Reinvestigation of the Reaction of Coumalyl Chloride with Ammonia and Amines. α-Aminomethyleneglutaconic Anhydride: Structure and Properties

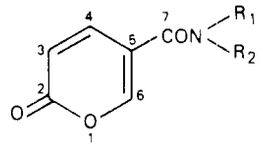
L. Tsai,* [1a] J. V. Silverton,[1b] and Howard T. Lingh[1c]

Laboratory of Biochemistry and Laboratory of Chemistry, National Heart, Lung and Blood Institute, National Institutes of Health, Bethesda, Maryland 20014

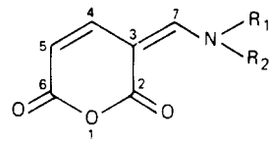
Received June 5, 1978

The reaction of coumalyl chloride with ammonia and amines has been reinvestigated. The product from the reaction with ammonia was deduced from spectroscopic data to be α-aminomethyleneglutaconic anhydride (**2a**) instead of coumalamide as previously reported. This structural assignment was confirmed by single-crystal X-ray analysis. The reaction with ethylenimine gave only a coumalamide derivative (**1b**), while aniline yielded both the amide (**1c**) and the anhydride (**2c**). Other amines, benzylamine, *tert*-butylamine, diethylamine, and pyrrolidine, gave only the corresponding N-substituted anhydrides as sole products. The reactivity of **2a** toward alkali, ammonia, and *tert*-butylamine has been studied.

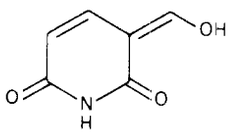
Among the derivatives of coumalic acid, the description of the amide has remained unclear in the literature.[2] von Pechmann[3] in 1901 described briefly a neutral compound, $C_6H_5NO_3$, mp 230–234 °C dec, obtained from coumalyl



1 a: $R_1 = H$, $R_2 = H$
b: $R_1-R_2 = (CH_2)_2$
c: $R_1 = H$, $R_2 = C_6H_5$



2 a: $R_1 = H$, $R_2 = H$
b: $R_1 = CH_2C_6H_5$, $R_2 = H$
c: $R_1 = C_6H_5$, $R_2 = H$
d: $R_1 = t\text{-}Bu$, $R_2 = H$
e: $R_1 = C_2H_5$, $R_2 = C_2H_5$
f: $R_1-R_2 = (CH_2)_4$



3

chloride and ammonia, for which he suggested the name "isocoumalinsäureamid" and the structure **2a.** In 1955, Wiley and Knabeschuh[4] reported coumalamide (mp 244–245 °C dec) (**1a**), but did not consider its possible identity with von Pechmann's "isocoumalinsäureamid". Wiley and co-workers[4,5] also described coumalamides derived from various amines and emphasized their characteristic UV absorption at 330–370 nm, which does not seem compatible with simple derivatives of coumalic acid (λ_{max} 290 and 245 nm). In view of this ambiguous situation concerning the structure of the coumalyl chloride–ammonia product, we decided to reinvestigate this problem. We report here the examination of a series of reaction products from coumalyl chloride and amines and show that they fall into two categories, distinguishable by their spectroscopic properties.

Results and Discussion

A. Coumalyl Chloride and Ammonia. Treatment of coumalyl chloride with concentrated ammonium hydroxide according to Wiley's procedure[4] gave a crystalline compound: mp 250–252 °C dec; *m/e* 139 (M^+, $C_6H_5NO_3$); λ_{max} (MeOH) 328 nm (ϵ 2.48 × 10^4). In the ^1H NMR spectrum in Me_2SO-d_6 (Table I), only two protons (δ 5.54 and 7.57) are coupled to each other (J = 9 Hz). These signals can be assigned to olefinic protons of an α,β-unsaturated carbonyl system, and the coupling constant of 9 Hz suggests a cis olefin. The broad signal at δ 9.24 is probably due to an intramolecularly bonded NH, and the δ 7.93 signal could be an aldehyde proton, a heteroaromatic ring proton, or a vinyl proton carrying an electronegative substituent. Upon exchange with D_2O, the signal at δ 9.24 disappears and the δ 7.93 signal sharpens. The ^1H NMR spectra of coumalic acid and its derivatives[6] (Table II) are recognizable by the three ring protons which are coupled to one another, resulting in three sets of doublets of doublets. Therefore, on the basis of the UV and ^1H NMR spectra (Table I), the coumalyl chloride–ammonia product cannot possess a coumalamide structure (**1a**) as suggested by Wiley et al.[4] Instead, the observed data can be accommodated by the isomeric structures **2a, 3,** or their possible tautomeric states. We favor structure **2a** over **3** because the compound does not give a color reaction with ferric chloride reagent. Indeed, von Pechmann[3] suggested structure **2a** for his "isocoumalinsäureamid", but he could not provide any proof of structure. In order to establish unambiguously this novel structure, α-aminomethyleneglutaconic anhydride (**2a**), we carried out a single-crystal X-ray analysis.

B. X-Ray Analysis. The structure was solved using MULTAN.[7] Standard refinement techniques,[8] with weighting following Peterson and Levy[9] and scattering factors as given in XRAY 72,[8] allowed recognition of all hydrogen atoms. The model was refined to an R factor of 0.037 (based on observed reflections) with isotropic thermal parameters for hydrogen atoms and anisotropic thermal parameters for all others. The atomic parameters are given in Table III, and the bond lengths and angles are shown in Figure 1.[10]

The molecule is very nearly planar, and, although significant on the χ^2 test, the deviations from planarity are very small. The deviations from the plane of the ring for O-8, O-7, C-9, and N-10 are −0.021, −0.003, +0.018 and −0.027 Å, respectively. Even H-110, attached to N-10, is only 0.115 Å out of the plane. The pattern of bond lengths essentially supports **2a** as the structure, but on the basis of the bond lengths there appears to be no formally single or double bonds apart from the C–O bonds. C_4–C_5 is longer than the expected value for a double bond, C_3–C_9 is comparable in length with an aromatic bond, and C_2–C_3 and C_5–C_6 are somewhat longer than aromatic bonds but by no means equal in length to single bonds. The C–N bond, 1.296 Å, has a length intermediate between that found in Schiff bases (ca. 1.26 Å)[11] and that found in pyridine (1.340 Å).[12] The general appearance of the molecule suggests a conjugated system extending over most of the molecule. The possibility that the crystal might be a disordered mixture of tautomers appears to be eliminated by consideration of the anisotropic thermal parameters and the fact that the hydrogen atoms could be refined without any difficulty.

