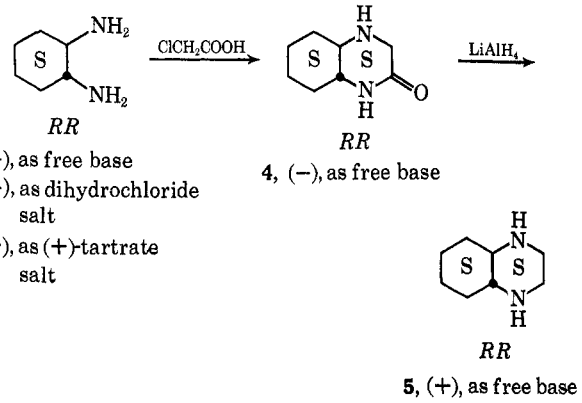
SCHEME II



(±)-*trans*-cyclohexane-1,2-diamine with glyoxal to (±)-*trans*-decahydroquinoxaline.

To this earlier report is now added the observation that, with the conditions previously utilized,[5] **3a** was reductively cycloalkylated with glyoxal to optically active **5**. This success not only simplified the preparation of **5**, but also provided a measure of insight into the mode of formation of **5** *via* the reductive cycloalkylation of **3a**.

If the reductive cycloalkylation of **3a** to **5** had proceeded *via* either the intermediate addition compound (aminol) or dehydration compound (5,6,7,8,9,10-hexahydroquinoxaline), chiral integrities of the bridge carbon atoms of **5** would be expected to have been preserved. However, if formation of **5** in whole or part resulted from the intermediate, aromatic 5,6,7,8-tetrahydroquinoxaline (which could conceivably form by dehydrogenation of the hexahydroquinoxaline), then **5** would have been in part, at least, a racemic mixture. The result of this experiment indicates that the aromatic tetrahydroquinoxaline was not significantly present during the reductive cycloalkylation of **3a** to **5**.

Experimental Section[6]

(+)-*trans*-Cyclohexane-1(*S*),2(*S*)-dicarboxylic Acid (1).—(±)-*trans*-Cyclohexane-1,2-dicarboxylic acid[7] was resolved (68% yield) by the procedure of Applequist and Werner:[3] mp 183–185°, $[\alpha]^{26}D$ +22.25° (*c* 1.88, Me_2CO) [lit.[3] mp 183.5–185°, $[\alpha]^{30}D$ + 22.3° (*c* 5.3, Me_2CO)].

(+)-*trans*-Cyclohexane-1(*S*),2(*S*)-diamine Dihydrochloride (2b).—This material (**2b**) was prepared (13% yield) *via* the Schmidt reaction utilized by Yashunskii,[8] as modified by Brill and Schultz,[2] for the preparation of the corresponding cis isomer: $[\alpha]^{24}D$ +16.14° (*c* 0.21, H_2O) [lit.[9] $[\alpha]^{25}D$ ±15.8° (*c* 20)]. *Vide infra* for the optical activity of the enantiomeric hydrochloride.

(−)-*trans*-Cyclohexane-1(*S*),2(*S*)-diamine (−)-Tartrate (2c).—Commercial, redistilled 1,2-diaminocyclohexane[10] was resolved with (−)-tartaric acid (90% yield) by the procedure of Reinbold and Pearson[11] to give **2c**, $[\alpha]^{24}D$ −18.05° (*c* 0.44, H_2O). Its antipodal (+)-tartrate salt (**3c**) had $[\alpha]^{24}D$ +14.19° (*c* 0.32, H_2O) [lit.[11] $[\alpha]_{589}$ +12.1° (*c* 1, H_2O), lit.[12] $[\alpha]D$ +12°].

