molecular weight in *m/e*, 13 (2), *m/e* 285, 15 (1), *m/e* 285, 21 (5), *m/e* 283, 24 (7), *m/e* 283.

1-Benzyl-5-carbomethoxy-1,2,3,4-tetrahydroquinoline (19).—A solution of 2.5 g (0.009 mol) of mixture **18** in 10 ml of toluene was heated under reflux with 1 g of 5% Pd–C for 26 hr. The catalyst was filtered and washed with ether. The washings were combined with the toluene solution and concentrated *in vacuo*. The residue was chromatographed on 100 g of Woelm neutral alumina. With benzene as the eluent, 1.3 g (51%) of compound **19** was obtained. Recrystallization from ethanol afforded an analytical sample of **19**: mp 77–78°; ir ($CHCl_3$), 5.84, 6.29, 14.4 μ; nmr ($CDCl_3$), τ 2.6–3.5 (m, 8), 5.55 (s, 2), 6.17 (s, 3), 6.5–7.1 (m, 4), 7.8–8.2 (m, 2).

Anal. Calcd for $C_{18}H_{19}NO_2$: C, 76.84; H, 6.81; N, 4.98. Found: C, 76.65; H, 6.72; N, 4.99.

5-Carbomethoxyquinoline (21).—A solution of 102 mg of compound **19** in 5 ml of absolute ethanol was treated with 500 mg of 5% Pd–C for 2 hr at atmospheric pressure and room temperature. *An evolution of gas was noted.* The catalyst was filtered and washed with ethanol. The washings were combined with the filtrate and concentrated *in vacuo* whereupon a solid residue was formed. Recrystallization from ether at −70° gave 55 mg (81%) of compound **21**: mp 39–41°; ir ($CHCl_3$), 5.82, 6.64 μ; nmr ($CDCl_3$), τ 0.50–0.70 (m, 1), 1.51–1.75 (m, 1), 2.10–2.30 (m, 2), 2.65–2.74 (m, 2), 6.00 (s, 3).

5-Carbomethoxyquinoline (21) by Known Synthesis.—A solution of 25 mg of quinoline-5-carboxylic acid in 50 ml of methanol was treated with excess diazoamethane. Evaporation of the solvent left a residue which was purified through preparative scale gas chromatography on a 5-ft, 20% SE-30 column at a flow rate of 90 ml/min and a column temperature of 190°. There was thus obtained 16 mg of ester **21**, mp 39–31° (undepressed on admixture with **21** from above).

Registry No.—**2**, 2409-87-2; **10**, 16675-55-1; **12**, 16675-56-2; picrate of **12**, 16675-57-3; **13**, 16675-58-4; **15**, 16675-59-5; **16**, 16675-60-8; **19**, 16675-61-9; **21**, 16675-62-0.

Mass Spectrometry in Structural and Stereochemical Problems. CLX.[1] On the Supposed *peri* Interaction in 4-Isobutylquinoline[2]

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In a previous publication from this laboratory,[3] the mass spectrum of 4-isobutylquinoline was reported. At 70 eV the base peak appeared at *m/e* 170, corresponding to the loss of a methyl radical. Even at 12 eV, this peak was second only to the molecular ion (*m/e* 185) in intensity, indicative of a highly facile mode of decomposition. Such behavior has been noted in 8-alkylquinolines, *e.g.*, 8-propylquinoline[3] where it has been attributed to ring closure with the suitably situated nitrogen atom. Since the concept of *peri* interactions in mass spectral fragmentations is being recognized more frequently,[4] the preferred loss of a methyl radical was

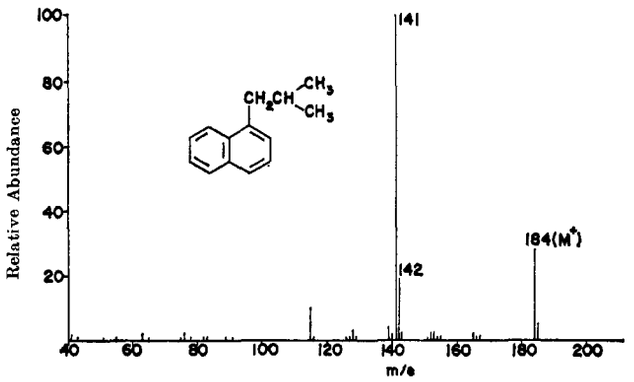


Figure 1.—Mass spectrum of 1-isobutylnaphthalene.