It seemed worthwhile to investigate the unusual bonding quantum mechanically, and an INDO[13] calculation was car-

Table I. ^{1}H NMR[a] and UV Absorption of α-Aminomethyleneglutaconic Anhydrides

compd	H-4	H-5	$J_{4,5}$	H-7	$J_{7,NH}$	NH	other	λ_{max} MeOH, nm	$\epsilon \times 10^{-4}$	λ_{max} MeOH, nm	$\epsilon \times 10^{-4}$
2a	7.57 (d)	5.54 (d)	9.0	7.93 (s)		9.24		328	2.48		
2b	7.14 (d)	5.70 (d)	9.5	7.45 (d)	14		4.64 (d, J = 6 Hz, CH); 7.4, 7.2 (m each, phenyl)	338	3.47	347 (sh)	3.30
2c	7.26 (d)	5.83 (d)	9.3	7.89 (d)	13.7	11.36	7.4, 7.2 (m each, phenyl)	370	4.27	290	0.50
2d	7.18 (d)	5.66 (d)	9.5	7.50 (d)	15	9.91	1.45 (s, $C(CH_3)_3$)	337	4.14	345 (sh)	3.90
2e	7.45 (d)	5.68 (d)	10.0	7.89 (s)			1.36 (t, CH_3); 3.51 (m, CH_2)	355.5	3.80	282	0.70
2f	7.58 (d)	5.62 (d)	10.0	8.03 (s)			1.98, 2.16, 3.67, 3.75 (t each, $(CH_2)_4$)	357	3.16	287	0.60

[a] Chemical shifts are given in parts per million (δ) downfield from Me_4Si; J values are in hertz. Solvents are Me_2SO-d_6 for **2a** and $CDCl_3$ for **2b–f.**

Table II. ^{1}H NMR[a] and UV Absorption of Coumalate Derivatives

compd	H-3	H-4	H-6	$J_{3,4}$	$J_{3,6}$	$J_{4,6}$	other	λ_{max}, nm	$\epsilon \times 10^{-4}$	λ_{max}, nm	$\epsilon \times 10^{-4}$	solvent[c]
coumalyl chloride[b]	6.51	7.87	9.68	10.0	1.0	2.8		258	1.37	290 (sh)	0.29	C
								265	1.06			
methyl coumalate	6.38	7.82	8.38	10.0	1.0	2.5	3.90 (s, OCH_3)	245	1.08	286	0.45	M
1b	6.36	7.80	8.38	10.0	1.2	2.5	2.34 (s, $N(CH_2)_2$)	251	1.65	285	0.53	C
1c	6.38	7.75	8.17	10.0	1.5	2.5	7.16–7.52 (m, phenyl)	257	1.35	280 (sh)	1.16	M

[a] Chemical shifts are given in parts per million (δ) downfield from Me_4Si in $CDCl_3$; J values are in hertz. [b] From ref 5. [c] M = methanol; C = cyclohexane.

Table III. Atomic Parameters[a]

atom	x/a	y/b	z/c	U (11)	U (22)	U (33)	U (12)	U (13)	U (23)
O(1)	9 554 (3)	8 285 (1)	3 159 (1)	451 (6)	306 (5)	265 (5)	8 (4)	−71 (4)	−1 (4)
C(2)	7 910 (4)	7 601 (1)	2 424 (1)	373 (7)	302 (7)	264 (6)	33 (5)	−12 (5)	−14 (5)
C(3)	6 532 (3)	7 918 (1)	1 274 (1)	306 (6)	331 (7)	254 (6)	38 (5)	−9 (5)	3 (5)
C(4)	6 950 (4)	8 883 (1)	953 (1)	335 (7)	375 (8)	285 (6)	36 (6)	−34 (5)	50 (6)
C(5)	8 581 (4)	9 522 (1)	1 692 (1)	412 (7)	315 (8)	370 (7)	−4 (6)	−46 (6)	56 (6)
C(6)	9 977 (4)	9 229 (1)	2 846 (1)	366 (7)	316 (7)	335 (7)	3 (6)	−14 (6)	−4 (5)
O(7)	7 795 (3)	6 809 (1)	2 850 (1)	730 (8)	302 (6)	341 (6)	0 (5)	−89 (5)	44 (4)
O(8)	11 548 (3)	9 709 (1)	3 602 (1)	631 (8)	387 (6)	406 (6)	−86 (5)	−156 (5)	−22 (5)
C(9)	4 784 (4)	7 282 (1)	486 (1)	327 (7)	379 (8)	269 (6)	45 (6)	−8 (5)	−14 (5)
N(10)	4 354 (4)	6 381 (1)	659 (1)	501 (8)	348 (7)	354 (7)	1 (6)	−78 (6)	−40 (5)
H(4)	600 (4)	906 (1)	14 (2)	45 (4)					
H(5)	891 (4)	1 017 (1)	146 (1)	46 (5)					
H(9)	379 (4)	753 (1)	−26 (1)	36 (4)					
H(10	315 (5)	597 (1)	4 (2)	82 (7)					
H(110)	528 (5)	609 (1)	130 (2)	61 (6)					

[a] Atomic parameters are multiplied by 10^4 for C, N, and O and by 10^3 for H. U values for hydrogen are given in the column designated U (11). Hydrogen atoms are numbered to correspond to the atoms to which they are attached. The temperature factor used was

$$\exp[-2\pi^2(\sum_i\sum_j h_i h_j a_i^* a_j^* U_{ij})].$$

ried out to obtain Mulliken total overlap populations,[14] which are shown in Figure 2. Since such calculations are somewhat dependent on the method of calculation, several simple molecules of known geometry were also investigated and the results are given in Table IV to provide a basis for comparison.

