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REACTIONS OF IMINES WITH *t*-BUTYL ISOCYANIDE[1]

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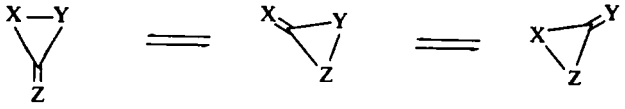
Abstract—The reactions of N-aryl imines with *t*-butyl isocyanide have been studied. Reaction only occurs with acid catalysis in non-basic solvents. The products from these reactions have been identified as 2,3-bis(t-butylimino)azetidines and 3-t-butylamino-2-phenylindoles. Detailed chemical and spectral data are given in support of these assigned structures. Some preliminary reports on the chemistry of these products are described including a novel dehydrogenation by a peracid.

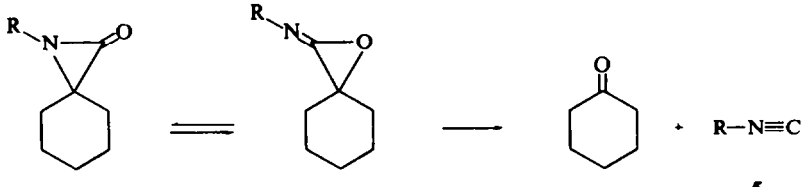
OBSERVATIONS that the presence of hereto atoms in the methylenecyclopropane π network apparently allows exceptionally facile molecular reorganization (equation 1)[2,3] have prompted us to search for new examples of structure **1** and their chemistry.



(1)

1

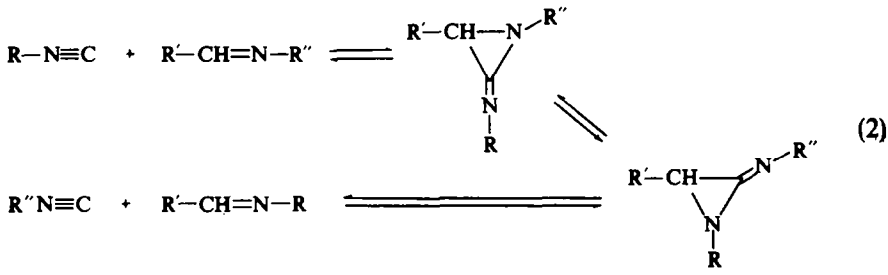
One of our approaches to this problem was based on the observed dissociation of a heteromethylenecyclopropane (**2**) into a ketone (**4**) and an isocyanide (**5**).[4] This result suggested to us that heteromethylenecyclopropanes might be generated by the reverse of this dissociation if suitable acceptors and conditions were chosen. For this



2 **3** **4** **5**

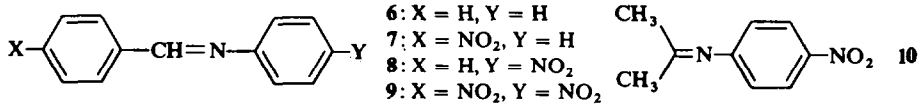
reason, the isomerization sequence depicted in Eq 2 was attempted under various conditions. Although these attempts have not yet produced the additional examples of the isomerization illustrated in equations 1 and 2, we have found a number of new and potentially useful reactions between isocyanides and imines.

Our initial experiments were conducted in carbon tetrachloride between 100–



(2)

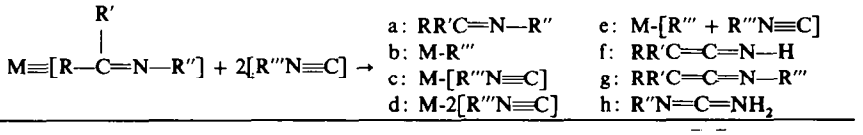
120° in sealed tubes. In these experiments, imines **6–10** were reacted with t-butyl isocyanide.* Two principal types of adducts could be isolated in yields which were highly dependent on the substituents. Imines **8**, **9** and **10** yielded 2:1 isocyanide : imine adducts



in 51–70% yields. Imines **6** and **7** formed 1:1 adducts as major (27–41%) products and 2:1 adducts in poor yield. No 1:1 adducts were formed from imines **8–10**.

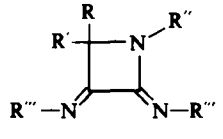
Structures of the 2:1 *adducts.* The 2:1 adducts were identified as such by their elemental analyses and mass spectra. The latter revealed significant peaks which were indicative of fragmentation products shown in Table 1. Each 2:1 adduct showed an IR peak at about 1720 cm^{-1} and a more intense peak at 1670 cm^{-1}. No absorption

TABLE 1. MASS SPECTRA OF 2:1 ADDUCTS



in the NH region was observed. The NMR spectra of adducts **6–9** all showed t-butyl peaks at approximately δ 1·07 and 1·48 as well as a singlet at about δ 5·5 which did not exchange with D_2O. The adduct from **10** lacked the 5·5 peak but showed two closely spaced t-Bu (δ 1·40 and 1·38) peaks and one 6-proton Me singlet at δ 1·80. No change had occurred in the number of aryl protons.

A number of general structures (**11–14**) can be written for the 2:1 adducts which are consistent with a lack of NH absorption and the maintained identity of the various



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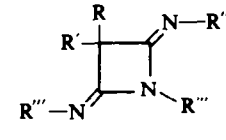

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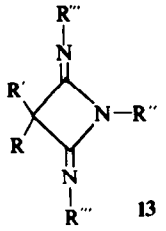
* This isocyanide was chosen because of its relative thermal stability.



