through a short column of alumina (Woelm, neutral) to remove considerable tar. The filtrate was evaporated and the residual resin was extracted several times with boiling *n*-hexane. The *n*-hexane extract was introduced onto an alumina column (Woelm, neutral; 10 g), the column was washed with *n*-hexane, and the product was eluted with benzene–hexane (1:1). 2-Nitro-4,5-dimethoxy-2′-ethylbiphenyl (VIII) could not be induced to crystallize and was purified only by a short-path distillation at 100° (0.3 mm) to give 1.45 g (42%) of a yellow oil; nmr spectrum in carbon disulfide showed a singlet at 7.45 (H-3) and a singlet at 6.51 (H-6).

*Anal.* Calcd for $C_{16}H_{17}NO_4$: N, 4.9. Found: N, 4.6.

**B. From 4-Iodo-5-nitroveratrole (VII) and *o*-Iodoethylbenzene.**—A mixture of 1.55 g of 4-iodo-5-nitroveratrole and 2.3 g of *o*-iodoethylbenzene was heated to 190° in a nitrogen atmosphere and 2.5 g of copper powder[16] was added over 1 hr. The resulting mixture was then heated to 210–215° for 2 hr, cooled, and extracted with hot methanol. On concentrating and cooling the methanol extract, 0.4 g (44%) of 2,2′-dinitrobiveratrole was obtained, mp 218–220° after recrystallization from ethanol; nmr spectrum in deuteriochloroform showed a singlet at 7.83 (H-3 and H-3′), a singlet at 6.72 (H-6 and H-6′), and a singlet at 3.95 and 4.05 ($OCH_3$).

*Anal.* Calcd for $C_{16}H_{16}N_2O_8$: C, 52.8; H, 4.4. Found: C, 52.3; H, 4.3.

The 2,2′-dinitrobiveratrole mother liquors were evaporated and the residual oil was extracted with several portions of hot *n*-hexane. After chromatography of the hexaneextracted material on alumina (Woelm, neutral; 3 g), followed by a short-path distillation at 100° (0.3 mm) of the crude product eluted from the column with benzene–hexane (1:1), 0.40 g (28%) of 2-nitro-4,5-dimethoxy-2′-ethylbiphenyl (VIII) was obtained as a yellow oil.

**4-Ethyl-6,7-dimethoxycarbazole (XI).**—2-Nitro-4,5-dimethoxy-2′-ethylbiphenyl (VIII) was reduced to the corresponding amine in quantitative yield by hydrazine–Raney nickel.[17] The crude amine was purified by short-path distillation at 80° (0.3 mm) to give 2-amino-4,5-dimethoxy-2′-ethylbiphenyl (IX) as a colorless oil; nmr spectrum (carbon disulfide) showed a singlet at 6.13 (H-3) and a singlet at 6.40 (H-6).

(17) D. Balcom and A. Furst, *J. Am. Chem. Soc.*, **75**, 4334 (1953).

A solution of 600 mg of the amine IX in 1 ml of concentrated sulfuric acid and 5 ml of water was cooled to 5° and treated dropwise with a solution of 160 mg of sodium nitrite in 2 ml of water. After allowing the diazonium solution to stand for 5 min at 5°, 200 mg of sodium azide in 5 ml of water was added all at once. As the mixture stood at room temperature overnight, nitrogen was slowly evolved and a dark orange oil was deposited on the wall of the flask. The mixture was extracted with chloroform and the dried chloroform extract evaporated *in vacuo* at 30–35° to give 490 mg (74%) of quite pure 2-azido-4,5-dimethoxy-2′-ethylbiphenyl (X) as a light brown oil: nmr spectrum, singlet at 6.56 (H-3 and H-6).

The azido compound was dissolved in 10 ml of *n*-hexyl ether, 100 mg of 30% palladium–charcoal was added, and the mixture was heated to 235–240°[18] in a nitrogen atmosphere. After 1 hr the evolution of nitrogen ceased and the mixture was refluxed for 15 min longer and then filtered while hot. The product crystallized from the cooled filtrate and was removed by filtration, washed with *n*-hexane, recrystallized from ethanol, and sublimed at 135° (0.3 mm) to give 253 mg (58%) of 4-ethyl-6,7-dimethoxycarbazole (XI): mp 144–146°; ultraviolet spectrum, $\lambda_{max}$ 237 mμ (ε 47,400), 265 (16,300), 302 (18,500), 328 (5740) 340 (5740), and $\lambda_{min}$ 220 mμ (ε 25,200), 260 (15,400), 279 (6400), 319 (5270), 331 (5650).

