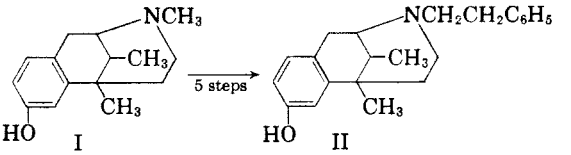
which was *N*-demethylated by the method of von Braun.[5] Phenylacetylation of the resultant secondary amine produced the amide which, on reduction with ethereal lithium aluminum hydride, yielded (±)-2'-hydroxy-5,9-dimethyl-2-phenethyl-6,7-benzomorphan (II) isolated as the *hydrobromide* salt, m.p. 166–170°[6] (*Anal.* Calcd. for $C_{22}H_{28}BrNO$: C, 65.68; H, 7.01. Found: C, 65.40; H, 7.00). The free *base* (*Anal.* Calcd. for $C_{22}H_{27}NO$: C, 82.20; H, 8.47. Found: C, 82.27; H, 8.48) melted at 180–181°.

Treatment of the hydrochloride salt of I in water with (±)-α-bromocamphor-π-sulfonic acid [(+)-3-bromo-8-camphorsulfonic acid] ammonium salt[7] gave, after fractional crystallization of the diastereoisomeric salts and neutralization of these salts with aqueous ammonium hydroxide, (−)-I, m.p. 183–184.5°, $[\alpha]_D^{20}$ −84.8° (*c*, 0.92, abs. alcohol) (*Anal.* Calcd. for $C_{15}H_{21}NO$: C, 77.88; H, 9.15. Found: C, 77.91; H, 8.97); *hydrobromide*, m.p. 238–241°, $[\alpha]_D^{20}$ −52.0 (*c*, 2.00, water) (*Anal.* Calcd. for $C_{15}H_{22}BrNO$: C, 57.68; H, 7.10. Found: C, 57.66; H, 7.34) and (+) -I, m.p. 183–184.5°, $[\alpha]_D^{20}$ +84.3 (*c*, 0.83, abs. alcohol) (*Anal.* Calcd. for $C_{15}H_{21}NO$: C, 77.88; H, 9.15. Found: C, 77.75; H, 9.25); hydrobromide, m.p. 238–242°, $[\alpha]_D^{20}$ +52.1° (*c*, 1.46, water) (*Anal.* Calcd. for $C_{15}H_{22}BrNO$: C, 57.68; H, 7.10. Found: C, 57.93; H, 7.18).

As described in the preparation of (±) - II, (−)-I and (+)-I gave, respectively, (−)-II *hydrobromide*, m.p. 284–287°, $[\alpha]_D^{20}$ −84.1° (*c*, 1.12, 95% ethanol) (*Anal.* Calcd. for $C_{22}H_{28}BrNO$: C, 65.68; H, 7.01. Found: C, 65.82; H, 7.02); base, m.p. 159–159.5°, $[\alpha]_D^{20}$ =121.6° (*c*, 0.74, 95% ethanol) (*Anal.* Calcd. for $C_{22}H_{27}NO$: C, 82.20; H, 8.47. Found: C, 81.95; N, 8.44) and (+)-II *hydrobromide*, m.p. 284–287°, $[\alpha]_D^{20}$ +84.4° (*c*, 1.47, 95% ethanol) (*Anal.* Calcd. for $C_{22}H_{28}BrNO$: C, 65.68; H, 7.01. Found: C, 65.65; H, 7.15); *base* m.p. 159–160°, $[\alpha]_D^{20}$ +120° (*c*, 0.60, 95% ethanol) (*Anal.* Calcd. for $C_{22}H_{27}NO$: C, 82.20; H, 8.47. Found: C, 82.35; H, 8.41).