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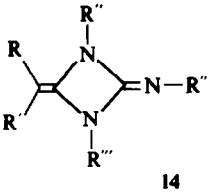
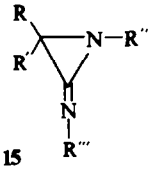


14

R groups. Structures **12–14** could conceivably arise from the attack of isocyanide on **16** which could, in turn, be formed from **15**. Structure **11** would arise (*vide infra*) by a route which does not include the heteromethylenecyclopropane structure (**15**). Although the t-Bu absorption at approximately δ 1·07 is suggestive of the existence of



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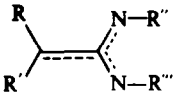
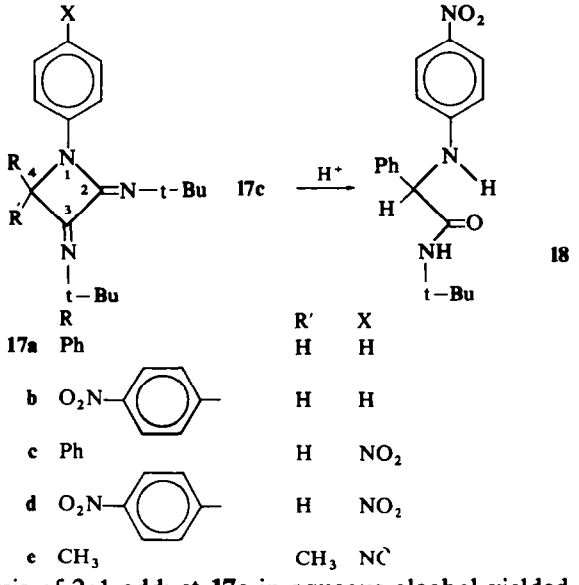


16

a tri-substituted nitrogen,[5] structure **11** is supported by the mass spectral formation of fragment *a* (Table 1). This mass spectral evidence was not regarded as totally conclusive since structures **12–14** might yield fragment *a* by the reverse of their hypothetical formations (*via* **16** and **15**). For this reason, independent structural evidence was sought by chemical degradation.

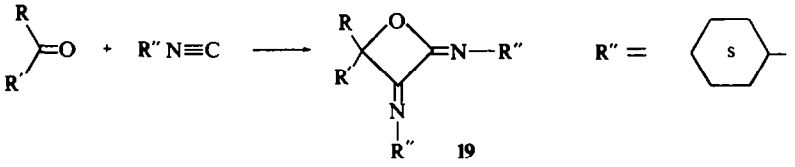


	R	R′	X
17a	Ph	H	H
b	O_2N–	H	H
c	Ph	H	NO_2
d	O_2N–	H	NO_2
e	CH_3	CH_3	NC

Acid hydrolysis of 2:1 adduct **17c** in aqueous alcohol yielded t-butyl amide **18**. This compound was identified by its spectral properties and by comparison with an authentic sample synthesized by an alternative method. Isolation of this compound thus eliminates from consideration structures **12–14**. We have, therefore, assigned **17** (i.e. general structure **11**) as the structure of a 2:1 adduct.

While this manuscript was in preparation, a report appeared concerning 2:1

isocyanide: carbonyl adducts isolated from the boron trifluoride catalyzed reactions of cyclohexyl isocyanide with acetone and acetaldehyde.[6] The structure (**19**) proposed for these adducts is similar to that assigned by us to **17**. The infrared absorption reported for **19** at 1705 and 1738 cm^{-1} is in satisfactory agreement with our observed

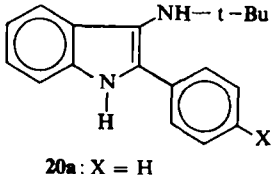


values of 1670 and 1720 cm^{-1}. The latter absorptions may be assigned to conjugated and non-conjugated four-membered ring imine groups respectively.

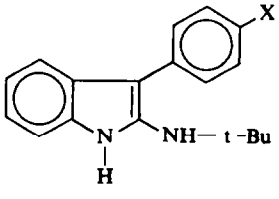
From model compounds (e.g. benzylidine-t-butyl imine), the chemical shift of the t-Bu groups of **17** are expected at around δ 1·30. The observed chemical shift of one t-Bu group in **17** (**a–d**) at about δ 1·07 requires that this t-Bu group be shielded. Inspection of molecular models reveals that the most reasonable conformation of compounds **17a–d** is one in which the C-4 aryl group is perpendicular to the ring. In this conformation the C-3 t-butylimino substituent would be positioned above the plane of this aryl group and thus be deshielded.

Structure of the 1:1 *adducts.* Although the mass spectral data served to confirm the 1:1 composition implied by elemental analysis, the fragmentation patterns did not provide any clear structural information. The lack of IR absorption between 1600 and 2900 cm^{-1} excluded structures with C=N or C≡N groups. The presence of NH was indicated in both the IR and NMR spectral of the 1:1 adducts. The NMR spectra revealed two peaks at approximately δ 2 and 8. These peaks were attributed to NH groups on the basis of their broadness and their facile exchange with D_2O. The NH group which gives rise to the approximately δ 2 absorption could readily be acetylated to a product mono-amide with a N-H peak at approximately δ 9·3. In addition to the NH peaks, the NMR spectra of the 1:1 adducts had a t-Bu peak at δ 1·0 as well as aryl absorption. Careful integration of the spectra showed that one aryl proton had been lost from the aniline portion of the precursor schiff base.

Consideration of this spectral evidence suggested two possible structures, **20** and **21**.



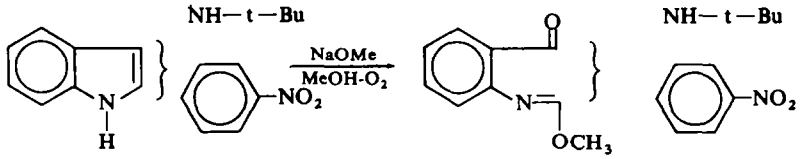
20a: X = H
b: X = NO_2



21a: X = H
b: X = NO_2

Structure **21** would require an intermediate of the type suggested in Eq. 2. An equally reasonable route (*vide infra*) to **20** can also be formulated.

