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Research Article

Branched 2-Amino-1,3-Dicyanocyclopenta-1,3-Diene

Francisco Ros*

Department of Medical Chemistry, Institute of Medical Chemistry, Madrid, Spain

ABSTRACT

Reaction of 2-chloroisobutyrophenone with two equivalents of malononitrile anion furnishes 2-amino-1,3-dicyano-5,5-dimethyl-4-phenylcyclopenta-1,3-diene. The cyclic compound represents the novel 2-amino-1,3-dicyanocyclopentadiene structure. The unique 1-cyano-2-amino-3-cyano arrangement in the cyclopentadiene brings about a strong polarization of the electronic configuration of the diene system that is conformed by two opposite dipolar halves. The polarized electronic configuration accounts for the extreme persistence manifested by the cyclopentadiene. The compound owns a vivid lemon-hued yellow color consequent to an unusually intense n absorption of a cyano group in the extensively conjugated compound. This is built up by consecutive one-pot reaction of two molecules of malonon itrile carbanion and the ketonic substrate followed by a new tandem carbon-carbon cyclization with final elimination of cyanate ion.

Keywords: 2-Halo ketones; Crowded substitution; Tandem nitrile reaction; Cyclizations; UV/visible spectroscopy; Reaction mechanisms

INTRODUCTION

We have been interested in the synthesis of branched-chain organic compounds by nucleophilic substitution on activated tertiary alkyl halides with resonance stabilized carbanions [1-5]. When the carbanion is also tertiary the substitution brings about a compound with two contiguous quaternary carbon atoms [6]. With tertiary 2-halo ketones as substrate, products arising from rival nucleophilic addition of the carbanions to the carbonyl group may be obtained [7,8]. Thus, 2-chloroisobutyrophenone (PhCOCClMe2) and ethyl cyanoacetate or methylmalononitrile (NCCMeCN-) carbanions produce the normal compounds of substitution, whereas this same 2-chloro ketone and nitromethane carbanion give the oxygen-rearranged tertiary 3-nitro allylic alcohol that results from the dechlorinated 2-nitro epoxide of addition to the carbonyl and which is isomeric to the substitution product [9].

Based on these grounds, it was reckoned that the reaction of 2-chloroisobutyrophenone with malononitrile anion would supply the normal alkylate since this nucleophile is less bulky than ethyl cyanoacetate and methylmalononitrile anions concerning the crowded substitution at the tertiary carbon of the 2-halo ketone. Nevertheless, attack of malononitrile anion to the carbonyl group alike to the attack of nitromethane anion was not disrespected on account of the smallness of the former. The reaction was undertaken and was conducted with two-fold excess of the reactant anion with the only intention of compensating a neutralization of this reactant in the course of the reaction, so protecting the reaction yield. Such neutralization could occur by proton transfer from the emerging alkylated malononitrile having one acidic hydrogen easily removable (as contiguous to two cyano groups) to reactant malononitrile anion.

The molecular ion in the mass spectrum of the compound isolated from the reaction did not agree with the molecular mass of the desired alkylate nor of an isomer, indicating that a more complex transformation had taken place. Also, the elemental analysis pointed out the absence of oxygen in the compound, which was striking and outstanding as such a loss of oxygen had not previously been observed in reactions of 2-chloroisobutyrophenone. These indications turned out the finding of the structure of the compound to be puzzling. Moreover, the compound exhibited a striking intrinsic neat lemon color that was unknown in the colorless class of alkylates of ketones and analogous substrates.

The compound has been proven to be 2-amino-1,3-dicyano-5,5-dimethyl-4-phenylcyclopenta-1,3-diene (1) whose structure has been fully elucidated by means of a complete spectroscopic examination, which else required a thorough examination of nuclear magnetic resonance data. Moreover, the structure is upheld by the mechanism of formation of the compound. The infrared and ^{13}C NMR spectra of 1 provide the clues to the striking stability that was manifest in the compound. The electronic spectrum has been carefully analyzed about the coloration presented by the cyclopentadiene (Scheme 1).

Correspondence to: Francisco Ros, Department of Medical Chemistry, Institute of Medical Chemistry, Madrid, Spain, E-mail: iqmr322@iqm.csic.es

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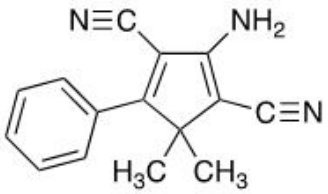


Scheme 1: 2-amino-1,3-dicyano-5,5-dimethyl-4-phenylcyclopenta-1,3-diene.

METHODS

2-Chloroisobutyrophenonone was prepared by a literature procedure [10]. 2-Bromoisobutyrophenone and all other reagents were commercially obtained. Commercial absolute ethanol was directly used. Dimethylsulfoxide was distilled from calcium hydride under reduced pressure. Thin layer chromatography: Merck silica gel 60 F_{254}. HPLC: Waters 2695 chromatograph, C18 column (3.5 µm, 2.1 × 50 mm). Melting point apparatus: Reicher Jung hot-stage microscope. IR spectrometry: Perkin Elmer 681 spectrophotometer. UV-Vis spectrometry: Jas.co V-730 spectrophotomer. NMR spectrometry: Bruker-400 spectrometer. Mass spectrometry: Finnigan TSQ 70 and high-resolution Agilent 650 spectrometers. Elemental anaysis: Elemental Analyser Leco CHNS-932.2-Amino-1,3-dicyano-5,5-dimethyl-4-phenylcyclopenta-1,3-diene (1, $C_{15}H_{13}N_3$).