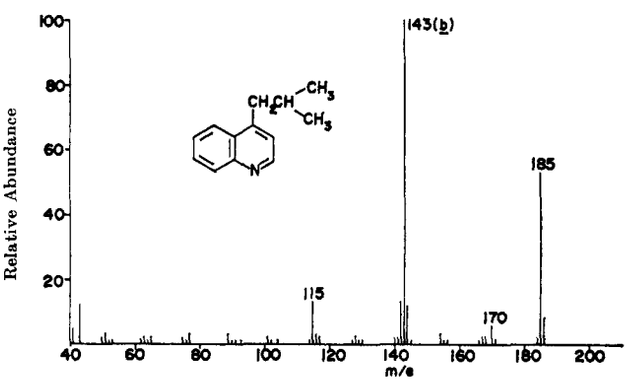


Figure 2.—Mass spectrum of 4-isobutylquinoline.

rationalized in terms of a cyclized structure (a), which would imply that in this instance (contrary to 8-propylquinoline) the presence of the heteroatom played no significant role in promoting this decomposition.

Accordingly, similar behavior would be expected in the hydrocarbon analog, *i.e.*, 1-isobutylnaphthalene. Consequently, this compound was prepared, as well as 1- and 2-butylnaphthalene. The occurrence of *peri* interaction would be expected to produce distinct qualitative differences between the 1- and 2-alkylnaphthalenes. In fact, the spectra of the three butylnaphthalenes are essentially identical. The reproduced spectrum (Figure 1) of 1-isobutylnaphthalene is representative. No evidence of significant *peri* interaction was obtained.

The dichotomy of these results cast suspicion on the original 4-isobutylquinoline spectrum.[3] The sample previously investigated was of commercial origin, and we were unable to determine the synthetic route used for its preparation. Gas chromatographic analysis revealed it to be a mixture of two major components in approximately 2:1 ratio, the greater one being 8-*t*-butylquinoline (as demonstrated by nmr spectroscopy) and the lesser one being quinoline. The presence of the former provides a simple explanation for the facile loss of a methyl radical.[3]

Consequently, authentic 4-isobutylquinoline was prepared by an unambiguous route as described in the Experimental Section. Its mass spectrum (Figure 2) is in marked contrast to that previously reported[3] and is completely consistent with the spectra[3] of other alkylquinolines. Thus the base peak at *m/e* 143 (70 eV) is due to the ubiquitous McLafferty rearrangement (I →

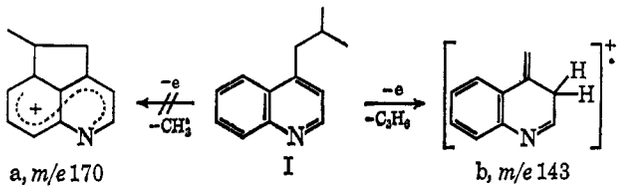
(1) For paper CLIX, see A. V. Robertson, M. Marx, and C. Djerassi, *Chem. Commun.*, 414 (1968).

(2) Support by the National Institutes of Health (Grant No. GM 11309) is gratefully acknowledged.

(3) S. D. Sample, D. A. Lightner, O. Buchardt, and C. Djerassi, *J. Org. Chem.*, **32**, 997 (1967).

