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"Bicyclobenzodiazepinones" from 3-Oxo-1,2-diazetidinium Hydroxide, Inner Salts

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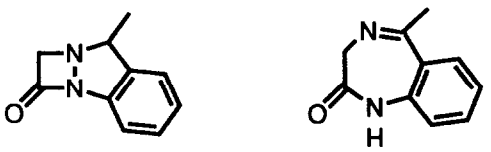
Abstract: *1,3-Dipolar cycloaddition of benzyne with 3-oxo-1,2-diazetidinium hydroxide, inner salts leads to tricyclic adducts which have been termed "bicyclobenzodiazepinones" because of their structural relationship to 1,4-benzodiazepinones. In analogous fashion, cycloaddition of benzyne with 3-oxopyrazolidinium hydroxide, inner salts, leads to homologous tricyclic adducts. Efforts to convert these readily accessible condensed aza-β-lactams and aza-γ-lactams to benzodiazepinones and benzodiazocinones are described. Several novel ring cleavage reactions leading from the above "bicyclobenzodiazepinones" to indazoles are reported.*

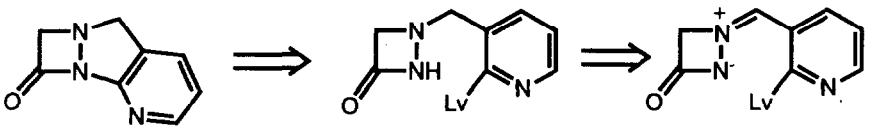
The 1,2-diazetidin-3-one ring system has received considerable attention in recent years as a highly strained aza analogue of the β-lactam family of antibiotics.[1] However, the structural similarity of certain 1,2-diazetidin-3-one derivatives (**1**) to isomeric compounds related to the 1,4-benzodiazepinone family of minor tranquilizers (**2**) appears not to have been previously recognized. With this in mind efforts have been made to synthesize compounds of type **1**, and to examine their possible conversion into 1,4-benzodiazepinones.



1 **2**

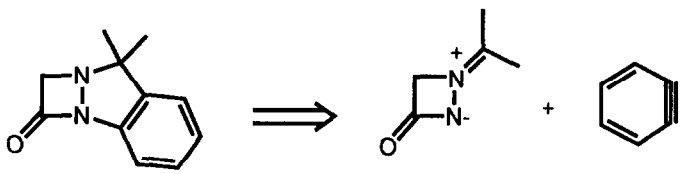
Figure 1

Inspection of the "bicycloaryldiazepinone" structure **1** reveals several possible synthetic strategies dictated by the number of structurally diverse 3-oxo-1,2-diazetidinium hydroxide, inner salts that are available,[2] and by the fact that homologous 3-oxopyrazolidinium hydroxide, inner salts, are also well known and should provide less strained model systems upon which preliminary investigations might be carried out.[3] One possible route is shown retrosynthetically in Scheme 1, and relies upon intramolecular attack of N-2 of the 1,2-diazetidin-3-one ring onto an appropriately substituted pendant heteroaromatic ring (illustrated here by a pyridine ring), with dis-



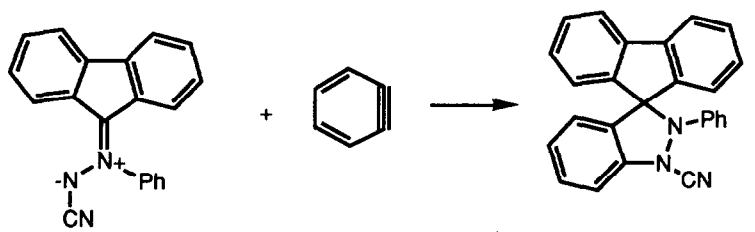
Scheme 1

placement of a leaving group (Lv). A second approach, illustrated in Scheme 2, utilizes a 1,3-dipolar cycloaddition reaction of an aryne across the 1,3-dipole of a 3-oxo-1,2-diazetidinium hydroxide, inner salt. The wide variety of 1,3-dipolar cycloaddition reactions which benzyne has been shown to undergo[4] lends strong support for this concept. In particular, the addition of benzyne to the azomethineimine ylid **3**[5] (see Figure 2) bodes well



Scheme 2

for the proposed reaction with the structurally and electronically similar diazetidinium ylids. Although the proposed aryne addition is conceptually attractive due to its directness and simplicity, it must be borne in mind that 3-oxo-1,2-diazetidinium hydroxide, inner salts have been shown to undergo 1,3-dipolar cycloadditions in only a limited number of very special cases. Thus, 1-(diphenylmethylene)-4-methyl-3-oxo-1,2-diazetidinium and