Method A

To a well stirred solution of sodium ethoxide in ethanol [freshly prepared in a dry atmosphere (calcium chloride) from 0.24 g sodium (10.4 mmol) and 5 cm^3 ethanol] 0.69 g malononitrile (10.4 mmol) dissolved in 2 cm^3 ethanol was slowly added dropwise by syringe, followed by addition of 0.95 g 2-chloroisobutyrophenone (5.2 mmmol). An intense yellow coloration immediately appeared accompanied by a slight and short evolution of heat. After 2 h, 15 cm^3 H_2O was added and the precipitate was filtered off and washed with H_2O. Recrystallization from dichloromethane/heptane (v/v 1/1) afforded 0.76 g 1 (62%), lemon-hued yellow crystals. M.p:175°C-177°C (corrected, subl.); HPLC retention time [40%-95% aq. acetonitrile (0.1% trifluoroacetic acid), 5 min gradient time]: 2.79 min, 100% purity; 1H NMR (400 MHz, $CDCl_3$): δ=7.50 (s, 1 C_6H_5), 4.94 (s, 1 NH_2, exchangeable with D_2O), 1.41 (s, 2 CH_3) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ=23.6 (CH_3), 54.5 (C-5), 89.1 (C-1), 107.4 (C-3), 113.3 [(C=N)-1], 116.4 [(C≡N)-3], 127.9 (C_6H_5), 129.2 (C_6H_5), 130.7 (C_6H_5), 132.0 (C_6H_5), 152.0 (C-2), 174.9 (C-4) ppm; IR (KBr): V=3405 (s, NH_2), 3220 (m, NH_2), 2228 (w, C≡N), 2185 (s, C=N), 1658 (s, C=C), 1619 (m, C=C) cm^{-1}; IR (carbon tetrachloride):=3412 (w, NH_2), 3242 (w, NH_2), 2227 (w, C≡N), 2200 (m, C≡N), 1653 (s, C=C), 1617 (w, C=C) cm^{-1}; UV-Vis (acetonitrile, c=3.4.10-5 mol dm^{-3}): λ max (ε)=362(3180), 273 (sh, 7410), 247 (15000), 221 (17900) nm (mol^{-1} dm^3 cm^{-1}); UV-V is (99% aq. acetonitrile containing 0.2 mol dm^{-3} hydrogen chloride, c=3.3.10-5 mol dm^{-3}): λ max (ε)=399 (3970), 340 (3210), 276 (7330), 251 (12000), 223 (16100) nm (mol^{-1} dm^3 cm^{-1}); MS (70 eV): m/z=235 (50, M+), 220 [100, (M-CH_3)+]; HRMS: m/z=236.1173 [(M+H)+, calcd. for $C_{15}H_{14}N_3$ 236.1182]; Elemental analysis (C, H, N) was in good agreement (± 0.3%) with the calculated values.

The use of 2-bromoisobutyrophenone in place of 2-chloroisobutyrophenone in Method A afforded 0.66 g 1 (54%) with melting point and 1H NMR spectrum identical to the product obtained by 2-chloroisobutyrophenone.

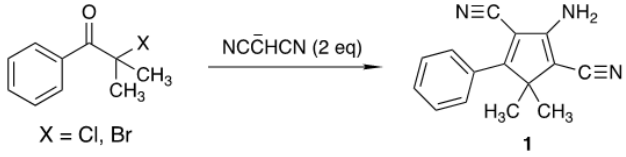
Method B

To a well stirred solution of 225 mg potassium tert-butoxide (2.00 mmol) in 2 cm^3 DMSO under nitrogen 132 mg molonitrile (2.00 mmol) dissolved in 1 cm^3 DMSO was slowly added dropwise by syringe, and 183 mg 2-chloroisobutyrophenone (1.00 mmol) in 1 cm^3 DMSO was then added. After 1 h the mixture was poured into H_2O and extracted by diethyl ether. The ethereal extract was washed with H_2O, dried over sodium sulfate, and the ether was removed. The crude product obtained was purified by TLC using benzene/ethyl acetate (v/v 10/1) as developing solvent (Rf 0.27) and diethyl ether as extracting solvent, which afforded 168 mg 1 (71%) with melting point and HPLC retention time coincident with the sample obtained by Method A.

The use of 2-bromoisobutyrophenone in place of 2-chloroisobutyrophenone in Method B afforded 90 mg 1 (38%) with melting point and 1H NMR spectrum identical to the product obtained by 2-chloroisobutyrophenone.