(+)-*trans*-Cyclohexane-1(*S*),2(*S*)-diamine (2a).—Solid potassium hydroxide was added to 50 ml of an aqueous, stirred solution containing 6.4 g of **2c** until two layers formed. The amine was separated and distilled from solid potassium hydroxide to give 2.25 g (81%) of colorless liquid **2a**, bp 104–110° (40 mm), $[\alpha]^{25}D$ +35.47° (*c* 4.74, Me_2CO). The optical antipode (**3a**) had bp 105–110° (40 mm), $[\alpha]^{25}D$ −35.20° (*c* 6.78, Me_2CO) [lit.[11] bp 75–80° (16 mm); lit.[13] bp 82° (14 mm), $[\alpha]D$ −36°]. The hydrochloride salt (**3b**) obtained upon passing hydrogen chloride gas into a diethyl ether solution of (−)-*trans*-cyclohexane-1(*R*),2(*R*)-diamine (**3a**) had $[\alpha]^{24}D$ −17.18° (*c* 0.51, H_2O) and $[\alpha]^{24}D$ −15.58° (*c* 20, H_2O) [lit.[9] $[\alpha]^{25}D$ ±15.8° (*c* 20)].

(−)-*trans*-9(*R*),10(*R*)-Decahydroquinoxalin-2-one (4).—Compounds **3b** and **3c** were cyclized with chloroacetic acid to **4** in 30% yields by the procedure of Brill and Schultz,[2] except that potassium bicarbonate was used instead of ammonium hydroxide: mp 196–197.5°, $[\alpha]^{24}D$ −70.33° (*c* 0.24, 95% EtOH).

Anal. Calcd for $C_8H_{14}N_2O$: C, 62.30; H, 9.15; N, 18.17. Found: C, 62.44; H, 9.12; N, 18.34.

The optical antipode of **4**, (+)-*trans*-9(*S*),10(*S*)-decahydroquinoxalin-2-one, was similarly prepared: mp 196–198°, $[\alpha]^{24}D$ +71.17° (*c* 0.45, 95% EtOH).

(+)-*trans*-9(*R*),10(*R*)-Decahydroquinoxaline (5). A. From 4.—Compound **4** was reduced to **5** with lithium aluminum hydride (50% yield) by the described procedure:[2] mp 176–177°, $[\alpha]^{24}D$ +16.31° (*c* 0.46, H_2O), $[\alpha]^{24}D$ +14.72° (*c* 0.4, 95% EtOH), and $[\alpha]^{24}D$ +10.72° (*c* 0.48, $CHCl_3$) [lit.[2] mp 176–177°, $[\alpha]^{26}D$ +10.4° (*c* 10, $CHCl_3$)]

Anal. Calcd for $C_8H_{16}N_2$: C, 68.52; H, 11.50; N, 19.98. Found: C, 68.79; H, 11.69; N, 20.35.

B. From 3a.—(−)-*trans*-Cyclohexane-1(*R*),2(*R*)-diamine was reductively cycloalkylated (30% yield) with glyoxal over platinum oxide catalyst by the earlier reported procedure.[5] The **5** obtainied had mp 176–177°, $[\alpha]^{24}D$ +16.40° (*c* 0.38, H_2O).

Registry No.—**2a**, 21436-03-3; **2b**, 32044-18-1; **2c**, 32044-19-2; **3a**, 20439-47-8; **3b**, 32044-21-6; **3c**, 32044-22-7; (−)-**4**, 32044-23-8; (+)-**4**, 32044-24-9; **5**, 32044-25-0.

(6) Melting points, uncorrected, were determined on a Thomas–Hoover apparatus. All optical activities were determined in a Rudolph Model 63 polarimeter using a 2-dm tube. Microanalyses were performed by PCR, Gainesville, Fla.

(7) C. C. Price and M. Schwarcz, *J. Amer. Chem. Soc.*, **62**, 2891 (1940).

(8) V. G. Yashunskii, *Zh. Obshch. Khim.*, **28**, 1361 (1958); *Chem. Abstr.*, **52**, 19979*f* (1958).

(9) R. G. Asperger and C. F. Liu, *Inorg. Chem.*, **4**, 1492 (1965).

(10) Aldrich Chemical Co.

(11) P. E. Reinbold and K. H. Pearson, *Talanta*, **17**, 391 (1970). Their salt was named D(−)-*trans*-1,2-diaminocyclohexane L(+)-tartrate, although neither reference to nor proof of a known absolute configuration for the diaminocyclohexane moiety is presented. As written by Eliel (E. L. Eliel, "Stereochemistry of Carbon Compounds," McGraw-Hill, New York, N. Y., 1962, p 90), the use of only one configurational symbol is inadequate for naming a compound having two asymmetric atoms, even if the two centers are alike, as they are in (−)-*trans*-cyclohexane-1,2-diamine.