3 **4**

Figure 2

1-(diphenylmethylene)-3-oxo-1,2-diazetidinium hydroxide, inner salts (**5**) undergo 1,3-dipolar cyclizations only with dialkyl acetylenedicarboxylates[6] (Figure 3). Attempts to extend this reaction to compounds with substitution other than diphenylmethylene at the 1-position (e.g. phenylmethylene, dimethylmethylene) were unsuccessful. In

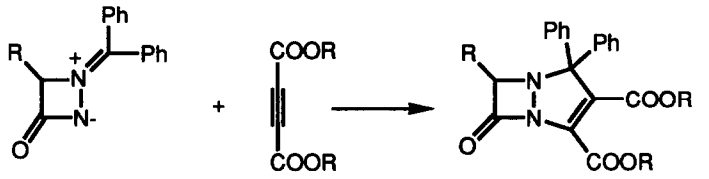


Figure 3

5 6

addition, the dialkyl acetylenedicarboxylate cycloaddition compounds **6** were prone to decomposition by dimerization and/or extrusion of carbon monoxide. Another peculiar aspect of the reported cycloaddition chemistry of 3-oxo-1,2-diazetidinium hydroxide inner salts is the observation that inner salts derived from the condensation of 3-oxo-1,2-diazetidinium tosylate with aromatic aldehydes, but not those derived from aromatic or aliphatic ketones, undergo 1,3-dipolar cyclization reactions with enamines **7** (Figure 4) to give adducts **8**.[6] Finally, this 1,3-dipolar cycloaddition approach, unlike the route depicted in Scheme 1, is necessarily limited to the formation of 8-monosubstituted or 8,8-di-substituted "bicycloaryldiazepin-ones", since 1-methylene-3-oxo-1,2-diazetidinium hydroxide, inner salt itself is not known.

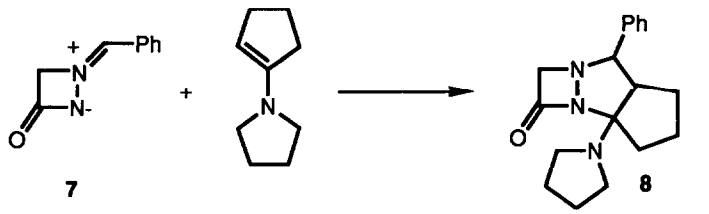


Figure 4

7 8

Regiochemistry is a further concern. It has been reported that the reaction of 3,3-dimethyl-5-carbomethoxy-3H-pyrazole (**9**) with diphenylketene gives the bicyclic diazetidinopyrazole **10**[7] (Figure 5), apparently because of the greater nucleophilic character of N-2 over N-1 of the azo compound. Since reactants

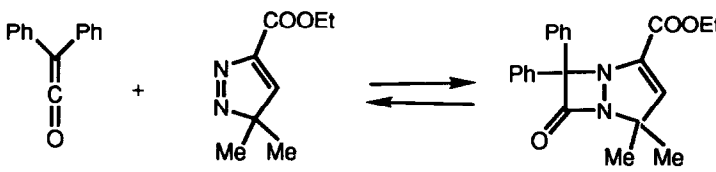
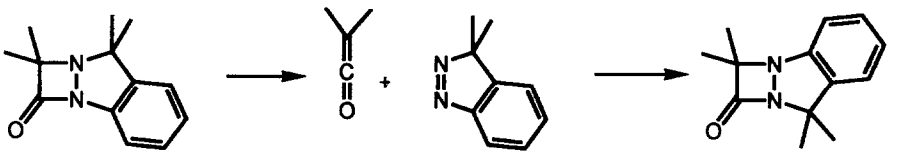


Figure 5

9 10

and product are reported to exist in facile equilibrium with each other in this system, the possibility exists that our target "bicyclobenzodiazepinone", regardless of its mode of preparation, might also undergo retro [2+2] cycloaddition to give a cis-azo compound and a ketene, which could then recombine as shown in Scheme 3 to produce the other (and in this case, unwanted) regioisomer. With these potential problems and limitations in mind, model studies using the less strained pyrazolidin-3-one ring system were undertaken.



Scheme 3

Our model reactions for an investigation of the route shown in Scheme 1 utilized pyridine and quinoline as the heteroaromatic components upon which cyclization was to take place. Treatment of an aqueous solution of pyrazolidin-3-one (**11**) hydrochloride[8] with potassium bicarbonate followed by addition of pyridine-3-carboxaldehyde 1-oxide (**12**) led to the formation of **13** as a highly water-soluble crystalline solid in 68% yield. Substrates **16** and **17** were prepared in 90% and 83% yield respectively by addition of 2-chloroquinoline-3-carboxaldehyde (**14**) or 2-iodoquinoline-3-carboxaldehyde (**15**) to a methanolic solution of pyrazolidin-3-one.

