crystals: mp >300 °C; 76%; IR (KBr) 3300–2360 (br), 1640, 1580, 1395, 1290, 1170, 1035, 825, 800 cm^{-1}; NMR (Me_2SO-d_6) 2.10 (s, 6, 2 CH_3), 5.99 (d, 1, =CH, J = 9 Hz), 7.51 (m, 3, COOH, NH, and =CH). The crude acid **8** (12 mmol), thionyl chloride (35 mmol), and 30 mL of anhydrous chloroform were refluxed for 6 h and evaporated to dryness in vacuo, and the crude **9** was purified by sublimation at 100 °C (0.1 mmHg) to give white crystals: 55%; mp 120–121 °C; IR (KBr) 3015, 2910, 1680, 1600, 1450, 1365, 1295, 1120, 1040, 795, 755 cm^{-1}; NMR (Me_2SO-d_6) 2.15 (s, 3, CH_3), 2.55 (s, 3, CH_3), 6.57 (d, 1, =CH, J = 9 Hz), 8.20 (d, 1, =CH, J = 9 Hz). Anal. Calcd for $C_8H_8N_2SO$: C, 53.31; H, 4.47; N, 15.54. Found: C, 53.08; H, 4.52; N, 15.27.

4-Amino-5-(*o*-methoxyphenyl)-2,4-dihydro-3(3*H*)-1,2,4-triazolethione *p*-Nitrobenzaldehyde Anil. A solution of 4.0 mmol of 4-amino-5-(*o*-methoxyphenyl)-3(4*H*)-1,2,4-triazolethione[1] and 20 mmol of *p*-nitrobenzaldehyde in 100 mL of anhydrous methanol was refluxed for 1 h and allowed to stand for 24 h. Evaporation in vacuo and chilling at ice-bath temperature gave 0.30 g (19%) of orange crystals of the title compound, mp 209–211 °C. Anal. Calcd for $C_{16}H_{13}N_5SO_3$: N, 19.71. Found: N, 19.73.

Registry No. 1a, 20939-15-5; **1b**, 22706-11-2; **1c**, 73396-58-4; (*Z*)-**2a**, 73396-59-5; (*Z*)-**2b**, 73396-60-8; (*Z*)-**2c**, 73396-61-9; (*Z*)-**3a**, 73396-62-0; (*Z*)-**3b**, 73396-63-1; (*Z*)-**3c**, 73396-64-2; **4a**, 73396-65-3; **4b**, 73396-66-4; **4c**, 73396-67-5; **5**, 73396-68-6; **6**, 1192-72-9; (*Z*)-**7**, 73396-69-7; (*Z*)-**8**, 73396-70-0; **9**, 73396-71-1; potassium 3-pivaloyldithiocarbazinate, 73396-72-2; hydrazine, 302-01-2; pivalic acid hydrazide, 42826-42-6; carbon disulfide, 75-15-0; methyl propiolate, 922-67-8; 4-amino-5-(*o*-methoxyphenyl)-2,4-dihydro-3(3*H*)-1,2,4-triazolethione *p*-nitrobenzaldehyde anil, 73396-73-3; *p*-nitrobenzaldehyde, 555-16-8.

Steric Inhibition to Cyclization of β-Keto Amides to Indeno[1,2,3-*de*]quinolinones and Related Compounds

B. Staskun

Department of Chemistry, University of the Witwatersrand, Johannesburg, South Africa

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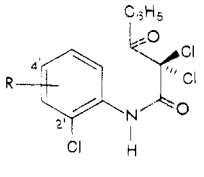
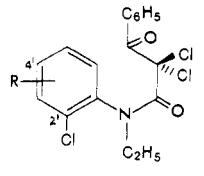
The preferred conformation of *N*-ethyl-2,2,2′-trichlorobenzoylacetanilide (**1f**) was deduced from ^1H NMR data and served to account for the failure of **1f** to cyclize in H_2SO_4 in terms of a steric hindrance to attainment of the requisite conformation for ring closure. Consistent with this view was the observation that pentachlorodihydroquinolinone **7a** with H_2SO_4 underwent ring opening to give as chief product alkene **8**, and only a minor amount of indenoquinolinone **2**. Substrate **7a** was formed, in preference to amide **11**, from difluorooxyborane **6a** and SO_2Cl_2, on allowing HCl to escape from the reaction mixture.

