NEW COMPOUNDS

Synthesis of Some New Nortricyclanes

David B. Knight*

Department of Chemistry, University of North Carolina at Greensboro, Greensboro, North Carolina 27412

Pelham Wilder, Jr. and Roy F. Gratz

Department of Chemistry, Duke University, Durham, North Carolina 27706

The synthesis of eight new derivatives of nortricyclane is reported.

We report the synthesis of several new substituted nortricyclanes. Entry into the nortricyclyl ring system was gained utilizing reactions reported by Rondestvedt and Ver Nooy (*8*). Thus treatment of 5-*endo*-phenylnorbornene-6-*exo*-carboxylic acid (**1a**) with bromine in base gives (3*S**,5*R**)-3-bromo-5-phenylnortricyclane (**2a**). Reaction of **2a** with lithium carbonate in water (*7*) affords the corresponding alcohol (3*S**,5*R**)-3-hydroxy-5-phenylnortricyclane (**3a**).

Treatment of **2a** with silver tosylate in acetonitrile gives the tosylate (3*S**,5*R**)-5-phenylnortricycl-3-yl tosylate (**4a**). On hydrolysis in aqueous dioxane tosylate **4a** was converted to alcohol **3a** (Scheme I).

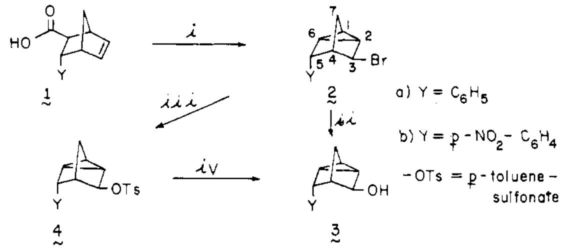
A similar series of reactions was carried out beginning with 5-*endo*-(*p*-nitrophenyl)norbornene-6-*exo*-carboxylic acid (**1b**), giving rise to the *p*-nitrophenyl substituted compounds **2b**, **3b**, and **4b**. In addition catalytic hydrogenation of **2b** using platinum oxide in methanol afforded the corresponding substituted aniline (3*S**,5*R**)-3-bromo-5-(*p*-aminophenyl)nortricyclane (**2c**).

All nortricyclane derivatives prepared in this study exhibited strong absorption in the IR region at around 800 cm^{-1}. Lippincott (*5*) has attributed this absorption to a vibrational mode characteristic of the nortricyclane cage. Pollard (*6*) has reported that this absorption in monosubstituted nortricyclanes appears as a doublet and that in disubstituted derivatives it appears as a triplet.

The NMR spectra of these substituted nortricyclanes showed several similarities, which are summarized in Table I. In each there was aryl absorption at around δ 7.2–7.4. Also there were broadened singlet absorptions at around δ 2.9–3.2 due to the benzylic hydrogens at C_3. At δ 3.7–3.8 there were poorly resolved three-line absorptions due to the hydrogens at C_5 that are α to hydroxyl or bromine. Assignments of these chemical shifts are based on comparison with the chemical shifts of similar hydrogens in 3-bromonortricyclane (**9**), 3-hydroxynortricyclane (**8**), and in 3-phenylnortricyclanone (**5**).

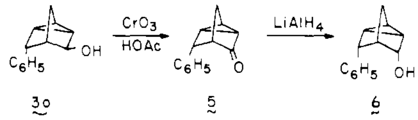
Assignments of relative configuration in **2**, **3**, and **4** as indicated are supported by chemical and spectral evidence. Alcohol **3a**, mp 80–81 °C, was oxidized to the ketone **5** using chromic anhydride in acetic acid. Reduction of **5** with lithium aluminum hydride afforded alcohol **6**, mp 39–40 °C, which is epimeric with **3a** (Scheme II). The NMR spectra of epimeric alcohols **3a** and **6** in deuteriochloroform show important differences. Absorption of the aromatic ring hydrogens in **3a** occurred at δ 7.21 and was essentially a sharp singlet. The aromatic hydrogens of **6** show complex absorption of at least nine lines centered at δ 7.33. An inspection of models indicates that the aromatic ring in **6** and the hydroxyl group syn to it are favorably disposed to be hydrogen bonded. Similar intramolecular hydrogen bonding involving π-type acceptors in bridged polycyclic compounds have been reported (*1*,*4*,*9*). The aromatic ring hydrogens in **6** are rendered magnetically nonequivalent due in part to the hydrogen bonding with the hydroxyl group or by virtue of the diamagnetic anisotropy of the C_3–O bond. The infrared spectrum of **6** indicates extensive hydrogen bonding as shown by intense absorption at 3505 cm^{-1}, which is present in addition to absorption at 3605 cm^{-1} due to free OH stretching.