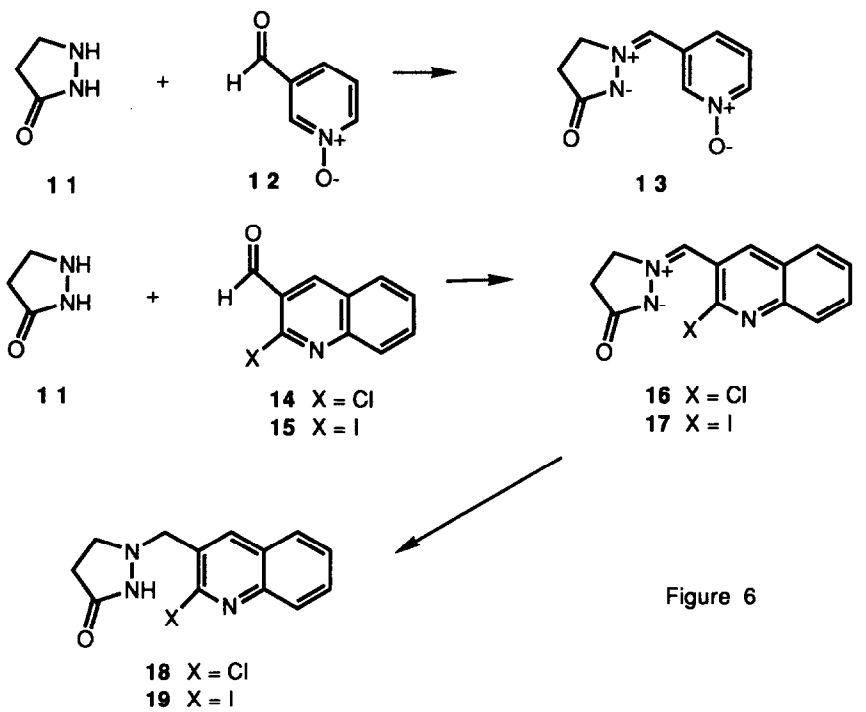
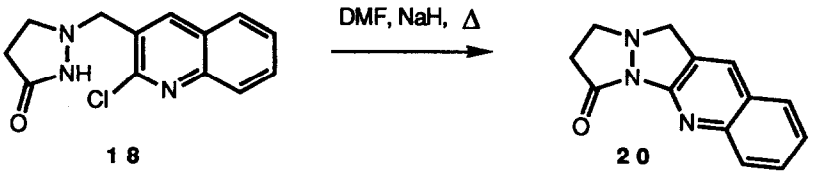


Figure 6

Treatment of **16** and **17** with one equivalent of sodium borohydride in methanol resulted in clean reduction of the iminium bond to give pyrazolidin-3-ones **18** and **19** in 83% and 79% yield respectively. Attempted reduction of the iminium bond of **13** under analogous conditions failed to yield any isolable products, probably because of rapid over-reduction.

A wide range of basic conditions (N,N-dimethylformamide, tetrahydrofuran, isopropanol, and chlorobenzene as solvents with sodium hydride, potassium tert-butoxide, DBU, sodium bicarbonate, or silver carbonate as bases) was explored in an attempt to achieve cyclization of **18** and **19**. Best results were obtained by treatment of **18** with sodium hydride in N,N-dimethylformamide under reflux for 20 hours (Figure 7), which



18 **20**

Figure 7

gave the desired ring closed product **20** in 22% yield. Similar attempts to form **20** from the iodo compound **19** under the same conditions unfortunately led only to decomposition of **19**; no trace of **20** could be detected.

Although only limited success had been achieved with these model reactions utilizing the pyrazolidin-3-one ring system, it was hoped that similar reactions utilizing the 1,2-diazetidin-3-one ring system might be more satisfactory, since N-2 of the diazetidin-3-one ring system is more nucleophilic than N-2 of the pyrazolidin-3-one system (due to reduced delocalization of electron density into the carbonyl group of the more highly strained diazetidinone ring). Unfortunately, attempts to synthesize the requisite diazetidinium hydroxide inner salts from 3-oxo-1,2-diazetidinium tosylate and the appropriate pyridine and quinoline aldehydes led only to polymeric materials which were not further characterized. Thus, although the route shown in Scheme 1 was successful for the formation of "bicycloaryldiazocinone" **20**, the inaccessibility of the required diazetidinium hydroxide, inner salts, for extension of this reaction led us to abandon this initial route to our desired "bicycloaryldiazepinones".