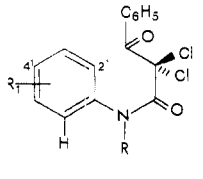
In the course of the conversion of β-keto amides **1** to indeno[1,2,3-*de*]quinolinones **2** by using concentrated sulfuric acid,[1] substrates **1d** and **11** each yielded a yellow,



1a, R = H
b, R = 3′,4′—diCH$_3$
c, R = 4′—Br—3′,5′—diCH$_3$
d, R = 4′—Cl—3′,5′—diCH$_3$



1e, R = H
f, R = 4′—Br—3′,5′—diCH$_3$
g, R = 4′—Cl—3′,5′—diCH$_3$



1h, R = H; R$_1$ = 2′,4′—diCH$_3$
i, R = H; R$_1$ = 4′—Cl—2′,3′—diCH$_3$
j, R = H; R$_1$ = 4′—Cl—3′,5′—diCH$_3$

1k, R = C$_2$H$_5$; R$_1$ = 2′,5′—diCH$_3$
l, R = C$_2$H$_5$; R$_1$ = 4′—Cl—3′,5′—diCH$_3$
m, R = i—C$_3$H$_7$; R$_1$ = 3′,5′—diCH$_3$

high-melting product which we suspect[2] to be indenoquinolinones **2a** and **2c**, respectively. The related 4′-bromo amide **1c** likewise underwent cyclization to an indenoquinolinone product, but in contrast, the corresponding *N*-ethyl derivatives, **1f** and **1g**, under similar conditions, gave neither **2** nor quinolinone **3** and were recovered largely unchanged.[3] The difficulties with **1f** and **1g** seemingly stem from steric factors, for which there appear to be few relevant precedents in the literature.

Koelsch and Britain[4] cyclized *N*-alkylbenzoylacetanilides to *N*-alkylquinolinones with sulfuric acid when the alkyl group was primary but not when it was secondary, as in **4a**. Failure in the latter instance, in their view, probably resulted from steric inhibition of N–Ar conjugation, an interpretation supported by UV properties of related *N*-alkyl-*p*-nitroacetanilides. In strong acid media, however, the aforementioned N-lone-pair participation may be of little importance,[2] and we prefer to rationalize the behavior of substrates such as **1f**, **1g**, **4a**, and **4b**, primarily in terms of steric hindrance to attainment of the conformation requisite for ring closure.[2] With a view to substantiating this suggestion, amide **1f** was selected for a conformational analysis, utilizing the results of ^1H NMR spectral studies with a variety of aniline derivatives[5,6] and our findings[3] with representative β-keto amides **1**. Some general conclusions concerning the steric preferences of the latter compounds were drawn from the following results.

Amides **1h** (δ 7.4), **1i** (δ 7.2), and **1j** (δ 7.2) each showed an "acylation shift" ($CDCl_3$) of the ortho proton comparable to that in the corresponding acetanilide, supporting

(1) B. Staskun, *Tetrahedron*, **28**, 5069 (1972).
(2) B. Staskun, *J. Org. Chem.*, **39**, 3494 (1974).
(3) B. Staskun, unpublished results.
(4) C. F. Koelsch and J. W. Britain, *J. Org. Chem.*, **24**, 1551 (1959).
(5) R. F. C. Brown, L. Radom, S. Sternhell, and I. D. Rae, *Can. J. Chem.*, **46**, 2578 (1968).
(6) R. E. Carter, *Acta Chem. Scand.*, **21**, 75 (1967).

