amines which gives exclusively the succinamic acid with the phenyl and carboxyl group on the same carbon atom.[6] Since the anhydride I is opened in strong alkali to give the *endo-cis* diacid II without any appreciable isomerization to a *trans*-diacid, the *endo*-configuration for the amide group in III is most likely.

The reduction of amide acid III with excess lithium aluminum hydride in tetrahydrofuran led to amino alcohol V in good yield. This basic product was characterized as the fumarate. In pharmacological tests, V showed no analgesic activity.[7] Although in a preliminary experiment, selective reduction of III as the sodium salt in tetrahydrofuran with lithium aluminum hydride to the amino acid followed by esterification with diazomethane to the amino ester IV appeared to proceed in low yield, it was not pursued further due to the lack of analgesic activity for compound V.

EXPERIMENTAL[8]

Phenylmaleic anhydride. Phenylmaleic anhydride was prepared by the method of Miller and Mann.[3a] From 51.7 g. (0.294 mole) of phenylsuccinic anhydride and 105 g. (0.588 mole) of *N*-bromosuccinimide, there was obtained 34.2 g. (67%) of the anhydride, m.p. 121–123°. As reported by Rondesvedt and Filbey,[3b] the use of a nichrome wire stirrer was found to be essential to the success of this reaction.

exo-2-Phenyl-endo-5-norbornene-2,3-dicarboxylic acid anhydride (I). A solution of 34 g. (0.195 mole) of phenylmaleic anhydride and 2.58 g. (0.390 mole) of freshly distilled cyclopentadiene in 150 ml. of benzene was stirred under nitrogen at room temperature for 22 hr. and at 50° for 5 hr. The solvent was removed under reduced pressure on the steam cone. The oily residue crystallized from ether–petroleum ether (b.p. 30–60°).The yield in three crops was 36.2 g. (77%) of anhydride (I) m.p. 65–70°.

From an ether–petroleum ether recrystallization of 0.17 g. of the anhydride (I), m.p. 69–70°, there was obtained 0.09 g., m.p. 69–70°; λ_{max}^{KBr} 5.41, 5.61 μ (anhydride $C{=}O$).

Anal. Calcd. for $C_{15}H_{12}O_3$: C, 74.99; H, 5.03. Found: C, 75.00; H, 5.22.

In the initial experiment, the total noncrystalline product was saponified by the method of Miller and Mann[3a] to give recrystallized II, m.p. 171–172°, in 65% yield. A sample of the diacid II was cyclized to the crystalline anhydride I, m.p. 68–69° by refluxing in acetyl chloride. Thereafter the anhydride I was crystallized directly from the Diels-Alder preparations.

exo-2-Phenyl-endo-3-pyrrolidinecarbonyl-5-norbornene-endo-2-carboxylic acid (III). Thirty-five milliliters of pyrrolidine was reacted with 3.75 g. (0.081 mole) of 53% sodium hydride–mineral oil. The suspension was stirred for 1 hr. at room temperature. A total of 6.50 g. (0.027 mole) of anhydride I was added in portions. The suspension was stirred for 1 hr. and allowed to stand overnight at room temperature. The pyrrolidine was removed under vacuum and the residue was dissolved in water. On acidification, a white solid precipitated which did not dissolve when ether was added. The solid was collected by filtration, washed with water and ether, and air-dried. The crude solid, m.p. 150–151°, was recrystallized from methylene chloride–ether in three crops, all melting at 150–151.5°, totaling 7.29 g. (87%) of amide III.

A recrystallization of 0.25 g. of III, m.p. 150–151.5°, from methylene chloride–ether, gave 0.14 g., m.p. 150.5–151.5°; λ_{max} 5.78 (carboxyl $C{=}O$), 6.24 μ (amide $C{=}O$).

Anal. Calcd. for $C_{19}H_{21}NO_3$: C, 73.29; H, 6.80; N, 4.50. Found: C, 73.16; H, 6.83; N, 4.44.

