Photolysis of 1,1-Dimethyl-*trans*-decalin-10-carbonyl Azide. An Analog of the *A/B/E* Rings of Some Diterpenoid Alkaloids[1a]

Walter L. Meyer and Alfred S. Levinson

Department of Chemistry, Indiana University, Bloomington, Indiana[1b]

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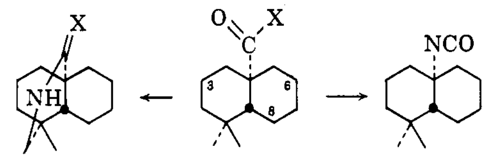
Photolysis of 1,1-dimethyl-*trans*-decalin-10-carbonyl azide in hexane solution at 0° affords 35% of the corresponding 10-isocyanate, 10% of the 10-carboxamide, 15% of a γ-lactam, and 10% of 1-aminomethyl-1-methyl-*trans*-decalin-10-carboxylic acid lactam. This result is discussed with respect to diterpenoid alkaloid synthesis and the general selectivity of the acyl azide photolysis reaction.

The tricyclic amine system Ia constitutes one of the major structural units of many diterpenoid alkaloids. In considering possible approaches to the synthesis of these natural products, we were attracted to sequences involving carbocyclic intermediates having an angular functional group which would be utilized for stereoselective elaboration of the nitrogenous ring at a suitable stage.[2] One type of reaction which seemed particularly favorable for the ultimate ring closure in such a synthetic scheme involved photolysis of an angular azidomethyl,[3] N-haloaminomethyl,[4] azidocarbonyl,[5] or related function, such that the reactive nitrogen species so produced could attack a methyl group at the eventual 4-position of the alkaloid, *e.g.*, IIa → Ib. Such a synthesis would utilize intermediates with symmetrical (*gem*-dimethyl) substitution at the potential 4-position, and the need for prior stereoselective introduction of an asymmetric center there would be avoided. In order to evaluate the utility of such an approach, and particularly to examine the question of whether six-membered ring formation would compete favorably with alternative five-membered ring closures involving attack at one of the methylene groups of the carbocyclic system, we undertook a model study with the 1,1-dimethyl-10-substituted *trans*-decalins (II).[6] This paper reports the results of such photolysis of the acyl azide IIa.

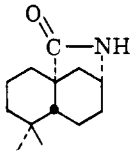
1,1-Dimethyl-*trans*-decalin-10-carboxylic acid (IIb)[7] was readily converted to the corresponding acid chloride, but this reacted only slowly with dicyclohexylammonium azide in tetrahydrofuran.[8] Although infrared absorption at 4.7 and 5.9 μ indicated that the mixture contained some of the acyl azide IIa after forty-six hours at room temperature, considerable amounts of unchanged acid chloride (5.6 μ) remained, and appreciable quantities of the isocyanate III (4.4 μ) were also present. Apparently steric hindrance to nucleophilic attack at the angular carbonyl group makes the substitution reaction so slow that the rate of rearrangement of the azide, even at room temperature, approaches that of its formation.[9,10] The best synthesis of the azide IIa involved treatment of the acid chloride with anhydrous hydrazine in benzene followed by nitrous acid oxidation of the resulting hydrazide IIc, m.p. 166–167°. In order to avoid concomitant thermal rearrangement to the isocyanate, no attempt was made to isolate the azide prepared in this manner, but its infrared spectrum indicated the absence of hydrazide and isocyanate contaminants.



Ia, X = H_2
b, X = O

IIa, X = N_3
b, X = OH
c, X = $NHNH_2$
d, X = NH_2

III



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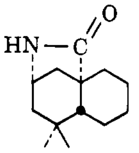

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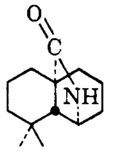
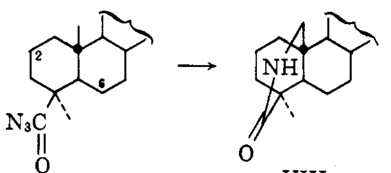
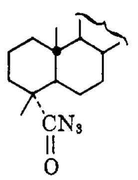


VI



VII

VIII



IX

Photolysis of the azide in *n*-hexane at 0° afforded a mixture of four major components which were separated by chromatography. The predominant product, formed in 35% yield,[11] was readily recognized as the isocyanate III by its characteristic 4.4-μ infrared absorption.[12] The other three major products, produced in 8, 9, and 14% yields,[11] were all amidic in nature as

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(1) (a) Abstracted in part from the Ph.D. dissertation of A. S. Levinson, Indiana University, 1963; preliminary communication, W. L. Meyer and A. S. Levinson, *Proc. Chem. Soc.*, **15** (1963); (b) contribution no. 1078.

