30 min isopropyl bromide (5 mL) was added and the reaction was maintained at room temperature for 48 hr. The solution was diluted with water (350 mL), the excess alkyl halide removed on a steam bath, the solution cooled, and the product collected by filtration to give 1.95 g (76.5%) of material, melting at 175-180°. Recrystallization from 95% ethanol, after treatment with activated charcoal, gave an analytical sample: mp 185.5-187°; ir 2.90 and 3.14 (NH_2), 3.37 broad (CH), 5.89 (CO), 5.99 ($CONH_2$) and 6.29μ (phenyl); uv (λ max) 248 (ϵ 21,300), 256-260 (shoulder, ϵ 16,800), and 280 mμ (shoulder, ϵ 7.110); pmr ($CDCl_3$) δ 7.5-7.1 (3H, multiplet, aromatic), 6.95 and 6.10 (1H, each, broad singlet, $CONH_2$), 6.37 (1H, triplet, J = 4 cps, vinyl), 3.15-2.30 (5H, multiplet, aliphatic), 1.00 (3H, doublet, J = 7 cps, methyl), 0.80 (3H, doublet, J = 7 cps, methyl).

Anal. Calcd for $C_{16}H_{17}NO_2$: C, 75.29; H, 6.66; N, 5.49. Found: C, 75.01; H, 6.79; N, 5.73.

Attempted preparation of compound 5c in THF afforded 2% of the anticipated product and acidification of the aqueous phase led to the isolation of starting indenone 2 in 76.5% recovery, while the reaction in acetone led only to the isolation of starting indenone 2 (63%), as evidenced by congruent melting points and infrared spectra.

2-Carboxamido-2-allyl-4,5-dihydroacenaphthen-1-one (5d).

Sodium hydride (0.52 g of 50% NaH in mineral oil, 10.8 mmoles) was carefully added to a suspension of compound 2 (2.13 g, 10 mmoles) in THF (30 mL) in a Erlenmeyer flask fitted with a drying tube (Drierite). The mixture was stirred at room temperature for 1 hr, after which allyl bromide (5 mL) was added and the mixture stirred at room temperature for 24 hr. The solution was then diluted with water (200 mL), ex-

cess alkyl halide and THF were removed on a steam bath, and the aqueous phase extracted with three 200 mL portions of chloroform. The chloroform layer was dried (magnesium sulfate), treated with activated charcoal, filtered, and concentrated at reduced pressure. The resulting oil crystallized from ethyl acetate-cyclohexane to give 5d (1.60 g, 63%), melting at 103-104°. Recrystallization from ethyl acetate-cyclohexane gave an analytical sample, mp 105.5-106.5°: ir 2.82 (NH), 3.18 (NH), 5.90 (CO), 5.99 ($CONH_2$), and 6.27 μ (phenyl); uv (λ max) 247 (ϵ 21,500), 256-260 (shoulder, ϵ 17,300), and 280 mμ (shoulder, ϵ 6,330); pmr ($CDCl_3$) δ 7.60-7.18 (3H, multiplet, aromatic), 6.75 (2H, broad singlet, $CONH_2$), 6.30 (1H, triplet, J = 4 cps, ring vinyl), 5.90-4.80 (3H, complex multiplet, vinyl side chain), 3.15-2.5 (6H, multiplet, methylene).

Anal. Calcd for $C_{16}H_{15}NO_2$: C, 75.89; H, 5.93; N, 5.53. Found: C, 75.97; H, 6.11; H, 5.49.

This compound was also prepared in acetone to give 41.5% of material, melting at 102-103.5°, possessing an infrared spectrum identical to the above.

Spiro [4',5'-dihydroacenaphthen-1'-one-2',3-succinimide] (6).