The fate of the approach illustrated in Scheme 2 relies upon 1) the propensity of the inner salts to undergo cycloaddition reactions, 2) generation of a benzyne intermediate in the presence of 3-oxo-1,2-diazetidinium and 3-oxopyrazolidinium hydroxide, inner salts, and 3) the stability of the products under the reaction conditions employed. The latter two factors are interrelated and in principle can be controlled by the method of benzyne generation chosen.

Of the wide range of available routes to benzyne intermediates,[9] those involving generation of an intermediate ortho-substituted phenyl anion were excluded from consideration because of the demonstrated ability of aryl anions to add to the iminium bond of 3-oxo-1,2-diazetidinim and 3-oxopyrazolidinium hydroxide, inner salts.[10] The most attractive of the many alternative routes to arynes, which avoids highly basic and nucleophilic phenyl anion intermediates, is thermolysis of benzenediazonium-2-carboxylates, prepared by diazotization of anthranilic acids.

Attempts to generate benzenediazonium-2-carboxylate from anthranilic acid in the presence of the 1,3-dipole with which it was to react failed to yield any isolable products. For example, 1-(diphenylmethylene)-3-oxo-1,2-diazetidinium hydroxide, inner salt, was dissolved in 1,2-dichloroethane at 40 °C. Concomitant, dropwise addition of solutions of anthranilic acid in 1,2-dichloroethane:1,2-dimethoxyethane, and isoamylnitrite in 1,2-dichloroethane, to the reaction solution was accompanied by evolution of gas. However, removal of the solvent under reduced pressure after a short reaction time yielded a black intractable residue. Addition of

preformed benzenediazonium-2-carboxylate to a solution of 1-(diphenylmethylene)-4-methyl-3-oxo-1,2-diazetidinium hydroxide, inner salt, in 1,2-dichloroethane at 60 °C, followed by removal of solvent, likewise produced only a dark gummy residue. Although an infrared spectrum of this residue exhibited a strong absorption band at 1810 cm^{-1}, as expected for the desired "bicyclobenzodiazepinone", all attempts at isolation of the component responsible for this carbonyl band by chromatography over silica gel, alumina, fluorisil or cellulose resulted only in its decomposition.

In an attempt to minimize formation of the large amounts of impurities which were formed under the above conditions, we attempted to achieve a lower concentration of benzyne at a lower temperature (40 °C) by using tetrahydrofuran rather than dichloroethane as solvent (benzenediazonium-2-carboxylate decomposes 4.5 times slower in tetrahydrofuran than it does in dichloroethane[4]). Using the less strained 3-oxo-pyrazolidinium hydroxide, inner salts as models, these modified conditions indeed led successfully to "bicyclobenzodiazocinones" **24**, **25** and **26** in 78-55% yield (Figure 8). These reaction conditions were then applied successfully to

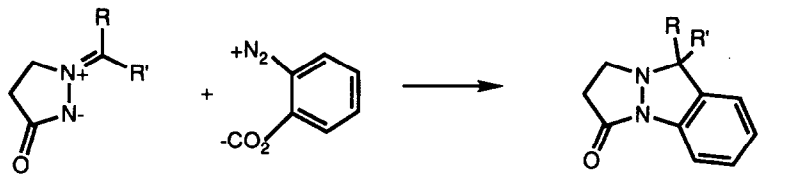


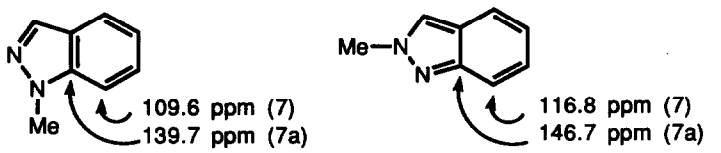
Figure 8

21 R=R'=Ph
22 R=H, R'=Ph
23 R=H, R'=o-Cl-Ph

24 R=R'=Ph
25 R=H, R'=Ph
26 R=H, R'=o-Cl-Ph

the preparation of "bicyclobenzodiazepinones". 1-(Diphenylmethylene)-3-oxo-1,2-diazetidinium hydroxide, inner salt, (**27**) was treated with benzenediazonium-2-carboxylate in tetrahydrofuran at 40 °C. Evaporation of the solvent left a solid residue rather than the intractable tar obtained under the previously employed reaction conditions. The solid residue could then be recrystallized from ethanol:tetrahydrofuran to give a product in 74% yield whose infrared spectrum exhibited a strong absorption band at 1785 cm^{-1}. Similar reaction conditions using 1-(diphenylmethylene)-4-methyl-3-oxo-1,2-diazetidinium hydroxide, inner salt, (**28**) and (Z)-4,4-dimethyl-1-(phenylmethylene)-3-oxo-1,2-diazetidinium hydroxide, inner salt, (**29**) produced analogous results. The spectral data for these reaction products clearly indicated that the desired benzyne 1,3-dipolar cycloaddition reaction had occurred, but gave no information about the retro [2+2] cycloaddition pathway outlined above (Scheme 3) as a possible subsequent event. Two of the benzyne adducts **30** and **32** (see Figure 11) were subjected to single crystal x-ray analysis, but the structures could not be solved because of crystal twinning.[11] Consequently, an indirect method of structure determination was sought.