Scheme I

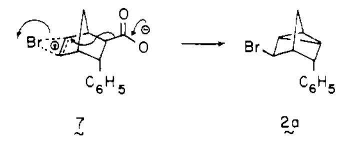


i) Br_2 in NaOH ; ii) Li_2CO_3 in H_2O ; iii) AgOTs in CH_3CN ; iv) Dioxane/ H_2O

Scheme II



Scheme III



Other chemical evidence supporting our structural assignments derives from a study of the fate of optical activity in the reaction sequence **1a** → **4a**. Carboxylic acid **1a** was partially resolved as its brucine salt. Optically enriched **1a**, $[\alpha]_D$ +18.3°, gave on treatment with bromine in base optically active (–)-**2a**, $[\alpha]_D$ –4.7°. The sign of the rotation of active **2a** (and all other optically active compounds in this study) was deduced from ORD curves obtained in 95% ethanol. Involved in the formation of **2a** from **1a** is an addition of bromine and a loss of carbon dioxide and the apparent stereospecificity of this process is of interest. A bromonium ion such as **7** is implicated (Scheme III) in this reaction and there is a wealth of evidence that suggests that such a bromonium ion would form on the exo face of **1a**. That

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Table I. Proton NMR Assignments for New Nortricyclane Derivatives

compd	R_1	R_2	R_3	chemical shift δ (ppm) H_3	H_5	aryl
2a	C_6H_5	Br	H	3.01 br s	3.86 br t	7.25 s
2b	p-$NO_2C_6H_4$	Br	H	3.26 br s	3.71 br t	7.76 q
3a	C_6H_5	OH	H	2.91 br s	3.80 br t	7.21 s
3b	p-$NO_2C_6H_4$	OH	H	3.20 br s	3.70 br t	7.80 q
6	C_6H_5	H	OH	3.11 br s	3.78 br t	7.33 m
5	C_6H_5			3.28 br s		7.21 s
8	H	OH	H		3.80 br t	
9	H	Br	H		3.88 br t	

active (−)-**2a** was formed suggests that there was no change in the position of the phenyl substituent. The most likely mode of forming the enantiomer of (−)-**2a** would involve a phenyl migration during the formation of **2a**. If no rearrangement involving the phenyl ring occurred, then the configuration at C_3 would be unchanged and the incoming bromine atom would necessarily be anti to the phenyl group.

As optical purities of **1a** and **2a** were not determined this argument is not conclusive but in conjunction with other chemical and spectral evidence is supportive of our configurational assignments.

Other reactions in this sequence exhibit a degree of stereospecificity as well. Hydrolysis of optically active (−)-**2a** in the presence of lithium carbonate gives the active alcohol (+)-**3a**. Treatment of active **2a** with silver tosylate gives tosylate **4a** of unspecified rotation. However, hydrolysis of this tosylate in aqueous dioxane yields active (+)-**3a**.

Experimental Section

Melting points and boiling points are uncorrected. Elemental analyses of all new compounds reported are by Galbraith Laboratories, Knoxville, Tenn., or by M-H-W Laboratories, Garden City, Mich., and were within acceptable limits (<0.30%). NMR spectra were recorded on Varian Model A-60 or T-60 spectrometers. Mass spectra were recorded using a Finnigan Model 3100D mass spectrometer. ORD measurements were carried out on a JASCO ORD-UV-CD instrument. Infrared spectra were obtained using Perkin-Elmer Model 457 or 137 spectrometers or a Beckmann Model IR-10 spectrometer.

5-endo-Phenylnorbornene-6-exo-carboxylic Acid (1a) and 5-endo-(p-Nitrophenyl)norbornene-6-exo-carboxylic Acid (1b). Racemic **1a**, mp 115–116 °C (lit. (*2*,*8*) mp 115.5–116 °C), was prepared by the method of Rondestvedt and Ver Nooy, using the experimental procedure of Trivette (10). Racemic **1a** was resolved as its brucine salt, formed in ethanol. An analytical sample of the brucine salt had mp 80–90 °C and on the basis of elemental analysis appeared to be solvated with 1 mol of ethanol.