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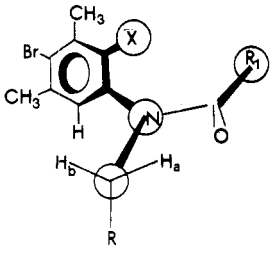


X=Cl; R=CH_3; R_1=$C_6H_5COCCl_2$

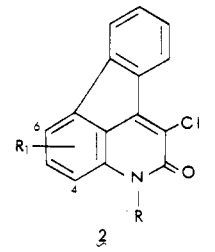
Figure 1. Conformation for **1f** which accommodates both a trans carbonyl group and the nonequivalence of the methylene protons.

a cis carbonyl conformation in the former compounds, i.e., with the amido carbonyl pointing toward the arylamido ring.[5] A like conformation is assigned in the 2′-chloro NH derivatives **1a**, **1b**, **1c**, and **1d**, in which the signal for the ortho proton appeared at unusually low field (near δ 8.0).[7] In contrast, the *N*-alkyl β-keto amides **1k**, **1l**, and **1m** exhibited hardly any "shift"; i.e., the relevant ortho proton resonance (δ 6.58, 6.50, and 6.20, respectively) differed only slightly from that in the corresponding arylamine, (δ ~6.3). By analogy with the *N*-alkylacetanilides,[6] these keto amides accordingly are assigned a trans conformation for the carbonyl, and this assumption is extended to **1f** (δ 6.96).

Particularly noteworthy in the ^{1}H NMR spectrum of **1f** was a symmetrical 12–14 peak multiplet for the geminal methylene protons of the *N*-ethyl group. Nonequivalence of the geminal protons was also observed in the simpler *N*-ethyl amide **1e**, although absent in **1l**, and was indicative of a rotational barrier[8,9] about the Ar–N bond, affording a diastereomeric environment in each of the 2′-chloro compounds.

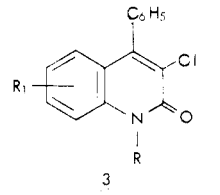
Figure 1 shows a conformation for **1f** which accommodates both a trans carbonyl group and the nonequivalence of the methylene protons and is presumably of lowest energy.[10] In a space-filling (Catalin) model (with sp^2 N), protons H_a and H_b (in Figure 1) were situated in dissimilar environments (lying in the vicinity of the CO group and the phenyl ring, respectively), establishing a difference in chemical shift. This shift is related to the proportion of preferred conformer (Figure 1) among the various conformer populations and would be expected to increase with the size of the substituents X and R.[11]

When an attempt was made to align the keto carbonyl group in the (Catalin) model for proper electrophilic attack on the arylamido ring, the N–Ar bond rotated concomitantly with introduction of unfavorable steric interactions between the 2′-Cl and N–Et substituents. An analogous hindrance did not arise in **1c**, thus affording an explanation for the difference in chemical behavior. In the event of the aforementioned steric constraint being overcome, cyclization of **1f** in sulfuric acid would be expected to lead to carbonium ion **5a**, of a type postulated to intervene[1] in the conversion of **1** to **2**. Moreover, it was evident from a (Catalin) model of **2** that species **5** would likewise be sterically impeded from transforming to either of the (planar) systems **2** or **3**. Chemical observations corroborating this latter assessment are now presented.

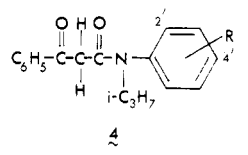


2

a, R=H; R_1=4-Cl-5-CH_2Cl-6-CH_3
b, R=C_2H_5; R_1=4-Cl-5-CH_2Cl-6-CH_3
c, R=C_2H_5; R_1=4-Cl-5,6-diCH_3