Bouchet, Fruchier, and Joncheray have reported the completely assigned ^{13}C NMR spectra of 1-methyl-1H-indazole and 2-methyl-2H-indazole (Figure 9),[12] which show markedly distinct absorptions for the 7 and 7a carbon atoms. In the case of product **32**, whose two possible regioisomers are shown in Figure 10, attack of a



33 34

Figure 9

nucleophile such as methylamine on the carbonyl carbon should result in cleavage of the carbonyl carbon-nitrogen bond. Oxidation of the resulting dihydroindazole would then yield a 1- or 2-alkyl substituted indazole. This reaction would provide a product whose ^{13}C NMR spectrum could then be correlated to the previously assigned ^{13}C NMR spectra of 1-methyl-1H- and 2-methyl-2H- indazole.

Addition of methylamine to the adduct obtained from the addition of benzyne to (Z)-1-(phenylmethylene)-4,4-dimethyl-3-oxo-1,2-diazetidinium hydroxide, inner salt (**29**), followed by air oxidation, gave an 81% yield of indazole **36** or **38**. Although all the absorbances in the ^{13}C NMR spectrum of this product could not be unambigously assigned, the C-7 and C-7a resonances at 116.9 and 146.7 ppm correlated well with the C-7 and

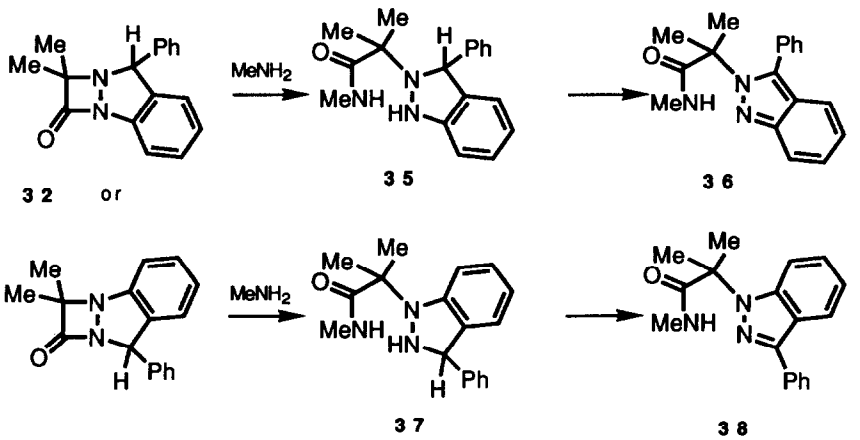
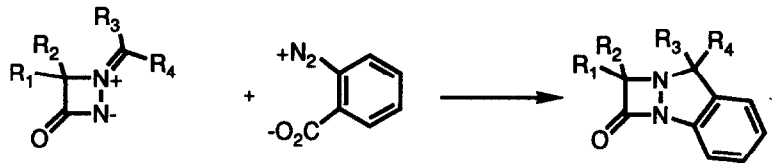


Figure 10

C-7a resonances for 2-methyl-2H-indazole, and very poorly with those for 1-methyl-1H-indazole. Consequently, the indazole obtained from the reaction of "bicyclobenzodiazepinone" **32** with methylamine has been assigned structure **36**. Since **36** must arise from **35**, we conclude that the products obtained from the reaction of benzyne with diazetidinium hydroxide, inner salts, are simple cycloaddition products and not the isomers arising from a subsequent retro [2+2]/[2+2] cycloaddition sequence.

With the regiochemistry of the products from the cycloaddition of benzyne to 3-oxo-1,2-diazetidinium hydroxide, inner salts, now established, the scope of the reaction was further explored. Generation of benzyne in the presence of a range of inner salts gave the expected "bicyclobenzodiazepin-ones" in widely varying isolated yields. In all cases, with the exception of the reaction of benzyne with **42** and **43** (see Figure 11), examination of the crude reaction mixture by ^1H NMR indicated clean addition of benzyne to the inner salt. The low yield of **44** was apparently due to rapid decomposition of the product during isolation. Examination of the ^1H NMR

spectrum of the crude reaction product obtained from **41** and benzyne indicated that **46** was formed as a 1:1 mixture of diastereoisomers which decomposed over a period of days. In the case of efforts to form **47**, examination of the crude reaction mixture gave no indication of the presence either of product or of unreacted inner salt; the cycloaddition adduct appears to be extremely unstable even under the mild reaction conditions employed. The single case where no reaction was observed to have taken place, and unreacted inner salt was