*Anal.* Calcd for $C_{16}H_{17}NO_2$: C, 75.3; H, 6.7; N, 5.5. Found: C, 75.0; H, 6.6; N, 5.7.

**Registry No.**—IIa, 14171-79-0; IIb, 14120-07-1; IIc, 14120-08-2; IIIa, 14120-09-3; IIIb, 14120-10-6; IIIc, 14120-11-7; VI, 3899-65-8; VII, 14120-13-9; VIII, 14120-14-0; XI, 14120-16-2; 2,3-dimethoxycarbazole, 14120-17-3; 2-chloro-4-ethylcyclohexanone, 14120-18-4; 2,2′-dinitrobiveratrole, 14172-77-1; IX, 14120-15-1; X, 14271-19-3.

**Acknowledgment.**—The authors are indebted to Dr. Charles Sederholm for the preparation of the calculated ABX spectra and for many helpful discussions.

(18) Nitrogen was evolved smoothly at this temperature; however, no decomposition of the azide occurred during 1 hr in the absence of a catalyst.

# Cyclizations of Anthranilate–Acetylenedicarboxylate Adducts. A Facile Route to 2,8-Dicarboalkoxy-4(1H)-quinolinones[1]

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Isatoic anhydrides (**1**) and anthranilic esters (**2**) react with acetylenedicarboxylates to give Michael adducts (**3**) which cyclize to 2,8 dicarboalkoxy-4(1H)-quinolinones (**4**) upon heating. The synthesis is limited by steric and electronic features in the initial anhydrides and esters which inhibit formation of the intermediate enamines (**3**).

The Conrad–Limpach reaction of β-dicarbonyl compounds with arylamines[2,3] is traditionally employed as the most general synthesis of 4(1H)-quinolinones; it was used for the preparation of the majority of quinolinones examined in the antimalarial program during World War II. This method, however, suffers from several significant disadvantages. A major problem has been the direction of the reactants, arylamine and β-keto ester, toward formation of the desired cyclization precursor, a substituted aminocrotonate, rather than toward the competitive product, an anilide, which leads to 2(1H)-quinolinones (Knorr synthesis).[4] In some cases no aminocrotonate formation was observed.[5] Similar problems are encountered with the closely related Gould–Jacobs reaction, which involves thermal cyclization of α-carbethoxy-β-anilinoacrylic esters.[6]

(1) This investigation was supported in part by N.S.F. Postdoctoral Fellowship to N.D.H. at Princeton University and in part by grants to Princeton University from the National Cancer Institute, National Institutes of Health (CA-02551) and to Lehigh University from the U. S. Army Medical Research and Development Command (Contract No. DA-49-193-MD-3011). This is contribution no. 254 from the Army Research Program on Malaria.

(2) R. C. Elderfield in "Heterocyclic Compounds," R. C. Elderfield, Ed., John Wiley and Sons, Inc., New York, N. Y., 1952, pp 1–343.

(3) R. H. Reitsema, *Chem. Rev.*, **43**, 43 (1948).

(4) C. R. Hauser and G. A. Reynolds, *J. Am. Chem. Soc.*, **70**, 2402 (1948).

(5) F. Misani and M. T. Bogert, *J. Org. Chem.*, **10**, 347 (1945).

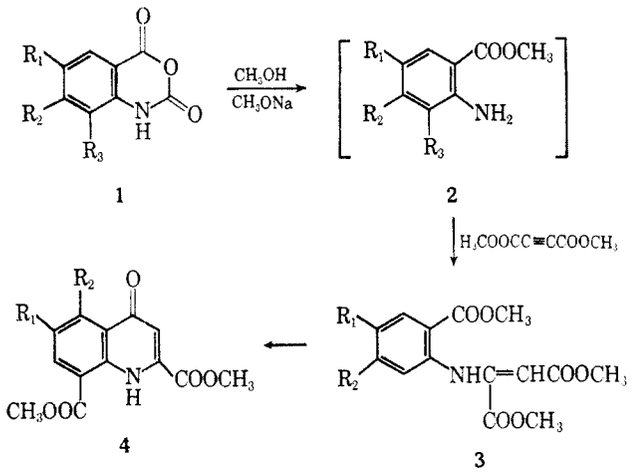
(6) R. G. Gould, Jr., and W. A. Jacobs, *J. Am. Chem. Soc.*, **61**, 2890 (1939).