The active acid **1a**, $[\alpha]_D$ +18.3°, had mp 115–116 °C. A duplicate experiment yielded (+)-**1a** having $[\alpha]_D$ +17.3°.

In the preparation of **1b**, glacial acetic acid was used as solvent for the reaction of cyclopentadiene and *p*-nitrocinnamic acid. The reaction, held at 85 °C, in this solvent is complete in 3 days rather than the reported 6 weeks required when carried out in toluene at 55 °C. Pure **1b**, had mp 175–176 °C. (lit. (*8*) 176–176.5 °C).

(3S*,5R*)-3-Bromo-5-phenylnortricyclane (2a) and (3S*,5R*)-3-Bromo-5-(p-nitrophenyl)nortricyclane (2b). To 300 mL of 3% aqueous sodium hydroxide warmed to 60–65 °C was added 0.10 mol of acids **1a** or **1b**. The salts were stirred until complete solution had occurred. To the stirred, warm salt solutions was added rapidly a solution of bromine in 3% aqueous sodium hydroxide until the bromine color was no longer discharged. Brownish oils separated from the resulting mixtures. The cooled reaction mixtures were treated with dilute sodium thiosulfate solution to remove unreacted bromine and the mixtures were extracted with ether. The ether layers were washed with water and dried over anhydrous magnesium sulfate, and the ether was removed under reduced pressure. The resulting oils were taken up in ligroin (60–90 °C) and were chilled in a refrigerator. Addition of a seed crystal caused rapid formation of white glistening plates of **2a**, mp 47–48 °C (lit. (*8*) 48.5 °C) in 41% yield. IR (KBr) 820 (s), 815 (s), 805 (s) cm^{-1}.

White crystals of **2b**, mp 118–119 °C (lit. (*8*) 119–119.5 °C), formed in 52% yield.

Optically active (−)-**2a** was prepared on a smaller scale by the same method as used for racemic **2a**. The sign of the rotation was determined by obtaining the ORD curve in 95% ethanol.

(3S*,5R*)-3-Hydroxy-5-phenylnortricyclane (3a) and (3S*,5R*)-3-Hydroxy-5-(p-nitrophenyl)nortricyclane (3b). The procedure used to prepare **3a** and **3b** was similar to that of Roberts (*7*) for the preparation of 3-hydroxynortricyclane. A suspension of 0.001–0.01 mol of nortricyclyl bromides **2a** and **2b** in a 3 M excess of lithium carbonate in 150 mL of water was heated at reflux for 2–3 days. The reaction mixtures were extracted with either methylene chloride or ether. The organic extracts were washed with water and dried over anhydrous magnesium sulfate and the organic solvents were removed under reduced pressure. The resulting viscous oils were recrystallized from hexane or ligroin (60–90 °C). A 53% yield of **3a**, mp 80–81 °C, was obtained. IR (KBr) 3390 (m, OH), 820 (m), 813 (m), 805 (m) cm^{-1}.

Alcohol **3a** was characterized as the monophthalate ester, mp 160.1–161.5 °C (from 3:1 hexane–ethyl acetate).

Alcohol **3b**, mp 101.5–102 °C, was obtained in 34% yield: mass spectrum *m/e* 231 (parent ion); IR ($CDCl_3$) 3610 (s, free OH), 3440 (s, br, H-bonded OH), 1520 (s, asym N-O str), 1355 (s, sym N-O str), 830 (s), 825 (sh), 810 (s) cm^{-1}.

Active (+)-**3a** was prepared by the same method used for the racemic material, except on a smaller scale. The sign of the rotation was determined by obtaining the ORD curve in 95% ethanol.