(4) H. Budzikiewicz, C. Djerassi, and D. H. Williams, "Mass Spectrometry of Organic Compounds," Holden-Day, Inc., San Francisco, Calif., 1967, p 518.

b), while m/e 142 is associated with benzylic fission with loss of a propyl radical and m/e 115 with subsequent expulsion of the elements of hydrogen cyanide (appropriate metastable peak observed). *peri* interactions thus do not exist in 1-alkylnaphthalenes or 4-alkylquinolines.



a, m/e 170 I b, m/e 143

Experimental Section[5]

Butylnaphthalenes.—The three butylnaphthalenes were prepared by a Wurtz–Fittig coupling reaction[6] and purified by vpc.

4-Isobutylquinoline.—The synthesis was based on a modification[7] of the Blaise–Maire synthesis[8] of 4-alkylquinolines, which involves as a precursor a 2-chloroethylalkylketone obtained by condensation of a dialkycadmium reagent with the appropriate acid chloride.[9]

Isobutylmagnesium bromide was prepared from 7.9 ml of isobutyl bromide (0.073 mol) and 1.77 g of magnesium turnings (0.073 g-atom) in dry ether. This Grignard reagent was treated with 7.36 g of finely powdered dry cadmium chloride (0.040 mol) to produce diisobutylcadmium. The ether was removed by heating and replaced with benzene. After cooling of the vigorously stirred suspension in an ice bath, a solution of 5.7 ml of 3-chloropropionyl chloride (0.059 mol) in benzene was added slowly with continuous stirring. Ice-bath temperature was maintained for 0.5 hr and was followed by a 45-min reflux. The reaction mixture was then cooled and filtered, and the precipitate washed with benzene. After extraction with 10% aqueous sodium bicarbonate and drying with magnesium sulfate, the benzene solvent was evaporated under water aspiration, leaving 1-chloro-5-methyl-3-hexanone (1.1 g) as a sweet-smelling oil which was used directly in the next step.

To an absolute ethanol solution of 35.1 g of stannic chloride pentahydrate (0.10 mol) and 1.45 ml of distilled aniline (0.155 mol) was added 1.1 g of above described chloro ketone. The solution was then heated under reflux for 4 hr. Upon cooling, the ethanol solution was poured into water; the pH was adjusted to neutral by the addition of solid sodium bicarbonate; and the product was extracted with ether. The ether was then partially evaporated and extracted three times with 10% aqueous hydrochloric acid. The aqueous extract was neutralized with aqueous ammonia and extracted three times with ether. The residue after removal of the ether was heated with excess acetic anhydride at steam-bath temperature for 2 hr in order to facilitate separation of unreacted aniline.

The acetic anhydride solution was mixed with ether and extracted three times with 10% aqueous hydrochloric acid; the aqueous extract was then neutralized and extracted with ether as above, giving in poor yield a solution of tertiary amine in ether. This ether solution was dried with magnesium sulfate, filtered, and evaporated. The resultant red, viscous oil was purified by vpc and shown to contain two components, only one of which was of low enough volatility to be the desired product. The structure was confirmed by proton nmr spectroscopy and the compound was characterized as its picrate (yellow needles, mp 168.5–170°, with sintering at 165° after three recrystallizations from 95% ethanol).

Anal. Calcd for $C_{19}H_{18}O_7N_4$: C, 55.03; H, 4.39; N, 13.53. Found: C, 55.24; H, 4.41; N, 13.59.

Registry No.—I, 7661-51-0; picrate of I, 16727-90-5; 1-isobutylnaphthalene, 16727-91-6.

(5) The mass spectral data were obtained by Mr. R. G. Ross on an MS-9 mass spectrometer at 70 eV, utilizing a heated glass inlet system at 180° with steel manifolding.

(6) E. Vogel, "Practical Organic Chemistry," 3rd ed, John Wiley and Sons, Inc., New York, N. Y., 1966, pp 511–512.

(7) J. Kenner and F. S. Statham, *Ber.*, **69**, 16 (1936).