(12) R. S. Treptow, *Inorg. Chem.*, **5**, 1593 (1966). The salt was named *l*-chn *d*-tartrate, indicating that it was the salt of the (−)-free amine base with (+)-tartaric acid. In point of fact, the salt *itself*, as cited in the experimental details above, had a (+) rotation.

(13) F. M. Jaeger and L. Bijkerk, *Proc. Kon. Ned. Akad. Wetensch.*, **40**, 12 (1937); *Chem. Zentr.*, **108** (II) 1196 (1937).

Reactions of 2-Dichloromethylene-3-oxazolin-5-ones with Toluene under Friedel–Crafts Conditions

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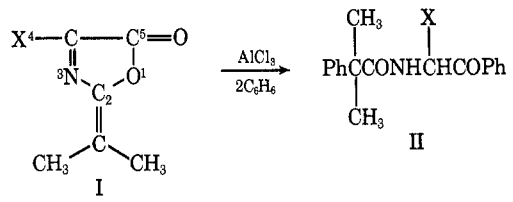
Received March 17, 1970

In our previous paper[1] it was reported that 2-isopropylidene-3-oxazolin-5-ones (I) react with benzene in the presence of anhydrous aluminum chloride to give 1:2 adducts, *N*-(α-phenylisobutyryl)-α-amino ketones (II), by 1,4 addition to the double bond system followed by ring opening.

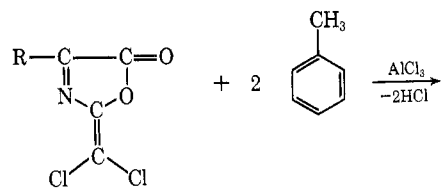
It was of interest to determine what reaction would occur when related pseudoxazolones containing a di-

(1) Y. Iwakura, F. Toda, and Y. Torii, *J. Org. Chem.*, **32**, 3202 (1967).

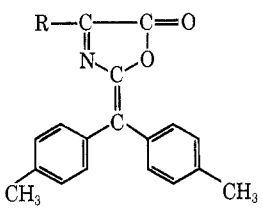


X = Me, *i*-Pr, *i*-Bu, Ph

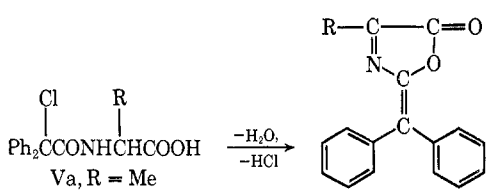
chloromethylene group, for example, 2-dichloromethylene-3-oxazolin-5-ones (III),[2] are treated under similar conditions. The major products isolated after the reaction of III with excess toluene in the presence of anhydrous aluminum chloride were shown to be 2-ditolylmethylene-3-oxazolin-5-ones (IV) by ir and nmr spectral comparison with the model compounds 2-diphenylmethylene-3-oxazolin-5-ones (VI), synthesized from *N*-diphenylchloroacetyl-DL-α-amino acids by a well-established route. Carbonyl absorption at 1770 cm^{-1} supports cyclic structures for the addition products.