RESULT AND DISCUSSION

Reaction of 2-chloroisobutyrophenone with malononitrile anion (Scheme 2) using two equivalents of the sodium salt of malonitrile in ethanol at room temperature smoothly gave 1 in 62% yield. An intense yellow coloration turned up immediately on reaction accompanied by a slight and nonpersistent evolution of heat, which indicates that formation of the cyclopentadiene takes place within seconds. The reaction was optimized concerning leaving group and solvent (Table 1). The lower yields observed with 2-bromoisobutyrophenone are presumably due to the better leaving-group ability of bromide ion, which facilitates side reactions.



Scheme 2: Reaction of 2-chloroisobutyrophenone with malononitrile anion.

Table 1: Reaction of PhCOC(CH_3)2X and (NC)2CH- to give 1[a].

X	Solvent	Yield/%
Cl[b]	EtOH[c]	62
Cl[d]	DMSO[e]	71
Br[b]	EtOH[c]	54
Br[d]	DMSO[e]	38

Note: [a]With two equivalents of $(NC)_2CH^-$ at room temperature. [b]$(NC)_2CHNa$ from $(NC)_2CH_2$ and EtONa. [c]2 h reaction time. [d]$(NC)_2CHK$ from $(NC)_2CH_2$ and Me_3COK. [e]1 h reaction time.

Structure

Accurate mass determination concerning the molecular ion of the obtained compound by high resolution mass spectrometry indicated the complete elemental composition in agreement with molecule 1, i.e. $C_{15}H_{13}N_3$, which was fully

supported by chemical elemental analysis. Both determinations pointed out that the oxygen in 2-chloroisobutyrophenone had been done away with in the course of the reaction, as mentioned in Introduction. Moreover, just the molecular formula ($C_{15}H_{13}N_3$) reveals the implication of two and not one molecule of reactant malononitrile in the structure of the compound since more than thirteen carbon atoms exist in the molecule. This enlightens the previously not well-pondered employment of two equivalents of malononitrile anion for the reaction, as above referred to. Furthermore, the molecular formula suggests the loss of a cyano moiety (CN) from malononitrile as three and not four nitrogen atoms are present together with the correct count of carbons. Such losses of an oxygen and a cyano group suggest the production of one and stable cyanate ion, which is supported by the reaction mechanism below. The molecular formula besides dismisses a dialkylation of malonitrile (C20H12N2O2) that is possible at nitriles bearing two removable hydrogen atoms [11,12].

In the IR spectrum of the obtained compound, two C≡N groups (V=2228, 2185 cm^{-1}) clearly manifested as two neat peaks in the specific IR range of C≡N groups conjugated with carbon-carbon double bonds [13-16], which is in agreement with structure 1. The two C=CC≡N groups showed in the solid-state IR spectrum and likewise in the spectrum in solution, and remarkably showed much different intensities (ca. 1:5). This indicates that the two cyano groups are not on the same carbon of a C=CC≡N2 group, i.e. not like C=C(C≡N)2. The C≡N peak at lower wavenumber (V), which besides shows the higher intensity, would correspond to the cyano group in resonance with the liable amino group of structure 1 throughout the C=C bond. This strong resonance weakens the C≡N bond with respect to the other cyano group in the structure and accounts for the stretching absorption at lower frequency. The significantly higher intensity of this peak results from a large change in bond dipole during the stretching [17], which is favored in this weakened and highly polarized C≡N bond [13]. This effect of a mutant dipole (the transition dipole) on absorption intensity manifests even more strikingly for these two cyano groups in the electronic spectrum below.

With reference to the two C=CC≡N units of structure 1, the disparate intensities observed in IR spectrum for the cyano groups indicate a diminution of normal conjugation through carbon 2 and 3 joining the units, differently from substituted cyclopendiene. Thus, an increased conjugation in the ring of 1 would uniform the disparate peaks for the cyano groups as would diminish the independence of the C=CC≡N units. Furthermore, two C=C stretching's are shown by the spectrum (V=1658, 1619 cm^{-1}) at positions that besides are strikingly and significatively coincident with the single C=C stretching's of 2-amino-1-cyanoethene (H2NCH=CHC≡N, V=1655 cm^{-1}) and 1-cyano-2-phenylethene (PhCH=CHC≡N, V=1622 cm^{-1}) [18], which are archetype compounds standing for the two independent C=C moieties of 1. Also, the intensities of the C=C IR absorptions of 1 are in correspondence with those of the latter archetype compounds. In a conjugated diene, interaction between the two C=C stretchings occurs and produces two new combination stretchings in place of two independent C=C stretchings [13,19]. However, this effect is not observed at all in 1,3-cyclopentadiene 1 as stated, which strongly supports a lessening of conjugation in the ring also pointed out by the disparate absorptions for the cyano groups.

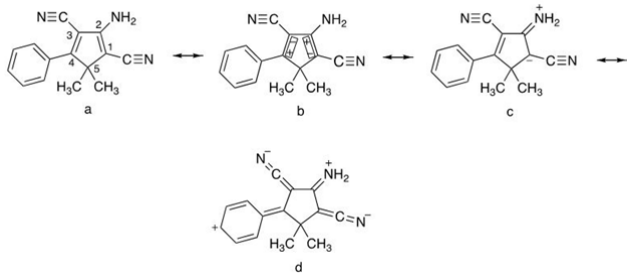
The IR spectrum also showed two distinc bands for the symmetric and asymmetric NH stretchings of a primary amino group (R-NH_2). The NH_2 group also showed in 1H NMR as a slightly widened signal that was exchangeable with deuterium; further, the 1H NMR spectrum is in agreement with structure 1 and displaying the correct ratios of hydrogens.