The results appear to substantiate the crystallographic discussion based on bond lengths. C_4–C_5 has an overlap intermediate between that of benzene and that of a true double bond. C_2–C_3, C_3–C_4, and C_5–C_6 have overlaps slightly less than that in benzene, and C_3–C_9 is comparable with benzene. The value for the C–N bond is greater than that for pyridine and, in fact, intermediate between those calculated for a single and a triple bond. The carbonyl overlap populations are slightly less than that calculated for an isolated bond, and the C–O bonds of the ring have overlaps slightly greater than that calculated for methanol. It would seem that there is a small involvement of the oxygen atoms in the conjugated system. The small net partial negative charge on the nitrogen atom is also interesting.

The molecular packing is shown in Figure 3. The relatively high density of the crystals is probably a consequence of the network of hydrogen bonds. Both hydrogen atoms of the nitrogen atom appear to be involved in hydrogen bonds to O-8 atoms in different molecules. The N–O distances are 2.920 and 2.918 Å. There also appears to be an intramolecular hydrogen bond to O-7. The distances of H-110 to O-7 and O-8, 2.180 and 2.288 Å, respectively, are both less than the sums of the appropriate van der Walls radii. The intramolecular hydrogen bond may well persist in solution and may account for the ^{1}H NMR spectrum, as mentioned earlier.

C. Coumalyl Chloride and Amines. Wiley et al.[4,5] reported the preparation of coumalamides by the reaction of coumalyl chloride and amines. For comparison, we elected to repeat Wiley's reaction with benzylamine[4] and ethylenimine.[5] With benzylamine, we obtained a product [mp 177–178 °C;

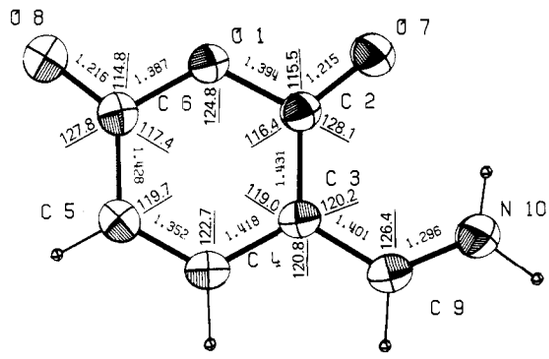


Figure 1. X-ray structure of **2a** (ORTEP drawing[10]).

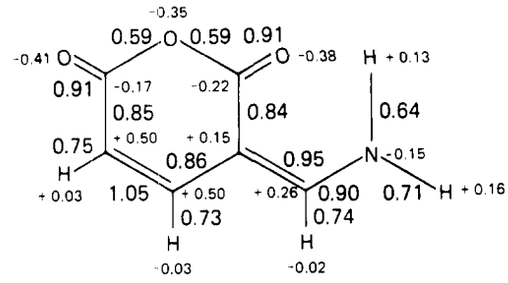


Figure 2. INDO results; the large numbers are total overlap populations, and the small ones are partial charges.

Table IV. Results of INDO Calculations on Some Simple Molecules

bond	total overlap population	compound
$C(sp^3)$–H	0.679	ethane
$C(sp^2)$–H	0.730	propene
$C(sp^2)$–H	0.691	benzene
C(sp)–H	0.720	acetylene
$C(sp^3)$–$C(sp^3)$	0.723	ethane
$C(sp^3)$–$C(sp^2)$	0.750	propene
C=C	1.109	propene
C–C	0.956	benzene
C≡C	1.551	acetylene
C–O	0.563	methanol
C=O	0.952	formaldehyde
C=O	0.886	formic acid
C–O	0.691	formic acid
C–N	0.655	methylamine
C–N	0.858	pyridine
C≡N	1.070	methyl cyanide
O–H	0.506	methanol
N–H	0.602	methylamine

λ_{max} (MeOH) 338 nm (ϵ 3.47 × 10^4), 347 sh (3.3 × 10^4)] in good agreement with properties reported by Wiley et al.[4] The ^1H NMR spectrum (Table I) requires that this compound cannot be *N*-benzylcoumalamide (**1**; R_1 = H, R_2 = $CH_2C_6H_5$), but must be structure **2b.** On the other hand, the product from the reaction with ethylenimine, mp 119–120 °C (lit.[5] mp 121 °C), exhibits UV and ^1H NMR spectra (Table II) very similar to those of methyl coumalate. Thus, one can readily recognize this compound as a coumalamide (**1b**). These observations indicate a dichotomy in the reaction of coumalyl chloride and amines, viz., (a) the normal reaction resulting in the formation of an amide, and (b) a rearrangement reaction leading to a glutaconic anhydride derivative (**2**). We were thus prompted to examine further the reaction with other amines. The spectral data of the products are summarized in Table I and show that the isolated products are mainly the result of the rearrangement reaction.[15] The anhydride function in **2** does not seem to be particularly reactive toward amines; thus, in general only 1 mol of amine is used in the reaction. However, the poor solubility of the product may be an important factor in this reaction. The reaction with aniline is unique in that both the coumalamide **1c** and the rearranged compound **2c** were obtained. The ^{13}C NMR data are given in Table V. They also serve to distinguish the α-aminomethyleneglutaconic anhydride structure **2** from the coumalamide structure **1.**

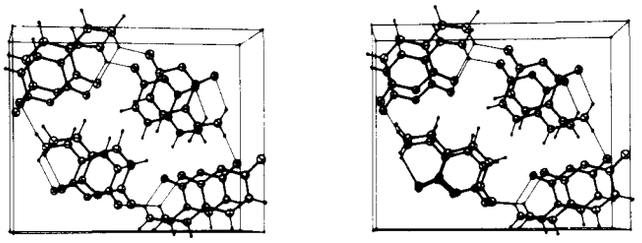
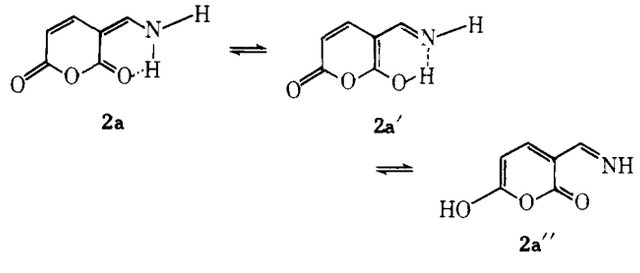


Figure 3. Molecular packing of **2a** showing the hydrogen bonds.