Iodolactonization of III *to give* VI. A solution of 0.1 g. of III in 3 ml. of 0.5*N* sodium bicarbonate was combined with a solution of 0.25 g. of iodine and 0.5 g. of potassium iodide in 1.5 ml. of water. The mixture was allowed to stand at room temperature overnight. The dark gummy precipitate was washed with water and dissolved in a mixture of methylene chloride and aqueous sodium thiosulfate. The organic layer was dried over magnesium sulfate and the solvent was removed under vacuum. The oily product crystallized from acetone—ether. One recrystallization from acetone—ether gave 0.03 g. of VI, m.p. 222–225°; λ_{max} 5.59, 5.85 (lactone $C{=}O$), 6.22 (amide $C{=}O$), 6.30 μ (aromatic $C{=}C$).

Anal. Calcd. for $C_{19}H_{20}NO_3I$: C, 52.19; H, 4.61; N, 3.20. Found: C, 52.20; H, 4.70; N, 3.41.

1-(endo-2-Hydroxymethyl-exo-2-phenyl-5-norbornene-3-ylmethyl)pyrrolidine (V). A suspension of 7.5 g. (0.198 mole) of lithium aluminum hydride in 250 ml. of dry tetrahydrofuran was stirred at room temperature for 2 hr. and then was heated to reflux and a solution of 15.09 g. (0.0485 mole) of III in 750 ml. of hot tetrahydrofuran was rapidly added. The mixture was heated under reflux for 66 hr. While stirring, the mixture was cooled and carefully decomposed with 22.5 ml. of water. After stirring for 2 hr. the inorganics were removed by filtration and washed with ether. Concentration of the ethereal filtrate gave 12.97 g. of viscous yellow oil, V; $\lambda_{max}^{CHCl_3}$ 3.0 (br., —OH), 6.24, and 6.67 μ (aromatic).

The hydrogen fumarate was prepared from 1.59 g. (0.00563 mole) of V and 0.66 g. (0.00563 mole) of fumaric acid in isopropyl alcohol. The 1.51 g. of fumarate, m.p. 197–200° (67%), was recrystallized from methanol–isopropyl alcohol to give 1.33 g., m.p. 203–205°; λ_{max} 3.0–4.0 (br., carboxyl —OH), 5.90 (carboxyl $C{=}O$), 6.08 ($C{=}C$), 6.24 (aromatic $C{=}C$), 6.32 μ (carboxylate $C{=}O$).

Anal. Calcd. for $C_{19}H_{25}NO \cdot C_4H_4O_4$: C, 69.15; H, 7.32; N, 3.51. Found: C, 69.30; H, 7.43; N, 3.46.

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(6) R. Anschutz, *Ann.*, **354**, 117 (1907).

(7) We are indebted to W. M. Govier, M.D., and our Department of Pharmacology for these results.

(8) Melting points were determined with a Kofler microhotstage. Infrared spectra were obtained in Nujol mull with a Perkin-Elmer Model 21 Spectrometer unless otherwise noted.

Bicyclic Bases. II. 3-Aminomethyl-2-norbornenearylmethanols

George I. Poos and Margaret M. Lehman

Received September 28, 1960

This note describes an exploratory attempt to find interesting pharmacological activity within a series of basically substituted norbornenearylmethanols.

Our investigation started with the reaction product of *trans*-benzoylacrylic acid and cyclopentadiene which was reported by Winternitz, Mousseron and Rouzier[1] to be a crystalline mixture containing 60% of the *exo-trans*-isomer II and 40% of the *endo-trans*-isomer I. The French workers separated the mixture by a laborious process

