methyl would lead to triphenylcarbinol (equation 2). Homolytic induced decomposition of the peroxide by I without attack on the solvent would probably lead to high yields of alkali benzoate, whether the reaction proceeded by direct metal atom (or electron) transfer to the peroxide (equation 3) or by attack of the organic free radical to

$$Ph_2C{-}O^-M^+ + PhCOOOCOPh \longrightarrow Ph_2CO + PhCOO^-M^+ + PhCOO\cdot \quad (3)$$

give an unstable initial product (equation 4).

$$Ph_2\dot{C}{-}O^-M^+ + PhCOOOCOPh \longrightarrow PhCOOC(Ph)_2O^-M^+ + PhCOO\cdot \quad (4)$$

Effective scavenging of the benzoyloxy radicals by ketyl would convert these to alkali benzoate with no loss of carbon dioxide (equation 5), while less

$$Ph_2\dot{C}{-}O^-M^+ + PhCOO\cdot \longrightarrow Ph_2CO + PhCOO^-M^+ \quad (5)$$

efficient scavenging would permit carbon dioxide production. A remaining possible course for the reaction would involve the decomposition of the peroxide through purely nucleophilic attack of I which might lead to products in which the peroxide linkage remained intact (equation 6). These considerations led us to investigate the reaction of alkali benzophenone ketyl with benzoyl peroxide in benzene.

$$Ph_2\dot{C}{-}O^-M^+ + PhCOOOCOPh \longrightarrow PhCOOO^-M^+ \text{ or } M_2O_2 + ? \quad (6)$$

We find that the reaction proceeds rapidly at room temperature with the production of nearly quantitative yields of benzoic acid (on work-up) and nearly quantitative recovery of the benzophenone employed in the ketyl preparation. No peroxidic products could be detected. The stoichiometry of the reaction, then, is given by the sum of equations 3 and 5, and reactions 2 and 6 are excluded.

While the data do not permit distinction between the mechanisms of equations 3 and 4, the direct atom (or electron) transfer has the virtue of simplicity. The experimental result is novel in that it is the first reported example of the induced decomposition of benzoyl peroxide by an anion-radical and in that it is a rare example of a homolytic decomposition of benzoyl peroxide in benzene which does not lead to attack on the solvent.

Experimental

Reaction of Ketyl with Benzoyl Peroxide. Method 1.—Sodium benzophenone ketyl was prepared under solvent (benzene) vapor pressure in a vessel with two arms separated by a sintered glass disk. When the reaction of the sodium with the benzophenone had produced an intensely colored blue solution, this solution was filtered into the other arm of the vessel, which contained a solution of benzoyl peroxide. The blue color was immediately discharged, and a white gelatinous precipitate appeared. Upon dissolution of this precipitate in water, followed by acidification and cooling, benzoic acid was deposited. No other products were isolated. The methods described below were employed for determinations of yields.

Method 2.—A solution of 0.169 mole of benzoyl peroxide in benzene was placed in a graduated dropping funnel, which was in turn attached to a 500-ml. round-bottomed flask. In the flask was placed sodium–potassium alloy (0.16 mole of each alkali metal) and benzophenone (0.318 mole), along with 100 ml. of benzene and a magnetic stirring bar. The entire apparatus was degassed and flushed with prepurified nitrogen. Stirring of the benzophenone solution generated the ketyl, which was titrated with the peroxide solution from the dropping funnel. The titration was carried out over several hours, with continual stirring, and with the exercise of caution to avoid adding excess benzoyl peroxide at any time (*i.e.*, sufficient peroxide to cause complete disappearance of the blue color was never added). This precaution was taken in order to minimize the possible reaction of the peroxide with the metal directly. The experiment consisted, then, of successive periods in which the ketyl was alternately generated and titrated with the peroxide. A 0.0878 mole sample of benzoyl peroxide was allowed to react.