IIIa, R = Me
b, R = *i*-Pr
c, R = *i*-Bu



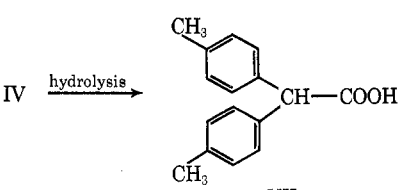
IVa, R = Me
b, R = *i*-Pr
c, R = *i*-Bu



Va, R = Me
b, R = *i*-Bu

VIa, R = Me
b, R = *i*-Bu

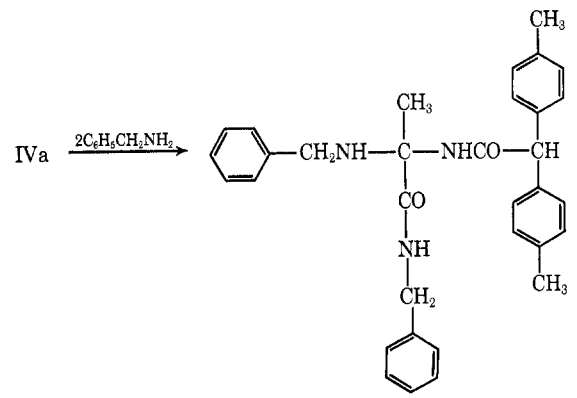
The nmr spectra are consistent with the assigned structures; the characteristic A_2B_2 pattern of the aromatic protons indicates para substitution of the tolyl groups. Substitution of two chlorine atoms of III could proceed by successive addition of toluene and elimination of labile hydrogen chloride as suggested by Steglich.[2] Di(*p*-tolyl)acetic acid (VII) was obtained from acid hydrolysis of IV.



VII

(2) W. Steglich, H. Tanner, and R. Hurnaus, *Chem. Ber.*, **100**, 1824 (1967).

It has been reported[3] that pseudoxazolones generally add 2 mol of primary amine. Compound IVa reacted spontaneously with 2 mol of benzylamine to give the 1:2 adduct VIII, presumably by 1,4 addition followed by ring opening.



VIII

Experimental Section

Reaction of 2-Dichloromethylene-3-oxazolin-5-ones with Toluene under Friedel–Crafts Conditions.—A sample of IIIa (2.22 g, 0.012 mol) in 100 ml of dry toluene was added dropwise to a stirred slurry of 7.14 g (0.054 mol) of anhydrous aluminum chloride in 50 ml of dry toluene. The reaction temperature was kept at 0° by the use of an ice bath. After the solution had been stirred for 2 hr, 40 ml of 18% HCl was added. The toluene layer was washed twice with 200-ml portions of water and dried (Na_2SO_4). After removal of toluene, the resulting solid was recrystallized from ethanol to give 1.91 g (53%) of IVa as a yellow solid: mp 141–142.5°; δ (CCl_4) 2.25 (s, 3) and 2.35 (s, 6). Similarly prepared were IVb [mp 128–132°; 84%; δ 1.3 (d, 6), 2.35 (s, 6), 3.00 (septet, 1)] and IVc [mp 118–119°; 54%; δ 0.95 (m, 6), 2.30 (s, 6), 2.40 (m, 3)].

Satisfactory analyses (0.35% for C, H, N) were reported for IVa and IVc. *Anal.* for IVb: C, 79.51. Calcd: C, 78.97.

Preparation of *N*-Diphenylchloroacetyl-DL-amino Acids (V).—To 7.3 g of DL-alanine, 21 g of *N*-chlorodiphenylacetyl chloride[4] in 200 ml of ethyl acetate was added. The mixture was refluxed for 14.5 hr. The reaction mixture was filtered, and the filtrate was washed with 200 ml of water and dried (Na_2SO_4). After removal of ethyl acetate, the resulting solid was recrystallized from benzene–cyclohexane to give *N*-diphenylchloroacetyl-DL-alanine, yield 9.7 g (38%), mp 134–135°.

Anal. Calcd for $C_{17}H_{16}ClNO_3$: C, 64.26; H, 5.07; N, 4.41; Cl, 11.16. Found: C, 64.48; H, 5.07; N, 4.17; Cl, 10.97.

Similarly prepared was *N*-diphenylchloroacetyl-L-leucine, yield 61%, mp 123–125°.

Anal. Calcd for $C_{20}H_{22}ClNO_3$: C, 66.75; H, 6.16; N, 3.89; Cl, 9.85. Found: C, 66.19; H, 6.05; N, 4.01; Cl, 9.79.

Synthesis of 2-Diphenylmethylene-3-oxazolin-5-ones (VI).—2-Diphenylmethylene-4-methyl-3-oxazolin-5-one (VIa) was prepared by the method used for the preparation of 2-dichloromethylene-3-oxazolin-5-ones (III) by Steglich, *et al.*[2]

N-Diphenylchloroacetyl-DL-alanine (6.8 g, 0.02 mol) was treated with 2 ml of phosphorus oxychloride and 7.4 ml of pyridine in 30 ml of methylene chloride to obtain 3.1 g (yield 59%) of 2-diphenylmethylene-4-methyl-3-oxazolin-5-one (VIa). The solid was recrystallized from ethanol: mp 155–156°; δ ($CDCl_3$) 7.65 (s, 3).