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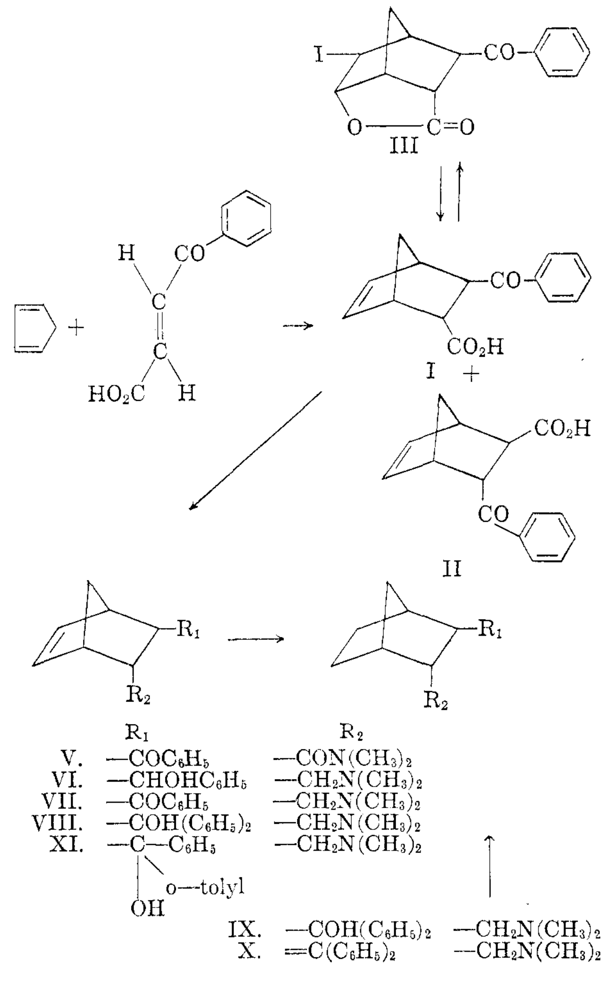
(1) F. Winternitz, M. Mousseron, and G. Rouzier, *Bull. soc. chim. France*, 170 (1955).

involving twenty recrystallizations and assigned structures based on bromolactone and hydroxylactone formation from I but not from II. We obtained the mixture of adducts as reported[1] and separated by iodolactonization. The pure crystalline iodolactone III was obtained in a yield of 48%. From the iodolactonization, an acidic fraction was obtained which afforded a crystalline mixture in 39% yield. This crystalline acidic product was largely an iodohydrin mixture (IV) based on analysis and spectra. Reduction of the iodolactone III with zinc in ethanol gave an excellent yield of the pure *endo*-acid I. With the impure iodohydrin mixture, a longer reduction time was required and a 75% yield of pure *exo*-acid II was obtained.



	R$_1$	R$_2$
V.	$-COC_6H_5$	$-CON(CH_3)_2$
VI.	$-CHOHC_6H_5$	$-CH_2N(CH_3)_2$
VII.	$-COC_6H_5$	$-CH_2N(CH_3)_2$
VIII.	$-COH(C_6H_5)_2$	$-CH_2N(CH_3)_2$
XI.	$-\underset{\mathrm{OH}}{\mathrm{C}}(o\text{—tolyl})-C_6H_5$	$-CH_2N(CH_3)_2$
IX.	$-COH(C_6H_5)_2$	$-CH_2N(CH_3)_2$
X.	$=C(C_6H_5)_2$	$-CH_2N(CH_3)_2$

Because of the greater abundance of I from the reduction step, subsequent reactions were carried out with this isomer.

By the mixed anhydride technique,[2] the acid I was converted to its dimethylamide (V) in 60% yield. Attempts to improve this yield by varying the quality and quantity of the reagents employed were fruitless; however, in all cases the balance of material was recovered as pure starting acid I. Reduction of ketoamide V with excess lithium aluminum hydride in tetrahydrofuran afforded the amino alcohol VI in good yield as a mixture of steroisomers. More than half of this mixture was a single isomer melting at 125°.