The ^{13}C NMR spectrum and the 1H-^{13}C NMR Heteronuclear Multiple Bond Correlation (HMBC) supply additional data and disclose the full structure of the compound. The ^{13}C spectrum neatly displays the two cyano groups present in the molecule as their carbon atoms lie within the particular narrow range of C≡N carbons (Table 2) [20] with no overlapping by the sp^2 carbons of the molecule.

Table 2: ^{13}C chemical shifts for cyclopentadiene 1 in $CDCl_3$ as the solvent.

Pos.	δ /ππμ	Pos.	δ /ππμ
methyl	23.6	phenyl	127.9
C-5	54.5	phenyl	129.2
C-1	89.1	phenyl	130.7
C-3	107.4	phenyl	132
(C°N)-1	113.3	C-2	152
(C°N)-3	116.4	C-4	174.9

As the most relevant feature of the ^{13}C spectrum, the most deshielded carbon (Table 2, C-4) lies well above the usual range of phenyl and ethylenic sp^2 carbons, instead lying just on the average for a carboxylic acid sp^2 carbon [20]. Hence such carbon can be assigned confidently to carbon 4 of structure 1 (see resonance structure a in Scheme 3), since this carbon has a likeness to a C(=O)OH carbon having a cationic character. This remarkable cationic character of C-4 is due to the conjugation of the C=C bond with strongly electron-withdrawing C≡N, as if for a keto group similar to structure b (Scheme 2). In addition, the phenyl group acts as a hydroxyl group as to delocalization of the positive charge at C-4. Carbon C-2, which is at the same ring localization as C-4 with respect to the electron-withdrawing C=CC≡N units, is actually clearly paired with C-4 in the spectrum (Table 2), although not so much deshielded as the mesomeric effect of the NH_2 group lessens the positive charge at the carbon. The positive charges at C-2 and C-4 conform the positive ends of two dipoles, and these are equivalent by resonance to their corresponding π bonds in structure a.



Scheme 3(a-d): cationic character of C-4 is due to the conjugation of the C=C bond with strongly electron-withdrawing C≡N.

The HMBC correlation (Figure 1) first shows the carbon backbone of an isobutyrophenone moiety in the compound. Thus, the hydrogens of the methyl groups correlate with their own sp^3 carbons, with the next isopropyl sp^3 carbon and, finally, with the most deshielded sp^2 carbon at α position to the phenyl group,

i.e. the above pointed out C-4. This α carbon correctly correlates with the phenyl hydrogens thus fulfilling the isobutyrophenone backbone.

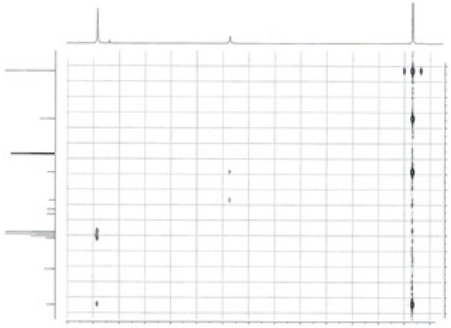


Figure 1: ^{1}H-^{13}C NMR HMBC correlation for cyclopentadiene 1 in $CDCl_3$. Horizontal axes: 1H NMR spectrum, δ 1.0 to 8.0 ppm; Vertical axes: ^{13}C spectrum, δ 20 to 180 ppm.

In addition, the methyl hydrogens correlate by the other side of the isopropyl group with the most shielded sp^2 carbon, and therefore a C=C unit is attached to the central isopropyl carbon. This is further bound to the previously indicated α carbon and thus constitutes a quaternary carbon center. No hydrogen atoms otherwise available, such C=C unit bears a C≡N group, and not the existing NH_2 group, at the carbon next to the quaternary carbon. This is so since the HMBC correlation relevantly reveals that the NH_2 does actually not correlates with an sp^2 and an sp^3 carbons (as it would correspond to attachment to C-1) but with two sp^2 carbons (Figure 1). The NH_2 is instead located at the other end of the present C=C unit (C-2) wherefrom shields strongly by resonance the alternative carbon of this unit, which actually is the most shielded ethylenic sp^2 carbon in the spectrum (C-1 in Table 2, Scheme 3c). Moreover, the NH_2 besides correlates with this most shielded carbon (Figure 1). Location of the remaining C≡N for NH_2 on this C=C unit, which would result in a 1-cyano-2-cyano-3-amino arrangement in the molecule, is contrary to the observed ^{13}C chemical shifts and the HMBC correlation.