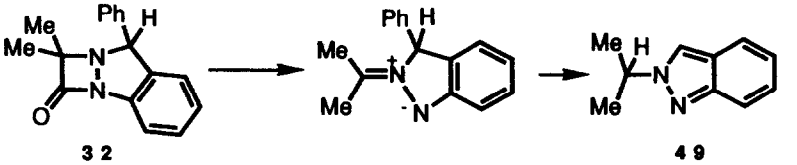


Ylid	R_1	R_2	R_3	R_4	Product	%yield
27	H	H	Ph	Ph	**30**	74
28	H	Me	Ph	Ph	**31**	55
29	Me	Me	H	Ph	**32**	48
39	H	H	p-Cl-Ph	p-Cl-Ph	**44**	8
40	H	H	p-OMe-Ph	p-OMe-Ph	**45**	51
41	H	Me	H	styryl	**46**	0
42	H	Me	Me	Me	**47**	0
43	H	H	H	p-OMe-Ph	**48**	0

Figure 11

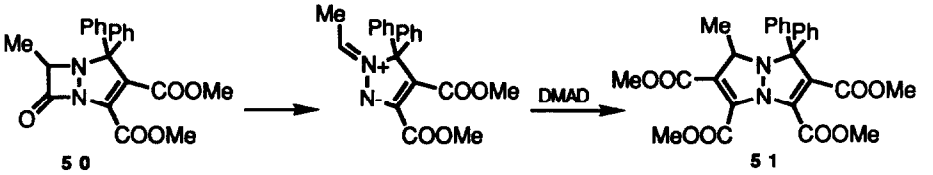
recovered, was the attempted reaction of **43** with benzyne. The failure in this case appears to be due to the insolubility of **43** in tetrahydrofuran. Even very slow decomposition of benzenediazonium 2-carboxylate in a dilute slurry of inner salt **43** and tetrahydrofuran failed to yield any cycloadduct. The reactivity of benzyne with solvents in which **43** is soluble (e.g. dimethyl sulfoxide, N,N-dimethylformamide) precluded further investigation of this specific reaction.

Experiments with **32** indicated that the primary mode of decomposition for these "bicyclobenzodiazepinones" involves loss of carbon monoxide from the diazetidine ring. When **32** was dissolved in carbon tetrachloride and allowed to stand at room temperature for a period of a week, or when the solution was heated under reflux for several hours, **32** decomposed to give a compound whose ^1H NMR spectrum indicated the presence of nine aromatic protons and an isopropyl group. The infrared spectrum indicated the absence of a carbonyl group, and the mass spectrum displayed a molecular ion peak at 236 mass units. These data, along with the ^{13}C NMR spectrum (see Experimental Section), indicate that **32** undergoes loss of carbon monoxide and relocation of the benzyhydryl hydrogen atom to give 2-isopropyl-3-phenylindazole, as shown in Figure 12. This mode of decomposition is consistent with observations by Taylor, Haley, and Clemens[2b] that **50** loses carbon monoxide to give an intermediate ylide which can be trapped with dimethyl acetylenedicarboxylate to give **51** (Figure 13).



32 49

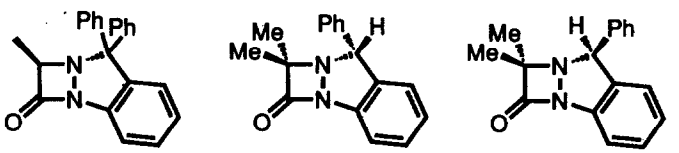
Figure 12



50 51

Figure 13

Although the reaction of **28** and **29** with benzyne could in principle lead in each case to the formation of two diastereomers, evidence could be found for only one. It has been shown previously that 1,4-dialkyl-1,2-diazetidin-3-ones adopt a conformation in which the 1- and 4-substituents are trans to each other.[2] Extrapolation of these results to the present system suggests the stereochemistry of **31** as shown in Figure 14. The formation of only one diastereoisomer in the case of **32** may be due to steric factors. Molecular models show that severe



31 32a 32b

Figure 14

steric interactions exist between the 8-phenyl and one of the 1-methyl groups of isomer **32a**, while such unfavorable steric interactions are absent in **32b** (Figure 14). NOE studies on **32** show a strong enhancement of the benzhydryl proton upon irradiation of one of the methyl groups, which is consistent with **32b** and not with **32a** (see Experimental Section).