5-Phenylnortricyclane-3-one (5). In a 250-mL three-necked round-bottom flask equipped with mechanical stirring, an addition funnel, and a reflux condenser was placed 3.0 g (0.016 mol) of alcohol **3a** and 50 mL of glacial acetic acid. The solution was cooled in an ice water bath while 1.5 g (0.015 mol) of chromic anhydride in 25 mL of 80% acetic acid was added dropwise. The reaction was stirred at room temperature overnight. Workup was accomplished by diluting the reaction mixture with 100 mL of water, extracting with three 100-mL portions of ether, and neutralizing. The extracts were dried over anhydrous magnesium sulfate, and the solvent was evaporated. The resulting oil was distilled, bp 100–115 °C (0.3 mm), yielding 2.0 g (68%) of **5**. IR (neat) 1735 (s, C=O), 825 (s), 800 (s) cm^{-1}.

A 2,4-dinitrophenylhydrazone derivation of **5** was prepared. After five recrystallizations from ethanol–ethyl acetate, the melting point was 160–161 °C.

(3R*,5R*)-3-Hydroxy-5-phenylnortricyclane (6). In a three-necked 250-mL round-bottomed flask equipped with magnetic stirring, reflux condenser and drying tube, and pressure equalizing dropping funnel was placed 0.25 g (0.0066 mol) of lithium aluminum hydride stirred in anhydrous ether. A solution of 0.8 g (0.0043 mol) of **5** in 50 mL of anhydrous ether was added dropwise. The reaction was stirred at room temperature for 4 h, at which time 50 mL of wet ether followed by 25 mL of 10% HCl were added. The ether layer was separated and the aqueous layer was extracted with 50 mL of ether. The combined ether layers were dried over anhydrous magnesium sulfate and solvent was removed under reduced pressure. The resulting oily residue was recrystallized five times from hexane to give alcohol **6**: mp 39–40 °C; IR (neat) 3604 (s, free OH), 3505 (s, H-bonded OH), 830 (s), 815 (s), 810 (s) cm^{-1}.

(3S*,5R*)-5-Phenylnortricycl-3-yl Tosylate (4a) and (3S*,5R*)-5-(p-Nitrophenyl)nortricycl-3-yl Tosylate (4b). To a solution of 0.0085 mol of bromides **2a** and **2b** in 30 mL of acetonitrile held at reflux was added 0.0090 mol of silver *p*-toluenesulfonate dissolved in 50 mL of acetonitrile. An immediate turbidity and white flocculent precipitate was observed. Heating was continued for 30 min after which the mixture was cooled and filtered. Removal of solvent left a greenish oil which was crystallized from either methanol, **4a**, or carbon tetrachloride, **4b**. Tosylate **4a** had mp 108–109 °C and was obtained in 22% yield. IR (KBr) 1360 (s, asym S–O str), 1180 (s, sym S–O str), 820 (s), 814 (s), 805 (s) cm^{-1}.

Tosylate **4b** was isolated in 38% yield. The product melted over the range 138–145 °C, the melting point varying with the rate of heating. IR (KBr) 1510 (s, asym N–O str), 1330 (s, sym N–O str), 1355 (s, asym S–O str), 1160 (s, sym S–O str), 820 (s), 810 (s), 800 (s) cm^{-1}.

Treatment of active (−)-**2a** with silver tosylate gave **4a** of unspecified rotation. Hydrolysis of this tosylate in 70% aqueous dioxane at 100 °C for 3 h gave active (+)-**3a**.

(3S*,5R*)-3-Bromo-5-(p-aminophenyl)nortricyclane (2c). A solution of 11.2 g (0.038 mol) of nitrobromide **3b** in 300 mL of methanol was placed in a Parr hydrogenation bottle. A few milligrams of platinum dioxide was added and **3b** was reduced at an average pressure of 36 psi. After the theoretical amount of hydrogen was absorbed, the solution was treated with charcoal and the mixture was filtered. Solvent was removed under reduced pressure leaving a residue that was crystallized from ligroin giving 7.5 g (75%) of slightly off-white crystals, mp 86–87.5 °C. IR (KBr) 3400 (m, N–H str), 820 (s), 810 (s) cm^{-1}.

Amine **2c** was further purified by conversion to the hydrochloride salt and reconversion to the amine.

(3S*,5R*)-3-Bromo-5-(p-aminophenyl)nortricyclane Hydrochloride. Through a solution of 2.35 g (0.088 mol) of amine **2c** in 30 mL of anhydrous ether was passed hydrogen chloride formed by dropping concentrated H_2SO_4 onto ammonium chloride. Shortly after the addition of HCl began, a turbidity and white crystal formation was observed. HCl addition was continued for 15 min. A yield of 2.54 g (96%) of white crystals, mp 175–177 °C, was recovered.