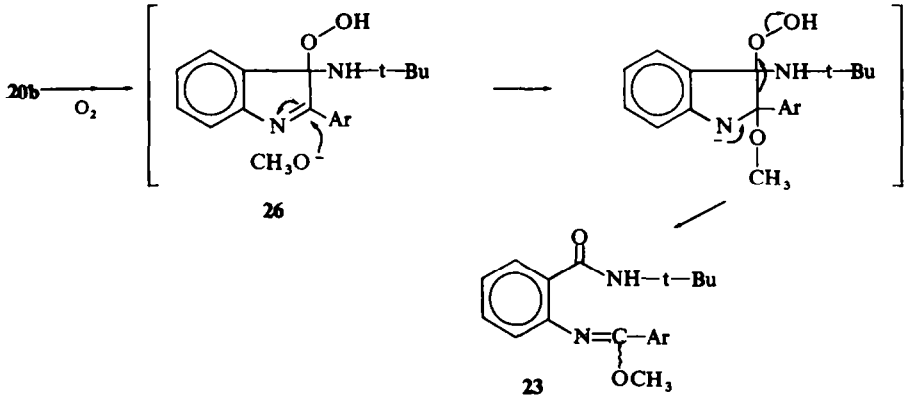
In order to decide between these structures chemical degradation was attempted. Although a number of reactions were investigated, the most fruitful results arose from the discovery of the ease with which the 1:1 adducts could be oxidized. For example, when dissolved in methanolic sodium methoxide the brick-red **22** underwent oxidation to orange imino ether **23**. Partial hydrolysis of **23** yielded amino amide **24** and *p*-nitrobenzoic acid **25**. Both compounds were shown to be identical in m.p. and spectral properties to authentic samples. This oxidation result established structures **20a** and **20b** for the 1:1 adducts. Autoxidation of **22** presumably produced



22 **23**

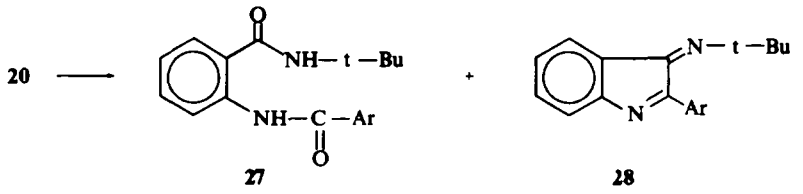
25 **24**

26 as an intermediate. Hydroperoxides analogous to **26** have been isolated by Witkop from the autoxidation of indoles.[7]

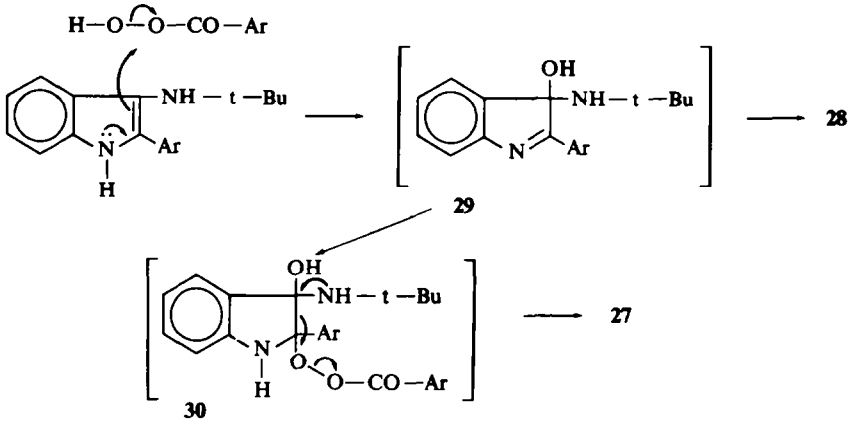


26 **23**

A second oxidative degradation was also carried out. Reaction of **20a** or **b** with *m*-chloroperbenzoic acid resulted in formation of two products, **27** and **28**. The former was favored by excess peracid. The latter predominated when stoichiometric amounts of peracid were slowly added to the indoles. The structure of **27** was established by its synthesis from **24**. The structure assigned to **28** was based on its spectral properties and its conversion back to **20** with sodium borohydride. A reasonable precursor of



both compounds is alcohol **29**. This alcohol can either dehydrate to give the novel overall result of dehydrogenation by a peracid or react with a second mole of peracid to produce **27** *via* **30**. Formation of **29** and its subsequent conversion to **27** finds precedent in the reaction of carbazoles with peracids.[8]



Mechanism of adduct formation. It is clear from inspection of the structures of the 1 : 1 and 2 : 1 adducts that these products were formed without the molecular scrambling of Eq. 2. The failure to observe reaction between these imines and isocyanide in polar solvents (including t-butyl isocyanide itself) under various conditions indicated possible acid catalysis. Trace amounts of acid present in non-polar halocarbon solvents are known to have large effects on reactions. The acid catalyzed nature of the reaction of carbonyl compounds with isocyanides to give **19** also suggested that our imine reactions involved similar catalysis.[6] Further indication of the acid catalyzed nature of these reactions was found in the formation of **17c** from t-butyl isocyanide and **8** at room temperature with trifluoroacetic acid catalysis. The production of **18** in approximately equal amounts made this a less desirable route to **17c** than the sealed tube reactions. Similarly, the indoles could be formed at room temperature from imines and t-butyl isocyanide in a hydrochloric acid–carbon tetrachloride mixture. In this case, the indole was isolated from the reaction mixture as a hydrochloride salt.

The overall reaction scheme is summarized in Fig. 1. It is clear that partitioning between paths 1 and 2 is dependent on the nucleophilicity of the aniline ring. The failure of t-butyl isocyanide to react with imines in the absence of acid catalysis apparently frustrated our efforts to realize the reactions in equation 2. Hopefully, the

information obtained thus far will allow suitable modifications of reactants and conditions in order to reach the originally desired goal.

