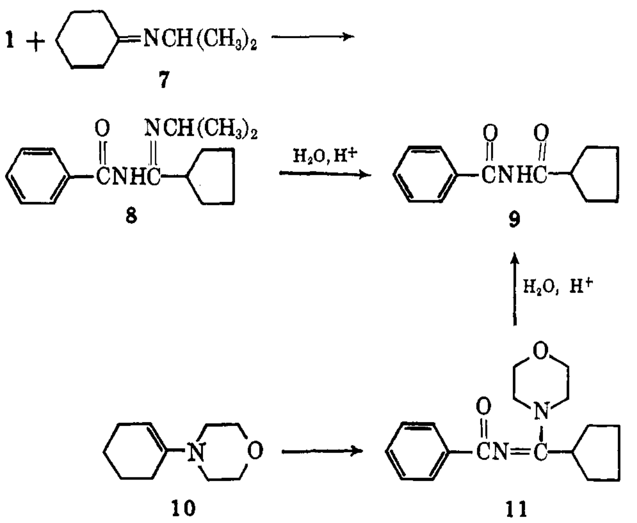

Experimental Section[7]

General Procedure.—Benzoyl azide (1) was added to the imine or enamine in either acetonitrile or benzene. The same results were obtained when either solvent was used; however, the reaction proceeded at a faster rate in the more polar solvent. The reaction was exothermic and the temperature of the mixture was maintained at 25 ± 5° by means of intermittent cooling. Nitrogen was evolved and after standing for 16 to 20 hr., the solvent was removed under reduced pressure. After examining the crude product, it was subjected to hydrolysis by allowing it to stand in excess 10% hydrochloric acid solution for 12 to 16 hr. The precipitated imide was removed by filtration.

N-Isobutyrylbenzamide (4). A.—The reaction of 1 (28 g., 0.19 mole) and 2a (20 g., 0.20 mole) in acetonitrile gave a 25-g. yield of crude 3a: infrared absorptions 3.0, 4.95, and 6.2–6.4 (s) μ. Compound 3b, prepared in the same manner as 3a, had a similar spectrum. Hydrolysis of 3b (2.95 g., 0.014 mole) gave an 1.78-g. (69%) yield of 4, which had an infrared spectrum identical with that of the material prepared subsequently by the reaction of 1 and 5. The n.m.r. spectrum (CCl_4) of crude 3b showed a doublet at 1.22 (isopropyl group), a single peak at 2.92 (N-methyl) which overlaps the peaks due to the tertiary proton of the isopropyl group, peaks at 7.47 and 8.40 (aromatic protons), and a broad peak at 11.61 (>N-H) p.p.m.

B.—The reaction of 1 (14 g., 0.095 mole) and 5 (10 g., 0.10 mole) in benzene (50 ml.) gave a 22-g. yield of crude 6 as an oil: infrared absorptions (neat) 2.95 (w) and 6.2–6.4 (s) μ; n.m.r. spectrum (CCl_4) doublet centered at 1.24 and septet at 3.06 (isopropyl group), peak at 3.12 (dimethylamino group), and peaks at 7.66 and 8.39 (aromatic protons) p.p.m. Hydrolysis of 6 (22 g., 0.10 mole) gave a 16-g. (88%) yield of 4: m.p. 153–154° (lit.[8] m.p. 154–155.5°); infrared absorption (KBr) 5.83 μ; n.m.r. spectrum (CH_2Cl_2) doublet at 1.28 and septet at 3.73 (isopropyl group), peaks at 7.88 and 9.28 (aromatic protons), and broad peak at 9.12 (>N-H) p.p.m.

Anal. Calcd. for $C_{11}H_{13}NO_2$: C, 69.1; H, 6.9. Found: C, 69.2; H, 7.2.

N-(Cyclopentylcarbonyl)benzamide (9). A.—The reaction of 1 (14 g., 0.095 mole) and 7 (14 g., 0.1 mole) in acetonitrile gave an 11-g. (45%) yield of crude 8, m.p. 70–72°. A sample recrystallized from a hexane–pentane mixture melted at 73.5–75°: infrared absorption (KBr) 6.3 (s) μ; n.m.r. spectrum doublet at 1.21 and broad peak at 3.83 (isopropyl group), two broad peaks at 1.85 (methylene protons of the cyclopentane ring) and 2.91 (tertiary proton of the cyclopentane ring), peaks at 7.43 and 8.36 (aromatic protons), and a broad peak at 11.85 (>N-H) p.p.m.