The recent discovery that the anil intermediates required in the quinolinone synthesis are conveniently available as their tautomeric enamines by the addition of amines to acetylenic esters offers a facile synthesis of 4(1H)-quinolinones. These adducts have already been exploited as intermediates in other versatile heterocyclic syntheses.[7-10]

### Formation of the Enamine Adducts

We have found that dimethyl acetylenedicarboxylate reacts smoothly with isatoic anhydrides (**1**) in methanol containing catalytic amounts of sodium methoxide to give Michael adducts (**3**) in high yield. These enamines (**3**) almost certainly arise by Michael addition of the primary amino group of the methyl anthranilates (**2**), generated *in situ*[11] by the reaction of the isatoic anhydrides with sodium methoxide, to the acetylenic triple bond. The isatoic anhydrides were refluxed in a stirred suspension of methanolic sodium methoxide containing the required amount of dimethyl acetylenedicarboxylate; the appearance of a clear yellow-brown solution served as a convenient indicator that all of the isatoic anhydride had been cleaved to the methyl anthranilate (**2**) (Scheme I).

SCHEME I




Continuation of the reflux for several hours, followed by work-up, led to the isolation of the pure enamines (**3**) in 60–80% yield. The methyl anthranilates (**2**) could also be generated independently from the corresponding isatoic anhydrides and subsequently condensed under the same conditions with dimethyl acetylenedicarboxylate. However, since substituted isatoic anhydrides are often more amenable to synthesis by reaction of anthranilic acids with phosgene[12] or with ethyl chloroformate,[13] or by oxidation of isatins,[14] than are the corresponding anthranilates, their direct synthetic utilization is to be preferred over the two-step procedure.

Steric and electronic features in the isatoic anhydrided or anthranilic esters have a marked effect on the facility with which the Michael adducts are generated. No addition took place with dimethyl acetylenedicarboxylate when a nitro substituent occupied a position *ortho* or *para* to the amino function. The isatoic anhydrides (**1**) ($R_1 = NO_2$, $R_2 = R_3 = H$; $R_1 = Cl$, $R_2 = H$, $R_3 = NO_2$) were converted to the corresponding methyl anthranilates under the reaction conditions, but no subsequent reaction with dimethyl acetylenedicarboxylate was observed. Similarily, methyl 2-amino-3-nitrobenzoate (**2**) ($R_1 = R_2 = H$, $R_3 = NO_2$) was recovered unchanged after prolonged refluxing in the presence of dimethyl acetylenedicarboxylate. A low yield (22%) of the Michael adduct was obtained when methyl 2-amino-4-nitrobenzoate was employed; similar dependence of anil formation in nitro-substituted anilines upon the position of the nitro function is well known.[5,15]

There appears to be some steric inhibition to the formation of Michael adducts when substituents occupy a position *ortho* to the amino group. Both 5,7-dibromo- and 5,7-dichloroisatoic anhydride (**1**) ($R_1 = R_3 =$ halogen, $R_2 = H$) and their corresponding anthranilic acid esters were found to be inert toward Michael addition to dimethyl acetylenedicarboxylate. Similarly, 2,6-dichloro-4-nitroaniline could be refluxed with acetylenedicarboxylate in methanol for 24 hr without detectable adduct formation. Since chloro and bromo substituents *para* to the amino group exhibit no adverse influence on the yield of the adducts, a steric "*ortho* effect" appears to be operating. The lack of reactivity of 2,6-dichloro-4-nitroaniline cannot be ascribed to a wholly electronic effect because 4-nitroaniline is able to undergo adduct formation.

Efforts to obtain analogous Michael adducts from other acetylenic components such as phenylacetylene, diphenylacetylene, ethyl propiolate and ethyl phenylpropiolate were unsuccessful, despite the observation by James and Fanta[8] that some secondary amines can be added to ethyl propiolate.