When the generation of the ketyl became noticeably slow, the experiment was halted, and the benzene was removed under vacuum. Small bits of alkali metal were visible in the residue but they were not quantitatively recovered. Extraction of the residue with ethyl ether led to the recovery of 0.306 mole of crude benzophenone (m.p. 44.5–47.0°, mixed m.p. 45.0–47.0°, infrared spectrum identical with benzophenone). The residue from the ether extraction was completely water-soluble and led to 0.175 mole of benzoic acid (recovered in two fractions, m.p. 121.5–122.5° and 121.0–122.0°, infrared spectrum identical with benzoic acid) corresponding to a 100% yield based on the peroxide.

In a duplicate run, potassium metal was employed instead of the alloy. Again the yield of benzoic acid and the recovery of the benzophenone were greater than 95%. Other runs with the alloy gave similar results.

In a control experiment, potassium metal was employed and stirred with benzoyl peroxide in benzene for 14 hr. The benzoyl peroxide was recovered nearly quantitatively.

Titration of Benzoyl Peroxide and Iodine with Ketyl.—In these experiments a filtered solution of potassium benzophenone ketyl was employed to titrate a weighed quantity of iodine (and, separately, benzoyl peroxide) in an all-glass apparatus which permitted the preparation and storage of the ketyl solution in a reservoir and subsequent transference through filters to a buret. The appearance of a permanent blue color would ideally be taken as the end point, but this was never achieved in the titration of peroxide. In two sets of such experiments in which a slowly fading end point was obtained, the molar ratio of ketyl to benzoyl peroxide treated was calculated, on the assumption that the reaction with iodine is quantitatively given by eq. 7, to be 2.3 and 1.7.

$$2Ph_2\dot{C}{-}O^-K^+ + I_2 \longrightarrow 2Ph_2CO + 2K^+I^- \quad (7)$$

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A Convenient Synthesis of Axial Amines

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The established procedure for the preparation of an axial amine is the hydrogenation of the appro-

priate cyclohexanone oxime in the presence of platinum oxide in acetic acid or some other acid medium. Shoppee and co-workers[1,2] have prepared several steroid amines by this method. Catalytic reduction, however, does not in all cases proceed in a stereoselective manner[2]; the equatorial amine is also produced in varying amounts, making the isolation of the axial amine difficult. Some axial amines have been prepared by the reaction of ammonia on the *p*-toluenesulfonates from the corresponding equatorial alcohols,[1,3,4] but this method, involving a pressure reaction, is neither very convenient nor gives a high yield. When the axial carboxylic acid (or appropriate derivative) is available, stereospecific conversion to the axial amine can be carried out by the Schmidt, Curtius, Hofmann, or Lossen rearrangements.[5]

The reaction of an azide with a secondary halide has been established[6] to be stereospecific and to involve Walden inversion. Nucleophilic substitution reactions of secondary tosylates also result in Walden inversion.[7] The following sequence of reactions was therefore examined for the preparation of axial amines and found to be satisfactory:

Equatorial alcohol ⟶ equatorial tosylate ⟶ axial azide ⟶ axial amine

A suitable medium for the reaction between a tosylate and sodium azide is *N*,*N*-dimethylformamide or *N*,*N*-dimethylacetamide,[8] to which some water has been added to increase the solubility of sodium azide. A side reaction at this stage is detosylation to produce alkenes. In the absence of other functional groups, the azide can be easily reduced with lithium aluminum hydride. An alternative method would be hydrogenation in the presence of a catalyst.[6] For the reduction to the amine, it is unnecessary to isolate the pure azide; it is enough to wash out with water the formamide or acetamide used as the reaction medium. Since no epimeric amine appears to be formed as a by-product, the purification of the axial amine through the formation of its hydrochloride is both convenient and adequate.

The preparation of 3α-aminocholestane in 62% overall yield from cholestanyl-3β-tosylate without recourse to chromatography is described here as an example. Also described is the preparation of (+)-neomenthylamine. The synthesis of some other amines *via* the corresponding azides will be described elsewhere.