Oxidation of amino alcohol VI which was largely one largely one steroisomer with chromic anhydride-pyridine[3] gave the amino ketone VII as a gum, characterized as the fumarate salt. The yield of crude base was about 60% and of the pure salt about 45%. Similar oxidation of the crude base VI or of lower melting or non-crystalline fractions gave VII-fumarate but in lower yields. The major difficulty in this oxidation was a low material balance. Exhaustive extraction of the reaction mixtures or reduction of the chromium salts followed by extraction on the alkaline side never gave a recovery of organic material better than 65%. Alternate methods of oxidation failed—*e.g.*, the Oppenauer oxidation (aluminum isopropoxide-cyclohexanone in benzene), chromic acid in acetic acid, chromic acid in acetic acid with sulfuric acid and platinum catalyzed air oxidation all gave recovered starting material. An oxidation with chromic acid in aqueous pyridine proceeded but in low yield (33%).

Treatment of amino ketone VII with excess phenyllithium led to the aminomethylnorbornyldiphenylmethanol VIII as a noncrystalline product which was characterized as the hydrogen fumarate. Several attempts to dehydrate VIII to the corresponding diphenylmethylene derivative were unsuccessful. Because of the possible interference of the isolated double bond, amino alcohol VIII was hydrogenated to the norbornane derivative IX. In polyphosphoric acid at 100° for several hours, IX appeared to dehydrate to the extent of at least 50% as judged by the ultraviolet maximum at 245 mμ and the lack of —OH absorption in the infrared of the basic product. However, all attempts to obtain a crystalline salt of the gummy product X failed, possibly due to the presence of mixtures resulting from the rearrangement of the norbornane skeleton.

Amino ketone VII failed to react with *o*-tolylmagnesium bromide but was converted smoothly to the phenyl-*o*-tolylcarbinol XI with *o*-tolyllithium. Compound XI was noncrystalline and gave a mixture of fumarate salts, probably because of the introduction of a new asymmetric center in the molecule. Several recrystallizations served to separate a single, sharply melting salt from the mixture.

Compounds V, VI, VIII, and XI were examined for pharmacological activity, both as to gross behavioral effects and more detailed pharmacodynamic actions.[4] Behaviorally they may be

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[2] D. S. Tarbell, *J. Org. Chem.*, **22**, 248 (1957).

[3] G. I. Poos, G. E. Arth, R. E. Beyler, and L. H. Sarett, *J. Am. Chem. Soc.*, **75**, 422 (1953).

[4] We are indebted to W. M. Govier, M.D., and the Department of Pharmacology for the testing results.

best classified as weak convulsants having lethal doses in the range of 100 to 300 mg./kg., i.p. Compounds VII, VIII and probably V demonstrated multiple actions such as ganglionic blockade, antihistamine, anticholinergic, and antiserotonin activities. As compound IX produced mydriasis at low doses in behavioral testing, it probably also has autonomic activity although insufficient compound was available for accurate determinations. No analgesic or anti-inflammatory action was found in the series.

EXPERIMENTAL[5]

exo-3-Benzoyl-5-norbornene-endo-2-carboxylic acid (I) *and endo-3-benzoyl-5-norbornene-exo-2-carboxylic acid* (II). By the method of Winternitz *et al.*[1] 248.1 g. (1.41 moles)of β-benzoylacrylic acid was dissolved in 1.2 l. of benzene with warming, and 103 g. (1.55 moles) of freshly distilled cyclopentadiene was added while stirring. The reaction mixture was stirred overnight at room temperature and then concentrated to dryness. The product was crystallized from ether-petroleum ether (b.p. 30–60°) in four crops, totaling 331.7 g. (97%) of the crystalline mixture of the *trans*-acids I and II, m.p. 102–134°; $\lambda_{\max}^{\text{Nujol}}$ 3.25–3.85 (–OH), 5.90 (carboxyl C=O), 5.96 (ketone C=O), 6.24 μ (aromatic C=C).