2-Pyrones are known to react with nucleophilic reagents at either the 2 or 6 position with concomitant ring opening.[16] The electrophilic character of position 6 in methyl coumalate in particular is enhanced by the presence of the carbomethoxy substituent at position 5, thus accounting for the facile reaction with cyanide ion,[17] aniline,[18] diazomethane,[19] and methanolic hydrogen chloride.[20] It is, therefore, reasonable to consider that the reaction of amine with coumalyl chloride could be initiated by attack at position 6 as shown in Scheme I, leading to the rearranged product **2.** The alternative attack at C-2 would result in structure **3,** which is not observed.

Among the amines examined, the ones that give mainly the rearranged compounds **2** are those having a pK_a in the range 10–11. The normal amides, **1b** and **1c,** are formed from the weaker bases, ethylenimine (pK_a 8) and aniline (pK_a 4.6); however, it is difficult to understand why ethylenimine gives only the normal amide **1b,** whereas aniline yields both the amide **1c** and the anhydride **2c.** The present data are too limited to clarify the situation.

D. Properties of α-Aminomethyleneglutaconic Anhydrides. α-Aminomethyleneglutaconic anhydrides, as a class of compounds, can be regarded as vinylogous carbamates. The amino function is practically neutral as indicated by the lack of change in the UV spectrum from neutral to acidic medium. Although the X-ray data show that a molecule of α-aminomethyleneglutaconic anhydride in the solid state exists in the form represented by **2a;** nevertheless, in solution other tautomeric forms, **2a′** and **2a″,** might be present. Examination



Scheme I

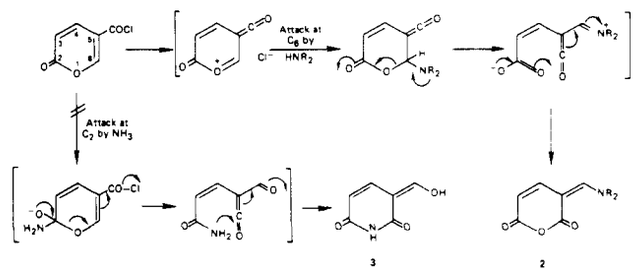


Table V. ^{13}C NMR Chemical Shifts[a] for Coumalate Derivatives and α-Aminomethyleneglutaconic Anhydrides

compd	C-2	C-3	C-4	C-5	C-6	C-7	other
methyl coumalate[b]	159.7	115.3	141.6	112.0	158.1	163.4	OCH_3: 52.5
1b	159.8	115.4	141.3	114.8	157.6	174.7	NCH_2–: 26.2
1c	160.1	115.9	141.4	116.1	153.9	161.0	phenyl: ipso, 137.0; ortho, 120.6; meta, 129.2; para, 125.3
2a[b,c]	162.2[e]	93.3	147.5	100.8	163.3[e]	159.6	
2b	161.8[e]	94.1	146.4	103.8	164.9[e]	157.4	phenyl: ipso, 134.9; ortho, 127.6; meta, 129.3; para, 128.8; NCH_2: 53.5
2c	*d*	96.1	145.7	106.1	*d*	149.6	phenyl: ipso, 145.5; ortho, 117.9; meta, 130.3; para, 126.7
2d	162.4[e]	93.4	147.4	102.6	165.0[e]	154.3	$C(CH_3)_3$: 54.9, 29.6
2e	162.7[e]	93.9	141.7	103.8	165.1[e]	152.1	$N(CH_2)_4$: 56.9, 50.6, 24.0, 26.3
2f	162.3[e]	92.3	141.0	104.3	165.1[e]	154.1	$N(CH_2CH_3)$: 54.7, 45.3, 14.3, 12.6

[a] In parts per million referenced to internal Me_4Si in $CDCl_3$, except **2a**. [b] Assignments were confirmed by coupled spectra and single-frequency selective decoupling. [c] In Me_2SO-d_6. [d] Not detected. [e] Interchangeable assignments.

Table VI. λ_{max} of α-Aminomethyleneglutaconic Anhydride (2a) in Various Solutions

solvent	λ_{max}, nm
water	332
dimethyl sulfoxide	332
methanol	328
dimethylformamide	328
acetonitrile	325
cyclohexane	324
2,2,2-trifluoroethanol	320

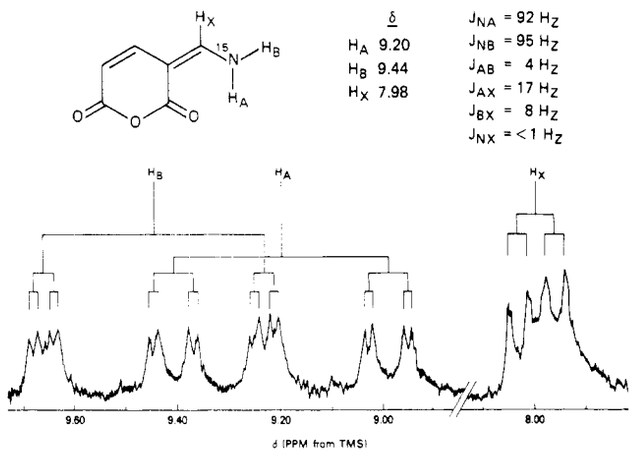


Figure 4. Low-field signals in the ^1H NMR spectrum of **2a**-^{15}N in Me_2SO-d_6.