3-Nortricyclyl Tosylate (10). The method of Hanack and Kaiser (*3*) was used to prepare 3-nortricyclyl tosylate, **8**, from 3-hydroxynortricyclane. A colorless oil was obtained which could be crystallized from hexane to give a 28% yield of product, mp 34–37 °C. These crystals slowly sublimed at 60 °C (2 Torr) to give white crystals, mp 42.5–43 °C (lit. (*3*) 41–43 °C). Tosylate **8** was also prepared by stirring 4.28 g (0.025 mol) of 3-bromonortricyclane in 10 mL of acetonitrile with 7.0 g (0.025 mol) of silver *p*-toluenesulfonate in 25 mL of acetonitrile. The mixture was stirred for 2 h, the precipitate of silver bromide was removed by filtration, and solvent was removed under reduced pressure. The residual oil was recrystallized from pentane to give 2.1 g (32%) of tosylate **10**.

Literature Cited

(1) R. Baker and L. Dyall, *J. Chem. Soc. B*, 1952 (1967).
(2) M. Beugelmans-Verrier, L. Nicolas, A. Gaudemen, and J. Parello, *Tetrahedron Lett.* 361 (1976).
(3) M. Hanack and W. Kaiser, *Justus Liebigs Ann. Chem.*, **657**, 12 (1962).
(4) D. Kleinfelter, T. Dye, J. Mallory, and E. Trent, *J. Org. Chem.*, **32**, 1734 (1967).
(5) E. R. Lippincott, *J. Am. Chem. Soc.*, **73**, 2001 (1951).
(6) G. Pollard, *Spectrochim. Acta*, **18**, 837 (1962).
(7) J. D. Roberts, E. Turnbull, W. Bennett, and R. Armstrong, *J. Am. Chem. Soc.*, **72**, 3116 (1950).
(8) C. Rondestvedt and C. Ver Nooy, *J. Am. Chem. Soc.*, **77**, 4878 (1955).
(9) P. v. R. Schleyer, D. Trifan, and R. Bacskai, *J. Am. Chem. Soc.*, **80**, 669 (1958).
(10) C. D. Trivette, Ph.D. Dissertation, Duke University, 1959.

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Synthesis and Spectral Properties of ω-Aroylacetophenone, Benzaldehyde, and Acetophenone Hydrazone Derivatives

Yousuf A. Al-Farkh, Farouk H. Al-Hajjar,* and Hayat S. Hamoud

Petroleum and Petrochemicals Division, Kuwait Institute for Scientific Research, Kuwait

The structures of ω-aroylacetophenone, benzaldehyde, and acetophenone *N*-(acyl- or benzoyl)hydrazones (IIIa–o, Va–i, and Vj–r, respectively) are supported by their NMR spectra, and the AB system, which appeared in the spectra of the former compounds, is discussed. The electronic spectra of ω-aroylacetophenone *N*-(acyl- or benzoyl)hydrazones (IIIa–o) are discussed in relation to those of the corresponding benzaldehyde *N*-(acyl- or benzoyl)hydrazones (Va–i).

In a previous publication (*1*), it was reported that the reaction of aroylphenylacetylenes (Ia–c) with the hydrazide derivatives (IIa–c) gave ω-aroylacetophenone *N*-(acyl- or benzoyl)-hydrazones (IIIa–i).

In order to study the spectral properties of these compounds, six more derivatives, in which the phenyl group is substituted by a chlorine atom (IIIj–l) and a methoxy group (IIIm–o), were prepared (cf. Figure 1) as described previously (*1*).

The structure of the reaction products (IIIa–o) was identified on the basis of spectroscopic evidence based on IR, NMR, and UV spectra (Tables I and II). The IR spectra show a sharp band in the region 3460–3300 cm^{-1} (ν(NH)) and a strong band in the region 1640–1620 cm^{-1} (ν(C=O)). The NMR spectra, however, support structure III, since they show a broad signal in the region δ 5.47–5.00 (NH) and a quartet (2 H) representing an AB system (J = 18 Hz) (*2*). The fact that these methylene groups behave as an AB system can be interpreted as being due to either the large anisotropic effect of the C=N– and the nitrogen lone pair or the restriction of the rotation by the weak

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