(2) For other approaches to this synthetic problem, see I. Iwai, A. Ogiso, and B. Shimizu, *Chem. Ind.* (London), 1288 (1962); J. A. Findlay, W. A. Henry, T. C. Jain, Z. Valenta, K. Wiesner, and C. M. Wong, *Tetrahedron Letters*, 869 (1962); ref. 5; and W. Nagata, *et al.*, *J. Am. Chem. Soc.*, **85**, 2342 (1963).

(3) D. H. R. Barton and L. R. Morgan, Jr., *J. Chem. Soc.*, 622 (1962).

(4) A. W. Hofmann, *Ber.*, **16**, 558, 586 (1883); K. Loeffler and C. Freytag, *ibid.*, **42**, 3427 (1909); S. Wawzonek and T. P. Culbertson, *J. Am. Chem. Soc.*, **81**, 3367 (1959); **82**, 441 (1960); E. J. Corey and W. R. Hertler, *ibid.*, **82**, 1657 (1960).

(5) J. W. ApSimon and O. E. Edwards, *Can. J. Chem.*, **40**, 896 (1962); see also W. Antkowiak, J. W. ApSimon, and O. E. Edwards, *J. Org. Chem.*, **27**, 1930 (1962).

(6) All synthetic compounds discussed herein are racemic, although only one enantiomer is depicted in each of the structural formulas and the prefix *dl* is omitted.

(7) W. L. Meyer and A. S. Levinson, *J. Org. Chem.*, in press.

(8) F. Weygand and M. Reiher, *Chem. Ber.*, **88**, 26 (1955).

(9) Other examples of the expected hindrance at this position have been observed; *cf.* ref. 7.

(10) We do not yet have any evidence which allows comparison of the rate of azide rearrangement in this very hindered system with less crowded azides. It is not impossible that there is steric acceleration of rearrangement as well as steric retardation of azide formation. The linear isocyanate would of course be less crowded by the axial methyl group than is the trigonal CON_3 function.

(11) Yields of all photolysis products are based on the hydrazide IIc.

(12) Only part of the isocyanate was isolated as such. The remainder hydrolyzed to the corresponding amine during chromatography.

evidenced by their infrared absorption in the 3.0–3.1-(N–H) and 5.9–6.0-μ (C=O) regions.

One of the amides, m.p. 145–146° (9% yield), was clearly the desired δ-lactam Ib. A mass spectrum established its molecular weight as the expected 207,[13] it had δ-lactam carbonyl absorption at 6.0 μ, and its n.m.r. spectrum showed the presence of only *one* C-methyl (9.12 τ) and *one* N–H (1.65 τ), but *two* protons on nitrogen-bearing carbon (multiplet centered at 187 c.p.s.[17]). That the N–H was the only proton on an atom adjacent to the N-methylene, and thus that this methylene, like the methyl, was attached to a quaternary center, was shown by a double resonance experiment[17] in which the N–H resonance was saturated. Under these conditions the CH_2 multiplet collapsed to the expected AB quartet, unperturbed by spin-coupling to any other hydrogen. These data are only compatible with the structure Ib.

A second of the amides, m.p. 75–77° (8% yield), also had carbonyl absorption at 6.0 μ, and was thus either another δ-lactam or an open-chain amide. That the latter was the case was suggested by its 6.2 μ infrared absorption, a band not usually shown by lactams,[14] and was supported by the absence of CHN proton resonance from its n.m.r. spectrum. Its identity as the amide IId, formed by abstraction of hydrogen from solvent by the intermediate nitrogenous species, was established by comparison with an authentic sample prepared by ammonolysis of the acid chloride.