The mixture of acids was separated by iodolactonization. A solution of 27.44 g. (0.113 mole) of total crystalline product from a small Diels Alder reaction in 686 ml. (0.343 mole) of 0.5*N* sodium bicarbonate was combined with 59.3 g. of iodine (0.468 eq.) in 115 g. of potassium iodide in 345 ml. of water and stored overnight at room temperature in the dark. The mixture was extracted three times with methylene chloride, which was washed with sodium thiosulfate solution and water and dried over magnesium sulfate. Removal of the solvent left 22.3 g. of brown solid, which, after decolorizing carbon treatment, was crystallized from methylene chloride–ether in two crops. The yield of iodolactone III was 20.0 g. (48%) m.p. 154–156°; $\lambda_{\max}^{\text{Nujol}}$ 5.62 (lactone C=O), 5.97 (ketone C=O), 6.25 μ (aromatic C=C). A 0.12-g. sample was recrystallized to give 0.09 g., m.p. 155.5-156°.

Anal. Calcd. for $C_{15}H_{13}IO_3$: C, 48.93; H, 3.56; Found: C, 48.95; H, 3.74.

The above sodium bicarbonate layer, containing the iodohydrin, was decolorized with sodium thiosulfate and acidified with 2*N* hydrochloric acid. The gummy precipitate was extracted with methylene chloride, which after drying over magnesium sulfate gave 22.7 g. of a buff-colored solid. This was crystallized from methylene chloride-petroleum ether in three crops, totaling 17.02 g. (39%) m.p. 169–182° dec.; $\lambda_{\max}^{\text{Nujol}}$ 3.74–.83 (—OH), 5.86 μ (ketone and carboxyl C=O). A 0.19-g. sample was recrystallized to give 0.09 g., m.p. 177–182° dec.

Anal. Calcd. for $C_{15}H_{15}IO_3$: C, 46.65; H, 3.92. Found: C, 49.63; H, 4.71.

Reduction of the iodolactone III back to the *endo*-acid I was accomplished by heating a mixture of 88.9 g. (0.241 mole) of III and 157 g. (2.41 moles) of zinc dust in 2 l. of ethanol under reflux for 2 hr. while stirring. The zinc dust was removed by filtration and the solvent was removed under vacuum. The residue was taken up in ether and washed well with 2*N* hydrochloric acid and water. The ether layer was dried over magnesium sulfate and the solvent was removed under vacuum. After decolorization, the 59-g. residue crystallized from methylene chloride–ether–petroleum ether in three crops, totaling 52.1 g. (90%) of I, m.p. 138.5–142.5°. Spectra were taken on a sample, m.p. 142.5–143.5°; $\lambda_{\max}^{\text{Nujol}}$ 3.25–4.50 (—OH), 5.90 (carboxyl (C=O), 5.97 (ketone C=O), 6.25 μ (aromatic C=C). Lit.[1] m.p. 136–137° for I.

Reduction of 2.0 g. (0.0052 mole) of impure iodohydrin (IV) by reflux with 3.60 g. (0.055 mole) of zinc dust in 40 ml. of ethanol was complete in 4 hr. The crystalline *exo*-acid II was isolated as above in 75.5% yield, 0.95 g., m.p. 127–128°; $\lambda_{\max}^{\text{Nujol}}$ 3.75 (—OH), 5.92, Shl. 6.00–.15 (ketone and carboxyl C=O), 6.25 μ (aromatic C=C). Lit.[1] m.p. 123–124° for II.