Anal. Calcd. for $C_{16}H_{22}N_2O$: C, 74.4; H, 8.6; mol. wt., 258. Found: C, 73.8; H, 8.3; mol. wt. (ebullioscopic in benzene), 257.

Hydrolysis of 8 (3 g., 0.012 mole) gave a 48% yield of 9 which had an infrared spectrum identical with that of the imide prepared subsequently from 1 and 10.[9]

B.—The reaction of 1 (28 g., 0.2 mole) and 10 (33 g., 0.2 mole) in benzene (50 ml.) gave a 59.5-g. yield of crude 11 as an oil: n.m.r. spectrum (CH_2Cl_2) broad peaks at 1.82 and 3.17 (protons of the cyclopentane ring), peak at 3.79 (protons of the morpholine ring), and peaks at 7.78 and 8.47 (aromatic protons) p.p.m. Hydrolysis of 59.5 g. of crude 11 gave a 35.5-g. (82%) yield of 9: m.p. (after one recrystallization from hexane) 140–141°; infrared absorptions (KBr) 5.83 and 6.0 μ; n.m.r. spectrum (CH_2Cl_2) broad peaks at 1.84 and 3.93 (protons of the cyclopentane ring), peaks at 7.95 and 8.34 (aromatic protons), and broad peak at 9.32 (>N-H) p.p.m.

Anal. Calcd. for $C_{13}H_{15}NO_2$: C, 71.8; H, 7.0. Found: C, 71.9; H, 7.1.

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[7] Melting and boiling points are corrected. The melting points were determined on a Fischer-Johns melting point block. N.m.r. spectra were measured at 60 Mc. on a Varian A-60 spectrometer with tetramethylsilane as an internal standard. The infrared spectra were determined on Baird AB-2 and MK-1A spectrophotometers.

[8] C. J. Eby and C. R. Hauser, *J. Am. Chem. Soc.*, **79**, 723 (1957).

[9] G. Stork, A. Brizzolara, H. Landesman, J. Szmuszkovicz, and R. Terrell, *ibid.*, **85**, 207 (1963).

Ketenes. VI. The Stereospecific Cycloaddition of Dimethylketene to *cis*- and *trans*-Butenyl Ethyl Ethers[1,2]

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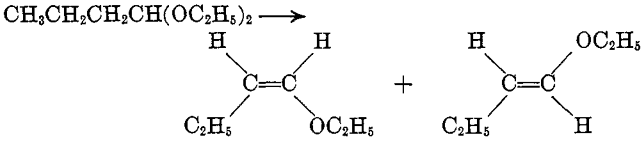
Received March 19, 1965

In an earlier paper in this series[3] we described the 1,2 cycloaddition of unsaturated ethers to dimethylketene to give 3-alkoxycyclobutanones and mentioned the probability that this cycloaddition is stereospecific. This paper is a more thorough treatment of that subject. 1-Butenyl ethyl ether, as prepared from butyraldehyde diethyl acetal, is a mixture of *cis* (1a) and *trans* (1b) isomers in the ratio of 2:1 as determined by g.l.p.c.[4] Careful fractionation through a 72-in. wire spiral column gave a fraction high (88%) in 1a and a fraction high (97%) in 1b.



1a 1b

When dimethylketene reacted with a mixture of 48% 1a and 52% 1b in benzene, the yellow color which is characteristic of dimethylketene persisted for 40 hr. This indicated that the cycloaddition was quite slow for at least one of the isomers. Analysis by g.l.p.c. of the low-boiling portion of the reaction mixture showed that it contained a substantial amount of unchanged 1b and no 1a. Analysis by g.l.p.c. of the high-boiling portion showed that it contained 76% *cis*-3-ethoxy-4-ethyl-2,2-dimethylcyclobutanone (2a), 10%

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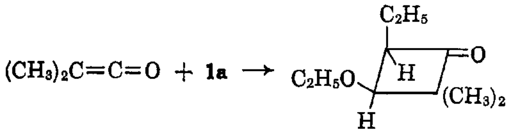
[1] Paper V: J. C. Martin, P. G. Gott, V. W. Goodlett, and R. H. Hasek, *J. Org. Chem.*, **30**, 4175 (1965).