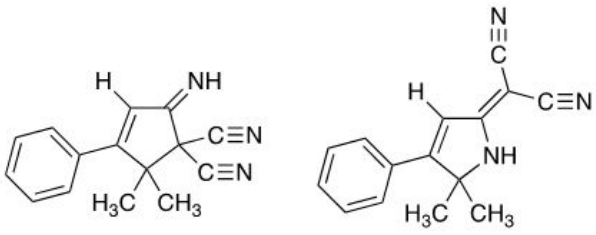
The efficient shielding of carbon C-1 by the resonance of the NH_2 group (Scheme 3c) places this carbon close to the lower limit for sp^2 carbons [19]. The negative charge at this carbon constitutes the negative end of a dipole (Scheme 3b) having the positive end at highly deshielded C-2 indicated previously. The negative end of the other dipole in the ring is placed at C-3, which is consistently paired with strongly shielded C-1 in the spectrum (Table 2). Carbon C-3 itself is significantly shielded with respect to the corresponding carbon of unsubstituted cyclopentadiene (δ=132 ppm). The positive end of this dipole at the left hand side of the ring lies at strongly deshielded C-4 noticed above.

No evidence for a partial π bond between C-2 and C-3 (Scheme 3b), which would go against the electrostatic dipole ends at these bridging carbons, has become apparent in the IR spectrum as pointed out above. The two independent and permanent dipoles are favorably oriented in a stabilizing manner [21] and constitute a double dipole. On account of the double dipole, the π system of the ring consists of two opposite dipolar halves. The dipoles are not of the maximal and like magnitude depicted in structure b as this is only a resonance contribution and the charges of the dipoles should actually not be equal.

Continuing the building of structure 1 by the HMBC correlation, the exclusively remaining =C(C≡N)-building block (C2N) is attached by the single bond to the previous ethylenic carbon bearing the NH_2 group because the NH_2 correlates with the sp^2 carbon of the unit (C-3 in Table 2, Figure 1). Finally, this =C(C≡N)-unit is in turn attached by the double bond to the previously indicated α carbon in the isobutyrophenone backbone. This ultimate attachment satisfies the only two remaining available valences according to the valence count, conforms for the molecule a second C=C bond conjugated with the previous one and closes the cyclopentadiene ring. With this, the elucidation of structure 1 becomes complete.

It remains to assign the two C≡N carbons in the ^{13}C spectrum to their corresponding carbons in the cyclopentadiene ring of 1 that is to C-1 and C-3. These C≡N carbons do not appear in the present 1H-13C correlation as are too far away from any protons. Since C-1 is more shielded than C-3, as disclosed by the correlation, the more shielded C≡N carbon should be attached to the former carbon simply by electrostatic considerations (Scheme 3b, Table 2), and likewise the less shielded C≡N carbon should correspond to C-3. Such structures could rotundly be dismissed by means of the spectroscopic data. Thus, the above-discussed IR information is in strong disagreement with the unconjugated C≡N groups of 2 and with the vicinal position of these groups in 3. In addition, the 1H spectrum does not display the single ethylenic proton of 2 and 3 but the two fold-intense signal of the amino protons of 1 which besides is exchangeable with deuterium, and further the ^{13}C spectrum shows two sp^3 carbons and not three as it would be for 2. The following ultraviolet-visible data definitively discourages these structures.

Structure 2 and 3, structural isomers of 1, needed be considered as the former come along by initial addition of malononitrile carbanion to the carbonyl of 2-chloroisobutyrophenone, which issues a precursor dechlorinated oxirane attached to malononitrile. Such an addition occurs in the above-mentioned reaction of nitromethane carbanion and the halo ketone [9] as well as in reactions of other carbanions with the same ketone [3,7,8]. The process will proceed from the precursor oxirane to 2 or 3 with participation of a second molecule of malononitrile carbanion.



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Electronic spectrum

The UV-Vis spectrum of cyclopentadiene 1 above 210 nm (Figure 2) displays in the 210-300 regions the three expected bands for a phenyl group conjugated with an unsaturated system [13] as in 1. Of these phenylic bands, the one at the highest wavelength shows as a shoulder (λ=273 nm) of the intermediate conjugation band that is specifically due to the 4-phenylcyclopenta-1, 3-diene core as the basic chromosphere. The high wavelength position of these latter two phenylic bands [13] indicates a high degree of conjugation in 1, which comprises the two cyano groups as well as the amino group as a typical auxochrome (Scheme 3d).

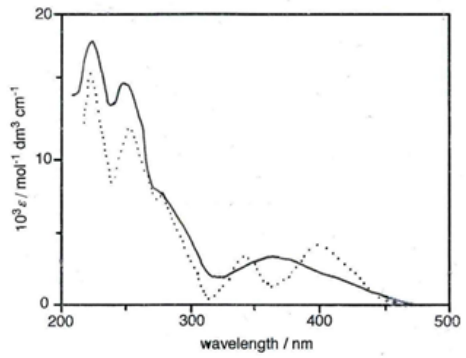


Figure 2: UV-Vis spectrum of cyclopentadiene 1. Solid line: Acetonitrile as the solvent; dotted line: 99% aqueous acetonitrile as the solvent containing ca. 5.103 excess hydrogen chloride with respect to 1.