The preponderant amidic product (14%) was a γ-lactam, for in addition to the correct molecular weight (207),[13] it had 5.9-μ carbonyl absorption and its n.m.r. spectrum showed the presence of *one* N–H (2.00 τ) and *one* CHN (207–218 c.p.s.), as well as two quaternary C-methyl groups (9.10 and 9.21 τ). Thus it is one of the lactams IV, V, or VI, which results from cyclization to the 6-, 3-, or 8-position of the bicyclic nucleus. Results of n.m.r. spin-decoupling experiments, although not conclusive, provide a distinct preference for the 6-substituted structure IV over the other two. The n.m.r. spectrum of the γ-lactam shows resonance from the carbocyclic methylene and methyne protons as a series of broad overlapping peaks between 40 and 130 c.p.s.[17] Spin-saturation[17] of the 207–218 c.p.s. CHN proton resonance causes no new one-proton singlet to replace any visible portion of this spectrum, and such should have occurred if the 9-methyne proton of the lactam were spin-coupled only to the CHN as it should be in structure VI. The CHN is certainly spin-coupled to ring protons which absorb in the 115 c.p.s. region, however, for saturation at that frequency causes the CHN resonance to sharpen considerably (to a partly resolved doublet). That no change in the 115-c.p.s. region occurs when the CHN is spin-saturated in turn renders structure V unlikely, for in that case the 115-c.p.s. resonant protons would be all or part of one or both methylenes at C-2 and C-4, and each of these AB systems should be isolated when decoupled from the CHN, their resonances sharpening appreciably (to quartets). Thus the 115-c.p.s. resonant protons which are coupled to the CHN seem to be coupled to other protons as well, as would be the case for the 7-methylene of lactam IV. The 5-methylene of lactam IV should decouple to an isolated AB system, and the observed sharpening of peaks in the 85–100-c.p.s. region of the spectrum produced by spin-saturation of the CHN could well be this system superimposed on the remainder of the skeletal proton resonance. It may also be noted that structure IV seems more in accord with formation of only one of the three γ-lactams than are either of the other possibilities. Confirmatory evidence for this structure is being sought.

Thus photolysis of 1,1-dimethyl-*trans*-decalin-10-carbonyl azide (IIa) produces 35% of the isocyanate III, 9% of the δ-lactam Ib, 8% of the amide IId, and 14% of a γ-lactam, probably IV.[15] Six-membered ring lactam formation is indeed realized to a significant extent, illustrating the feasibility of such an approach to diterpenoid alkaloid synthesis. The importance of several competitive reaction pathways will severely limit the practicality of acyl azide photolysis for such a purpose, however, unless techniques can be developed to minimize them.

It is interesting to compare the product distribution from this system with that observed in the only other reported examples of lactam formation under such conditions, for noteworthy differences as well as similarities are seen. In their initial study of the reaction, ApSimon and Edwards examined several diterpenoid resin acid azides (VII and IX), and observed, as we have, that the corresponding isocyanate was the major product in each case,[5] although neither their results nor ours establish that this rearrangement is truly photochemical rather than thermal in origin. In either event, however, unless it can be eliminated in some way, perhaps by control of temperature or wave length of irradiation, such rearrangement must be considered the most severe detriment to use of this photolysis for lactam synthesis, since it drastically limits the yield of lactam even when lactam formation is structurally specific.

More striking are the relative proportions of lactams from our angular azide IIa and the axial azides VII studied by ApSimon and Edwards. From each of the axial resin acid azides a δ-lactam VIII, arising from cyclization to the angular methyl, predominated extensively (5–10:1) over a γ-lactam formed by attack at either the 2- or 6-position.[5] It was not clear whether this resulted from a general selectivity for six-membered ring formation in photolysis of acyl azides (by virtue of preferential formation of a transition state of special geometry) in contrast to alkyl azides[3] or N-haloalkylammonium salts[4] which commonly form five-membered rings, whether it arose from a preference for attack at methyl rather than methylene groups, or whether it was simply a consequence of the proximity of the methyl and azide groups due to the geometry of the terpenoid system. Unfortunately an attempt to examine this point in an acyclic system (where the other photolytic reactions have been studied[3,4]) was inconclusive when *n*-hexanoyl azide gave no readily isolable lactam, but only the isocyanate and *n*-hexanamide.[5] In the angular azide IIa, the methyl and azide groups are in very nearly the same juxtaposition (1,3-diaxial)

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(13) We are grateful to Professors G. Berchtold and K. Biemann for the mass spectral data reported here.