With successful syntheses of "bicyclobenzodiazepinones" and "bicyclobenzodiazocinones" in hand, we briefly explored their chemistry. Treatment of **24** with m-chloroperoxybenzoic acid at room temperature in chloroform gave no indication of the presence of any compounds other than starting materials. Similarly, no reaction could be observed upon treatment of **24** under reflux in ethanol in the presence of an excess of 30% hydrogen peroxide. In contrast, however, treatment of **25** with m-chloroperoxybenzoic acid resulted in destruc-

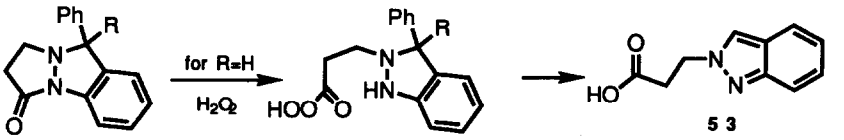


Figure 15

24 R=Ph
25 R=H

tion of **25** with no identifiable products being produced, while reaction with 30% hydrogen peroxide in isopropanol gave 3-phenyl-2H-indazole-2-propionic acid (**53**) in 40% yield (Figure 15). Heating **25** in aqueous isopropanol led to no change. The conversion of **25** to **53** probably involves nucleophilic attack by peroxide on the carbonyl carbon followed by irreversible oxidation of the intermediate dihydroindazole to the indazole. In none of the above cases was an N-oxide detected. Analogous negative results were obtained upon attempted oxidation of "bicyclobenzodiazepinones" with peroxide or peracids.

Several reactions leading to cleavage of the nitrogen-nitrogen single bond in 1,2-diazetidin-3-ones are known. Fahr and Fisher[13] have reported that treatment of 4-aryl-1,2-diphenyl-1,2-diazetidin-3-ones (**54**) with sodium carbonate in methanol yields two cleavage products, **55** and **57**; the former arises from direct attack of methoxide on the carbonyl group of the 1,2-diazetidin-3-one ring, while the latter is formed by initial deprotonation at C-4 of the 1,2-diazetidin-3-one ring to give intermediate **56**, which then suffers N-N cleavage with elimination of an anionic amide leaving group (Figure 16). Treatment of **54** either with sodium methoxide in methanol or with sodium tert-butoxide in tert-butanol led exclusively to **57**. Base-catalyzed N-N cleavage of

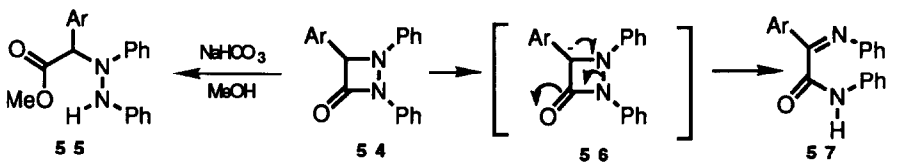


Figure 16

"bicyclobenzodiazepinones" in the fashion illustrated in Figure 16 would result in ring expansion (Figure 17) to generate the target benzodiazepinone (see Figure 1). In order to examine this concept, the model compound **30** was treated with sodium methoxide in methanol, conditions similar to those employed for the nitrogen-nitrogen

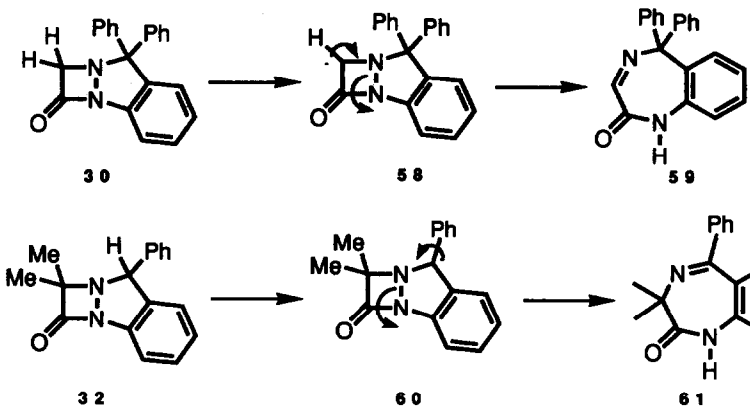


Figure 17

bond cleavage reaction reported by Fahr and Fisher. The only product isolated, however, was **62**, which resulted from attack by methoxide at the carbonyl group of **30** (Figure 18). Non-nucleophilic bases such as potassium tert-butoxide in tert-butanol resulted in complete consumption of **30**, but efforts to identify the components of the resulting complex mixture of products were unsuccessful. Similar results were obtained when

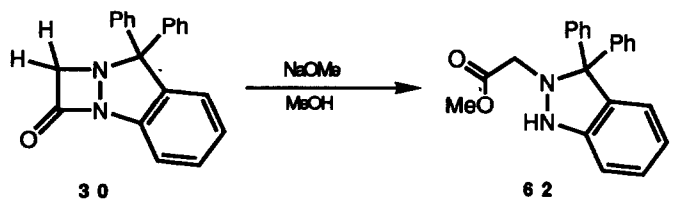


Figure 18

the reaction was carried out using LDA or lithium bis(trimethylsilyl)amide in tetrahydrofuran at -78 C. Attempts to trap the intermediate anion analogous to **58** (see Figure 17) using trialkylsilylchlorides or iodomethane as trapping agents were also unsuccessful.