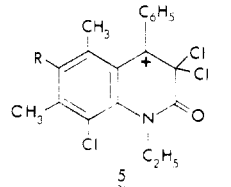


3



4

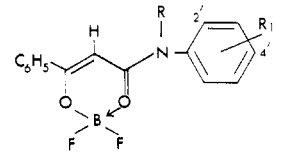
a, R=H
b, R=2′-CH_3



5

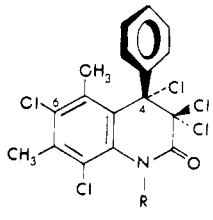
a, R=Br
b, R=Cl

We recently treated certain difluorooxyborane derivatives of type **6** with sulfuryl chloride to obtain the corresponding 2,2-dichloro-β-keto amides **1**.[12] The reaction between **6a** and sulfuryl chloride took an unexpected and different course on allowing HCl to escape to the atmosphere; the product mixture now contained a substantial proportion (>47%) of a new substance "A", and only a minor amount of **1l**. A molecular formula of $C_{19}H_{16}Cl_5NO$ was established from the elemental analysis and accurate mass spectral measurements of the molecular ion. The ^{1}H NMR spectrum ($CDCl_3$) revealed the presence in A of two intact (aromatic) Me groups (singlets at δ 1.72 and 2.58, respectively) and of an *N*-ethyl moiety with nonequivalent methylene protons (12-peak multiplet centered at δ 4.15). A strong IR absorption at 1710 cm^{-1} implicated an amide carbonyl group adjacent to a *gem*-dichloro function. These data accord with A having dihydroquinolinone structure **7a**, and its formation constitutes a novel synthesis of this ring system. The relatively upfield ^{1}H NMR absorption (δ 1.72) of the 5-Me group in **7a** derives from shielding by an out-of-plane 4-phenyl ring, while the presence in the



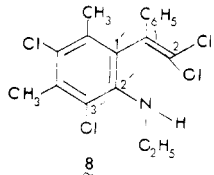
6

a, R=C_2H_5; R_1=3′,5′-diCH_3
b, R=$C_6H_5CH_2$; R_1=3′,5′-diCH_3
c, R=C_2H_5; R_1=4′-Br-2′-Cl-3′,5′-diCH_3