### Stereochemistry of the Enamine Adducts

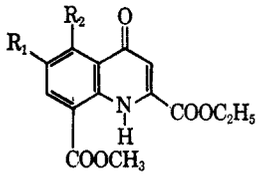
The demonstration by Kurtz[16] and co-workers and by Dolfini[17] that the chemical shift of the enamine (vinyl) proton in the nmr can be used to assign stereochemistry (maleate or fumarate) to amine–acetylene adducts is of importance here. The enamines prepared in this study were generated in basic media, when obtained from the isatoic anhydrides, and in nonbasic media, when obtained from the methyl anthranilates.[18] The same spectrum was obtained whether the enamine was generated in the presence or absence of sodium methoxide. Prolonged reflux in sodium methoxide did not produce an additional vinyl resonance.

Dolfini's results imply that in hydroxylic solvents of high proton mobility, such as might be expected in methanol or methanolic methoxide, protonation of the enolate anion generated upon amine addition to

(7) J. B. Hendrickson, R. Rees, and J. F. Templeton, *J. Am. Chem. Soc.*, **86**, 107 (1964).
(8) D. S. James and P. E. Fanta, *J. Org. Chem.*, **27**, 3346 (1962).
(9) E. C. Taylor and N. D. Heindel, *ibid.*, **32**, 1666 (1967).
(10) N. D. Heindel, T. A. Brodof, and J. E. Kogelschatz, *J. Heterocyclic Chem.*, **3**, 222 (1966).
(11) R. P. Staiger and E. B. Miller, *J. Org. Chem.*, **24**, 1214 (1959).
(12) E. C. Wagner and M. F. Fegley, "Organic Syntheses," Coll. Vol. III, John Wiley and Sons, Inc., New York, N. Y., 1955, p 488.
(13) E. Erdmann, *Ber.*, **32**, 2159 (1899).
(14) H. Wichelhaus, *ibid.*, **36**, 1736 (1903).
(15) S. Coffey, J. K. Thompson, and F. J. Wilson, *J. Chem. Soc.*, 856 (1936).
(16) A. N. Kurtz, W. E. Billups, R. B. Greenlee, H. F. Hamil, and W. T. Pace, *J. Org. Chem.*, **30**, 3141 (1965).
(17) J. E. Dolfini, *ibid.*, **30**, 1298 (1965).
(18) These enamines displayed only one vinyl proton resonance in the region 5.64–5.84 ppm, which did not appear to shift on dilution of the sample.

TABLE I

2-CARBOETHOXY-8-CARBOMETHOXY-4(1H)-QUINOLINONES



| $R_1$ | $R_2$ | Method | Yield, % | Mp, °C | Formula | Calcd, % C | Calcd, % H | Calcd, % N | Found, % C | Found, % H | Found, % N |
|---|---|---|---|---|---|---|---|---|---|---|---|
| H[c] | H[c] | A | 58[a] | 123–124 | $C_{14}H_{13}NO_5$ | 61.09 | 4.76 | 5.09 | 61.33 | 4.93 | 5.27 |
| | | B | 51[a] | | | | | | | | |
| Cl[d] | H[d] | B | 65 | 160–162 | $C_{14}H_{12}NO_5Cl$ | 54.28 | 3.91 | 4.52 | 54.07 | 3.74 | 4.57 |
| H[e] | $NO_2$[e] | B[b] | 58 | 178–179 | $C_{14}H_{12}N_2O_7$ | 52.33 | 4.08 | 8.72 | 52.19 | 3.78 | 8.73 |
|  | [f] | B | 82 | 209–210 | $C_{18}H_{15}NO_5$ | 66.46 | 4.65 | 4.30 | 66.05 | 4.25 | 4.37 |

[a] Represents yield based on methyl anthranilate since the intermediate adduct was not isolated. [b] Adduct was refluxed in diphenyl ether for 20 min instead of the usual 10 min. [c] Registry no. 14195-51-8. [d] Registry no. 14195-52-9. [e] Registry no. 14195-53-0. [f] Registry no. 14195-54-1.

the triple bond can occur intermolecularly to produce the fumarate isomers.[17] In addition, Huisgen has shown that fumarates are the most stable eventual products of primary amine additions to acetylenedicarboxylate, although maleates do appear as transient intermediates in solvents of low proton mobility.[19] The observed position of our enamine vinyl resonances compares favorably with the value for the anilino fumarates (5.40 ppm) reported by Huisgen. These structures (**3**) may thus be provisionally assigned transoid geometry.