(14) L. J. Bellamy, "The Infrared Spectra of Complex Molecules," 2nd Ed., Methuen and Co., London, 1958, p. 216 ff.

(15) Dr. R. F. C. Brown has recently informed us that he, too, has examined this photolysis, with similar results. We are grateful to Dr. Brown for communication of his results prior to their publication and for permission to cite them here.

as they are in the resin acid azides. If there had been a strong intrinsic preference for piperidone over pyrrolidone formation or methyl over methylene attack we would have expected this product to predominate here as it did in the resin acid system. That it does not (δ-lactam–γ-lactam = 2:3) implies that no such strong preference exists. It further suggests that not only the accessibility of δ-hydrogens but the inaccessibility of γ-hydrogens played an important part in the high selectivity observed with the resin acid azides; *i.e.*, that although the axial methyl group of the angular azide IIa and the angular methyl of the resin acid azide VII are about equally accessible, both γ-hydrogens in the latter system are considerably less available than is one of those in the former. Clearly the structural selectivity of lactam formation by acyl azide photolysis in such rigid systems is a rather sensitive function of the relative accessibility of γ- and δ-hydrogens for attack.

Only one of the three possible γ-lactams (IV, V, or VI) was formed in significant quantity from the angular azide IIa. It is attractive to consider that the axial hydrogens at the 3- and 8-positions are hindered by the axial 1-methyl group, and that thus the hydrogen at C-6, which suffers no such hindrance, is probably considerably more exposed to attack than are the other two. Such an argument, of course, predicts that our γ-lactam is IV, and its validity will be tested by confirmation of that structure for this product. It is also compatible, however, with the results from the diterpenoid systems VII, where both "available" γ-hydrogens (2 and 6) are likewise 1,3-diaxial to a methyl and are not appreciably attacked in comparison to the methyl. The proposition that a γ-hydrogen 1,3-diaxial to a methyl group is not attacked as effectively as is the methyl, while an axial γ-hydrogen not so hindered is attacked competitively with an axial γ-methyl, thus may serve as a useful working hypothesis for predicting products from such photolyses, at least for the present.[16]

Finally, photolysis of the angular azide IIa, like *n*-hexanoyl azide,[5] affords significant amounts of the amide IId. We found this result rather surprising, for the resin acid azides did not give a corresponding product, even when the azide group was equatorial and thus probably more exposed to solvent than is that of IIa.[5] The factors which regulate the relative importance of the solvent abstraction reaction as a competing process consequently remain obscure.

Comparison of the acyl azide with other photolytically active groups in this system as well as related work in other systems will be reported later.

Experimental[17]

1,1-Dimethyl-*trans*-decalin-10-carboxhydrazide (IIc).—The procedure follows ApSimon and Edwards.[5] A solution of 2.35 g. (0.0112 mole) of 1,1-dimethyl-*trans*-decalin-10-carboxylic acid (Ib),[7] m.p. 75–85°, in 11 ml. of thionyl chloride foamed spontaneously for 15 min. Ten drops of anhydrous pyridine were added, the solution was refluxed for 2 hr., and the mixture was concentrated *in vacuo* to a paste which was triturated with 75 ml. of benzene. The benzene solution was filtered into a mixture of 100 ml. of benzene and 10 ml. of 95% anhydrous hydrazine (Matheson Coleman and Bell) which was then stirred at room temperature for 2.5 hr. Solvent was removed *in vacuo* and the solid residue was recrystallized from 40 ml. of ethyl acetate to afford 1.87 g. (75%) of long fibrous colorless crystals of the hydrazide IIc, m.p. 164.5–166°. The analytical sample (from ether-hexane) had m.p. 166–167°; $\lambda_{max}^{CHCl_3}$ 2.88, 6.02, 6.16 μ; n.m.r. (CCl_4–$CDCl_3$ mixture), 9.11 (s), 9.22 τ (s).

Anal. Calcd. for $C_{13}H_{24}N_2O$: C, 69.60; H, 10.78; N, 12.49. Found: C, 69.7; H, 10.7; N, 12.7.