7

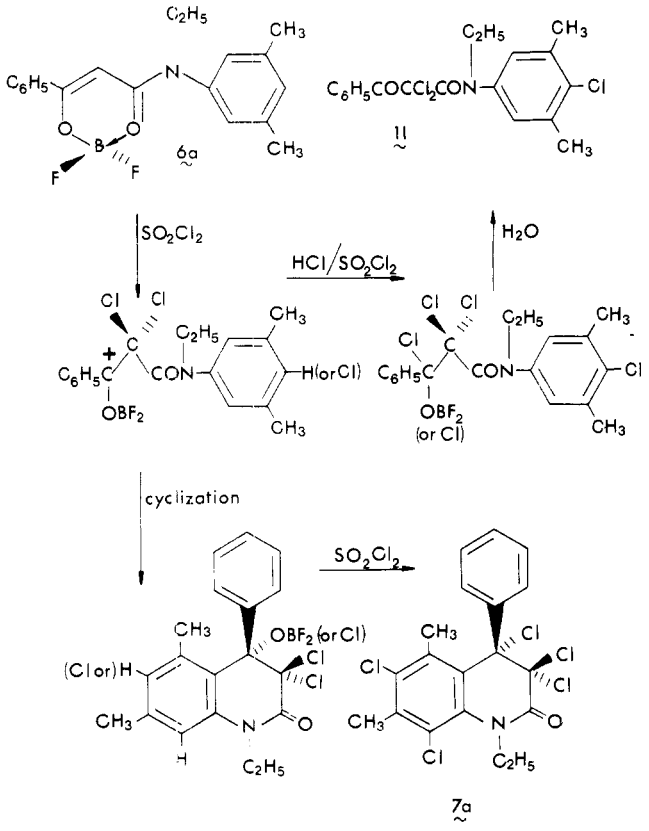
a, R=C_2H_5
b, R=$C_6H_5CH_2$



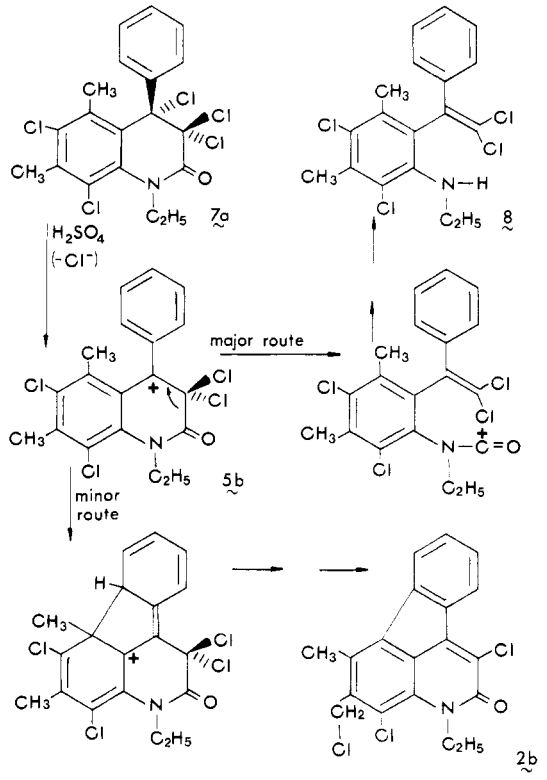
8

(7) Similar substantial "shifts" in acetanilides have been attributed to the deshielding influence of the cis carbonyl intramolecularly H-bonded to the Cl atom in an approximately planar situation.[5]
(8) W. B. Jennings, *Chem. Rev.*, **75**, 307 (1975).
(9) I. O. Sutherland, *Annu. Rep. NMR Spectrosc.*, **4**, 200 (1971).
(10) For a related preferred conformation (of a phthalimide derivative) see A. N. Lewin, J. Lipowitz, and T. Cohen, *Tetrahedron Lett.*, 1241 (1965).
(11) This expectation was borne out with certain *N*-benzyl ortho-substituted difluorooxyborane derivatives (**6**).[3]
(12) B. Staskun, *J. Org. Chem.*, **44**, 875 (1979).

Scheme I



Scheme II



spectrum of a multiplet (1 H) near δ 8.0 is attributed to anisotropic deshielding of an ortho proton by a neighboring Cl atom. Structure **7a** was supported from the ^{13}C NMR signals which correlated with the appropriate carbons, including peaks at δ 161.57 (C=O), 123.28 (CCl_2), and 88.14 (CCl). A tentative pathway for the production of **7a** from **6a** is outlined in Scheme I; in this view cyclization precedes introduction of (at least) the 8-Cl substituent.

The analogous *N*-benzyldihydroquinolinone **7b**, characterized from its elemental analysis and spectral properties, was formed on similar treatment of **6b** with sulfuryl chloride. Restricted rotation about the Ar–N bond in **7b** was revealed from the ^1H NMR spectrum which exhibited two doublets (J = 15 Hz) of an AB system for the methylene protons of the *N*-benzyl group.

In the expectation of generating carbonium ion **5b**, and hence forming indenoquinolinone **2** (vide supra), compound **7a** was warmed with concentrated sulfuric acid. In the event, only a minor amount of **2** resulted, and the chief reaction product, isolated after chromatography (43%), was a substance "B". From its elemental analysis ($C_{18}H_{17}Cl_4N$) and spectral (IR, ^1H NMR, ^{13}C NMR, and MS) properties, B is assigned the ring-opened structure **8**. The presence of an amino function in **8** was established from the IR peak at 3330 cm^{-1} (carbonyl absorption absent) and the ^1H NMR signal (1 H) near δ 3.4 (removed by D_2O), while evidence for the 3′-Cl substituent was provided from the nonequivalence of the methylene protons of the *N*-ethyl group [complex multiplet (2 H) overlapping the NH absorption]. In confirmation of an unsubstituted phenyl ring in **8** were the relatively high intensity ^{13}C NMR signals at δ 128.08, 128.50, and 128.94 and the ^1H NMR absorption band (5 H) at δ 7.3.

The conversion of **7a** to **8** suggests a potentially useful approach to the synthesis of tetrasubstituted olefins and is rationalized in Scheme II; as indenoquinolinone formation and loss of Cl^+ (to give **3**) are both sterically impeded (vide supra), relief of strain in **5b** is achieved preferentially by opening of the dihydroquinolinone ring.