Confirmation for this assignment is obtained by observations on the enamine from N-methyl-5-chloroisatoic anhydride and dimethyl acetylenedicarboxylate. This adduct is derived from a secondary amine and should therefore be of maleate geometry[19] and display a considerably more shielded vinyl proton resonance. In fact, a single vinyl peak at $\delta$ 4.70 ppm, a full 1-ppm separation from the corresponding Michael adduct lacking the N-methyl, was observed. This position compares favorably with the 4.82 ppm reported by Huisgen for maleate adducts from N-methylaniline.[19] Additional support for these stereochemical assignments is obtained from the cyclization results below.

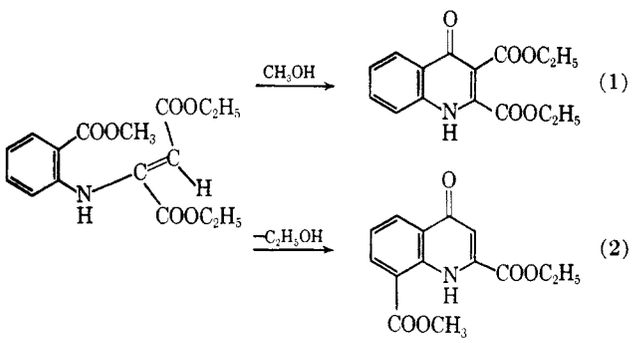
## Cyclization of the Enamine Adducts

Conversion of the intermediate Michael adducts (**3**) to 4 (1H)-quinolinones was most conveniently accomplished by either fusing at a temperature slightly above the melting point (method A) or by refluxing in diphenyl ether (method B).

In light of the previous studies on the behavior of similar enamines,[7-10] two possible cyclization routes, leading to isomeric products, appear possible. Analogy exists to support the expectation that the intermediate enamine might react with the electrophilic carbonyl at the *ortho* ring position[7-9,20] leading to 2,3-dicarbomethoxy-4(1H)-quinolinones. Alternatively, a Conrad–Limpach closure of the side-chain ester $\beta$ to the anilino nitrogen onto the unsubstituted *ortho* ring position would lead to isomeric 2,8-dicarbomethoxy-4(1H)-quinolinones.[10]

Since nmr data indicate that the adducts are fumarates, there is ample reason to anticipate the latter cyclization mode. The most convincing, chemical way of establishing the direction of closure appeared to be the di*ethyl* acetylenedicarboxylate adducts of the *methyl* anthranilates. In this case the products of the possible cyclization routes would be nonisomeric and nmr and combustion analyses would provide firm grounds for structural assignments (Scheme II).

SCHEME II



In all cases examined (See Tables I and II) the results clearly eliminated route 1. Even the enamine adduct of methyl 4-nitroanthranilate, the most likely candidate for a route 1 closure on electronic grounds, formed the corresponding route 2 product.

Predicted behavior upon thermal treatment was observed for the dimethyl acetylenedicarboxylate adduct from N-methyl-5-chloroisatoic anhydride. This material, presumably of maleate configuration,[19] was recovered in 85% yield after 1.5-hr boiling in diphenyl ether. The corresponding adduct from 5-chloroisatoic anhydride presumably of the required fumarate geometry cyclized to 2,8-dicarbomethoxy-6-chloro-4(1H)-quinolinone in 70% yield on 5–10 min of heating.

## Spectral Characteristics of the Quinolinones (4)

In confirmation of other observations on the lactam structure of 4(1H)-quinolinones,[21] all of the quinoli-

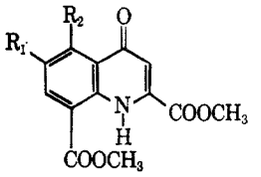
(19) R. Huisgen, K. Herbig, A. Siegl, and H. Huber, *Chem. Ber.*, **99**, 2526 (1966).

(20) While not strictly analogous, a recent azasteroid synthesis of Meyers represents a case of an enamine double bond displacing upon an adjacent carboethoxy function (A. I. Meyers and J. C. Sircar, *Tetrahedron*, **23**, 785 (1967)).

(21) A. R. Katritzky and J. M. Lagowski, *Advan. Heterocyclic Chem.*, **1**, 339 (1963).