The intensity at the maximum of the color band remaining in the spectrum is high (εmax ca. 3000 mol^{-1} dm^3 cm^{-1}), yet moderate with respect to the other mighty bands. A 20% of incident light is not absorbed at the maximum of the color band, which extends well into the visible region. These characteristics account for the firmness of the intrinsic and intense neat lemon-hued yellow color exhibited by cyclopentadiene 1.

The color band is due to an unusual n → π* absorption from a cyano group to a conjugated system with which the single lone electron pair at the cyano nitrogen atom is in immediate neighborhood via a π bond of the nitrogen bearing the lone electron pair, which itself does not participate in the conjugation. This kind of absorptions is in theory forbidden like the absorptions for a carbonyl group [13,17] so the high intensity observed for the present absorption is remarkable.

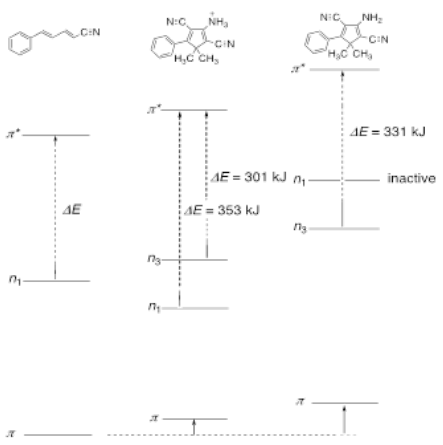
The n → π* absorption is due specifically to the cyano group at carbon C-3 of the 1,3-cyclopentadiene (1), not to the cyano at C-1. This assignation ensues the observation that in presence of hydrogen chloride, whereby the amino group of 1 is blocked by protonation, the spectrum displays an additional n → π* absorption, i.e. two n → π* bands around 350 and 400 nm (Figure 2). Group (CN)-1 is devoid of the mesomeric influence of the amino group in the presence of the acid whereas (CN)-3 is indifferent to this direct influence. Hence, the single n n → π* absorption in the spectrum of cyclopentadiene 1 is due to (CN)-3 and not to (CN)-1 according to the test. The phenylic bands of the protonated form of the cyclopentadiene are practically identical to the non-protonated form as are characteristic for the gross unsaturated system.

In 1, the omitted n → π* transition for (CN)-1, otherwise manifested in the protonated form, has collapsed because the requisite change in transition dipole [17] is too little. Thus, a single n electron on the (CN)-1 nitrogen atom of 1 is too loose already in the ground state as is strongly repelled on that nitrogen atom by the delocalized pair of electrons of the adjacent amino group by resonance. So the loose negative charge of the n electron will not significantly disperse to a greater extent in passing to the excited π* state, specially taking into account that conjugation is somewhat confined to only a moiety of the molecule (Scheme 3b). In other words, the amino group cannot excite in that manner the n negative charge at the alternative (CN)-3 group and, consequently, only the np* transition for this group is observed in the spectrum as only this n electron, and not the already excited electron at (CN)-1, is able to be further excited; excitation here referring to the change in magnitude of the electric dipole on the transition to the excited π* state. It is remarkable that the effect of this transition dipole is opposite to that of the stretching dipole that operates in the IR absorption for the (CN)-1 group, which increases with the bond stretch and gives rise to a strong IR absorption as above mentioned.

The forbidden n → π* (CN)-1 absorption in the electronic spectrum of 1 would lie still at longer wavelengths than the observable color (CN)-3 absorption because the n electron energy is higher for the former due to electron repulsion by the amino group. This typical auxochromic effect of the amino group is however concealed in such actually unobservable absorption. As a substitute for the no protonated cyclopentadiene, the existence of two discernible electronic moieties is plainly apparent by the two neatly separated np* absorptions in the protonated form (Figure 2).

2-Amino-1-cyanoethene (H2NCH=CHC≡N) represents a half of cyclopentadiene 1 assuming no conjugation in the ring (Scheme 3b), and is a colorless compound [18]. This is in agreement with the lack of color in 1 becoming from that half of the molecule as discussed, and supports the assignment of 3-cyano group at the other half of the molecule as the chromatic cyano group. 1-Cyano-2-phenylethene (N≡CCH=CHPh) representing the other half of the cyclopentadiene is colorless [22,23] (like H2NCH=CHC≡N) whereas cyclopentadiene 1 is colored due to this half. This indicates that the π separation between the two molecular moieties of 1 throughout carbon C-2 and C-3 (Scheme 3b) is not perfect since the conjugation of the π system in the ring lowers the excited state and will produce coloration.

1-Cyano-4-phenylbuta-1,3-diene (PhCH=CH-CH=CHC≡N) that wholly represents cyclopentadiene 1 (regardless of the 2-amino and 3-cyano groups) is a light-yellow colored compound [24] similarly to 1. In similarity with 1, the yellow coloration of the open diene should result from an n → π* transition of the 1-cyano group at grossly 400 nm, which empirically corresponds with the n → π* transition of the 3-cyano of 1 likewise producing a yellow color. Of these two n energy levels (Scheme 3, n1 for the open diene vs. n3 for the unprotonated cyclic diene), that one for the open diene is lower as the electron-repelling negative charge on the cyano nitrogen atom will be smaller in the former simply because of the larger distance from the positively charged phenylic end (5 vs. 3 bonds), which retrogradely counterbalances the negative charge at the nitrogen with increasing difficulty with distance. Also, the energy level for the inactive transition of the unprotonated cyclic diene (n1) before mentioned is still higher on account of the powerful electron-donating amino group.