of UV absorption in a number of solvents (Table VI) and in various concentrations shows only small shifts in λ_{max}, indicating that the molecule in solution is present predominantly in one tautomeric form, most likely **2a**, on the basis of the relative stability observed in other enaminones.[21] This is borne out by the ^{13}C NMR spectrum of **2a** in Me_2SO-d_6 (Table V), which exhibits sharp peaks for each C atom.[22]

Further evidence that **2a** is indeed the major tautomeric form present in solution is provided by the ^1H NMR spectrum of the ^{15}N derivative in Me_2SO-d_6. Figure 4 shows the signals due to the two NH and vinyl protons which constitute an ABX system as shown. The advantage of using ^{15}N derivatives to study keto–enol equilibrium has been well documented by the work of Dudek and Dudek.[23] The two large coupling constants (92 and 95 Hz) for the **2a**-^{15}N compound are strong indications that the tautomeric equilibrium is predominantly in favor of **2a** since the tautomeric form, **2a'** or **2a''**, would show only one one-bond ^{15}N–H coupling. We assign the δ 9.20 resonance to the intramolecularly hydrogen-bonded NH because of the large (17 Hz) coupling constant to the vinyl proton. The unusually low-field resonance (δ 9.44) of the other NH is probably due to the hydrogen bonding to the solvent. The striking feature of the spectrum is the very small (<1 Hz) coupling constant between ^{15}N and the vinyl proton.[24]

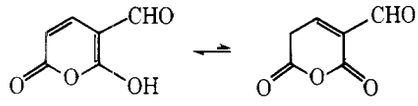
The above ^1H NMR results are consistent with the unusual planar geometry of the nitrogen atom shown in the X-ray structure of **2a**. The one-bond ^{15}N–H coupling constants (92 and 95 Hz) in **2a**-^{15}N are comparable with those ascribed to sp^2 hybridized nitrogen.[25] Numerically, the values for **2a** resemble that in 2,4-dinitroaniline (92.6 Hz), where the variation of $^1J(^{15}N–H)$ could be correlated with the hybridization of the nitrogen atom. Attempts were made,[26] following Edmiston and Reudenberg,[27] to obtain two centered localized molecular orbitals from the INDO quantum mechanical results, but the convergence was very slow and was by no means complete after 400 cycles.

The consideration of the tautomeric state for **2a** may be extended to include the N-substituted compounds **2b–f** on the basis of the similarity of their spectroscopic properties. The λ_{max} values in methanol (Table I) show bathochromic shifts due to substituents on nitrogen similar to those observed in a *cis-s-cis*-enaminone system.[28] For the three compounds (**2b, 2c,** and **2d**) derived from primary amines, the NH to vinyl proton (H-7) coupling is large (14–15 Hz) (Table I), suggesting a transoid relationship. Also, in compounds **2c** and **2f** the methylene protons attached to nitrogen are nonequivalent. The ^{13}C NMR spectra (Table V) of all of the compounds (**2b–f**) show single sharp peaks for each C atom in the molecule similar to those of **2a,** except for slight variations in chemical shifts due to the N substituents. These spectroscopic data are in good accord with the conclusion that all of these compounds are planar molecules existing primarily in the tautomeric forms represented by **2b–f.**

α-Aminomethyleneglutaconic anhydride (**2a**) is a stable, orange-pink crystalline solid. The color cannot be removed by repeated recrystallization, but some colorless crystals could be obtained by sublimation in vacuo. In polar solvents, **2a** gives light orange solutions whose color would intensify upon standing; e.g., in dimethyl sulfoxide, a very dark orange solution would result after standing for a few days, but it showed little change in UV and ^1H NMR spectra.

von Pechmann[3] reported the hydrolysis of "isocoumalinsäureamid" by hot alkali to "isocoumalinsäure", $C_6H_4O_4$. In our hands, treatment of **2a** by hot or cold 2 N KOH invariably led to intractable material. We observed the evolution of NH_3 upon dissolution of **2a** in alkali accompanied by an irreversible change in its UV spectrum and the formation of purple color upon treatment with $FeCl_3$ reagent. Treatment of **2a** with Na_2CO_3 or $NaHCO_3$ solution at room temperature for a few hours or brief heating at 80 °C provided an amorphous solid [*m/e* 140 (M^+, $C_6H_4O_4$); λ_{max} (MeOH) 344 and 276 nm] which could not be crystallized but possessed properties resembling

those of "isocoumalinsäure". The ^1H NMR spectrum in D_2O solution reveals two olefinic protons at δ 5.54 and 7.79 with a coupling constant of 9.5 Hz. There is also a singlet at δ 9.29 which can be attributed to an aldehyde proton. We thus tentatively assign structure **4** to this compound. On prolonged



4 **4′**

standing in D_2O–Na_2CO_3 solution, the proton signal at δ 5.54 disappears, indicating the exchange of H at C-5 with D, possibly due to equilibration with the tautomeric form (**4′**) at high pH.

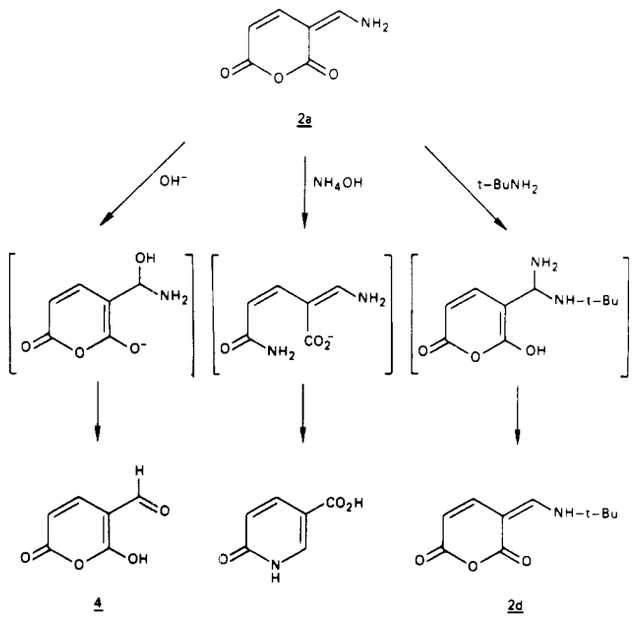
The reaction of **2a** with ammonia appeared to be quite different from that with dilute alkali as indicated by the change of the UV spectrum in 2 M NH_4OH. In fact, the UV spectrum changes progressively over a period of 10 h, resulting finally in a spectrum of 6-hydroxynicotinic acid, though in much reduced intensity and superimposed on some background absorption. A small yield of 6-hydroxynicotinic acid could indeed be isolated from a solution of **2a** in 2 M NH_4OH. On the other hand, *tert*-butylamine reacts smoothly with **2a**, yielding *tert*-butylaminomethyleneglutaconic anhydride (**2d**) as the only product. These observations reveal the multiplicity of nucleophilic sensitive sites in the molecule **2a** as expected. The behavior of **2a** toward a limited number of nucleophiles can be summarized in Scheme II. A full understanding of the reactivity of this novel heterocyclic system must await further study.