TABLE II

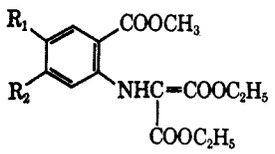
2,8-DICARBOMETHOXY-4(1H)-QUINOLINONES



| R1 | R2 | Method | Yield, % | Mp, °C | Formula | Calcd, % C | Calcd, % H | Calcd, % N | Found, % C | Found, % H | Found, % N |
|---|---|---|---|---|---|---|---|---|---|---|---|
| H | H | A | 71 | 157–158 | $C_{13}H_{11}NO_5$ | 59.77 | 4.24 | 5.36 | 59.58 | 4.51 | 5.28 |
| | | B | 73 | | | | | | | | |
| Cl | H | A | 67 | 194–195 | $C_{13}H_{10}NO_5Cl$ | 52.82 | 3.38 | 4.74 | 52.77 | 3.53 | 4.53 |
| | | B | 70 | | | | | | | | |
| Br | H | A | 66 | 208.5 | $C_{13}H_{10}NO_5Br$ | 45.90 | 2.96 | 4.12 | 45.88 | 3.13 | 4.29 |
| | | B | 71 | 209 | | | | | | | |
| I | H | A | 70 | 222 | $C_{13}H_{10}NO_5I$ | 40.32 | 2.60 | 3.62 | 40.36 | 2.84 | 3.57 |
| $CH_3$ | H | A | 82 | 208–209 | $C_{14}H_{13}NO_5$ | 61.09 | 4.76 | 5.09 | 61.36 | 4.97 | 5.08 |
|  | | A | 68 | 245 | $C_{17}H_{13}NO_5$ | 65.59 | 4.21 | 4.50 | 65.54 | 4.25 | 4.15 |
| H | $NO_2$ | A | 60 | 233 | $C_{13}H_{10}N_2O_7$ | 50.98 | 3.29 | 9.16 | 50.95 | 3.51 | 9.26 |

TABLE III

MICHAEL ADDUCTS WITH DIETHYL ACETYLENEDICARBOXYLATE



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| Starting material | Adduct R1 | Adduct R2 | Yield, % | Mp, °C | Formula | Calcd, % C | Calcd, % H | Calcd, % N | Found, % C | Found, % H | Found, % N |
|---|---|---|---|---|---|---|---|---|---|---|---|
| Methyl anthranilate | H | H | *a* | Liquid | | | | | | | |
| Methyl 5-chloroanthranilate[b] | Cl | H | 79 | 105–106 | $C_{16}H_{18}NO_6Cl$ | 54.01 | 5.10 | 3.93 | 53.92 | 4.98 | 4.05 |
| Methyl 3-amino-2-naphthoate[c] |  | | 87 | 121.5–123 | $C_{20}H_{21}NO_6$ | 64.68 | 5.70 | 3.77 | 64.79 | 5.68 | 3.80 |
| Methyl 4-nitroanthranilate[d] | H | $NO_2$ | 25 | 106.5–108 | $C_{16}H_{18}N_2O_8$ | 52.45 | 4.95 | 7.64 | 52.63 | 4.85 | 7.52 |

[a] Adduct was a viscous liquid which decomposed on attempted vacuum distillation. The infrared spectrum displayed the absence of the primary amine bands. The yield reported for the corresponding 4(1H)-quinolinone, in Table I, is based on methyl anthranilate. [b] Prepared by the reaction of 5-chloroisatoic anhydride with sodium methoxide in methanol, mp 74–76° (Heilbron, Dictionary of Organic Compounds, reports mp 76°. [c] Prepared by passing gaseous HCl through a methanol solution of the acid for 6 hr, mp 102–105° (Heilbron reports mp 104–105). [d] J. J. Blanksma and D. Hoegen, *Rec. Trav. Chim.*, **65**, 333 (1946).

nones prepared in this study showed a strong N–H absorption band between 3200 and 3255 $cm^{-1}$ and a strong amide carbonyl band at 1625–1640 $cm^{-1}$ (Nujol mull). The latter amide bands are essentially identical with those exhibited by 4(1H)-quinolinone itself and by 3-carbomethoxy-4(1H)-quinolinone.

The nmr spectra of the heterocycles derived from the diethyl acetylenedicarboxylate adducts of methyl anthranilates always showed the ethyl (methyl triplet at $\delta$ 1.50 ± 0.02 ppm, methylene quartet at 4.51 ± 0.01 ppm), and the methyl (singlet at 4.06 ± 0.03 ppm) ester groups. All the nmr spectra of the quinolinones from both dimethyl and diethyl acetylenedicarboxylate displayed the proton on C-3 as a doublet ($J$ = 1.5–2 cps) at $\delta$ 6.83–7.01 ppm. No other peak appeared to have a corresponding coupling constant and it is proposed that homoallylic splitting by the broadened N–H resonance is responsible for the multiplicity of the C-3 proton. Confirmation of the N–H–C-3 proton coupling was obtained by addition of $D_2O$, which caused diminution of the N–H resonance and the collapse of the C-3 proton to a singlet. Similar homoallylic coupling has been reported in $\alpha,\beta$-unsaturated ketones[22] and in related quinolinones.[9]