Experimental Section[13]

4′-Bromo-3′,5′-dimethyl-*N*-ethyl-2,2,2′-trichlorobenzoylacetanilide (1f) was prepared from *N*-ethyldifluorooxyborane **6c** and sulfuryl chloride in acetonitrile solution:[12] colorless crystals (from absolute ethanol), mp 115–116 °C; IR 1710 (keto C=O), 1650 cm^{-1} (amide C=O); ^1H NMR ($CDCl_3$) δ 1.12 (t, 3 H, CH_2CH_3), 2.32 (s, 3 H, $ArCH_3$), 2.50 (s, 3 H, $ArCH_3$), 2.7–4.6 (symmetrical 12-14-peak multiplet centered at δ 3.65, 2 H, CH_2CH_3), 6.96 (s, 1 H, 6′-H), 7.25–8.1 (m, 5 H, ArH); mass spectrum, m/e 475 (1 Br, 3 Cl; minor peak, M^+), 440 (1 Br, 2 Cl; M – 35), 370 (1 Br, 3 Cl; M – 105), 288 [1 Br, 1 Cl; Br(Cl)-$(CH_3)_2C_6HN(CO)C_2H_5$], 260 (1 Br, 1 Cl; 288 – 28).

3,4-Dihydro-5,7-dimethyl-1-ethyl-3,3,4,6,8-pentachloro-4-phenylquinolin-2-one (7a). Sulfuryl chloride (6 mL) was added in one portion to **6a** (1.8 g) contained in a 50-mL flask; an immediate and vigorous evolution of gas occurred. The flask was stoppered with cotton wool and left to stand at room temperature for 3 h; after ~45 min the solution rather suddenly developed an intense dark green color which gradually faded to pale yellow. Ice and water were added, and the mixture was stirred intermittently until the precipitated material had solidified. The colorless product was collected by filtration, washed with water, and air-dried (2.3 g, mp 155–170 °C); TLC (benzene) showed this to be a mixture with **7a** as a major component, easily distinguished (highest R_f value) from several minor products which included **11**. The latter substances were dissolved on swirling the mixture with warm (ca. 60 °C) ethanol (3 × 10 mL) providing a residue of **7a** (1.1 g; mp 183–195 °C; one spot on TLC) which was recrystallized as colorless crystals (from ethanol–dimethylformamide): mp 197–199 °C, raised to 205–207 °C on recrystallization

(13) All melting points were determined with a Kofler hot-stage apparatus and are uncorrected. IR spectra (KBr disk) were recorded on a Perkin-Elmer Model 521 spectrophotometer; ^1H NMR spectra were obtained at 60 MHz by using a Hitachi Perkin-Elmer R-20 instrument, with Me_4Si as internal reference (s, singlet; d, doublet; t, triplet; m, multiplet). Mass spectra (m/e) were measured on a Varian CH-5 spectrometer at 70 eV; the correct isotopic abundance ratios were observed in the compounds described. Microanalyses and ^{13}C NMR spectra were determined at the CSIR, Pretoria, South Africa.

from absolute ethanol; IR 1710 cm^{-1} (amide C=O); ^1H NMR ($CDCl_3$) δ 1.22 (t, J = 7 Hz, 3 H, CH_2CH_3), 1.72 (s, 3 H, $ArCH_3$), 2.58 (s, 3 H, $ArCH_3$), 4.0–4.3 (symmetrical 12-peak multiplet centered at δ 4.15, 2 H, CH_2CH_3), 7–7.6 (m, 4 H, ArH), 8.0–8.2 (m, 1 H, ArH); ^{13}C NMR ($CDCl_3$) δ 12.67 ($ArCH_3$), 19.03 ($ArCH_3$), 21.28 (CH_3CH_2), 45.22 (N–CH_2), 88.18 (C-4), 123.28 (C-3), 126.54, 128.03, 129.31, 129.53, 130.16, 130.66, 130.95, 133.64, 134.56, 137.06, 137.43, 161.57 (C=O); mass spectrum, m/e 449 (5 Cl, M^+), 414 (4 Cl, M – 35), 386 (4 Cl, 414 – 28), 379 (3 Cl, M – 70), 351 (3 Cl, 379 – 28), 344 (2 Cl, 379 – 35), 316 (2 Cl, 351 – 35).