The present work demonstrates the dual pathways in the reaction of coumalyl chloride and amines. It also establishes that coumalamide (**1a**) cannot be prepared by the reaction of coumalyl chloride and ammonium hydroxide and that this simple derivative of coumalic acid remains to be synthesized. The facile reaction of *tert*-butylamine with **2a** suggests that this could be a practical method for the preparation of other N-substituted α-aminomethyleneglutaconic anhydrides.

Experimental Section

Melting points were taken on a Kofler hot-stage and are uncorrected. Mass spectra were recorded on an LKB-9000 spectrometer using the direct inlet system at 70 eV. UV spectra were measured on a Cary 15 spectrophotometer. Microanalyses were performed by the Section on Microanalytical Services and Instrumentation, Laboratory of Chemistry, National Institute of Arthritis, Metabolism and Digestive Diseases. ^1H NMR spectra were determined on a Varian HR 220 MHz spectrometer operating at a probe temperature of 17 °C. ^{13}C NMR data were obtained on a JOEL FX-60 spectrometer at 15 MHz using a flip angle of 30° and a pulse repetition rate of 1 per second. Typical concentration was about 0.1 M solution, depending on the solubility of individual compounds.

Scheme II



Coumalyl chloride was prepared by the method of Fried and Elderfield.[19] Only freshly prepared samples were used in all experiments. Reaction of coumalyl chloride with ammonium hydroxide was carried out as described by Wiley and Knabeschuh.[4]

α-Aminomethyleneglutaconic anhydride (2a), mp 250–252 °C dec, was purified by recrystallization from a large volume of 50% ethanol. A colorless sample was obtained by sublimation at 160 °C and 0.05 mm pressure: MS *m/e* (relative intensity) 139 (100, M^+), 111 (21), 95 (22), 94 (18), 69 (12), 67 (74), 66 (15), 54 (10). Anal. Calcd for $C_6H_5NO_3$: C, 51.80; H, 3.623; N, 10.07. Found: C, 51.64; H, 3.61; N, 9.91.

α-Aminomethyleneglutaconic-^{15}N Anhydride (2a-^{15}N). To a solution of 273 mg (5 mmol) of ammonium-^{15}N chloride (99.6 atom % of ^{15}N; Merck, Canada) in 2.5 mL of water, chilled in a −5 °C bath, was added solutions of 500 mg (3.15 mmol) of coumalyl chloride in 5 mL of benzene and 1 mL of 10 N potassium hydroxide alternatively under vigorous stirring. At the completion of addition, the orange precipitate of **2a**-^{15}N was collected on a filter, washed with water, and dried in vacuo at 50 °C. Crystallization from 50% ethanol afforded 180 mg of pure material, mp 248–251 °C dec, whose UV spectrum was identical with that of **2a:** MS *m/e* (relative intensity) 140 (100, M^+), 112 (18), 96 (18), 95 (15), 68 (53), 55 (33).

Reaction of Coumalyl Chloride and Amines. The procedure described by Wiley and deSilva[5] for the preparation of *N*-coumalyaziridine (**1b**) was followed. All of the amines used were freshly redistilled. The workup of the reaction was modified according to the solubility of the product.

***N*-Phenylcoumalamide (1c):** mp 167–168 °C ($CHCl_3$); MS *m/e* (relative intensity) 215 (39, M^+), 187 (12), 123 (100),[29] 95 (31), 93 (39), 77 (10), 65 (12). Anal. Calcd for $C_{12}H_9NO_3$: C, 66.97; H, 4.216; N, 6.509. Found: C, 66.24; H, 4.10; N, 6.71.

***N*-Benzyl-α-aminomethyleneglutaconic Anhydride (2b):** mp 177–178 °C (CH_3OH); MS *m/e* (relative intensity) 229 (25, M^+), 92 (8), 91 (100), 65 (14). Anal. Calcd for $C_{13}H_{11}NO_3$: C, 68.11; H, 4.838; N, 6.111. Found: C, 67.79; H, 4.70; N, 5.68.

***N*-Phenyl-α-aminomethyleneglutaconic Anhydride (2c):**[30] mp 220–223 °C (EtOAc); MS *m/e* (relative intensity) 215 (100, M^+), 214 (47), 187 (20), 170 (47), 143 (20), 142 (10), 117 (20), 115 (20), 104 (23), 77 (60), 57 (33), 55 (33). Anal. Calcd for $C_{12}H_9NO_3$: C, 66.97; H, 4.216; N, 6.509. Found: C, 66.72; H, 4.24; N, 6.43.

***N*-*tert*-Butyl-α-aminomethyleneglutaconic Anhydride (2d):** mp 188–189 °C (CH_3OH); MS *m/e* (relative intensity) 195 (30, M^+), 180 (5), 140 (23), 139 (63), 122 (5), 111 (12), 95 (11), 94 (8), 79 (8), 67 (29), 57 (100). Anal. Calcd for $C_{10}H_{13}NO_3$: C, 61.52; H, 6.713; N, 7.176. Found: C, 61.30; H, 6.68; N, 7.15.