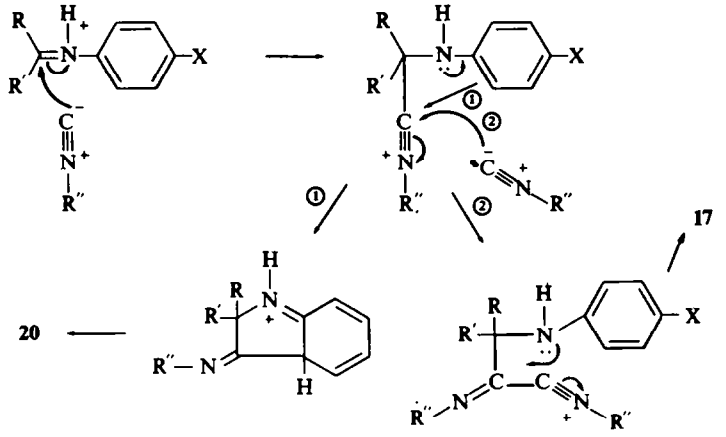


FIG. 1.

EXPERIMENTAL

The NMR spectra were taken on a Varian A-60A with TMS as internal standard. The IR spectra were taken on a Perkin–Elmer Infracord while the mass spectra were taken on a Hitachi Perkin–Elmer RMU-6E Mass Spectrometer. All new compounds reported had a molecular ion peak which agreed with the expected value. The CHN analyses are from Galbraith Laboratories, Inc., Knoxville, Tenn. A Cary 15 Recording Spectrophotometer was used for the UV spectra. M.ps are uncorrected and taken in a Thomas-Hoover Capillary M.P. Apparatus. Alumina used was Fisher Scientific Co. "Alumina Adsorption", and "5% alumina in benzene" means that 5% by wt of water was added to the alumina and that the column was packed in benzene.

t-Butyl isocyanide. t-Butyl isocyanide was prepared from N-t-butylformamide using the procedure of Ugi *et al.*[9] Imines **6**,[10] **7**,[11] **8**,[12] and **9**[13] were prepared by standard procedures.[14] 2-Propylidene-*p*-nitroaniline was prepared from 2,2-diethoxypropane[15] and *p*-nitroaniline using the method of Hoch,[16] b.p. 97–102°/0·3 mm, NMR (CCl_4) δ 1·98 (d, 6, broad peaks separated by 20 Hz), 6·74 (d, 2, J = 9 Hz), and 8·12 (d, 2, J = 9 Hz). The compound was not further characterized because of its sensitivity to moisture. It was used immediately after preparation.

1,4-Di-p-nitrophenyl-2,3-bis(t-butylimino)azetidine (**17d**). -*p*-Nitrobenzylidene-*p*-nitroaniline (500 mg, 1·8 mmol), t-butyl isocyanide (1·0 g, 12 mmol) and CCl_4 (11 g) were placed in a glass tube. The tube was flushed with N_2, sealed and heated at 120° for 13 hr. After cooling, the solvent was removed under reduced press. The remaining material was chromatographed on a 10% alumina in benzene column. The main fraction was concentrated and applied to a thick layer alumina plate. The plate was developed in benzene. The main fraction gave 560 mg (76% yield) after recrystallization from EtOH of product, m.p. 175–177°, IR (Nujol) cm^{-1} 1720, 1670, UV (abs. EtOH) λ_{max} mμ 376 (ε = 23,700), 288 (ε = 11,200), 240 (ε = 14,300); NMR ($CDCl_3$) δ 1·08 (s, 9), 1·48 (s, 9), 5·70 (s, 1), and 7·8 (m, 8). (Found: C, 63·35; H, 6·40; N, 15·86. Calcd for $C_{23}H_{27}N_5O_4$: C, 63·14; H, 6·22; N, 16·01).

1-p-Nitrophenyl-4-phenyl-2,3-bis(t-butylimino)azetidine (**17c**). Benzylidene-*p*-nitroaniline (4·05 g, 17·9 mmol), t-butyl isocyanide (3·3 g, 40 mmol) and CCl_4 (50 ml) were sealed in a glass tube and heated at 100° for 8 hr. The reaction mixture went from yellow to a dark red-brown in this time. After cooling, the solvent and excess isocyanide were removed under reduced press. The residue was chromatographed on 100 g alumina eluting with benzene. The first two fractions (300 ml) contained the product. Several crystallizations from cyclohexane and a few drops of pet. ether yielded 3·10 g (51%) bright yellow crystals: m.p. 141·5–143°; IR (Nujol) 1730, 1680, UV (abs EtOH) λ_{max} mμ 380 (ε = 23,800), 292 (ε = 5,080), λ_{sh} 227 mμ (ε = 32,700) and NMR (CCl_4) δ 1·13 (s, 9), 1·5 (s, 9), 5·52 (s, 1), 7·36 (s, 5), 7·49 (d, 2, J = 9 Hz), 7·97 (d, 2, J = 9 Hz). (Found: C, 70·36; H, 7·13; N, 14·58. Calcd for $C_{23}H_{28}N_4O_2$: C, 70·39; H, 7·19; N, 14·28%).

1-p-*Nitrophenyl*-2,3-*bis*(*t-butylimino*)-4,4-*dimethylazetidine* (**17e**). 2-Propylidene-*p*-nitroaniline (530 mg, 3·0 mmol), t-butyl isocyanide (830 mg, 10 mmol) and CCl_4 (9 ml) were placed in a glass tube. The tube was flushed with N_2, sealed and heated at 110° for 14 hr. The resulting dark brown mixture contained a small amount of brown solid which was not investigated further. The reaction mixture was washed out of the tube with chloroform and concentrated on a rotary evaporator. The residue was applied to a 5% alumina in benzene column. Elution with benzene followed by recrystallization from hexane gave 535 mg (52% yield) of product, m.p. 138–139°; IR (KBr) cm^{-1} 1725, 1665, UV (abs. EtOH) λ_{max} mμ 385 (ε = 24,300), 309 (ε = 2,520), 292 (ε = 2,850), 243 (ε = 7,730), 216 (ε = 12,200); NMR (CCl_4) δ 1·38 (s, 9), 1·40 (s, 9), 1·80 (s, 6), 7·83 (d, 2, J = 9 Hz), and 8·17 (d, 2, J = 9 Hz). (Found: C, 66·29; H, 8·27; N, 16·15. Calcd for $C_{19}H_{28}N_4O_2$: C, 66·25; H, 8·19; N, 16·27%).