Anal. Calcd for $C_{17}H_{13}NO_2$: C, 77.55; H, 4.98; N, 5.32. Found: C, 77.47; H, 5.07; N, 5.28.

Similarly prepared was 2-diphenylmethylene-4-isobutyl-3-oxazolin-5-one (VIb). The solvent for recrystallization was ethanol: mp 70–72°; yield 58%; δ 0.98 (m, 6) and 2.46 (m, 3, $-CHCH_2-$).

Anal. Calcd for $C_{20}H_{19}NO_2$: C, 78.66; H, 6.27; N, 4.59. Found: C, 78.65; H, 6.24; N, 4.67.

(3) Y. Iwakura, F. Toda, Y. Torii, and K. Tomioka, *Tetrahedron*, **24**, 575 (1968).

(4) J. H. Billman and P. H. Hidy, *J. Amer. Chem. Soc.*, **65**, 760 (1943).

Hydrolysis of 2-Ditolylmethylene-3-oxazolin-5-ones (IV).—A sample (1.16 g) of IV was dissolved in 10 ml of dioxane. To this solution, 2.5 ml of concentrated HCl was added, and the mixture was kept at 80–90° for 9 hr. After evaporation of the reaction mixture, 100 ml of ether and 50 ml of 7% HCl were added. The layer of ether was collected. After evaporation of the ether the resulting solid was recrystallized from cyclohexane, yield 71% (0.68 g). This compound is *p,p*-ditolylacetic acid (VII), mp 137–138° (lit.[5] mp 144°).

Anal. Calcd for $C_{16}H_{16}O_2$: C, 79.97; H, 6.71. Found: C, 79.73; H, 6.73.

Hydrolysis of 2-ditolylmethylene-4-isopropyl-3-oxazolin-5-one gave the same compound.

Reaction of IVa with Benzylamine.—A mixture of IVa (1.49 g, 0.005 mol) and benzylamine (2.68 g, 0.025 mol) in benzene (10 ml) was kept at 80° for 5 hr. The resulting solid was collected by filtration and recrystallized from cyclohexane to give 2.1 g of crystals (VIII), yield 83%, mp 111.5–112.0°.

Anal. Calcd for $C_{33}H_{35}N_3O_2$: C, 78.33; H, 6.98; N, 8.31. Found: C, 78.30; H, 7.15; N, 8.43.

Registry No.—IVa, 30318-25-3; IVb, 30318-26-4; IVc, 30318-27-5; Va, 30318-28-6; Vb, 30318-29-7; VIa, 30318-30-0; VIb, 30318-31-1; VII, 20809-78-3; VIII, 30318-33-3; toluene, 108-88-3.

(5) P. Fritsch and F. Feldmann, *Justus Liebigs Ann. Chem.*, **306**, 72 (1899).

The Preparation and Some Reactions of 9-(Disubstituted amino)-9*H*-pyrrolo[1,2-*a*]indoles

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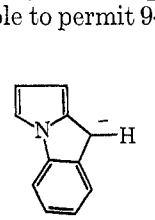
We wish to report a convenient method for the direct synthesis of 9-(*N,N*-disubstituted amino)-9*H*-pyrrolo-[1,2-*a*]indoles. At present, the only general procedure[2] for introducing substituents at the 9 position utilizes the anion I. Previous methods for preparing the 9*H*-pyrrolo[1,2-*a*]indole ring system II[3–5] also are not readily adaptable to permit 9-amino substitution.