[2] While this paper was in preparation, R. Huisgen, L. Feiler, and G. Binsch [*Angew. Chem.*, **76**, 893 (1964)] published similar work on the cycloaddition of diphenylketene to *cis*- and *trans*-propenyl propyl ethers.

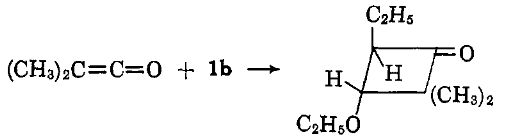
[3] R. H. Hasek, P. G. Gott, and J. C. Martin, *J. Org. Chem.*, **29**, 1239 (1964).

[4] All g.l.p.c. separations were made on a 0.25 in. × 6 ft. column packed with 20% Carbowax 20M on Chromosorb P. Compositions of mixtures are reported in area per cent.

trans-3-ethoxy-4-ethyl-2,2-dimethylcyclobutanone (**2b**), and 14% tetramethyl-1,3-cyclobutanedione. These results indicate that the *cis* ether is much more reactive in this cycloaddition than the *trans* ether.



2a



2b

The stereospecificity of the reaction was demonstrated by the treatment of dimethylketene with predominantly *cis* ether. When equimolar amounts of dimethylketene and 1-butenyl ethyl ether (88% **1a** and 12% **1b**) were combined in benzene, the yellow color owing to dimethylketene disappeared in a few hours. Analysis by g.l.p.c. showed that the high-boiling portion of the reaction mixture consisted of only one component, the *cis*-cyclobutanone **2a**. This compound was isolated and identified by its n.m.r. spectrum.[5]

The reaction of dimethylketene with the *trans* ether **1b** was markedly slower than that with the *cis* ether **1a**. The competing dimerization of dimethylketene to give tetramethyl-1,3-cyclobutanedione was predominant.

The structural assignments of **1a** and **1b** were made on the basis of their n.m.r. spectra. Karplus reported that in the n.m.r. spectra of ethylenic compounds, the *trans* coupling constant is larger than the *cis* coupling constant.[6] The values for **1a** and **1b** were $J = 6.0$ and 12.7 c.p.s., respectively.

The structural assignments of **2a** and **2b** were made on the basis of their n.m.r. spectra. Karplus showed that vicinal proton coupling constants depend on the dihedral angle involved.[7] If **2a** and **2b** are planar,[8] and the angle between geminal substituents is 110°, the dihedral angle for the *cis* form **2a** is 0° and for the *trans* form **2b** is 127°. By using the equation of Karplus, we determined that the coupling constant for **2a** should be larger than that for **2b**. The observed values for the two isomers formed were $J = 8.0$ and 6.9 c.p.s. The isomer with $J = 8.0$ c.p.s. was assigned the *cis* structure **2a** and the other isomer was assigned the *trans* structure **2b**.

The following conclusions were drawn from our work: (1) the 1,2 cycloaddition of dimethylketene to 1-butenyl ethyl ether is stereospecific, *i.e.*, the *trans* ether gives a *trans* adduct and the *cis* ether gives a *cis* adduct; and (2) the *cis* ether reacts much faster than the *trans* ether.

Experimental Section

***cis*- and *trans*-1-Butenyl Ethyl Ethers (1a and 1b).**—Butyraldehyde diethyl acetal (542 g., 3.7 moles) was distilled from phosphoric acid (0.4 ml.) through a 10-in. Vigreux column into a receiver containing potassium carbonate (10 g.). The distillate, b.p. 90–100°, consisted of a mixture of 1-butenyl ethyl ether and ethyl alcohol. It was decanted into a separatory funnel and washed with water until analysis by g.l.p.c. indicated that the alcohol was removed. The organic layer was dried over potassium carbonate and distilled through a 6-in. Vigreux column to give 130 g. (35%) of 1-butenyl ethyl ether, b.p. 92–97°.[9] Analysis by g.l.p.c. indicated that the ether was a mixture of *cis* and *trans* isomers in the ratio of 2:1. This mixture was fractionated through a 13 mm. × 72 in. nichrome wire spiral column, and the following fractions were selected as the best approximations of pure *cis* isomer, 50:50 mixture of *cis* and *trans* isomers, and pure *trans* isomer: I, 10 ml., b.p. 70.0–92.0° (mostly 89.0–92.0°), $n^{20}\text{D}$ 1.4039; II, 15 ml., b.p. 92.0–92.5°, $n^{20}\text{D}$ 1.4060; III, 10 ml., b.p. 92.5°, $n^{20}\text{D}$ 1.4059; and IV–XXVIII, 4-ml. fractions, b.p. 92.5–99.5°, $n^{20}\text{D}$ 1.4059–1.4068.