(1) C. W. Shoppee, D. E. Evans, H. C. Richards, and G. H. R. Summers, *J. Chem. Soc.*, 1649 (1956).

(2) C. W. Shoppee, R. J. W. Cremlyn, D. E. Evans, and G. H. R. Summers, *ibid.*, 4304 (1957).

(3) A. C. Cope, E. Ciganek, L. J. Fleckenstein, and M. A. P. Meisinger, *J. Am. Chem. Soc.*, **82**, 4651 (1960).

(4) R. D. Haworth, L. H. C. Lunts, and J. McKenna, *J. Chem. Soc.*, 986 (1955).

(5) For example, see J. Sicher, F. Šipoš, and M. Tichý, *Coll. Czech. Chem. Commun.*, **26**, 847 (1961).

(6) P. Brewster, F. Hiron, E. D. Hughes, C. K. Ingold, and P. A. Rao, *Nature*, **166**, 178 (1950).

(7) C. W. Shoppee and R. J. Stephenson, *J. Chem. Soc.*, 2230 (1954).

(8) Kindly supplied by E. I. du Pont de Nemours and Co., Inc., Industrial and Biochemicals Dept., Wilmington, Delaware.

Experimental[9]

Cholestanyl-3α-azide.—In a 250-ml. flask, equipped with a heating mantle and a magnetic stirrer, there were placed 100 ml. of dimethylacetamide[8] and 2.0 g. (3.6 mmoles) of cholestanyl-3β-tosylate. After a few minutes when the tosylate had dissolved, 0.3 g. (46 mmoles) of sodium azide and 4 ml. of water were added and the mixture maintained at 90–100° for 4 hr. Upon cooling, crude cholestanyl-3α-azide separated as a thick oil that solidified at room temperature. The entire mixture was then added to 500 ml. of water and extracted with three 60-ml. portions of ether. The combined ether fractions were washed with two 50-ml. portions of saturated sodium chloride solution in order to remove any residual dimethylacetamide. The ether solution was then dried and concentrated on a steam bath and used directly for reduction to the amine.

The azide could be isolated as a waxy solid, m.p. 52–55°, by complete evaporation of the ether solution. Recrystallization from an ethyl acetate–ethanol–water mixture gave the pure azide as colorless needles, m.p. 62.5–63.5°; $[\alpha]^{26}D$ +18.6° (chloroform, c = 1.01); λ_{max}^{Nujol} 4.75 μ (azide).

Anal. Calcd. for $C_{27}H_{47}N_3$: C, 78.39; H, 11.45; N, 10.16. Found: C, 78.59; H, 11.35; N, 10.21.

The azide may sometimes be obtained in a different form, m.p. 52.0–52.5°. The lower melting form changes to the higher melting form on standing for a few days.

3α-Aminocholestane.—The ether solution of cholestanyl-3α-azide obtained above was slowly added to a slurry of 0.5 g. (13 mmoles) of lithium aluminum hydride in 50 ml. of anhydrous ether, and gentle reflux was maintained for 3 hr. After cooling, the excess lithium aluminum hydride was destroyed by the addition of wet ether followed by 50 ml. of water. The aqueous layer was removed; the ether layer was washed with two 30-ml. portions of saturated sodium chloride solution and then dried. Purification of the amine was effected by passing hydrogen chloride through the ether solution, collecting the amine hydrochloride on a filter, and washing thoroughly with dry ether. The dry salt weighed 1.3 g. (83% yield based on cholestanyl tosylate). The salt was suspended in 20% aqueous potassium hydroxide solution and extracted with ether. On evaporation of the ether, cholestanyl-3α-amine was obtained as 0.9 g. (62% yield based on the tosylate) of a white wax, m.p. 87–88°; $[\alpha]^{26}D$ +28.6° (chloroform, c = 1.05) (lit[1] m.p. 87–88°; $[\alpha]D$ +27°).