In mice (subcutaneous administration) (−)-2'-hydroxy-2,5,9-trimethyl-6,7-benzomorphan (I) proved to be almost twice as effective (ED_{50} 1.7 mg./kg.) and less than half as toxic (LD_{50}>400 mg./kg.) as (+)-I while the *dextro*-isomer was inactive at 20 mg./kg., a convulsant dose. The (−)-2'-hydroxy-5,9-dimethyl-2-phenethyl-6,7-benzomorphan (II) (ED_{50} 0.11 mg./kg.) is 12–15 times more potent than (−)-I, almost 20 times more so than morphine. The (+) -II is also surprisingly effective (ED_{50} 6.7). Finally (±)-II (ED_{50} 0.25) has shown low physical dependence potency in the monkey.[8] Addiction studies in man[9] are in progress. Initial clinical experiments[10] with this racemate show it to be a promising agent for the relief of both acute and chronic pain.



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(5) J. von Braun, O. Kruber, and E. Aust, *Ber.*, **47**, 2312 (1914).

(6) After about a year the melting point had risen to 247–250°. Analysis and infrared data proved the new crystals to be another crystalline modification of II.

(7) From the Aldrich Chemical Co., Inc.

(8) G. Deneau, personal communication.

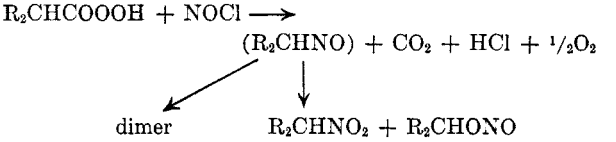
(9) Research Addiction Center, National Institute of Mental Health, Lexington, Ky.

(10) Large-scale preparation of this compound and clinical studies are due to the Smith Kline & French Laboratories, Philadelphia.

A New Reaction of Organic Peroxyacids

Sir:

If a primary or secondary peroxyacid is allowed to react with a nitrosating agent in an appropriate solvent in the cold, an instantaneous reaction occurs. The solution becomes deep blue or green, colors characteristic of monomeric C-nitroso compounds. Upon working up the crude products bis-nitroso compounds have been isolated, as well as nitro compounds and nitrite esters. The following equation approximates the reaction:



We will illustrate it by the results obtained in a typical experiment with peroxyphenylacetic acid.

Peroxyphenylacetic acid (12 g.) prepared by a modification of the method of Swern and coworkers[1] (purity by titration for active oxygen 95%, m.p. 76–77°), was allowed to react with nitrosyl chloride in petroleum ether at 0°; the solution became deep green in color. Three products were isolated from the reaction mixture: (a) bis-α-nitrosotoluene, an ether-insoluble solid, m.p. 120–121.5[2,3]; crude yield 0.7 g. λ_{max} 295 mμ, lit. 296 mμ.[3] *Anal.* Found C, 69.23; H, 5.83; N, 11.46. The infrared spectrum showed a strong peak at 8.53μ in chloroform and 8.55μ in a Nujol mull (lit.[3] 8.58μ), and the absence of the 6.25 and 6.45μ

(1) W. E. Parker, C. Ricciuti, C. L. Ogg, and D. Swern, *J. Am. Chem. Soc.*, **77**, 4037 (1955).

(2) R. Behrend and E. König, *Ber.*, **23**, 1776 (1890); *Ann.*, **263**, 210 (1891).

(3) E. Müller and H. Metzger, *Chem. Ber.*, **88**, 165 (1955).

peaks characteristic of the monomeric material.[4] (b) Benzyl nitrite, b.p. 31–32° at 1 mm., $n_D^{24.8°}$ 1.4986; crude yield 5 g. The ultraviolet and infrared spectra were identical with a sample synthesized by a different route.[5] (c) α-Nitrotoluene, b.p. 62–63° at 0.6 mm, $n_D^{24.8°}$ 1.5320; crude yield 4 g. The infrared spectrum was identical with a sample prepared by a different route.[5]

No tertiary carboxylic acid from which we have been able to make the peroxyacid has reacted with a nitrosating agent. We are currently investigating the mechanism, and the extensions to other reagents and peroxygen compounds. Preliminary results indicate that other electrophilic agents behave similarly. Dinitrogen tetroxide reacting with peroxyacid gives a nitro compound as the major product. The mechanism may be analogous to that indicated by Barry and Hartung[6] for the nitrosation of malonic acid involving the addition of nitrosyl chloride to an enol form of the acid.

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(6) R. H. Barry and W. H. Hartung, *J. Org. Chem.*, **12**, 460 (1947).