1,1-Dimethyl-*trans*-decalin-10-carbonyl Azide (IIa).—The procedure follows ApSimon and Edwards.[5] A solution of 1.500 g. (6.7 mmoles) of the hydrazide IIc, m.p. 164.5–166°, in 60 ml. of glacial acetic acid was cooled in an ice–water bath until the acetic acid partially froze. A solution of 0.923 g. (13.4 mmoles) of sodium nitrite in 1 ml. of water was added, and the mixture was removed from the ice–water bath and shaken until homogeneous (8 min.) and then 1 min. more. The solution was diluted with 100 ml. of ice water and the product was extracted promptly with five 20-ml. portions of cold *n*-hexane. The hexane solution was washed promptly with 25 ml. of ice-water, 25 ml. of ice-cold 5% sodium bicarbonate, and 25 ml. of ice-water, and dried over sodium sulfate. An aliquot had λ_{max}^{hexane} 4.70 and 5.84 μ, and showed no detectable absorption in the N–H, NCO, or hydrazide regions. A similarly obtained cyclohexane solution showed only strong end absorption below 220 mμ in the ultraviolet.

Photolysis of 1,1-Dimethyl-*trans*-decalin-10-carbonyl Azide (IIa).—A solution of acyl azide IIa, freshly prepared from 1.500 g. (6.7 mmoles) of hydrazide IIa and having no 4.4-μ absorption, in 350 ml. of *n*-hexane was irradiated for 8 hr. under dry deoxygenated nitrogen using an Hanovia 200-w. mercury lamp, Model 54A36. The quartz photolysis cell was immersed in an ice bath at 0° and cold water was circulated between the lamp and the reaction mixture. At the end of the irradiation period solvent was evaporated *in vacuo* to leave 1.214 g. of brown oil with λ_{max}^{film} 3.1 (broad, weak), 4.42, 5.9, 6.0–6.05 μ. Gas-liquid chromatography showed the presence of four major components in the ratio 3:2:4:2 in order of emergence, and also several minor components. A precipitate (0.7 mg.) present on the photolysis cell wall was not sufficiently soluble in suitable solvents to permit determination of its infrared spectrum.

The oil was chromatographed on 30 g. of Woelm neutral alumina (activity grade II), elution being effected with *n*-hexane, benzene, chloroform, and mixtures of these. The first fraction contained 0.196 g. of oily isocyanate III (14% based on hydrazide IIc); $\lambda_{max}^{CCl_4}$ 4.42 μ; n.m.r. (CCl_4), 9.06 (s), 9.18 τ (s).

Subsequent fractions were assayed by g.l.c., which showed the presence in each fraction of one or two of the original components and an additional substance which had not been present prior to chromatography. Fractions were combined on the basis of their content of the various initial components, and mixed fractions were rechromatographed on alumina. Before final product iso-

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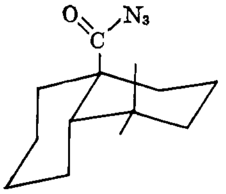
[16] Brown (see ref. 15) found that the *cis*-fused azide corresponding to IIa gave predominantly the *cis* δ-lactam corresponding to Ib. This, too, is in accord with such hypothesis that is applied to conformation i for the azide.



i

[17] Infrared spectra were obtained on Perkin-Elmer Models 21, 137, and 137G spectrophotometers, and n.m.r. spectra were obtained from dilute solutions using a Varian A-60 spectrometer or a Varian DP-60 spectrometer operating at 60 Mc. and equipped with a Model 3506 flux stabilizer. Resonance positions were determined relative to tetramethylsilane as an internal standard, the audio side-band technique being used for DP-60 spectra. N.m.r. spectra are described by the use of abbreviations, (s) for singlet, (d) for doublet, (t) for triplet, (q) for quartet, and (m) for multiplets not described by other symbols, with chemical shifts reported in τ units and line positions in c.p.s. downfield from tetramethylsilane. The spin-decoupling experiments were carried out by the procedure described by L. F. Johnson, "Varian Associates NMR/EPR Spectroscopy Technical Information Bulletin," Vol. III, No. 3, p. 5, 1962. Gas chromatograms were run on an F and M Model 609 chromatograph with nitrogen as the carrier gas and with a hydrogen flame detector, a 2-m. 9% silicone gum SE30 on Chromosorb W column being employed. The compositions of mixtures were estimated by measuring the ratios of individual peak areas. Melting points were taken in open capillary tubes, and are uncorrected. Microanalyses were by Alfred Bernhardt, Mulheim (Ruhr), Germany.