3-t-*Butylamino*-2-p-*nitrophenylindole* (**20b**). *p*-Nitrobenzylideneaniline (1·94 g, 8·6 mmol), t-butyl isocyanide (4·73 g, 57 mmol) and CCl_4 (25 ml) were placed in a glass tube. The tube was flushed with N_2, sealed and heated at 110° for 22 hr. After cooling and concentrating, the reaction mixture was chromatographed on an alumina in benzene column. The major product was 1·1 g of the indole (41% yield), m.p. 166–168°; IR (Nujol) cm^{-1} 3300, 1580, 1530; UV (abs. EtOH) λ_{max} mμ 420 (ε = 12,500), 355 λ_{sh} (ε = 9100), 275 (ε = 9600), 229 (ε = 21,500); NMR ($CDCl_3$) δ 1·00 (s, 9), 3·52 (s, 1), 7·34 (m, 4), 8·08 (s, 5); NMR after washing with D_2O ($CDCl_3$) δ 1·00 (s, 9). 7·34 (m, 4), and 8·08 (s, 4). The indole, a brick-red compound was crystallized from CCl_4–$CHCl_3$. (Found: C, 69·90; H, 6·38; N, 13·31. Calcd for $C_{18}H_{19}N_3O_2$: C, 69·88; H, 6·19; N, 13·58%).

1-*Phenyl*-4-p-*nitrophenyl*-2,3-*bis*(*t-butylimino*)*azetidine* (**17b**). A small amount of azetidine was obtained from the chromatography of the 3-t-butylamino-2-*p*-nitrophenylindole reaction mixture. The azetidine was recrystallized first from ethanol then from heptane, m.p. 147–152°; IR (Nujol) cm^{-1} 1720, 1670, UV (abs. EtOH) λ_{max} mμ 305 (ε = 12,700), 296 (ε = 12,800), 260 (ε = 8430), 224 (ε = 21,400), NMR ($CDCl_3$) δ 1·04 (s, 9), 1·46 (s, 9), 5·48 (s, 1), ~7·2 (m, 4), 8·2 (m, 5). (Found: C, 70·53; H, 7·24; N, 14·31. Calcd for $C_{23}H_{28}N_4O_2$: C, 70·29; H, 7·19; N, 14·28%).

3-t-*Butylamino*-2-p-*nitrophenylindole* (**20b**) (*alternative procedure*). *p*-Nitrobenzaldehyde anil (6·60 g, 29·2 mmol) and t-butyl isocyanide (4·13 g, 55 mole) were mixed with a small amount of CCl_4 in a 1 l. flask provided with a magnetic stirrer. CCl_4 (450 ml) saturated with dry HCl was then added to the slurry. A yellow solid separated immediately. The resulting slurry was then stirred for 3 days at room temp.

The reaction mixture was filtered through a Buchner funnel. The resulting light yellow powder (7·16 g) was placed in a seperatory funnel with $CHCl_3$ (300 ml) and $NaHCO_3$aq (500 ml) and shaken vigorously until all of the solid was in soln. The resulting dark red $CHCl_3$ soln was drawn off and dried with $MgSO_4$. The $CHCl_3$ was then evaporated at reduced press to leave the spectrally pure product as dark red crystals (6·18 g, 68% yield) m.p. 150–158°.

Reaction of benzaldehyde anil and t-butyl isocyanide at 100°. A soln of benzaldehyde anil (9·05 g, 50 mmol), t-butyl isocyanide (4·21 g, 70 mmol) and CCl_4 (30 ml) was sealed (flame) in a tube after flushing with N_2. The tube was heated at 100° for 12 hr. After cooling, the reaction mixture was filtered. The solid (2·56 g, 17% yield) was identified as 2-phenyl-3-t-butylaminoindole hydrochloride. The filtrate was concentrated under reduced press. Upon dilution with hexane, 1·35 g (10% yield) of **20a** was obtained. Recrystallization from heptane gave a melting range 146·5–148°; IR ($CHCl_3$) cm^{-1} 333, 1590, UV (abs. EtOH) λ_{max} mμ 309 (ε = 14,200, 241 (ε = 23,500, 206 (ε = 24,400), NMR ($CDCl_3$) δ 0·98 (s, 9), 272 (s, 1), and 7·0–7·9 (m, 10). The mass spectrum was identical with that of hydrochloride except for *m/e* at 38, 37 and 36. (Found: C, 81·88; H, 7·70; N, 10·61. Calcd for $C_{18}H_{20}N_2$: C, 81·78; H, 7·63; N, 10·60%).

The mother liquor from the indole crystallization contained a number of components (TLC). Chromatography on an alumina column followed by chromatography on a thick layer alumina plate gave two of these components.

One component could be purified by sublimation at 100°/0·2 mm. This was a 2:1 adduct of benzaldehyde anil and t-butyl isocyanide and assigned the structure **17a** on spectral evidence, m.p. 114–116°, IR (Nujol) cm^{-1} 1720, 1670; UV (abs. EtOH) λ_{max} mμ 328·5 (ε = 9650), λ_{sh} 298 (ε = 5050), λ_{max} 228 (ε = 23,200); NMR (CCl_4) δ 1·06 (s), 1·48 (s), 5·28 (s), and 7·2 (m). (Found: C, 79·23; H, 8·39; N, 12·21. Calcd for $C_{23}H_{29}N_3$: C, 79·49; H, 8·41; N, 12·09%).

The other component isolated was identified as 1,2,3,4-tetraphenyl-1,4-diazabutadiene, m.p. 139–141° (rptd. m.p. 141–142°)[17] UV (abs. EtOH) λ_{max} mμ 264 (ε = 27,700); NMR (CCl_4) δ 6·54 (m), 7·02 (m), 7·38 (m), 7·90 (m). The m.p. of this component was not depressed on admixture with an authentic sample.[17] (Found: C, 86·59; H, 5·67; N, 7·87. Calcd for $C_{26}H_{20}N_2$: C, 86·63; H, 5·59; N, 7·72%).