Anal. Calcd for $C_{19}H_{16}Cl_5NO$: C, 50.53; H, 3.57; Cl, 39.25; N, 3.10; m/e 448.9674 (M^+). Found: C, 50.55; H, 3.79; Cl, 39.28; N, 2.88; m/e 448.9728 (M^+).

The 1-benzyl analogue **7b** was similarly derived from difluorooxyborane **6b** (0.30 g) and sulfuryl chloride (1.5 mL); after extraction of the contaminants with warm ethanol, the residual **7b** (0.15 g, 40%) was crystallized from absolute ethanol: colorless crystals; mp 217–220 °C; IR 1720 cm^{-1} (amide C=O); ^1H NMR ($CDCl_3$) δ 1.65 (s, 3 H, $ArCH_3$), 2.52 (s, 3 H, $ArCH_3$), 5.12 (d, J = 15 Hz, 1 H, benzylic H), 5.47 (d, J = 15 Hz, 1 H, benzylic H), 7.0–7.6 (broad 4-phenyl multiplet superimposed on N-benzyl singlet, 9 H, ArH), 8.0 (m, 1 H, ArH); mass spectrum, m/e 511 (5 Cl, M^+), 476 (4 Cl, M – 35), 441 (3 Cl, M – 70).

Anal. Calcd for $C_{24}H_{18}Cl_5NO$: C, 56.12; H, 3.53; Cl, 34.51; N, 2.73; m/e 510.9831 (M^+). Found: C, 56.25; H, 3.68; Cl, 34.91; N, 2.53; 510.9869 (M^+).

Compounds **7a** and **7b** each gave a purple solution in concentrated sulfuric acid.

1-Phenyl-1-[(3′,5′-dichloro-4′,6′-dimethyl-2′-(ethylamino))phenyl]-2,2-dichloroethene(8). Concentrated sulfuric acid (1.6 mL) was added to a mixture of **7a** (0.80 g, 1.8 mmol) and silver sulfate (0.31 g, 1 mmol) after which the permanganate-colored mass was kept at 95 °C (oil bath) for 3 min with intermittent stirring; negligible hydrogen chloride was evolved in contrast to the reaction without silver sulfate. The orange mixture was diluted with ice and water and extracted with chloroform, and the organic phase was washed with water, dried (anhydrous sodium sulfate), and evaporated to leave an orange gum (0.8 g); TLC (benzene) showed several constituents, with **8** (highest R_f value) predominating and a minor amount of (suspected) **2b** (yellow spot). Separation of the gum on a column (Merck, Kieselgel 60; benzene) afforded **8** as an oil (0.30 g, 43%) which solidified on standing: colorless, shining plates (from acetone–ethanol); mp 112–113 °C; IR 3330 cm^{-1} (NH); ^1H NMR ($CDCl_3$) δ 1.11 (t, J = 7 Hz, 3 H, CH_2CH_3), 2.34 (s, 3 H, $ArCH_3$), 2.46 (s, 3 H, $ArCH_3$), ~3.1 (complex m, 2 H, CH_2CH_3), 3.4 (br s, NH, D_2O exchangeable), 7.1–7.5 (m, 5 H, ArH); ^{13}C NMR ($CDCl_3$) δ 16.08 ($ArCH_3$), 17.89 ($ArCH_3$), 19.13 (CH_2CH_3), 42.51 (CH_2CH_3), 122.17 (C-2), 125.16, 127.77, 128.08, 128.50, 128.94, 129.66, 130.60, 133.46, 135.03, 136.62, 137.06, 142.01 (C-1); mass spectrum, m/e 387 (4 Cl, M^+), 352 (3 Cl, M – 35), 351 (3 Cl, M – 36), 336 (3 Cl, 351 – 15), 323 (3 Cl, 351 – C_2H_4), 317 (2 Cl, M – 70).