Analysis by g.l.p.c. showed that fraction II consisted of 88% **1a** and 12% **1b**. Fractions XX–XXII were combined to give a mixture (8.3 g.) of **1a** and **1b**. Analysis by g.l.p.c. showed that the mixture consisted of 48% **1a** and 52% **1b**. Fractions XXV–XXVIII were combined, and analysis by g.l.p.c. showed that the mixture consisted of 3% **1a** and 97% **1b**.

Pure **1a** and **1b** were isolated by using a chromatographic unit equipped with a $^3/_8$ in. × 10 ft. column.[10]

1a had $n^{20}\text{D}$ 1.4054; n.m.r. spectrum (CCl_4), triplets at 0.91 and 1.18 (methyl groups), quintet at 2.07 (methylene group of ethyl group), quartets at 3.71 (methylene group of ethoxy group) and 4.31 (proton on >C=C< next to ethyl group), and doublet ($J = 6.0$ c.p.s.) with additional small splitting caused by the 3-methylene group at 5.88 (proton on >C=C< next to ethoxy group) p.p.m.

Anal. Calcd. for $C_6H_{12}O$: C, 72.0; H, 12.1. Found: C, 72.1; H, 12.1.

1b had $n^{20}\text{D}$ 1.4072; n.m.r. spectrum (CCl_4), triplets at 0.97 and 1.22 (methyl groups), quintet at 1.93 (methylene group of the ethyl group), quartet at 3.62 (methylene group of the ethoxy group), pair of triplets at 4.65 (proton on >C=C< next to ethyl group), and doublet ($J = 12.7$ c.p.s.) at 6.17 (proton on >C=C< next to ethoxy group) p.p.m.

Anal. Calcd. for $C_6H_{12}O$: C, 72.0; H, 12.1. Found: C, 72.1; H, 12.1.

Reaction of Dimethylketene with a Mixture of 1a and 1b.—Dimethylketene (5.8 g., 0.083 mole) was added by means of a syringe to a solution of **1a** and **1b** (8.3 g., 0.083 mole, fractions XX–XXII) in benzene (25 ml.). The reaction was slightly exothermic and the temperature of the mixture was maintained below 30° by intermittent cooling. After standing for 19 hr., the mixture still possessed the characteristic yellow color of dimethylketene; however, after 40 hr., the yellow color had disappeared. Analysis by g.l.p.c. showed that the reaction mixture consisted of 76% **2a**, 10% **2b**, 14% tetramethyl-1,3-cyclobutanedione, and unchanged **1b**. The mixture was distilled through a 3-in. Vigreux column to give 26 g. of forerun followed by 6 g. of material with b.p. 62–63° (5 mm.), $n^{20}\text{D}$ 1.4299. Analysis by g.l.p.c. showed that the 26 g. of forerun consisted of 87% benzene and 13% **1b**. The n.m.r. spectrum of this mixture verified the absence of the *cis* ether **1a**. Analysis by g.l.p.c. indicated that the 6 g. of material consisted of 85% **2a**, 12% **2b**, and 3% tetramethyl-1,3-cyclobutanedione.

Pure **2b** was isolated by g.l.p.c.[9]: $n^{20}\text{D}$ 1.4283; n.m.r. spectrum (neat), singlets at 1.09 and 1.13 (methyl groups), triplet at 0.97 and quintet at 1.60 (ethyl group), triplet at 1.21 and quartet at 3.49 (ethoxy group), quartet at 3.11 (proton on the carbon adjacent to the carbonyl group), and doublet ($J = 6.9$ c.p.s.) at 3.48 (proton on the carbon bearing the ethoxy group) p.p.m.

Anal. Calcd. for $C_{10}H_{18}O_2$: C, 70.6; H, 10.7. Found: C, 70.1; H, 10.6.

Reaction of Dimethylketene with 1a.—Dimethylketene (7.76 g., 0.11 mole) was added by means of a syringe to a solution of

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[5] N.m.r. spectra were recorded on a Varian A-60 instrument at 60 Mc. with tetramethylsilane as an internal standard.