(8) E. E. Blaise and M. Maire, *Bull. Soc. Chim. Fr.*, **3**, 658 (1908).

(9) J. Cason, *Chem. Rev.*, **40**, 15 (1947).

Quinazolines and 1,4-Benzodiazepines. XLI.[1] 1,3-Dihydro-2H-1,4-benzodiazepin-2-one 4-Oxide Previously Described as 1,3-Dihydro-2H-4,1,5-benzoxadiazocin-2-one

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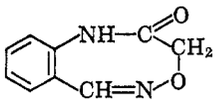
In a recent publication,[2] we reported the synthesis of a series of 5-substituted 4,1,5-benzoxadiazocin-2-ones by cyclization of 2′-aroyl- (or alkanoyl-) 2-haloacetanilide *syn*[3]-oximes in an alkaline medium. A similar mild alkaline treatment of 2-chloro-2′-formylacetanilide oxime **1** of unspecified configuration was reported by v. Auwers[4] to yield a compound described as 1,3-dihydro-2H-4,1,5-benzoxadiazocin-2-one (A). Since the steric configuration of the oxime is believed to determine the site of attack in intramolecular alkylation,[2] a 4,1,5-benzoxadiazocin-2-one resulting from the *syn*-oximes and a 1,4-benzodiazepin-2-one 4-oxide from the *anti* isomer, a study of the structure of the compound reported by v. Auwers was undertaken.[5]



A

A sample of **3**,[6] prepared as described by v. Auwers, when submitted to mass spectroscopy showed a strong peak at M − 16 indicating the loss of oxygen. This phenomenon is characteristic for nitrones but has not been seen with 4,1,5-benzoxadiazocin-2-ones.[2] The nitrone structure was corroborated by preparation of the nitrone **3**, identical with the material prepared directly from **1**, by rearrangement of 2-chloromethylquinazoline 3-oxide (**2**)[7] on treatment with dilute alkali. Catalytic reduction of the nitrone with Raney nickel catalyst removed the N-oxide oxygen and also reduced the 4,5 double bond resulting in the formation of the 1,3,4,5-tetrahydro-1,4-benzodiazepin-2-one (**5**). This compound was identical with the product prepared by reduction of the corresponding 1,3-dihydro-1,4-benzodiazepin-2-one (**8**) which had been synthesized from **7** according to the classical method shown. When

(1) Paper XL: J. V. Earley, R. I. Fryer, D. Winter, L. H. Sternbach, *J. Med. Chem.*, in press.

(2) A. Stempel, I. Douvan, E. Reeder, and L. H. Sternbach, *J. Org. Chem.*, **32**, 2417 (1967).

(3) The terms *syn* and *anti* are used as defined in ref 2, footnote 7. This is particularly important in a discussion of benzaldehyde oximes since these terms are then in conflict with the traditional definition in which the position of the oxime hydroxyl is considered in reference to the aldehydic hydrogen. To be consistent, in this report the configuration will be named based on the relationship of the oxime hydroxyl to the amino-substituted phenyl ring in both aldehydic and ketonic oximes.

(4) K. v. Auwers and E. Frese, *Ann. Chem.*, **450**, 273 (1926). These authors named the compound 4,5-benzo-7-oxy-oct-1,2,6-oxdiazin.

(5) While our work was in progress, the product of an analogous reaction carried out with 2,4′-dichloro-2′-formylacetanilide oxime, again of unspecified configuration, was reported in a Dutch patent to be 7-chloro-1,3-dihydro-2H-1,4-benzodiazepin-2-one 4-oxide but no proof of structure was offered: Grindstedvarket, A.S., Netherlands Patent 6,608,039 (Dec 12, 1966).

(6) In view of the evidence discussed below we shall present this compound as the N-oxide **3** rather than the earlier incorrect structure A.

(7) L. H. Sternbach and E. Reeder, *J. Org. Chem.*, **26**, 4936 (1961).