Scheme 5: The lateral amino group of cyclopentadiene 1 heightens the π ground-state energy level with respect to the open diene.

The lateral amino group of cyclopentadiene 1 heightens the π ground-state energy level with respect to the open diene (Scheme 3) by subtracting normal π conjugation from the ring with creation of an energetically unfavorable charge separation by the mesomeric effect (Scheme 2c). The effect of the 3-cyano group is alike to the amino group in heightening the π ground-state energy (Scheme 2d). These energy effects concerning the π conjugation energy are remotely minute [25] while the energy separation of π and π* states is enormous [17,26] (Scheme 3). Relative to the open diene, the π system of cyclopentadiene 1 becomes destabilized in a polar manner. In protonated 1, conjugation in the ring together with energy are saved with respect to the nonprotonated form (Scheme 3) as the strong competing interference of the amino group is now blocked. Thus, the π conjugation in the ring tends to the primitive unsubstituted cyclopentadiene. The π level of the protonated form is higher relative to the open diene due to the interference of the 3-cyano group in the above-indicated manner.

The n3 level of the protonated form (Scheme 3) is stabilized relative to the unprotonated form by the release of negative charge on the cyano nitrogen which accompanys the increase of conjugation in the ring. Consistently with this, the color n3 absorption appears at longer vawelengths than the color n3 → π* absorption of the nonprotonated form (Figure 2). Also, the n1 level lies below the n3 level congruently with the relative positions of the n1 level of the open diene and the n3 level of nonprotonated cyclic diene which were disclosed above as discussed. Moreover, the n1 level of the protonated cyclic diene is further depressed by the electron-withdrawing, inductive ammonium group. So, the n1 and n3 levels of the protonated and nonprotonated cyclic dienes are strikingly and remarkably inverted in these two forms of the cyclic diene.

As a result of the lowered n1 level of the protonated form, the n1 and shorter-wavelength absorption of this form appears fully in the ultraviolet (Figure 2, dotted line, λ max=340 nm). The energies of the nonbonding electrons at the cyano groups of the protonated form differ by the large quantity of 12 kcal per electron mole (50 kJ, Scheme 3). This outstanding responsiveness of nonbonding electrons to otherwise weak electronic effects agrees with the intrinsic mobility of the n1 electron of cyclopentadiene 1 which was above pointed out in connection with the transition dipole and the forbiddance of this transition.

Structure 2 and 3 considered for 1 are incompatible with the UV-Vis spectrum in the presence of hydrogen chloride. Thus, structure 2 cannot account for the two n bands under such conditions as the lone pairs of electrons on the cyano nitrogens are not in touch with the system, and in 3 the cyano groups, being vicinal as they are, cannot account for the two neatly separated n absorptions in the spectrum.

Stability

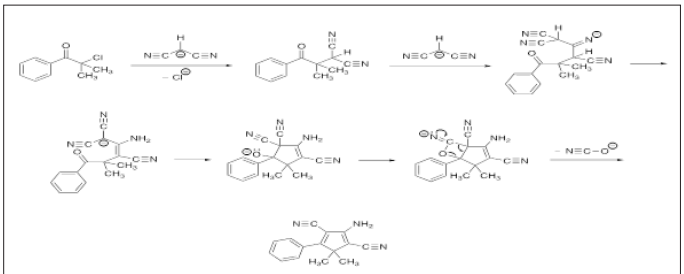
Cyclopentadiene 1 proved to be very much stable in solid state. It remained enterely unaltered at room temperature and light for a much extended period, as checked by high performance liquid chromatography. This characteristic of 1 is in sharp contrast with unsubstituted cyclopentadiene whose relative instability is well-known. The key to the remarkable stability of 1 is resonance structure b (Scheme 2) as a predominant contribution. According to the IR and ^{13}C data, the π electronic configuration in the ring is conformed by two opposite dipolar halves wherein conjugation throughout C-2 and C-3 is unimportant. The stabilized permanent double dipole of structure b suppresses conjugation throughout C-2 and C-3 in contrast with the partial π bond in unsubstituted cyclopentadiene, and brings about a π electronic configuration clearly different from the apolar configuration of unsubstituted cyclopentadiene.

The internal double dipole confers the ring of cyclopentadiene 1 with a certain dielectric character as contrary to a free electronic circulation in the π system. This electron mobility would be necessary to make occur covalent bond formation in a Diels-Alder dimerization of 1 in the manner of the spontaneous self-dimerization of unsubstituted cyclopentadiene. Such a process has however not been observed in 1 congruently with the dielectric double dipole. In energy terms, the stabilization energy of interaction between the two dipoles of the double dipole is not compensated by or bond formation in a Diels-Alder dimerization. It stands for the contrary concerning the individual charges of each dipole, which are actually compensated by the bonds formed. Anyway, the energy of stabilization of the double dipole is an exclusive factor in an energy balance for bond formation with respect to unsubstituted cyclopentadiene. Hence this non-compensated energy barrier qualitatively accounts for the greater stability of 1 relative to cyclopentadiene.