3-t-*Butylamino-2-phenylindole* (*alternative procedure*). Benzaldehyde anil (6·58 g, 36 mmol) and t-butyl isocyanide (5·05 g, 60 mmol) were mixed with a small amount of CCl_4 in 1 l. flask provided with a magnetic stirrer. CCl_4 (450 ml) saturated with dry HCl was then added to the slurry. The reaction mixture was stirred at room temp for 5 days.

The slurry was filtered to recover a pink-white powder (6·77 g). The powder was placed in a separatory funnel with $CHCl_3$ (250 ml) and saturated $NaHCO_3$ aq and vigorously shaken until all the powder dissolved. The $CHCl_3$ fraction was then separated and dried with $MgSO_4$. The $CHCl_3$ was evaporated at reduced press to leave crude product (5·82 g, 61% yield).

The crude product was recrystallized from heptane to give white crystals, m.p. 143–146°.

Trifluoroacetic acid, benzylidene-p-nitroaniline, and *t-butyl isocyanide*. Benzylidene-*p*-nitroaniline (1·130 g, 5·0 mmol), t-butyl isocyanide (1 g, 12 mmol) and trifluoroacetic acid (0·88 g, 7·7 mmol) in CH_2Cl_2 (50 ml) were stirred together for 2 hr at room temp. The reaction mixture was washed with Na_2CO_3 aq, dried ($MgSO_4$), and filtered. The solvent was removed under reduced press. The residue was applied to an alumina in benzene column. Elution with benzene followed by recrystallization from cyclohexane gave 567 mg (29% yield) of **17c**. Elution with $CHCl_3$ and recrystallization from $CHCl_3$–cyclohexane gave 487 mg of **18**. The NMR spectrum indicated that cyclohexane was present in a 1:1 ratio in the crystals (24%). The sample went from yellow to almost white at approximately 110° and it melted at 165–166·5°. *p*-Nitroaniline approximately 30% yield was obtained from the mother liquors of the amide crystallization.

Degradation of 2,3-*bis*(*t-butylimino*)-1-p-*nitrophenyl-2-phenylazetidine*. 2,3-Bis (t-butylimino)-1-*p*-nitrophenyl-2-phenylazetidine (328 mg, 0·84 mmol), conc H_2SO_4 (6 ml), EtOH (150 ml), and water (150 ml) were refluxed for 6 hr. On cooling, the reaction mixture was treated with CH_2Cl_2 and $NaHCO_3$ aq. The layers were separated. The water layer was extracted with CH_2Cl_2. The organic layers were combined, dried ($MgSO_4$), filtered and the solvent removed under reduced press. The residue was applied to a thick layer alumina plate which was developed in benzene. The middle fraction was recrystallized from $CHCl_3$–ether and identified as **18** on the basis of its spectral data, m.p. 163·5–165·5°, 61 mg (22%); IR (Nujol) cm^{-1} 333, 3279, 1681; NMR ($CDCl_3$) δ 1·26 (s, 9), 4·82 (s, 1), 5·70 (s, 1), 6·15 (s, 1, broad), 6·51 (d, 2, J = 9 Hz), 7·38 (s, 5), and 8·00 (d, 2, J = 9 Hz). The peak at 6·15 washed out in D_2O. (Found: C, 65·96; H, 6·29; N, 12·66. Calcd for $C_{18}H_{21}N_3O_3$: C, 66·04; H, 6·47; N, 12·84%).

Ethyl N-p-*nitrophenyl-2-phenylglycinate*. Ethyl chlorophenylacetate[18] (2·0 g, 10·1 mmol), *p*-nitroaniline (1·40 g, 10·1 mmol) and Et_3N (1·1 g, 11 mmol) were placed in a glass tube. After flushing the tube with N_2, the tube was sealed and then heated at 110–120° for 26 hr. The reaction mixture now consisted of yellow needles and a red viscous liquid. The reaction products were washed out of the tube using $CHCl_3$. The $CHCl_3$ was removed under reduced press and the residue was dissolved in a minimal amount of $CHCl_3$ and placed on a 5% alumina–benzene column (90 g of 5% alumina). The column was eluted with benzene. The first 150 ml of yellow fractions contained product. Later yellow fractions were mostly *p*-nitroaniline. After one recrystallization from cyclohexane 1·59 g (52% yield) of bright yellow crystals were collected, m.p. 116–119°, IR (Nujol) cm^{-1} 3330, 1725; NMR ($CDCl_3$) δ 1·18 (t, 3, J = 7 Hz), 4·22 (q, 2, J = 7 Hz), 5·12 (s, 1), ~5·85 (s, 1, broad), 6·51 (d, 2, J = 9 Hz), ~7·38 (m, 5) and 8·01 (d, 2, J = 9 Hz). The NMR spectrum of the product with a drop of Et_3N corresponded to the spectrum in ($CDCl_3$ + Et_3N) δ 1·18 (t, 3, J = 7 Hz), 4·19 (q, 2, J = 7 Hz, the two lower field peaks of the quartet were split with J = 1 Hz), 5·10 (d, 1, J = 6 Hz), 5·89 (d, 1, J = 6 Hz (broad peaks)), 6·48 (d, 2, J = 9 Hz), ~7·38 (m, 5) and 7·98 (d, 2, J = 9 Hz).

N-p-*Nitrophenyl-2-phenylglycine*. Ethyl N-*p*-nitrophenyl-2-phenylglycinate (0·710 g, 2·36 mmol), AcOH (9 ml), and conc HCl (4 ml) were refluxed together for 3 hr. The reaction mixture was partially concentrated and then transferred to a separatory funnel, and ether and water were added. The layers were separated. The water layer was extracted with ether twice, and the ether layers were combined and washed with water. After drying ($MgSO_4$), the soln was concentrated under reduced press. The residue was dissolved in a minimal amount of ether and diluted with cyclohexane until yellow crystals appeared. After one recrystallization, 0·475 g (74% yield) of product had been collected, m.p. 157–158·5°; IR (Nujol) cm^{-1} 3750, 1730, and 1690. The product was not soluble in CCl_4, $CHCl_3$ or water. The sodium salt was not sufficiently soluble in water for a NMR spectrum to be obtained.