## Experimental Section[23]

**Reaction of Isatoic Anhydrides (or Methyl Anthranilates) with Dimethyl Acetylenedicarboxylate. Formation of Michael Adducts (3).**—A suspension of 0.05 mole of the isatoic anhydride (1) (or the corresponding methyl anthranilate (2)) and 0.075 mole of dimethyl acetylenedicarboxylate in 40 ml of methanol containing 0.10 g of sodium methoxide was heated under reflux for 4 hr. The reaction mixture was concentrated to approximately half its volume and cooled. The canary yellow crystals which separated were collected by filtration and recrystallized from methanol.

Unsuccessful attempts were made to cause dimethyl acetylenedicarboxylate to react under these conditions with 5,7-dichloroisatoic anhydride, 5,7-dibromoisatoic anhydride, 5-chloro-7-nitroisatoic anhydride, methyl 4,6-dichloroanthranilate, methyl 4,6-dibromoanthranilate, methyl 4-bromo-6-chloroanthanilate, and methyl 5-nitroanthranilate.

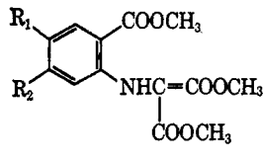
**Reaction of Methyl Anthranilates with Diethyl Acetylenedicarboxylate. Formation of Michael Adducts (5).**—In order to exclude the possibility of significant ester interchange, the

(22) N. S. Bhacca and D. H. Williams, "Applications of NMR Spectroscopy in Organic Chemistry," Holden-Day Inc., San Francisco, Calif., 1964, p 110.

(23) We are indebted for the microanalyses to Dr. George Robertson, Florham Park, N. J., and Dr. Velmer B. Fish, Lehigh University. Infrared spectra were obtained as Nujol mulls scanned on a Perkin-Elmer 237 and standardized against polystyrene. The nmr spectra were run in deuteriochloroform with tetramethylsilane as internal standard on a Varian A60.

TABLE IV

MICHAEL ADDUCTS WITH DIMETHYL ACETYLENEDICARBOXYLATE



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| Starting material | Adduct R1 | Adduct R2 | Yield, % | Mp, °C | Formula | Calcd, % C | Calcd, % H | Calcd, % N | Found, % C | Found, % H | Found, % N |
|---|---|---|---|---|---|---|---|---|---|---|---|
| Isatoic anhydride[a] | H | H | 93 | 92–93 | $C_{14}H_{15}NO_6$ | 57.34 | 5.15 | 4.76 | 57.15 | 5.08 | 4.69 |
| Methyl anthranilate | | | 77 | | | | | | | | |
| 5-Chloroisatoic anhydride[a] | Cl | H | 74 | 87–88.5 | $C_{14}H_{14}NO_6Cl$ | 51.30 | 4.32 | 4.27 | 51.17 | 4.27 | 3.88 |
| 5-Bromoisatoic anhydride[b] | Br | H | 81 | 96–97.5 | $C_{14}H_{14}NO_6Br$ | 45.18 | 3.79 | 3.77 | 45.26 | 3.85 | 3.70 |
| Methyl 5-bromoanthranilate[c] | | | 84 | | | | | | | | |
| Methyl 5-iodoanthranilate[d] | I | H | 61 | 119.5–120.5 | $C_{14}H_{14}NO_6I$ | 40.11 | 3.37 | 3.34 | 40.18 | 3.34 | 3.61 |
| 5-Methylisatoic anhydride[e] | $CH_3$ | H | 75 | 102–103.5 | $C_{15}H_{17}NO_6$ | 58.63 | 5.57 | 4.56 | 58.28 | 5.47 | 4.54 |
| Isatoic anhydride from 3-amino-2-naphthoic acid[f] |  | | 64 | 132–133.5 | $C_{18}H_{17}NO_6$ | 62.97 | 5.00 | 4.08 | 63.16 | 5.07 | 4.05 |
| Methyl 4-nitroanthranilate[g] | H | $NO_2$ | 22 | 135.5–136.5 | $C_{14}H_{14}N_2O_8$ | 49.72 | 4.18 | 8.30 | 49.57 | 4.03 | 8.78 |