The stabilized internal double dipole in 1 stabilizes the overall π electronic configuration in the ring since the double dipole represents a significant energy contribution [21]. The conjugation in the ring further extends to the outside of the ring (resonance structure d in Scheme 2), which gives rise to a close alternative distribution of positive and negative charges which likewise stabilizes the molecule.

Mechanism of formation

The mechanism of formation of 1 from 2-chloroisobutyrophenone and two molecular equivalents of malononitrile anion is depicted in Scheme 4. Nucleophilic substitution on the 2-chloro ketone by malononitrile carbanion takes place as the first step forming a carbon-carbon single bond and a quaternary carbon atom in the same manner that the bulkier methylmalononitrile carbanion [3]. The substitution of malononitrile anion at the crowded tertiary carbon of the 2-chloro ketone is supported by the fact that the cyclopentadiene was also obtained using instead 2-bromoisobutyrophenone having a better leaving group for the reaction (Table 1), which is in agreement with the occurrence of an SN2 substitution at the crowded tertiary carbon [2].



Scheme 6: The intermediate cross-coupled malononitrile carbanion.

Addition of a second molecule of malonitrile carbanion to a cyano group of alkylated malonitrile then takes place in the manner of a one-pot reaction. This addition anew provides a C-C bond and brings about a deprotonated imino group that converts into β-cyano enamine, which provides a C=C bond for the cyclopentadiene. The malononitrile carbanion built up in his step is stabilized by resonance with this C=C bond.

With a similarity to the preceding cross-coupling of malononitriles taking place during this reaction, self-coupling of nitriles under basic conditions is a documented process. Malononitrile itself dimerizes in the presence of sodium giving 2-amino-1, 3-tricyanopropene [16]. Furthermore, self-coupling eventually occurs as an undesired side reaction in the generation of nitrile anions from nitriles for synthetic purposes [12]. This troublesome process was prevented in the present preparation of a nitrile anion by reverse and slow addition of malononitrile onto an equivalent amount of the base in solution (Table 1), which gave a clear solution of malononitrile salt to the reaction.

The intermediate cross-coupled malononitrile carbanion (Scheme 4) constitutes the reactive species of a tandem reaction driving to the cyclopentadiene. The key cyclization step in the reaction is the intramolecular attack of the cross-coupled carbanion to the carbonyl group, which produces a third C-C bond and builds up the basic carbocyclic system. This addition likewise gives rise to an alkoxide anion bearing an adjacent cyano group. Thus the process proceeds with an intramolecular nucleophilic attack of the alkoxide oxygen to the cyano group giving rise to a nitranionic imino oxetane. This undertakes an interweaved electronic reorganization attended by production of a conjugated C=C bond and elimination of cyanate anion. This unusual final step formally represents a retro [2+2] process.

Intermolecular Pinner addition of alkoxides to nitriles is well known [26]. The present intramolecular variation of Pinner reaction in the last stage of the formation of cyclopentadiene 1 also takes place in the reaction between 2-chloroisobutyrophenone and phenylacetonitrile carbanion, which gives rise to a rearranged alkoxide that attacks the cyano group in the phenyl acetonitrile moiety and sets up a furane ring [3]. An analogous intramolecular addition of an organic nitranion rather than an alkoxide anion to a cyano group building up a pyrroline ring has been reported [27].

The driving force (G) of the overall reaction of 2-chloroisobutyrophenone and malononitrile anion is partly due to the greater stability of produced chloride and cyanate anions as bases compared with reactant malononitrile anion [9], and to the extensive conjugation in product 1. It is remarked that the reactivity of branched chain compounds is often inhibited with respect to their homologs for the sake of a lack of active hydrogen atoms, without regard for steric hindrance [28]. In cyclopentadiene 1 the quaternay carbon atom precludes the incurrence of a strongly favored cyclopentadienyl anion in a reactional process under basic conditions.

CONCLUSION

The results obtained from the study provide promising outcomes concerning the utilization of biological parameters and diagnostic criteria employed in clinical psychology. The 'A' isoform of MAO as a biomarker should be surveyed in different affective disorders in further studies. Especially, as an addition to the MAOA-VNTR polymorphism profiling, gene expression analysis of the same research group at different time intervals or stages of treatment or for various drugs in therapy would be considered for further enlightening studies.

The synthesis of cyclopentadiene 1 bearing the novel 1-cyano-2-amino-3-cyano arrangement in a cyclopentadiene ring has been achieved for the first time and by means of a new carbon-carbon cyclization reaction. As a result of this arrangement and in sharp contrast with unsubstituted cyclopentadiene, cyclopentadiene 1 possesses a polarized electronic configuration for the conjugated system in the ring, which consists of two opposite dipolar halves as manifested by spectroscopic data of the compound and by its stability as well.

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