Sodium hydride (1.10 g of 50% NaH in mineral oil, 22.9 mmoles) was added to a suspension of compound 2 (4.26 g, 20 mmoles) in THF (100 mL) in an Erlenmeyer flask fitted with a drying tube (Drierite). The mixture was stirred at room temperature for 1.5 hr; then ethyl bromoacetate (3.67 g, 23.7 mmoles) was added and the mixture stirred an additional 100 hr. The solution was poured onto 500 g of ice and the oily solid was collected by filtration and recrystallized from 50% ethanol to give 1.20 g (23.7%) of product, melting 222-227°. Recrystallization from 50% ethanol gave an analyticsl sample of white plates: mp 229.5-231.5°; ir 3.15 (NH), 5.62 and 5.86 (imide CO), 5.80 (CO), and 6.28 μ (aromatic); uv (λ max) 246 (ϵ 20,000), 255-264 (shoulder, ϵ 15,200), and 280 mμ (shoulder, ϵ 5,700); pmr (DMSO-d_6) *ed* 7.42 (3H, multiplet, aromatic), 6.16)1H, triplet, J = 4 cps, vinyl), and 3.05-230 (6H, multiplet, methylene).

Anal. Calcd for $C_{15}H_{11}NO_3$: C, 71.15; H, 4.35; N, 5.53. Found: C, 70.91; H, 4.59; N, 5.44.

1-(1',1'-Dicyanoethyl)-3,4-dihydronaphthalene (7).

Sodium hydride (1.37 g of 50% NaH in mineral oil, 28.5 mmoles) was slowly added to a solution of 1a (5.3 g, 27.3 mmoles) in DMSO (25 mL) in an Erlenmeyer flask fitted with a drying tube (Drierite). The solution was stirred for 1.5 hr at room temperature. Methyl iodide (4.2 g, 2.95 mmoles) was then added and the solution stirred an additional 14 hr, poured into 200 mL of water and the resulting solid collected by filtration to give 5.2 g (91%) of 7, melting at 50-52°. Compound 7 was also prepared in an analogous fashion using tetrahydrofuran as solvent to give 80% of 7, mp 51-52°. Recrystallization from 50% ethanol afforded white crystals: mp 56-57°; ir 3.42 (CH) and 4.48μ (CN); uv (λ max) 212 (ϵ 13,700), 218 (ϵ 13,900), 225 (ϵ 20,400), and 260 mμ (ϵ 6,600); pmr ($CDCl_3$) δ 7.3 (4H, multiplet, aromatic), 6.33 (1H, triplet, J = 4 cps), 2.5 (4H, multiplet, methylene) and 2.01 (3H, singlet, methyl).

Anal. Calcd for $C_{14}H_{12}N_2$: C, 80.74; H, 5.81; N, 13,46. Found: C, 80.68; H, 5.89; H, 13.33.

1-(1',1'-Dicarboxamidoethyl)-3,4-dihydronaphthalene (8).

Compound 7 (2.08 g, 10 mmoles) was added to polyphosphoric acid (60 g) and stirred on a steam bath for 24 hr. The dark red resolution was poured into 500 mL of water and the resulting solid (1.0 g, 48%) was collected by filtration. The infrared spectrum of this compound showed that it was identical to starting material. The mother liquor was extracted with three 300 mL portions of chloroform. The chloroform was dried (magnesium sulfate), decolorized (Norit), and concentrated at reduced pressure.

The resulting oil was recrystallized from ethyl acetate-cyclohexane to give 0.58 g of white crystals (24%): mp 182-183°; ir 2.9-3.15 (broad, NH_2), 3.42 (CH), 6.00 ($CONH_2$), and 6.05 μ ($CONH_2$).

Anal. Calcd for $C_{14}H_{16}N_2O_2$: C, 68.87; H, 6.55; N, 11.47. Found: C, 68.85; H, 6.75; N, 11.38.

2-Methyl-1-tetrylidenemalononitrile (9).

2-Methyl-1-tetralone was prepared in 57% yield by the method previously reported (14), bp 95-100° (1.0 mm) [lit (14) bp 115-116° (2.5 mm)]: ir 3.41 (CH), 5.95 (CO) and 6.25μ (phenyl); pmr ($CDCl_3$) δ 7.76 (1H, multiplet, aromatic), 7.05 (3H, multiplet, aromatic), 2.81-1.32 (5H, multiplet, methylene) and 1.00 (3H, doublet, J = 7 cps, methyl). The condensation with malononitrile was accomplished following a modification of the method of Mowry (15), but replacing benzene with isopropanol as solvent. 2-Methyl-1-tetralone (22.5 g, 14.1 mmoles), malononitrile (20 g, 30 mmoles), ammonium acetate (2g), and acetic acid (5 mL) were refluxed in isopropanol (190 mL) for 24 hr. The solution was concentrated to dryness at reduced pressure and the solid was dissolved in chloroform, washed with water, dried (magnesium sulfate), treated with activated charcoal, and concentrated at reduced pressure on a rotary evaporator. The resulting oil was crystallized from 95% ethanol to give 12.3 g (42%) of 9, melting at 77-79°. Recrystallization from 95% ethanol gave an analytical sample: mp 84.5-85.5°; ir 3.41 (CH) and 4.52μ (CN); uv (λ max) 235 (ϵ 7,600) and 309 mμ (ϵ 16,700).