lation, and in some cases before the second chromatography, each set of combined fractions was taken up in ether and extracted with 12% hydrochloric acid, thereby removing completely the substance which g.l.c. had shown to be present after but not before chromatography. One fraction of the initial chromatogram showed only the g.l.c. peak corresponding to this acid-soluble compound, and had $\lambda_{max}^{CCl_4}$ 2.95, 3.08, 5.90 (impurity?), 6.06 (all weak peaks); n.m.r. (CCl_4), 9.09 (s), 9.23 τ (s). This is thus tentatively characterized as 10-amino-1,1-dimethyl-*trans*-decalin, formed from the isocyanate during chromatography. The amine amounted to 0.24 g. (loss of weight on acid extraction), or the equivalent of an additional 19% of isocyanate III.

Isolation of the Amide IId.—The first amidic component to be eluted was isolated after two chromatograms as 0.047 g. (3.4% based on starting hydrazide IIc) of an oil which slowly crystallized. This was sublimed at *ca.* 60° (*ca.* 10^{-6} mm.) to afford the amide IId as white prisms, m.p. 75–77° (microscope hot stage); $\lambda_{max}^{CCl_4}$ 3.1, 6.0, 6.2 μ (weak); n.m.r. (CCl_4), 9.16 (s), 9.20 τ (s). The infrared and n.m.r. spectra of this sample were identical with those of material prepared by ammonolysis of the acid chloride, and the melting point of a mixture was undepressed. Mixed fractions contained an additional 0.059 g. of IId (according to g.l.c.) bringing the total yield to 8%.

Isolation of the γ-Lactam.—The second amidic product to be eluted was obtained after acid washing and two chromatograms as 0.159 g. of an oil (11% based on starting hydrazide). Mixed fractions contained, according to g.l.c., an additional 0.038 g. (total yield 14%). The oily γ-lactam was distilled in a Hickman still at 0.05 mm. (bath 130–136°) to afford the analytical sample, $\lambda_{max}^{CCl_4}$ 3.1, 5.9 μ; n.m.r. (CCl_4), 2.00 (s), 6.45 (s), 9.10 (s), 9.21 τ (s).

Anal. Calcd. for $C_{13}H_{21}NO$: C, 75.31; H, 10.21; N, 6.76; mol. wt., 207. Found: C, 75.2; H, 10.0; N, 6.7; mol. wt., 207 (mass spectrum[13]),

Isolation of the δ-Lactam Ib.—The final amidic product after acid washing and two chromatograms amounted to 0.115 g. (8% based on starting hydrazide) of white plates, m.p. 134–139°; $\lambda_{max}^{CCl_4}$ 3.12, 6.02 μ; n.m.r. (CCl_4), 1.65 (s), 170–205 c.p.s. (m), 9.72 τ (s). When the 160–220 c.p.s. region of the n.m.r. spectrum was scanned while a strong saturating rf field was applied 321 ± 10 c.p.s. to lower field from the 170–205-c.p.s. resonance, the 170–205-c.p.s. multiplet split to a symmetric AB quartet. Mixed fractions contained 0.013 g. bringing the total yield to 9%. After recrystallization from *n*-hexane the white prisms of δ-lactam Ib had m.p. 145.5–146.5°. The material sublimed readily at 100° (0.1 mm.) to afford the analytical sample, m.p. 145.5–146.5°.

Anal. Calcd. for $C_{13}H_{21}NO$: C, 75.31; H, 10.21; N, 6.76; mol. wt., 207. Found: C, 75.6; H, 10.1; N, 7.0; mol. wt., 207 (mass spectrum[13]).