***N,N*-Diethyl-α-aminomethyleneglutaconic Anhydride (2e):** mp 104 °C ($CHCl_3$–C_6H_{12}); MS *m/e* (relative intensity) 195 (100, M^+), 167 (12), 166 (13), 152 (96), 138 (18), 122 (44), 110 (18), 108 (48), 97 (23), 96 (12), 95 (27), 94 (27), 93 (12), 82 (34), 80 (67), 79 (52), 56 (96). Anal. Calcd for $C_{10}H_{13}NO_3$: C, 61.52; H, 6.713; N, 7.176. Found: C, 61.47; H, 6.72; N, 7.24.

***N,N*-Tetramethylene-α-aminomethyleneglutaconic Anhydride (2f):** mp 186–188 °C ($CHCl_3$–C_6H_{12}); MS *m/e* (relative intensity) 193 (93, M^+), 165 (59), 164 (69), 137 (62), 121 (21), 120 (76), 110 (10), 109 (5), 108 (17), 94 (24), 93 (100), 80 (17), 79 (45), 51 (55). Anal. Calcd for $C_{10}H_{11}NO_3$: C, 62.16; H, 5.739; N, 7.250. Found: C, 61.93; H, 5.63; N, 7.32.

Reactions with α-Aminomethyleneglutaconic Anhydride (2a). (A) With Alkali. A mixture of 167 mg (1.2 mmol) of **2a** and 4 mL of 5% sodium bicarbonate was stirred at 80 °C for 15 min, upon which a clear orange solution resulted. After cooling, the solution was passed through a short Dowex 50 (H^+ form) ion-exchange column and eluted with water. The eluent, about 50 mL, was lyophilized to give 160 mg of orange amorphous solid which became dark and resinous upon standing. Attempted crystallization from various organic solvents invariably resulted in dark red resinous material: MS *m/e* (relative intensity) 140 (71, M^+), 112 (100), 95 (19), 94 (38), 84 (76), 68 (24), 66 (24).

(B) With Ammonium Hydroxide. A mixture of 50 mg of **2a** and 5 mL of 2 M ammonium hydroxide was stirred at room temperature for 24 h. The orange solution was lyophilized overnight; the residue was dissolved in 4 mL of water and brought to pH 4 by a few drops of

88% formic acid. It was lyophilized again to give a brown resinous residue from which 22 mg of amorphous solid was obtained after trituration with a few drops of methanol. This was passed through a short column of silica gel (Brinkmann Instrument 70–325 mesh) and eluted with 1% formic acid in ethanol. The middle fractions afforded 5 mg of amorphous solid whose UV spectrum and TLC analysis (Kodak silica gel sheet; chloroform–isopropyl alcohol–88% formic acid, 1:2:0.2) were identical with those of an authentic sample of 6-hydroxynicotinic acid.

C. With *tert*-Butylamine. A mixture of 56 mg of **2a** and 1 mL of *tert*-butylamine was stirred at room temperature for 1 h. Dilution with 5 mL of ice water gave a pale yellow precipitate which was crystallized from methanol to yield 40 mg of *N-tert*-butyl-α-aminomethyleneglutaconic anhydride (**2d**), mp 185–188 °C.

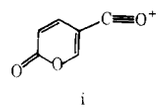
Crystallographic Data: $C_6H_5NO_3$; mol wt, 139.1; monoclinic; a = 3.7284 (4) Å; b = 14.118 (1) Å; c = 11.065 (1) Å; β = 91.44 (1); V = 582.25 Å^3; Z = 4; space group, $P2_1/c$ (No. 14); d_{calcd} = 1.586 g cm^{-3}, d_{measd} = 1.57 g cm^{-3}. Cell dimensions were obtained by least-squares analysis using reflections measured at ±θ on a diffractometer (Cu Kα radiation, λ = 1.5418 Å).

Data Collection. The crystal used was a platelet approximately 0.25 × 0.25 × 0.15 mm^{-3} and was mounted along a diagonal of the largest face. Intensities were measured with a computer-controlled diffractometer (Nonius CAD-4) using graphite-monochromatized Cu Kα radiation. There were 1149 unique reflections, 951 of which had $I_o > \sigma(I_o)$. Lorentz and polarization corrections were applied but not absorption corrections. There was no indication of significant radiation damage during data collection.

Registry No.—**1b,** 67598-05-4; **1c,** 67598-06-5; **2a,** 67598-07-6; **2b,** 67598-08-7; **2c,** 67598-09-8; **2d,** 67598-10-1; **2e,** 67598-11-2; **2f,** 67598,12-3; **4,** 67598-13-4; methyl coumalate, 6018-41-3; coumalyl chloride, 23090-18-8; ethylenimine, 151-56-4; aniline, 62-53-3; benzylamine, 100-46-9; *tert*-butylamine, 75-64-9; diethylamine, 109-89-7; pyrrolidine, 123-75-1.