Acetylation of this amine afforded 3α-acetamidocholestane, m.p. 216–218°; $[\alpha]^{26}D$ +35.8° (chloroform, c = 1.16) (lit[1].: m.p. 217°, $[\alpha]D$ +36°).

(+)-Neomenthylamine Hydrochloride.—To 31.1 g. (0.10 mole) of (−)-menthyl *p*-toluenesulfonate[10] dissolved in a mixture of 600 ml. of dimethylformamide and 90 ml. of water was added 34.5 g. (0.53 mole) of sodium azide. The mixture was stirred and kept at a temperature of 90° for 9 hr. The reaction mixture was then poured into 900 ml. of a saturated aqueous sodium chloride solution diluted with 100 ml. of water. It was then extracted with ether and the combined ether extracts were washed with the saturated sodium chloride solution and dried over anhydrous magnesium sulfate.[11]

(9) Microanalyses were performed by Alfred Bernhardt, Mülheim, West Germany. Melting points are uncorrected.

(10) H. Phillips, *J. Chem. Soc.*, 2552 (1925).

(11) In one experiment this ether solution was fractionally distilled; earlier fractions contained mostly 3-menthene. The azide fraction, b.p. 108–109°/20 mm.; $n^{21}D$ 1.4663; $[\alpha]^{22}D$ +96.3° (chloroform, c 5.62); λ_{max} 4.75 μ (azide), was found to be only 90% pure by gas chromatography. Also see J. H. Boyer, F. C. Canter, J. Hamer, and R. K. Putney, *J. Am. Chem. Soc.*, **78**, 325 (1956).

To a suspension of 5.7 g. (0.15 mole) of lithium aluminum hydride in 100 ml. of absolute ether there was added, over a period of 30 min., the dried ether extract from above. The mixture was stirred at room temperature for 1 hr. and then refluxed for 1 hr. more. The excess lithium aluminum hydride was destroyed with moist ether followed by water and the solid material was filtered off. The organic layer was washed twice with a saturated sodium chloride solution and dried over anhydrous magnesium sulfate. Hydrogen chloride gas was passed into this ether solution and the mixture was then allowed to evaporate. After washing the resulting residue with hexane, 6.57 g. (34%[12]) of white, crystalline neomenthylamine hydrochloride was obtained. Recrystallization from hexane gave a sample, m.p. 192.5–195.0°, $[\alpha]^{26}D$ +18.2° in chloroform (c = 2.17) (lit.,[13] m.p. 189° $[\alpha]$ +21.5°).

On acetylation of the neomenthylamine hydrochloride with acetic anhydride in the presence of sodium hydroxide solution there was obtained (+)-*N*-acetylneomenthylamine, m.p. 172–173.5° (softening at 169°), $[\alpha]^{17}D$ +52.9° in chloroform (c = 1.20) (lit.,[13] m.p. 169–170°, $[\alpha]D$ +53.0°).

By treating neomenthylamine hydrochloride with benzoyl chloride in a mixture of pyridine and benzene, there was obtaine (+)*N*-benzoylneomenthylamine, m.p. 124.5–125° (softening at 122°), $[\alpha]^{25}D$ +23.6° (chloroform, c = 2.79) (lit.,[13] m.p. 121.5°, $[\alpha]D$ +22.7°).

Acknowledgment.—This research was supported in part by a grant from the National Science Foundation.

(12) The optimum conditions for the best yield of neomenthylazide and therefore the amine have not been established.

(13) J. L. Simonsen, "The Terpenes," Vol. I, 2nd ed., Cambridge University Press, Cambridge, England, 1953, p. 245.