[a] Courtesy of Maumee Chemical Co. [b] R. Adams and H. R. Snyder, *J. Am. Chem. Soc.*, **60**, 1411 (1938). [c] Prepared by reaction of 5-bromoisatoic anhydride with sodium methoxide in methanol, mp 74° (Heilbron, Dictionary of Organic Compounds, reports mp 73–74°). [d] P. Petyunin and M. Konshin, *Chem. Abstr.*, **51**, 15522*i* (1957). [e] W. Panaotovic, *J. Prakt. Chem.*, [2] **33**, 58 (1886). [f] See ref 13. [g] See footnote *d*, Table III.

methyl anthranilates and diethyl acetylenedicarboxylate were stirred at room temperature in ethanol (base free) for 4 days. Concentration *in vacuo* precipitated crystals of the anthranilates. Nmr and elemental analysis showed that no transesterification had occurred.

The caution employed above may not have been required. Owing to the extremely sluggish reactivity of methyl 4-nitroanthranilate (no detectable reaction on stirring for 4 days at room temperature with diethyl acetylenedicarboxylate), this anthranilate was refluxed for 48 hr in ethanolic solution. Only 25% of the adduct was obtained (see Tables III and IV), but nmr and elemental analysis ruled out ester interchange in the product.

The Michael adduct of N-methyl-5-chloroisatoic anhydride[24] and dimethyl acetylenedicarboxylate was prepared by 4-hr reflux in methanolic methoxide as described above: yield, 64%; mp 108.5–110°.

*Anal.* Calcd for $C_{15}H_{16}NO_6Cl$: C, 52.72; H, 4.73; N, 4.10. Found: C, 53.00; H, 4.59; N, 4.02.

**Formation of 2,8-Dicarbomethoxy-4(1H)-quinolinones (4). Method A.**—In a 160 × 20 mm test tube (Pyrex) was placed 4.0 g of the Michael adduct (**3**). The material was heated carefully and intermittently with a microburner until a clear melt was formed. Heating was then increased slightly; the melt started to darken; and a vigorous evolution of methanol ensued. The solidified fusion product was dissolved in hot benzene–methanol (1:1), treated with charcoal, and filtered; the filtrate was concentrated and cooled. The tan crystals so obtained were sublimed at 150–175° (0.5 mm).

**Method B.**—A fine suspension of 1.5 g of the Michael adduct in 8 g of diphenyl ether was heated briefly (10 min) under reflux (free flame), cooled to room temperature, and poured with stirring into 30 ml of pentane. The filtered crystals were washed with pentane, dried *in vacuo*, and sublimed under the conditions described above.

**Registry No.**—**3** ($R_1$, $R_2$ = H), 14195-37-0; **3** ($R_1$ = Cl; $R_2$ = H), 14195-38-1; **3** ($R_1$ = Br; $R_2$ = H), 14195-39-2; **3** ($R_1$ = I; $R_2$ = H), 14195-40-5; **3** ($R_1$ = $CH_3$; $R_2$ = H), 14195-41-6; **3** ($R_1$, $R_2$ = $C_4H_4$), 14320-42-4; **3** ($R_1$ = H; $R_2$ = $NO_2$), 14195-42-7; **4** ($R_1$, $R_2$ = H), 14195-43-8; **4** ($R_1$ = Cl; $R_2$ = H), 14195-44-9; **4** ($R_1$ = Br; $R_2$ = H), 14195-45-0; **4** ($R_1$ = I; $R_2$ = H), 14195-46-1; **4** ($R_1$ = $CH_3$; $R_2$ = H), 14320-46-8; **4** ($R_1$, $R_2$ = $C_4H_4$), 14320-21-9; **4** ($R_1$ = H; $R_2$ = $NO_2$), 14320-47-9; **5** ($R_1$, $R_2$ = H), 14195-47-2; **5** ($R_1$ = Cl; $R_2$ = H), 14195-48-3; **5** ($R_1$, $R_2$ = $C_4H_4$), 14195-49-4; **5** ($R_1$ = H; $R_2$ = $NO_2$), 14195-50-7; Michael adduct of N-methyl-5-chloroisatoic anhydride and dimethyl acetylenedicarboxylate, 14195-55-2.

(24) This sample was courtesy of Maumee Chemical Co.