exo-3-Benzoyl-N,N-dimethyl-5-norbornene-endo-2-carboxamide (V). A suspension of 47.4 g. (0.1955 mole) of I in 300 ml. of dry toluene was cooled to −5°, and 21.8 g. (0.216 mole) of triethylamine was added. To the resulting solution, 23.4 g. (0.216 mole) of ethyl chloroformate in 100 ml. of dry toluene was added dropwise over 30 min. with stirring at −5° to 0°. The suspension was stirred at 0° for 2.25 hr. A solution of 9.75 g. (0.216 mole) of dimethylamine in cold toluene was added rapidly. The suspension was stirred at room temperature for 18 hr., and the organic layer was washed with water, 2*N* hydrochloric acid, water, 5% sodium bicarbonate, and water. The aqueous washes, at *p*H 8, were back-extracted with ether and similarly washed. The combined ethereal extracts were dried and concentrated, and the product was crystallized from ether–petroleum ether in two crops giving a total of 26.3 g. (50%) of V, m.p. 91–95°. A sample, m.p. 94–95°, was characterized; $\lambda_{\max}^{\text{Nujol}}$ 5.97 (ketone C=O), 6.11 (amide C=O), 6.25 μ (aromatic C=C).

Anal. Calcd. for $C_{17}H_{19}NO_2$: C, 75.81; H, 7.11; N, 5.20. Found: C, 76.08; H, 7.36; N, 5.26, 5.27 (Kjeldahl).

In a later preparation of amide V, from 16.25 g. (0.0672 mole) of I, using the above conditions, a 60.3% yield of V was isolated, m.p. 108.5–109°; $\lambda_{\max}^{\text{Nujol}}$ 6.00 (ketone C=O), 6.14 (amide C=O), 6.26 μ (aromatic C=C).

Anal. Calcd. for $C_{17}H_{19}NO_2$: N, 5.20. Found: N, 5.32, 4.93.

Infrared solution spectra of the two different melting amides were identical, although the solid state spectra differed in the finger-print region. A mixed m.p. of 94–95° and 108.5–109° amides melted at the higher temperature. A sample of V, m.p. 94–95°, was converted to V, m.p. 107.5–108.5°, by seeding an ether solution of the former with the latter. All of the evidence indicates that the two substances are isomorphic forms of V.

In the first amide V preparation above, the aqueous washes were acidified, and the precipitate was extracted into ether, which was dried over magnesium sulfate. The 13.43 g. (28.4%) of crude acidic material crystallized from methylene chloride-ether-petroleum ether to give 10.30 g. (21.7%) of recovered I, m.p. 143–144°.

endo-3-Dimethylaminomethyl-α-phenyl-5-norbornene-exo-2-methanol (VI). A solution of 23.7 g. (0.0881 mole) of V in 100 ml. of dry tetrahydrofuran was added slowly to a suspension of 10.0 g. (0.264 mole) of lithium aluminum hydride in 300 ml. of dry tetrahydrofuran. The mixture was refluxed for 20 hr., cooled in an ice bath, and decomposed slowly with 30 ml. of water. The mixture was stirred for 4.5 hr. at room temperature, and the precipitate was removed by filtration. The filtrate was concentrated and the residue crystallized from methylene chloride–ether–petroleum ether to give, in three crops, 13.1 g. (58%) of VI, m.p. 118–125°. A sample of VI, m.p. 124–124.5°, $\lambda_{\max}^{\text{Nujol}}$ 3.20, 3.29 μ (— OH), was characterized as the acid fumarate, which was obtained from isopropyl alcohol, m.p. 190°; $\lambda_{\max}^{\text{Nujol}}$ 3.0 (—OH), 5.80 (carboxyl C=O), 6.04 (C=C) , 6.36 μ (carboxylate C=O).

Anal. Calcd. for $C_{21}H_{27}NO_5$: C, 67.54; H, 7.29; N, 3.75. Found: C, 67.38; H, 7.63; N, 3.89, 3.85 (Kjeldahl).

A fourth crop of VI, 3.00 g. (total yield 71.3%), was crystallized from ether-petroleum ether, m.p. 78–90°. Recrystallization gave 0.56 g., m.p. 78–90°; $\lambda_{\max}^{\text{Nujol}}$ 3.20 (—OH), 6.24 and 6.68 μ (aromatic).

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[5] Melting points were taken on a Kofler block; infrared spectra were determined with a Perkin-Elmer Model 21 Spectrometer and ultraviolet spectra with a Cary Model 11 Spectrometer in methanol solution unless otherwise noted.

