USE OF A MODEL CHAIN OXIDATION REACTION FOR THE QUANTITATIVE DETERMINATION OF MORPHINE

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We have established that morphine is an inhibitor of the model chain reaction of the initiated oxidation of cumene by oxygen. Its inhibiting action is connected with the splitting out of mobile hydrogen atoms of phenolic hydroxyls in the reaction with the active centers of the chain process — cumyl peroxide radicals [1]:

Initiation of the chain (generation of $RO_2^{\bullet}$ radicals)	W_i — rate of initiation
Chain propagation	$RH + RO_2^{\bullet} \xrightarrow[+O_2]{K_3} RO_2^{\bullet} + ROOH$
Chain termination	$2RO_2^{\bullet} \xrightarrow{K_6}$ molecular products
	$InH + RO_2^{\bullet} \xrightarrow{K_7} In^{\bullet} + ROOH$
	$In^{\bullet} + RO_2^{\bullet} \xrightarrow{K_8}$
	$2In^{\bullet} \xrightarrow{K_9}$ molecular products

Where RH is a hydrocarbon (cumeme)
$RO_2^{\bullet}$ is a peroxide radical;
ROOH is a hydroperoxide;
InH is an inhibitor (morphine); and
$In^{\bullet}$ is an inhibitor radical.

We have found that morphine has an inhibition coefficient f (number of chains terminated by one inhibiting group of the inhibitor) of 2. This means that the radicals formed from the morphine molecules react only with the cumyl peroxide radicals and do not react with one another. The rate constant of inhibition for morphine is $K_7 = 2.5 \cdot 10^4$ liter/mole·sec, which is not less than that of the widely used antioxidant ionol. The experimental conditions and limits of calculating the kinetic parameters have been described elsewhere [2].

The value of the inhibition coefficient f found for morphine enables us to calculate, at a known rate of initiation W_i and from the experimentally determinable induction period τ (time of action of the inhibitor), the initial concentration of morphine in the reaction mixture and, consequently, its amount in the initial mixture analyzed.

Method of Determination. About 0.012 g(accurately weighed) of the mixture to be analyzed is dissolved in 20 ml of glacial acetic acid. About 0.020 g (accurately weighed) of the initiator azoisobutyronitrile (AIBN), 0.3 ml of the prepared solution of the mixture, and 4.7 ml of cumene are added to the reaction vessel through a glass funnel. The kinetic curve of the absorption of oxygen is recorded, and from this the induction period is determined graphically. The percentage of morphine referred to the dry substance is calculated from the formula

$$(InH) = 3.54 \frac{\tau \cdot B}{A} \%,$$

where A is the mass of the mixture being analyzed (g), and B is the mass of the AIBN (g).

The method of analysis is simple in performance, readily reproducible, and quick. The relative error of determination amounts to ±2%.

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ALKALOIDS OF *Buxus sempervirens*

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The alkaloids of *Buxus sempervirens* L. (common box) cultivated in the environs of the town of Kislovodsk had not been studied. We have begun an investigation of the alkaloids of this plant collected on May 21, 1978. The amounts of alkaloids were determined by chloroform extraction: in shoots of the first year — 2.39%; in young roots — 2.11%; in leaves and small branches — 1.64%: in the flowers 1.94%; and in branches several years old 1% of total alkaloids.

The etheral part of the total alkaloids isolated from 16 kg of thin branches and leaves was dissolved in benzene and was separated according to basicity by McIlvaine's solutions at pH 8.0-2.2 (pH interval 0.2).

The combined fractions of the total alkaloids with pH 8.0-7.4, 7.2-7.0, and 6.8-6.4 were chromatographed separately on a column of alumina (Brockmann activity grade II). Elution was carried out with ether—ethanol containing increasing concentrations of ethanol — 10, 20, 30, and 40%. In this way, bases were isolated with mp 241-243°C (ethanol), $[\alpha]_D$ +98.52°C (c 0.601; chloroform), $C_{25}H_{42}N_2O$ (I) mp 228-230°C (ethanol), $[\alpha]_D$ +68.78° (c 0.875; chloroform), $C_{26}H_{46}N_2O$ (II); and mp 200-202°C (ethanol); $[\alpha]_D$ +102.88° (c 0.522; chloroform), $C_{28}H_{50}N_2$ (III).

The mother liquor from the alkaloids (I), (II), and (III) was treated with acetone. The acetone-soluble part of the combined material was chromatographed on a column of alumina with eluation by ether—ethanol (4:3) and (1:1), fractions 1-8 were rechromatographed on a column of silica gel with elution by hexane—ether—ammonia (5:4:0.25) and (5:4:0.5).

The hexane—ether—ammonia (5:4:0.5) fraction yielded a base with mp 127-129° (ethanol) (IV).

Alkaloid (I) was identified as cyclobuxine D, (II) as cyclovirobuxine D, and (III) as cycloprotobuxine A (melting points and IR, NMR, and mass spectra of (I-III) and their derivatives) [1-3].

The IR spectrum of base (IV) contained absorption bands at 3030 and 1462 cm^{-1} (methylene of a cyclopropane ring), 3320 cm^{-1} (hydroxy group), and 2930 cm^{-1} (CH_2, CH_3). The main peaks in the mass spectrum are those of ions with m/z 57, 58, 70, 71, 72 (100%), 106, 365, 386, 400, and M^+ 430, which are characteristic for the mass-spectrometric fragmentation of the cycloprotobuxines [4]. From its spectral characteristics, this alkaloid was assigned to the bases of the 9β,19-cyclo-5α-pregnane type, which differs from the alkaloids of the *Buxus* genus isolated previously.

Thus, cyclobuxine D, cyclovirobuxine D, cycloprotobuxine A, and a base with mp 127-129°C have been isolated from *Buxus sempervirens* L.

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