Anal. Calcd for $C_{14}H_{12}N_2$: C, 80.74; H, 5.81; N, 13.46. Found: C, 80.44; H, 5.90; N, 13.54.

2-Carboxamido-3-methyl-4,5-dihydroacenaphthen-1-one (10).

A solution of 9 (9.9 g, 50 mmoles) in 100 mL of conc. sulfuric acid was warmed on a steam bath to 60°, removed, and the temperature rose to 76° in 10 min. When the temperatures began to drop, the solution was heated to 80°, allowed to cool to 40° (1 hr) and then poured onto 1 Kg of cracked ice. After 24 hr the resulting solid (yellow-white) was collected by filtration to give 9.52 g (84.2%) of crude product, mp 196-201°. The product was subjected to Soxhlet extraction with diethyl ether. The yellow color was not removed from the material in the cup, and evaporation of the ether yielded a material identical to that in the cup as shown by infrared comparison. Six recrystallizations from 95% ethanol (Norit) afforded a yellowish-white material which showed a narrow band on tlc (silica gel) eluted with chloroform, R_f .375-.50. The compound partially melted at 200° and completely melted at 217-220° with decomposition. This material was assigned structure 10 based on the following spectroscopic properties, but the slight yellow color is attributed to a small amount of tautomer 11, which exists in equilibrium with 10: ir 2.92 and 3.15 (NH_2), 3.42 (CH), 5.88 (CO), 6.00 ($CONH_2$) and 6.28 μ (phenyl); uv (λ max) 246 (ϵ 15,100), 255-260 (shoulder, ϵ 11,400), 272-275 (shoulder, ϵ 8,800), and 284-287 mμ (shoulder, ϵ 5,100); pmr (DMSO-d_6) δ 7.80 (1H, broad singlet, amide), 7.33 (4H, multiplet, aromatic and amide), 4.10 (1H, singlet, methine), 3.10-2.25 (multiplet, methylene), and 1.87 (3H, singlet, methyl).

Anal. Calcd for $C_{14}H_{13}NO_2$: C, 74.01; H, 5.73; N, 6.17. Found: C, 74.10; H, 5.66; N, 6.13.

S-Benzylisothiuronium 2-Carboxamido-3,4-trimethyleno-1-indanone-3-sulfonate (12a).

A mixture of 2 (2.0 g, 9.4 mmoles), sodium bisulfite (2.0 g, 19.2 mmoles) in 100 mL of 50% aqueous ethanol was warmed on a steam bath until a clear amber solution was formed (5 min). The solution was concentrated to a volume of 50 mL on a hot plate under a stream of air, cooled in an ice bath, and the clear amber solution treated with

S-benzylisothiuronium chloride (9.4 mmoles) to give 2.85 g (66%) of a beige precipitate, mp 141-144°. Recrystallization from 50% ethanol afforded colorless crystals: mp 146-147°; ir 2.80 and 3.0-3.4 broad (H-bonding), 5.85 (CO), 5.99 ($CONH_2$), and 8.1-8.8 μ (SO_3).

Anal. Calcd for $C_{21}H_{29}N_3O_5S_2$: C, 54.90; H, 5.00; N, 9.15; S, 13.96. Found: C, 54.59; H, 4.99; N, 9.08; S, 13.77.