Reactions of Acetylenes. I. *t*-Ethynyl Alcohol with Isocyanates

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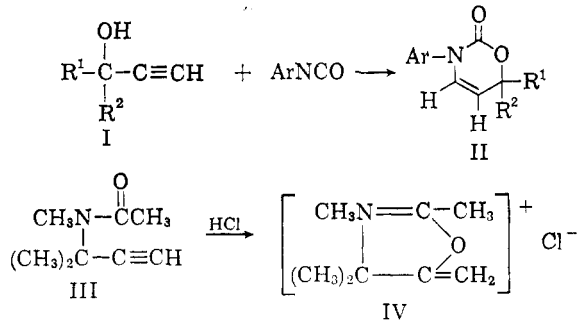
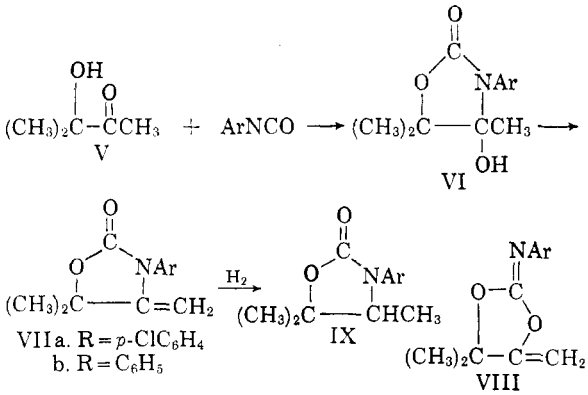
The recent publication[1] claiming the formation of 1,3-oxazine-2-ones (II) from the reaction of *t*-ethynyl alcohols (I) with an aryl isocyanate did not appear logical in view of previous findings from these laboratories.[2] This earlier work showed that N-acyl derivatives of *t*-ethynylamines (III) gave five-membered rings (IV) on cyclization with mineral acid. An examination of the n.m.r. spectrum of compound II (R^1 = R^2 = CH_3, Ar = *p*-ClC_6H_4) showed a series of four peaks centered at 5.93 τ. The coupling constants were small (about 3 c.p.s.), and the system was much closer to that expected for non-equivalent 1,1-hydrogens rather than either *cis* or *trans* 1,2-hydrogens. The availability of the keto alcohol



made possible an unequivocal alternative synthesis which proved the ring size. Treatment of V with *p*-chlorophenyl isocyanate and subsequent dehydration of the resulting carbinol (VI) gave a compound identical to that prepared from 3-methyl-1-butyn-3-ol (I. R^1 = R^2 = CH_3) and *p*-chlorophenyl isocyanate. Since this procedure has been used for the synthesis of oxazoles,[3] the identity of the



two materials established that the correct structure is VIIa and not II. The synthesis of oxazoles by the above procedure[3] would also appear to eliminate the possibility of an oxygen ring closure and thus rule out the other possible structure VIII.

Further proof of the exocyclic double bond, and therefore a five-membered ring, was obtained by hydrogenation of VII to give IX (Ar = C_6H_5). The n.m.r. spectrum of IX showed the doublet for the C-methyl split by the proton centered at 8.87 τ and a quartet centered at 5.91 τ for the hydrogen at the 4-position. Of interest also is the fact that the two methyl groups at the five position were chemically non-equivalent and showed their peaks at 8.52 τ and 8.62 τ.

In the reaction of ethynyl alcohols with phenyl isocyanate, the open chain urethane was isolated; this could be readily converted to the oxazolidinone by treatment with sodium ethoxide in ethanol.

Experimental

All melting points are uncorrected and were obtained in an open capillary tube.

3-*p*-Chlorophenyl-4-methylene-5-ethyl-5-methyloxazolidine-2-one.—This was prepared from *p*-chlorophenyl iso-

(1) S. L. Shapiro, V. Bandurco, and L. Freedman, *J. Org. Chem.*, **26**, 3710 (1961).

(2) N. E. Easton, R. Dillard, M. Livezey, D. E. Morrison, and G. F. Hennion, Am. Chem. Soc. Meeting, New York, 1960, Abstracts 44-O.