1,1-Dimethyl-*trans*-decalin-10-carboxamide (IId).—A 0.250-g. (0.0012 mole) sample of 1,1-dimethyl-*trans*-decalin-10-carboxylic acid (IIb), m.p. 90–95°, was converted to the acid chloride with 1 ml. of thionyl chloride and 2 drops of pyridine. The crude acid chloride in 25 ml. of benzene was added to a stirred mixture of 10 ml. of benzene[18] and *ca.* 40 ml. of anhydrous ammonia which was allowed to warm to room temperature overnight. The mixture was washed with water, dried over sodium sulfate, and concentrated *in vacuo* to 0.237 g. of tacky brown oil, which was chromatographed on 5 g. of Woelm neutral alumina (activity grade II) to afford 0.122 g. (48%) of oil which slowly crystallized. Sublimation at *ca.* 60° (*ca.* 10^{-6} mm.) afforded the amide IId as white prisms, m.p. 75–77° (microscope hot stage); $\lambda_{max}^{CCl_4}$ 3.1, 6.0, 6.2 μ (weak); n.m.r. (CCl_4), 9.16 (s), 9.20 τ (s).

Anal. Calcd. for $C_{13}H_{23}NO$: C, 74.59; H, 11.08; N, 6.69. Found: C, 75.0, 74.8; H, 10.9, 10.7; N, 6.75.

Acknowledgment.—We express thanks to the U. S. Public Health Service, National Institutes of Health, for a grant (A4215) in support of this work, and to Mr. A. O. Clouse for assistance with some of the n.m.r. determinations. The n.m.r. instruments were provided by grants from the U. S. Public Health Service and the National Science Foundation, to whom we are grateful.

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[18] Mr. N. G. Schnautz in our laboratory has found that tetrahydrofuran is a superior solvent for this reaction.

4-*t*-Butyl-3-cyclohexenone and 4-*t*-Butyl-3-cyclohexenols

ROBERT D. STOLOW, MARIA M. BONAVENTURA, AND JOHN W. LARSEN

Department of Chemistry, Tufts University, Medford 55, Massachusetts

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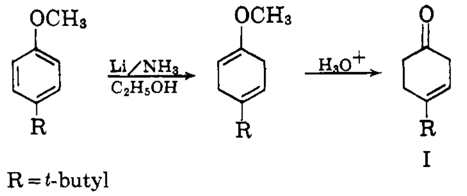
4-*t*-Butyl-3-cyclohexenone (I) was prepared from *p*-*t*-butylanisole. Reduction of I with lithium aluminum hydride gave 4-*t*-butyl-3-cyclohexenol (II). Addition of Grignard reagents to I gave 4-*t*-butyl-1-phenyl-3-cyclohexenol (III) and 4-*t*-butyl-1-methyl-3-cyclohexenol (IV). Nuclear magnetic resonance and infrared spectra of II–IV are discussed. The possibility of transannular intramolecular hydrogen bonding in II–IV and other 3-cyclohexenols is considered.

Preparations of 4-*t*-butyl-3-cyclohexenols were undertaken in order to permit study of transannular OH. . .π intramolecular hydrogen bonding in such compounds.[1] The key intermediate, 4-*t*-butyl-3-cyclohexenone (I), was prepared by a procedure analogous to that reported for synthesis of 4-isopropyl-3-cyclohexenone[2] and 4-methyl-3-cyclohexenone.[3]

Reduction of *p*-*t*-butylanisole with lithium in liquid ammonia plus ethanol presumably gave 4-*t*-butyl-2,5-dihydroanisole, which without isolation, was subjected to oxalic acid-catalyzed hydrolysis of the enol–ether function, to give 4-*t*-butyl-3-cyclohexenone (I), isolated by fractional distillation as a colorless liquid, b.p. 91° (8 mm.). Identification of I is based on ultraviolet spectra, infrared spectra, and gas chromatography, which when taken together, indicate a purity of 96 ± 2%, probable impurities being 4-*t*-butyl-2-cyclohexenone, *ca.* 3%; 4-*t*-butylcyclohexanone, up to 3%; and *p*-*t*-butylanisole, *ca.* 0.2%.



An earlier preliminary report of the preparation of I stated that "lithium metal in ethylenediamine has been used to reduce *t*-butylphenol in good yield to

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[1] J. W. Larsen, B. S. thesis, Tufts University, 1962.

[2] N. A. Nelson and G. A. Mortimer, *J. Org. Chem.*, **22**, 1146 (1957), and references cited.

[3] E. A. Braude, and A. A. Webb, with (in part) M. U. S. Sultanbawa, *J. Chem. Soc.*, 3328 (1958).