N-t-*Butyl*-2-p-*nitroanilino*-2-*phenylacetamide*. N-*p*-Nitrophenyl-2-phenylglycine (226 mg, 0·83 mmol), Et_3N (0·3 ml, 2·1 mmol), $SOCl_2$ (0·07 ml, 0·97 mmol), and dry benzene (5 ml) were placed in a dry flask equipped with a magnetic stirrer and a Drierite drying tube. On mixing a red color appeared which faded within 5 min. The reaction mixture was stirred at room temp for 1 hr before t-butylamine (0·1 ml, 0·95 mmol) was added. The mixture turned red orange and was stirred at room temp for 2 hr. CH_2Cl_2 and water were

added and the layers separated. The organic layer was washed with water, dried over $MgSO_4$, filtered, and solvent was removed under reduced press. The residue was applied to a thick layer plate and developed in benzene. The bright yellow fraction contained the product, 75 mg, 27% yield, m.p. 164–165. This material was identical by direct comparison with that isolated by hydrolysis of **17c**.

3-Acetyl-t-butylamino-2-phenylindole. 3-t-Butylamino-2-phenylindole (500 mg, 1·89 mmol) and NaOAc (700 mg, 8·5 mmol) were refluxed in 7 ml Ac_2O for 1 hr. The solvent was evaporated under reduced press. $CHCl_3$ and NaOH aq were added to the residue. The layers were separated, and the $CHCl_3$ layer dried ($MgSO_4$) and filtered. The solvent was removed under reduced press to yield approximately 600 mg of crystalline solid. The product was recrystallized from MeOH–benzene, m.p. 231–232°; IR (Nujol) cm^{-1} 3100 and 1620; NMR ($CDCl_3$) δ 1·32 (s, 9), 1·96 (s, 3), 7·46 (m), and 8·98 (s, broad).

The analytical sample was prepared by sublimation, 110°/0·02 mm. (Found: C, 78·23; H, 7·28; N, 9·21. Calcd. for $C_{20}H_{22}N_2O$: C, 78·40; H, 7·24; N, 9·14%.

3-Acetyl-t-butylamino-2-p-nitrophenylindole. 3-t-Butylamino-2-*p*-nitrophenylindole (260 mg, 0·84 mmol) and NaOAc (200 mg, 2·4 mmol) were refluxed for 2 hr in 4 ml Ac_2O. The product was isolated by the same procedure used for 3-acetyl-t-butylamino-2-phenylindole. The product was recrystallized from EtOH, 180 mg (60% yield), m.p. 274–276°; IR (Nujol) cm^{-1} 3150, 1620, 1580, 1510, 1335, 851, and 736; NMR ($CDCl_3$) δ 1·36 (s), 1·98 (s), 7·46 (m), 7·98 (d, J = 9 Hz), 8·36 (d, J = 9 Hz), and 9·6 (s). (Found: C, 68·20; H, 5·90; N, 11·82. Calcd. for $C_{20}H_{21}N_3O_3$: C, 68·36; H, 6·02; N, 11·96%).

Oxidative degradation of 2-p-nitrophenyl-3-t-butylaminoindole. 2-*p*-Nitrophenyl-3-t-butylaminoindole (2·30 g, 7·45 mmol) and NaOMe (2·52 g, 47 mmol) in MeOH (140 ml) were stirred at room temp for 2 days under O_2. The solvent was removed under reduced press and the residue mixed with $CHCl_3$. After washing the $CHCl_3$ mixture with water, the soln was dried ($MgSO_4$), filtered, and evaporated under reduced press. This residue was applied to a 5% alumina in benzene column. Elution with 50% $CHCl_3$–benzene (vol) yielded 1·3 g of ether **23** (50% yield), m.p. 150–152°, IR ($CHCl_3$) cm^{-1} 3250, 1640, and 1595; NMR ($CDCl_3$) δ 1·37 (s, 9), 4·02 (s, 3), ~6·2 (m, 1), ~7·4 (m).

An analytical sample of **23** crystallized from benzene–cyclohexane melted 153–155°. (Found: C, 64·42; H, 5·95; N, 12·01. Calc. for $C_{19}H_{21}N_3O_4$: C, 64·21; H, 5·96; N, 11·83%).

Ether **23** (100 mg, 0·28 mmol) was refluxed for 6 hr in 10 ml of 6M HCl. Upon cooling the soln was evaporated to dryness under reduced press. The residue was dissolved in sat Na_2CO_3 aq and extracted with $CHCl_3$. The water soln was acidified and then filtered. The solid collected was dried and identified as *p*-nitrobenzoic acid (20 mg, 43% yield), m.p. 235–237°. Its m.p. was undepressed on admixture with an authentic sample.

Ether **23** (1·17 g, 3·30 mmol) and toluenesulfonic acid (50 mg, 0·26 mmol) were stirred together in 20 ml water and 30 ml dioxan for 8 hr at room temp. Na_2CO_3 aq was added until the soln was basic, and the soln was placed on a rotary evaporator to remove the dioxan. $CHCl_3$ was then added and the layers separated. The organic layer was dried ($MgSO_4$) and filtered. The solvent was removed under reduced press. The residue was applied to an alumina in benzene column and eluted with benzene. After concentrating the benzene soln, it was applied to a thick layer alumina plate and developed in benzene. The major cut was freed from inorganics and recrystallized twice from benzene to give 240 mg (40% yield) of 2-amino-N-t-butylbenzamide, m.p. 123–124·5° (rptd. m.p. 126–127°).[19] The m.p. of the product was not depressed on admixture with an authentic sample.

Peracid oxidation of 3-t-butylamino-2-p-nitrophenylindole (**20b**). 3-t-Butylamino-2-*p*-nitrophenylindole (6·00 g, 194 mmol) was dissolved in $CHCl_3$ (300 ml) and placed in a one l three-necked round bottom flask. The flask was equipped with a magnetic stirrer, $CaCl_2$ drying tube, and an addition funnel. The indole soln was maintained at 0° by an ice bath. A soln of *m*-chloroperbenzoic acid (6·66 g, 0·0338 mole, in 250 ml $CHCl_3$) was added slowly with vigorous stirring over a period of 1 hr to the cold reaction vessel. The reaction mixture was allowed to stand at ice bath temp for 1 hr and then extracted twice with Na_2CO_3 aq. The $CHCl_3$ layer was then separated, dried with $MeSO_4$, and the solvent evaporated at reduced press.