Anal. Calcd. for $C_{17}H_{23}NO$: C, 79.33; H, 9.01; N, 5.44. Found: C, 79.44; H, 9.24; N, 5.54.

endo-3-Dimethylaminomethyl-5-norbornen-2-yl exo-phenyl ketone (VII). Pyridine, 200 ml., was cooled in an ice bath and 13.3 g. of chromic oxide was added in portions with thorough mixing. To the resulting complex was added a solution of 13.32 g. of aminoalcohol VI in 80 ml. of pyridine. The resulting dark mixture was allowed to stand at room temperature for 22 hr. and then was treated with 280 ml. of water. This mixture was extracted three times with ether, washing each ether extract with a small portion of water, which was added to the pyridine-water reaction mixture. The combined ethereal extracts were dried over magnesium sulfate and concentrated to dryness, finally with pumping under high vacuum, to give 8.39 g. (63%) of crude VII as a dark oil; λ_{max}^{neat} 5.96 μ (ketone C=O), 6.25 μ (aromatic C=C).

The hydrogen fumarate prepared from 3.39 g. (0.0133 mole) of VII and 1.54 g. (0.0133 mole) of fumaric acid in isopropyl alcohol–ether amounted to 3.67 g. (over-all 47%) melting at 144–146°; λ_{max}^{Nujol} 3.0 (broad, —OH), 5.78 (carboxyl C=O), 5.92 (ketone C=O), 6.03 (C=C), 6.35 μ (carboxylate C=O); λ_{max} 244 mμ (ϵ 16,500).

Anal. Calcd. for $C_{17}H_{21}NO \cdot C_4H_4O_4$: N, 3.77. Found: N, 3.97, 3.89 (Kjeldahl).

endo-3-Dimethylaminomethyl-α,α-diphenyl-5-norbornene-exo-2-methanol (VIII). A solution of phenyllithium was prepared by adding in portions under nitrogen 2.88 g. (0.146 g.-atom) of lithium wire to a solution of 32.8 g. (0.208 mole) of bromobenzene in 100 ml. of anhydrous ether. The mixture was stirred with a Hershberg stirrer until the reaction was complete. At the same time, the pure amino ketone VII was isolated by dissolving its fumarate in water, making the solution strongly basic with sodium hydroxide, extraction with ether, washing, drying, and concentration. A solution of 26.6 g. (0.104 mole) of *endo*-3-dimethylaminomethyl-5-norbornen-2-yl *exo*-phenyl ketone (VII) in 100 ml. of anhydrous ether was then added to the phenyllithium solution at a rate to maintain reflux (15 min.). The resulting reaction mixture was stirred at room temperature overnight and hydrolyzed by adding 33 ml. of water dropwise. When all of the solid had dissolved, the layers were separated and the aqueous part was extracted with ether. The combined ethereal solutions were washed with water, treated with charcoal, concentrated to dryness and the residue dried by distilling benzene from it. The product was 33.4 g. of VIII a brown gum; $\lambda_{max}^{CCl_4}$ 3.30 (—OH), 5.98 (very weak C=O), 6.26 μ (aromatic C=C).

Combination of 10.12 g. (0.034 mole) of this product with 3.54 g. (0.034 mole) of fumaric acid in isopropyl alcohol led to 9.13 g. (over-all 74%) of the fumarate, m.p. 212–214°. A sample of this salt, washed with hot ethanol, showed a m.p. of 214–215.5°; λ_{max}^{KBr} 3.25, 3.33, 4.14 (—OH), 6.28 μ (aromatic C=C). There was only benzene ring absorption in the ultraviolet spectrum above 210 mμ.