References and Notes

(1) (a) Laboratory of Biochemistry; (b) Laboratory of Chemistry; (c) Montgomery County, Maryland High School Intern, 1977.
(2) There are a few reports of coumalamides in patents [(a) H. Martin, W. Baumann, H. Zaeslin, and H. Gysin, U.S. Patent 2 364 304, 1944; *Chem. Abstr.*, **39,** P4196 (1945); (b) J. R. Geigy, A.-G. Swiss Patent 215 240, 1941; *Chem. Abstr.*, **42,** P3782f (1948); (c) J. R. Geigy, A.-G. British Patent 586 135, 1947; *Chem. Abstr.*, **42,** P2272d (1948); (d) J. R. Geigy, A.-G. Swiss Patent 222 387, 1942; *Chem. Abstr.*, **43,** P821h (1949); and (e) J. R. Geigy, A.-G. Swiss Patents 220 966–9, 1942; *Chem. Abstr.*, **43,** P2239h (1949)], but these are mainly amides of 4,6-dimethylcoumalic acid (isodehydroacetic acid).
(3) H. von Pechmann, *Ber.*, **34,** 1406 (1901).
(4) R. H. Wiley and L. H. Knabeschuh, *J. Am. Chem. Soc.*, **77,** 1615 (1955).
(5) R. H. Wiley and C. L. deSilva, *J. Org. Chem.*, **21,** 841 (1956).
(6) W. H. Pirkles and M. Dines, *J. Heterocycl. Chem.*, **6,** 1 (1969).
(7) P. Main, M. M. Woolfson, and G. Germain, MULTAN, a computer program for the automatic solution of crystal structures, Universities of York and Louvain (1971).
(8) J. M. Stewart, G. J. Kruger, H. L. Ammon, C. Dickinson, and S. R. Hall, XRAY 72, Technical Report TR-192, Computer Center, University of Maryland, 1972.
(9) S. W. Peterson and H. A. Levy, *Acta Crystallogr.*, **10,** 70 (1957).
(10) C. K. Johnson, ORTEP, Oak Ridge National Laboratory Report ORNL-3794, 1965. The numbering used in the discussion of the X-ray results is that given in Figure 1.
(11) (a) K. Ezumi, H. Nakai, S. Sakata, K. Nishikida, M. Shiro, and T. Kubota, *Chem. Lett.*, 1393 (1974); (b) J. Bernstein, *J. Chem. Soc., Perkin Trans. 2,* 946 (1972); (c) H. B. Burgin and J. D. Dunitz, *Helv. Chim. Acta,* **53,** 1747 (1970).
(12) B. Bak, L. Hansen-Nygaard, and J. Rastrup-Andersen, *J. Mol. Spectrosc.*, **2,** 361 (1958).
(13) J. A. Pople, D. L. Beveridge, and P. A. Dobosh, "CNDO/INDO Program", Program 141, Quantum Chemistry Program Exchange, Indiana University, 1970.
(14) R. S. Mulliken, *J. Chem. Phys.*, **23,** 1833 (1955).
(15) A U.S. patent[2a] describes a compound, *N,N*-diethyl-1,2-pyrone-5-carboxamide [bp 100–105 °C (0.35 mm)], which is quite different from compound **2e.** We were unable to isolate from our reaction any product corresponding to the reported property. The UV spectrum of the reaction mixture before workup showed only absorption due to compound **2e.**
(16) N. Pashusherina, N. D. Dmitrieva, E. A. Luk'yanets, and R. Ya. Levina, *Russ. Chem. Rev. (Engl. Transl.),* **36,** 175 (1967).
(17) G. Vogel, *J. Org. Chem.*, **30,** 203 (1965).
(18) H. von Pechmann and W. Welsh, *Ber.*, **17,** 2384 (1884).
(19) J. Fried and R. C. Elderfield, *J. Org. Chem.*, **6,** 577 (1941).
(20) H. von Pechmann, *Justus Liebigs Ann. Chem.*, **273,** 164 (1893).
(21) G. O. Dudek and R. H. Holm, *J. Am. Chem. Soc.*, **84,** 2691 (1962).
(22) The poor solubility of this compound in most solvents prevents the study of the ^{13}C NMR spectrum in solvents other than dimethyl sulfoxide.
(23) G. O. Dudek and E. P. Dudek, *J. Am. Chem. Soc.*, **86,** 4283 (1964); **88,** 2407 (1966).
(24) One other case of such a small coupling constant was observed by Dudek and Dudek[23] for *N*-methyl-2-hydroxy-1-naphthaldehydimine-^{15}N.
(25) T. Axenrod in "NMR Spectroscopy of Nuclei Other than Protons", T. Axenrod and G. A. Wedd, Eds., Wiley, New York, N.Y., 1974, pp 82–86.
(26) B. Tinland, "Molecular Orbital Localization Program", Program 191, Quantum Chemistry Program Exchange, Indiana University, 1973.
(27) C. Edmiston and K. Reudenberg, *Rev. Mod. Phys.*, **35,** 457 (1963).
(28) C. Kashima, M. Yamaoto, and N. Sugiyama, *J. Chem. Soc. C,* 111 (1970).
(29) The *m/e* 123 peak is prominent in this spectrum as well as those of methyl coumalate and *N*-coumalylaziridine (**1b**). It is probably due to the ion i and



i

can be considered as the characteristic peak for coumalate derivatives. In contrast, in all of the spectra of the anhydrides (**2a–f**), the *m/e* 123 peak is either missing or present in less than 2%.
(30) H. von Pechmann [*Justus Liebigs Ann. Chem.*, **273,** 180 (1893)] described a compound, $C_{12}H_9NO_3$, mp 220–223 °C, of unknown constitution arising from aniline and coumalic acid followed by treatment with acetic anhydride. We have repeated von Pechmann's experiment and established that this unknown compound was identical in every respect with **2c.**

Intramolecular Photochemistry of Vinylogous Imides. An Efficient Photochemical Ene Reaction

Fred M. Schell* and Phillip M. Cook

Department of Chemistry, University of Tennessee, Knoxville, Tennessee 37916

Received May 19, 1978

Pyrex filtered irradiation of a vinylogous imide derivative of dimedone was found to produce intramolecular ene products rather than the expected cycloaddition product. The stereochemistry of the products was determined using chemical and spectroscopic techniques.

In recent years the photochemistry of vinylogous imides has been studied by several groups. Early examples of vinylogous imide photocycloaddition were provided by Wiesner, who produced cyclobutanes using methyl acrylate[1] and allene[1,2] as the olefin components in intermolecular reactions and a terminal allene in an intramolecular reaction.[3] Likewise, Cantrell[4] reported successful photocycloaddition of cyclopentene to a vinylogous imide. More recently, Tamura[5] has described the production of **2** and **3** by irradiation of **1.** In analogy with these previous reports, it was anticipated that **5** would undergo intramolecular 2 + 2 cycloaddition when submitted to Pyrex filtered irradiation. It was found, however,

0022-3263/78/1943-4420$01.00/0