[6] M. Karplus, *J. Chem. Phys.*, **30**, 11 (1959).

[7] M. Karplus, *J. Am. Chem. Soc.*, **85**, 2870 (1963).

[8] The question of whether cyclobutanes have a puckered or planar configuration has been discussed at some length by A. Wilson and D. Goldhamer, *J. Chem. Educ.*, **40**, 504 (1963). A. Bauder, F. Tank, and H. Günthard [*Helv. Chim. Acta*, **46**, 1453 (1963)] have presented convincing evidence that *cyclobutanones are planar*. Although the use of a puckered model for our calculations would change the absolute values for *J*, the *cis* isomer would still have the higher relative value when ring puckering is less than about 35°.

[9] R. I. Longley, Jr. [U. S. Patent 2,667,517 (1954) (to Monsanto Chemical Co.)] reported two fractions, b.p. 91–94°, $n^{25}\text{D}$ 1.4045, and b.p. 94–96°, $n^{25}\text{D}$ 1.4039.

[10] The unit was an Aerograph Autoprep Model A-700 made by Wilkens Instrument and Research.

1-butenyl ethyl ether (11.1 g., 0.11 mole of fraction II) in benzene (25 ml.). The reaction was slightly exothermic, and the temperature of the mixture was maintained below 30° by intermittent cooling. After standing for 16 hr., the mixture had completely lost its yellow color. Analysis by g.l.p.c. of the reaction mixture showed only one major product peak, no evidence of any isomeric cyclobutanone, and the presence of a small amount of tetramethyl-1,3-cyclobutanedione. Distillation of the mixture gave, after removal of the solvent, 13 g. (69%) of pure **2a**: b.p. 66-67° (6 mm.); $n^{20}\text{D}$ 1.4304; n.m.r. spectrum (neat), singlets at 1.07 and 1.19 (methyl groups), triplet at 0.97 and quintet at 1.66 (ethyl group), triplet at 1.19 and quartet at 3.58 (ethoxy group), quartet at 3.28 (proton on the carbon adjacent to the carbonyl group), and doublet (J = 8.0 c.p.s.) at 3.88 (proton on the carbon bearing the ethoxy group) p.p.m.

Anal. Calcd. for $C_{10}H_{18}O_2$: C, 70.6; H, 10.7. Found: C, 70.3; H, 10.6.

Reaction of Dimethylketene with 1b.—Dimethylketene (7.2 g., 0.103 mole) was added by means of a syringe to a solution of **1b** (10.3 g., 0.103 mole, fractions XXV-XXVIII) in benzene (25 ml.). The reaction was slightly exothermic and the temperature of the mixture was maintained below 30° by intermittent cooling. After standing for 19 hr., the mixture still possessed the characteristic yellow color of dimethylketene; however, after 40 hr., the yellow color had disappeared. Analysis by g.l.p.c. showed that the reaction solution consisted of 57% tetramethyl-1,3-cyclobutanedione, 38% **2b**, 5% **2a**, benzene, and unchanged **1b**. The mixture was distilled to give 23 g. of forerun followed by 0.3 g. of material with b.p. *ca.* 65° (6 mm.). The forerun consisted of 31% **1b** and 69% benzene. The n.m.r. spectrum of this mixture verified the absence of **1a**. The 0.3 g. of higher boiling material was a mixture of 30% **2a** and 70% **2b**.

Ketenes. VII. Some Reactions of 3-Ethoxy-2,2-dimethylcyclobutanone with Aromatic Amines[1]

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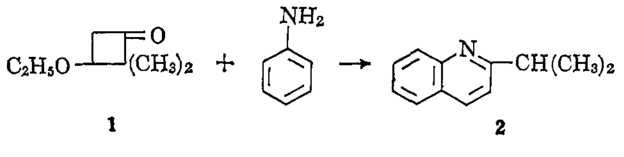
Received March 19, 1965