Anal. Calcd for $C_{18}H_{17}Cl_4N$: C, 55.56; H, 4.40; Cl, 36.44; N, 3.60. Found: C, 55.61; H, 4.52; Cl, 36.16; N, 3.37.

Compound **8** dissolved easily in chloroform, acetone, and benzene but was sparingly soluble in ethanol and in hot 2 M HCl.

Continued elution of the Kieselgel column with benzene–acetone (10:1 to 5:1) and evaporation of the appropriate combined fractions yielded ~50 mg of suspected indenoquinolinone **2b**: yellow crystals (from acetone–methanol); mp 145–155 °C; IR 1650 (amide C=O), 760 cm^{-1} (four adjacent protons); mass spectrum, m/e 377 (3 Cl, M^+), 349 (3 Cl, M – C_2H_4), 342 (2 Cl, M – 35), 314 (2 Cl, 349 – 35).

Registry No. 1f, 73396-48-2; **1l**, 52827-58-4; **2b**, 73396-49-3; **6a**, 73396-50-6; **6b**, 73396-51-7; **6c**, 73396-52-8; **7a**, 73396-53-9; **7b**, 73396-54-0; **8**, 73396-55-1.

Pteridines. 47. Preparation and Chemistry of 2-Amino-6-carbalkoxy-3-cyano-5-substituted Pyrazine 1-Oxides: Synthesis of Pterin-6-carboxaldehyde[1,2]

Edward C. Taylor* and Donald J. Dumas

Department of Chemistry, Princeton University, Princeton, New Jersey 08544

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A new procedure for the synthesis of 2-amino-3-cyano-5-substituted pyrazines **9**, useful intermediates for the synthesis of pteridines, is described. Oximation of β-keto esters **2** followed by reaction with aminomalononitrile provides 2-amino-6-carbalkoxy-3-cyano-5-substituted pyrazine 1-oxides **5**. Protection of the amino group as its ((dimethylamino)methylene)amino derivative **9** followed by S_N2 decarbalkoxylation provides pyrazines **10** which on removal of the protecting group and deoxygenation give pyrazines **8**. This method is designed to be of use in cases where the β-keto ester cannot be converted directly to the corresponding α-keto aldoxime **3**. The procedure is applied to the synthesis of 2-amino-3-cyano-5-(dimethoxymethyl)pyrazine (**8a**), an intermediate in the synthesis of pterin-6-carboxaldehyde (**1**).

Over the past few years we have developed a versatile new synthetic approach to pteridines which utilizes as its key first (and unequivocal) step the cyclization of an α-oximinocarbonyl compound with an α-aminonitrile to give a 2-amino-3-cyano- (or carbalkoxy-) pyrazine 1-oxide which can then be converted to pteridines and pterins by a series of simple deoxygenation and cyclization steps.[3] We describe in this paper a further extension of this procedure to the preparation of 2-amino-3-cyano-5-(dimethoxymethyl)pyrazine (**8a**) (see Scheme I), which has been shown previously to be an effective intermediate for the synthesis of pterin-6-carboxaldehyde (**1**),[4] a naturally-occurring pterin of particular interest as an intermediate for the synthesis of pteroic acid,[5–8] folic acid,[5–7] and various analogues of these two natural products.[6,9–12]

(1) For the previous paper in this series see E. C. Taylor and A. J. Cocuzza, *J. Org. Chem.*, **44**, 302 (1979).

(2) We are indebted to F. Hoffmann-La Roche & Co., Ltd., for support of this work.

(3) For reviews of this approach to pteridine synthesis, see (a) E. C. Taylor in "Chemistry and Biology of Pteridines", W. Pfleiderer, Ed., Walter de Gruyter, Berlin, 1976, pp 543–73; (b) E. C. Taylor, R. N. Henrie II, and D. J. Dumas in "Chemistry and Biology of Pteridines", R. L. Kisliuk and G. M. Brown, Eds., Elsevier/North-Holland, New York, 1979, pp 71–75; (c) preceding papers in this series.

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