Anal. Calcd. for $(C_{23}H_{27}NO)_2 . C_4H_4O_4$: C, 76.69; H, 7.47; N, 3.58. Found: C, 76.33, 76.41; H, 7.38, 7.66; N, 3.25, 3.51.

endo-3-Dimethylaminomethyl-α,α-diphenylnorbornane-exo-2-methanol (IX). A solution of 5.67 g. of the crude amino alcohol VIII from the previous experiment in 50 ml. of methanol was shaken under 3 atm. of hydrogen with 0.2 g. of 10% palladium-on-carbon for 3.5 hr. The catalyst was removed by filtration and the filtrate was concentrated to dryness under vacuum. The residue was dissolved in ether and extracted into dilute hydrochloric acid; the aqueous layer was made basic and extracted with ether. After drying over magnesium sulfate, the ether solution was treated with decolorizing carbon, filtered, and concentrated to dryness to give IX as a yellow gum (5.13 g.). From 0.26 g. of this base and 0.090 g. of fumaric acid in isopropyl alcohol-ether, there was obtained 0.26 g. of the hydrogen fumarate, m.p. 185–192°. Recrystallization from methanol-isopropyl alcohol-ether gave pure IX hydrogen fumarate, m.p. 191–192°; ultraviolet and infrared spectra consistent with structure.

Anal. Calcd. for $C_{23}H_{29}NO \cdot C_4H_4O_4$: C, 71.81; H, 7.37; N, 3.10. Found: C, 71.70; H, 7.52; N, 3.14.

endo-3-Dimethylaminomethyl-α-phenyl-α-o-tolyl-5-norbornene-exo-2-methanol (XI). A solution of *o*-tolyllithium was prepared from 6.45 g. (0.0375 mole) of *o*-bromotoluene and 0.52 g. (0.075 g.-atom) of lithium in 20 ml. of ether. This was treated with a solution of 4.78 g. (0.0187 mole) of amino ketone VII in 20 ml. of ether and worked up as described under the preparation of VIII. The product was 5.94 g. of a yellow oil; λ_{max}^{neat} 2.85, 3.29 (—OH), 6.25 μ (aromatic C=C).

From 3.16 g. of this product and 1.06 g. of fumaric acid in isopropyl alcohol–ether, there was obtained 2.37 g. (56%) of XI hydrogen fumarate melting at 174–189°; ultraviolet and infrared spectra consistent with structure.

A recrystallization of this material from isopropyl alcohol–ether gave a sample of XI hydrogen fumarate melting at 190.5–192.5° in about 50% recovery.

Anal. Calcd. for $C_{24}H_{29}NO \cdot C_4H_4O_4$: C, 72.54; H, 7.18; N, 3.02. Found: C, 72.28; H, 7.42; N, 3.07, 2.81.

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Carbamoylation of Some Cyclic 1,3-Dicarbonyl Compounds with Urea

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The general class of tricarbonylmethane compounds contains examples with a wide variety of physiological actions as antifungal, anthelmintic, and antibacterial.[1] However, only the tetracycline incorporate a carbamoyl moiety as part of the tricarbonylmethane system. We wish to report a method of preparing 2-carbamoyl derivatives of some cyclic 1,3-dicarbonyl compounds through the use of readily accessible intermediates, *i.e.*, cyclic 1,3-dicarbonyl compounds and urea. The interest of others in such compounds has been disclosed using acetyl cyanate as an intermediate.[2]

Urea has found application as a source of the elements of cyanic acid as in the preparation of urethanes by reactions with alcohols and in the preparation of substituted ureas by reaction with amines.[3] The zinc chloride catalyzed carbamoylation of resorcinol under Friedel-Crafts conditions by means of urea has been reported.[4] Since organic acids catalyze the decomposition of urea, presumably *via* cyanic acid,[5] it was hoped that compounds

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[1] C. H. Hassel, *Experimentia*, **6**, 642 (1950); C. H. Hassel in J. W. Cook, *Progress in Organic Chemistry*, vol. 4, 115, Academic Press, New York, 1958.

[2] M. M. Shemyakin, *et al.*, *Zhur. Obshchei Khim.*, **30**, 542 (1960).

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