The sodium salt of the sulfonic acid could also be isolated; however, an analytical sample could not be prepared. Thus indenone 2 (33 g, 15.5 mmoles) and sodium bisulfite (19 g, 18.2 mmoles) were placed in 200 mL of 50% ethanol. The mixture was heated on a hot plate and concentrated to 50 mL. A chloroform extract of the clear amber solution was dried (magnesium sulfate), decolorized with Norit, and concentrated to dryness at reduced pressure to give 0.5 g of starting material. The aqueous phase was decolorized with Norit and concentrated to dryness at reduced pressure to give 47.5 g of sodium 2-carboxamido-3,4-trimethyleno-1-indanone 3-sulfonate (12b), mp 185-187° (dec). Acidification of a colorless solution of the sodium sulfonate salt 12b in water afforded a yellow solution from which indenone 2 was isolated. Recrystallization of 12b from 95% ethanol-THF (a small amount of undissolved material was removed by filtration) afforded white crystals: mp 187-188° with decomposition to an orange material which is undoubtedly indenone 2 formed by a retro-Michael reaction on heating; ir 2.8-3.4 (H-bonding), 5.80 (CO), 6.00 ($CONH_2$), and 8.2-8.6μ (broad SO_3).

A good elemental analysis could not be obtained for this compound.

Anal. Calcd for $C_{13}H_{12}NO_5SNa \cdot H_2O$: C, 46.50; H, 4.17; N, 4.17. Found: C, 45.87; H, 4.35; N, 4.00.

Sodium 2-Carboxamido-2-methyl-3,4-trimethyleno-1-indanone-3-sulfonate (13).

A solution of 12b (6.34 g, 20 mmoles) in dimethylformamide (50 mL) was treated with sodium hydride (1.20 g of 53% NaH in mineral oil, 27 mmoles) After 20 min methyl iodide (10 mL) was added and the reaction was kept at room termperature for 100 hr. The resuting solid was collected by filtration and washed with ether and chloroform to give 2.75 g (42%) of material which did not melt at 360°. The compound gave a positive test for sulfate with barium chloride, after digestion with nitric acid. The infrared spectrum exhibited peaks at 2.90 (NH), 5.90 (CO), 6.00 ($CONH_2$), and 8.2-8.65 μ (SO_3). The compound was soluable in water and upon acidification afforded 2.5 g (55%) of 5a, as evidenced by congruent infrared spectrum and melting point. The ether-chloroform solution was extracted with water, and acidification of the aqueous phase yielded an additional 0.5 g (11%) of 5a.

2-(8-Carboxy-3,4-dihydro-1-naphthyl)propanoamide (14).

A mixture of indenone 2 (1.4 g, 6.5 mmoles), 10% sodium hydroxide (10 mL) and 95% ethanol (15 mL) was stirred at room temperature until a homogenous amber-colored solution was obtained (30 min). Methyl iodide (5 mL) was added and the solution was stirred an additional 12 hr at room temperature. The reaction mixture was diluted with 200 mL of water, acidified to pH 3 with 20% sulfuric acid, and the excess methyl iodide was removed on a steam bath. The resulting solid was collected, yielding 1.18 g (74%) of 14, mp 190-192°. An analytical sample was prepared by recrystallization from 95% ethanol: mp 197.5-199°; ir 2.90 and 3.05 (NH_2), 3.30-4.00 (H-bonded COOH), 5.88 (COOH, 6.10 ($CONH_2$), and 6.30 μ (phenyl); uv (λ max) 263 (ϵ 7,500) and 305 mμ (ϵ 1,180); pmr (DMSO-d_6) δ 7.29 (3H, multiplet, aromatic), 6.68 (2H, multiplet, amide), 6.29 (1H, triplet, J = 4.5 cps, vinyl), 3.4 1H, quartet, J = 7 cps, methine) 2.8-1.9 (broad multiplet, obscured DMSO, methylene) and 1.21 (3H, doublet, J = 7 cps, methyl). This compound was soluble in sodium bicarbonate.

Anal. Calcd for $C_{14}H_{15}NO_3$: C, 68.55; H, 6.12; N, 5.71. Found: C, 68.75; H, 6.37; N, 5.81.

Compound 14 was also synthesized from 5a by the following procedure. A mixture of 5a (1.4 g, 6.2 mmoles), 10% sodium hydroxide (15 mL) and 95% ethanol (15 mL) was stirred at room temperature for 12 hr, then diluted with 200 mL of water and acidified to pH 3 with 20% sulfuric acid. The solid was collected by filtration to give 1.20 g (74%) of 14, as shown by identical infrared spectrum and melting point.

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Note

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