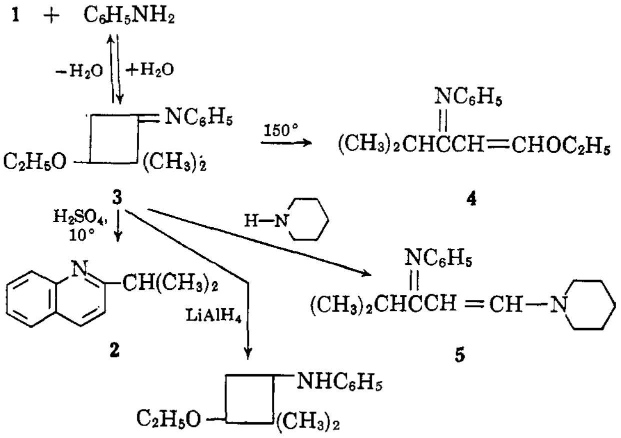
In an earlier paper in this series[2] we described the preparation of 3-ethoxy-2,2-dimethylcyclobutanone (1) from dimethylketene and ethyl vinyl ether. This paper is a report of some investigations of the reactions of 1 with aromatic amines. Aniline and 1, when refluxed in toluene with *p*-toluenesulfonic acid as a catalyst and with the water which was formed allowed to remain in the system, gave a 52% yield of 2-isopropylquinoline (2). A substantial amount (27%) of formanilide was obtained as a by-product in the reaction. This quinoline synthesis was extended to a few substituted anilines to give the new quinolines listed in Table I. The yields varied markedly with the nature and position of the substituent, but not enough examples were run to allow generalized predictions regarding substituents. It appears that *meta*-substituted anilines, particularly those with electron-donating groups, give the best yields. *m*-Toluidine and *m*-phenetidine gave a 70% yield of 2-isopropyl-7-methylquinoline[3] and a 55% yield of 7-ethoxy-2-isopropylquinoline, respectively. *o*- or *p*-Anisidine gave very low yields of the corresponding quinolines. *m*-Chloroaniline gave a 55% yield of a mixture of 5- (and 7-) chloro-2-isopropylquinoline.



The exact mechanism for the formation of 2 is not clear. However, it was observed that modifications of the reaction conditions led to the formation of entirely different products. For instance, the anil of 1, N-(3-ethoxy-2,2-dimethylcyclobutylidene)aniline (**3**), was prepared in 61% yield by heating **1** and aniline in the presence of aniline hydrochloride in toluene at 48° *in vacuo* and by removing water as it was formed. This low temperature was essential to the success of the reaction, as was demonstrated when this reaction was tried in refluxing toluene. At the higher temperature the water removed was 76% of the theoretical amount, but no **3** was obtained. Small amounts of ethyl alcohol, 3-methyl-2-butanone, N,N′-diphenylformamidine, unchanged **1**, and aniline, together with a large amount of black syrup, were produced.

The formation of **3** was found to be readily reversible. Exposure of **3** to atmospheric moisture for several hours gave **1** and aniline. When **3** was heated at 150° for 30 min., a ring-opening reaction to give N-(3-ethoxy-1-isopropylallylidene)aniline (**4**) in 82% yield took place. The reaction has a formal resemblance to the ring-opening reactions of 3-dialkylaminocyclobutanones having one or more α-hydrogen atoms.[4] N-(1-Isopropyl-3-piperidinoallylidene)aniline (**5**) was produced in 44% yield by the action of piperidine on **3** in refluxing toluene (Scheme I). We found that this ring-opening reaction was not confined to the anil; 3-ethoxy-2,2-dimethylcyclobutanone (**1**) and piperidine on refluxing in toluene underwent a similar reaction to give 4-methyl-1-piperidino-1-penten-3-one (**6**).[5] Treatment of **3** with cold, concentrated sulfuric acid gave 2-isopropylquinoline (**2**) in 76% yield.

SCHEME I



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[1] Paper VI: J. C. Martin, V. W. Goodlett, and R. D. Burpitt, *J. Org. Chem.*, **30**, 4309 (1965).

[2] R. H. Hasek, P. G. Gott, and J. C. Martin, *ibid.*, **29**, 1239 (1964).

[3] By analogy to other quinoline syntheses, the 7-methyl isomer rather than the 5-methyl isomer was the expected product. This was verified by the n.m.r. spectrum of our compound.

[4] R. H. Hasek and J. C. Martin, *J. Org. Chem.*, **28**, 1468 (1963).

[5] One rationale for this reaction presupposes that the ethoxy group of **1** is replaced by the piperidino group to give 2,2-dimethyl-3-piperidinocyclobutanone as an intermediate. According to reference **4**, this would be expected to open to **6**.