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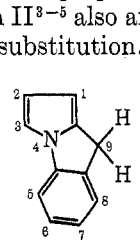
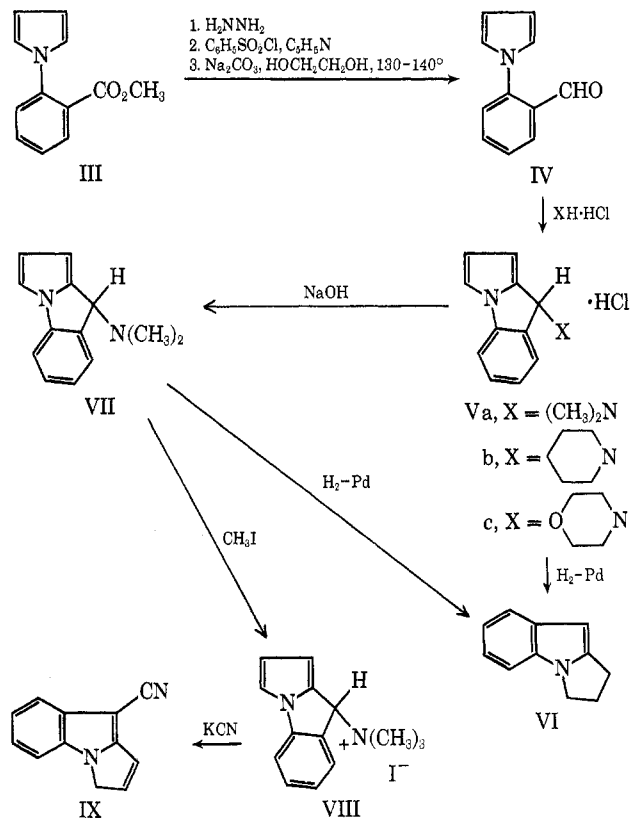


II

N-(*o*-Formylphenyl)pyrrole (IV) is prepared from *N*-(*o*-carbomethoxyphenyl) pyrrole (III) by a McFadden–Stevens reaction (Scheme I). Compound IV is converted directly to compounds Va–c by a Mannich reaction. The trimethylammonium iodide VIII also was prepared from Va. With two exceptions where acetaldehyde was successfully utilized as the carbonyl component,[6,7] Mannich reactions on pyrrole compounds have been limited to the use of formaldehyde.

SCHEME I



Catalytic reduction of the dimethylamino compound either as the free base VII or the hydrochloride salt Va is accompanied by prototropic tautomerism to give the known indole VI.[5] This is consistent with the work of Laschtuvka and Huisgen.[5]

Treatment of the quaternary ammonium compound VIII with potassium cyanide gave 9-cyano-3*H*-pyrrolo-[1,2-*a*]indole (IX). It was reported by Franck and Bernady[2] that treatment of the anion I with ethyl chloroformate or carbon dioxide also gives a 9-substituted 3-H derivative. As prototropic tautomerism took place in the former case where the pyrroloindole VIII is the electrophile as well as in the latter case where the pyrroloindole system (I) is the nucleophile and as the amino substituted compounds Va–e occur as 9-H derivatives, it appears that the 3-H compounds are the thermodynamically more stable products when the 9 position has an electron-withdrawing substituent and that 9-H compounds are favored when there is an electron-donating substituent at the 9 position.

Experimental Section

A Varian A-60A, Perkin-Elmer 137, and Cary recording spectrophotometer Model 14 were employed for obtaining spectral data. Uv. and ir spectra appear in Table I.

***o*-(Pyrrol-1-yl)benzohydrazide.**—Methyl *o*-(pyrrol-1-yl)benzoate[8] (III) (60.4 g, 0.3 mol), anhydrous hydrazine (200 ml), and ethanol (200 ml) were combined and stirred at reflux for 3 hr. The reaction mixture was next concentrated to a thick residue by rotary evaporation with the aid of heat. The residue crystallized to give a quantitative yield of product which was recrystallized

(1) Merrell National Laboratories, Division of Richardson-Merrell, Inc., Cincinnati, Ohio 45215.

(2) R. W. Franck and K. F. Bernady, *J. Org. Chem.*, **33**, 3050 (1968).

(3) E. E. Schweizer and K. K. Light, *ibid.*, **31**, 2913 (1966).

(4) G. R. Allen, Jr., and M. J. Weiss, *ibid.*, **30**, 2904 (1965). The 7-benzyloxy derivative was prepared in this paper.

(5) E. Laschtuvka and R. Huisgen, *Chem. Ber.*, **93**, 81 (1960).

(6) U. Eisner, *J. Chem. Soc.*, 854 (1957).

(7) W. Herz and U. Toggweiler, *J. Org. Chem.*, **29**, 213 (1964).

(8) A. D. Josey and E. L. Jenner, *ibid.*, **27**, 2466 (1962).