The dark tar-like residue was chromatographed on a basic alumina column (activity 10%) in benzene. Two major products were isolated by elution with benzene in approximately equal quantities.

The first fraction from the column was evaporated. The residue recrystallized from cyclohexane to give orange crystals m.p. 155–160°. This compound was shown to be from the following spectral and analytical results: IR (Nujol) 1600 cm^{-1}; UV (abs. EtOH) λ_{max} mμ 386 (ε 5,060), 282 (ε 19,400), 244 (ε 19,300), λ_{sh} 230 (ε 17,100); NMR ($CDCl_3$) δ 1·58 (s, 9), 7·48 (m, 4), 8·21 (q, 4, J = 9 Hz). (Found: C, 70·35; H, 5·46; N, 13·42. Calc. for $C_{18}H_{17}N_3O_2$: C, 70·34; H, 5·58; N, 13·67%).

The second fraction eluted from the column crystallized from concentrated benzene soln. The orange-

yellow crystals were recrystallized from 95% EtOH to give yellow plates, m.p. 202–204°; IR (Nujol) cm^{-1} 3344, 1689, 1645; NMR ($CDCl_3$) δ 1·50 (s, 9), 6·39 (s, 1), 7·0 to 8·9 (m, 8), 12·42 (s, 1), (washing with D_2O did not change the spectrum). (Found: C, 63·28; H, 5·64; N, 12·34. Calc. for $C_{18}H_{19}N_3O_4$: C, 63·33; H, 5·61; N, 12·37%).

This compound was identified as 2-(*p*-nitrobenzoylamino)-N-t-butylbenzamide from spectral data and a mixed m.p. with an authentic sample.

Synthesis of 2-(p-*nitrobenzoylamino*)-N-*t-butylbenzamide* (**27**). A sample of **20** (420 mg, 2 mmol) was dissolved in 50 ml benzene. To this soln was added pyridine (2 ml) and *p*-nitrobenzoyl chloride (556 mg, 3 mmol). The reaction was refluxed for 2 hr and filtered. The benzene soln was then dried with $MgSO_2$ and the benzene evaporated at reduced press to leave a yellow powder. This powder was recrystallized from 95% EtOH to yield yellow plates of 2-(*p*-nitrobenzoylamino)-N-t-butylbenzamide, m.p. 202–204°.

3-*t-Butylimino*-2-p-*nitrophenyl*-3-H-*indole* (*modified procedure*). 3-t-Butylamino-2-*p*-nitrophenylindole (6·0 g, ·0195 mole) was dissolved in 500 ml $CHCl_3$ and placed in a one liter flask equipped with a magnetic stirrer, $CaCl_2$ drying tube, and a special addition funnel for slow addition. The indole soln was maintained at 0° with an ice bath. A *m*-chlorperbenzoic acid soln (3·34 g, ·0195 mole in 250 ml $CHCl_3$) was added very slowly with vigorous stirring over a period of 6 hr and allowed to stand overnight in the ice bath. The $CHCl_3$ was evaporated at reduced press and the residue was recrystallized twice from cyclohexane to yield 3·25 g (54·5% yield) of 3-t-butylimino-2-*p*-nitrophenyl-3-*H*-indole.

Sodium borohydride reduction of 3-t-*butylimino*-2-p-*nitrophenyl*-3-H *indole*. 3-t-Butylimino-2-*p*-nitrophenyl-3-*H* indole (150 mg, 48 mmol) was dissolved in MeOH (50 ml). This soln was placed in an Erlenmeyer flask provided with a magnetic stirrer. The reaction vessel was cooled in an ice bath and the $NaBH_4$ soln (60 mg. 1·5 mmol in 10 ml MeOH) was added with vigorous stirring. When addition was completed, dil HCl was added until the reaction mixture was slightly acid. The EtOH was then evaporated and the resulting oil dissolved in $CHCl_3$. The $CHCl_3$ soln was then washed through a column of alumina (activity 10%) and the $CHCl_3$ evaporated at reduced press. The resulting oil was shown to be 3-t-butylamino-2-*p*-nitrophenyl indole by comparison of R_f values on TLC (alumina) and its NMR spectrum with a known sample.

Peracid oxidation of 3-t-*butyl*-2-*phenyl indole*. 3-t-Butyl-2-phenyl indole (2·0 g, 7·6 mmol) was dissolved in $CHCl_3$ (300 ml) and placed in a one liter 3-necked flask equipped with a magnetic stirrer, $CaCl_2$ drying tube, and an additional funnel. A soln of *m*-chloroperbenzoic acid (1·31 g, 7·6 mmol in 150 ml $CHCl_3$) was added very slowly with vigorous stirring to the reaction flask cooled in an ice bath. As the peracid was added a color change from straw-yellow to orange was noted. The peracid soln was added over a 5 hr period and the reaction mixture was washed with a sat Na_2CO_3aq. The $CHCl_3$ soln was evaporated to dryness at reduced press to leave an orange-yellow solid (1·84 g, 92% yield). The solid was recrystallized twice from 95% EtOH to yield orange crystals of 2-phenyl-3-(t-butylimino)-3-*H* indole, m.p. 87–90°; IR (Nujol) cm^{-1} 1634; UV (abs. EtOH) λ_{max} mμ 258·0 (ε 29,200), 393·0 mμ (ε 3120); NMR ($CDCl_3$) δ 1·55 (s, 9), 7·0 to 7·8 (m, 7), 8·3 (m, 2). (Found: C, 82·64; H, 6·74; N, 10·70. Calc. for $C_{18}H_{18}N_2$: C, 82·41; H, 6·92; N, 10·68%).

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