Attempts to effect ring expansion of **32** to a 1,4-benzodiazepinone met with slightly different results. Addition of **32** to a preformed solution of lithium diisopropylamide in tetrahydrofuran at -78 C immediately produced a deep red solution. Aqueous workup of the reaction mixture gave 3-phenyl-1H-indazole (**63**) as the major product (Figure 19). Nitrogen-nitrogen bond cleavage did not take place, probably because of stereoelectronic constraints imposed by annulation of a ring at the 1- and 2- positions of the 1,2-diazetidin-3-one ring; models clearly indicated that the requisite antiperiplanar relationship of the electron pair at position 8 and the N-N bond cannot be achieved. 3-Phenyl-1H-indazole is most likely formed from **32** via the intermediate anion **60** which gives the ketone enolate **64** by C-N cleavage. Whether **63** is formed from **64** by direct hydrolysis of the isobutyryl grouping, or by elimination of dimethylketene, is not known. We conclude that base-catalyzed ring expansion of "bicyclobenzodiazepinones" to give benzodiazepinones is not a feasible concept.

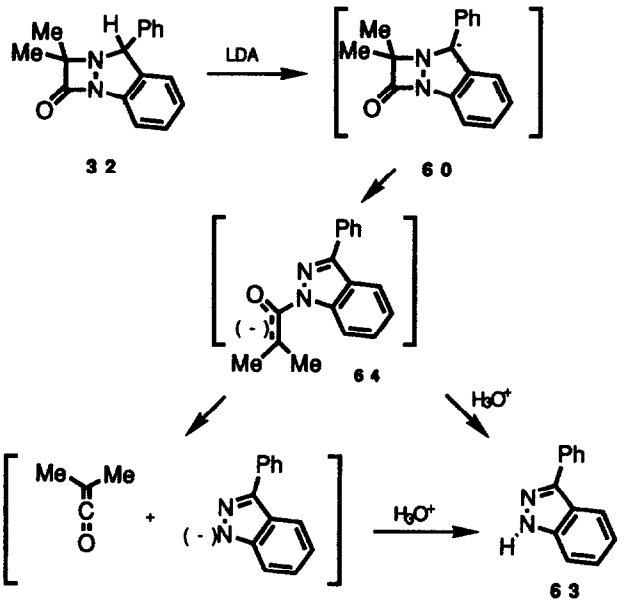


Figure 19

Several examples of reductive cleavage of the N-N bond in 1,2-diazetidin-3-ones are known. Schenck and Engelhard[14] reported reduction of 1,2-diaryl-1,2-diazetidin-3-ones with hydrogen in the presence of a palladium catalyst (Figure 20). Also, the reduction of 1-(diphenylmethyl-ene)-3-oxo-1,2-diazetidinium hydroxide, inner salt, with Raney nickel has been reported by Greenwald and Taylor.[2a] We therefore briefly

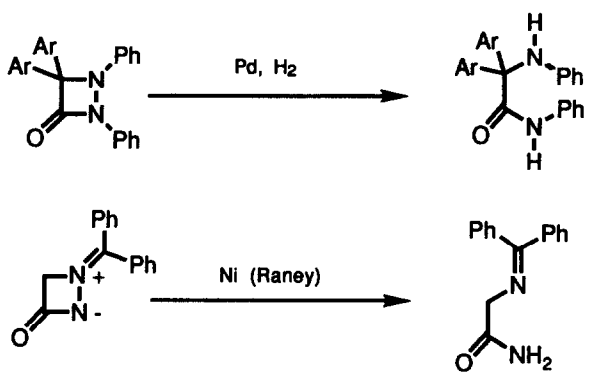


Figure 20

examined the possibility that a similar reductive cleavage of the N-N bond in our "bicyclobenzodiazepinones" and "bicyclobenzodiazocinones" might be effected. Treatment of **25** with W-2 Raney nickel in ethanol under reflux for three hours led very surprisingly to **64** in 23% yield as the sole reaction product (Figure 21). The purported intermediate **65** could actually be isolated in 28% yield when the reduction was carried out under milder conditions (use of partially deactivated W-2 Raney nickel, or lowering the reduction time from 3 hours to 30 minutes). However, attempts to reduce **24** and **26** using the conditions employed for the reduction of **25** were

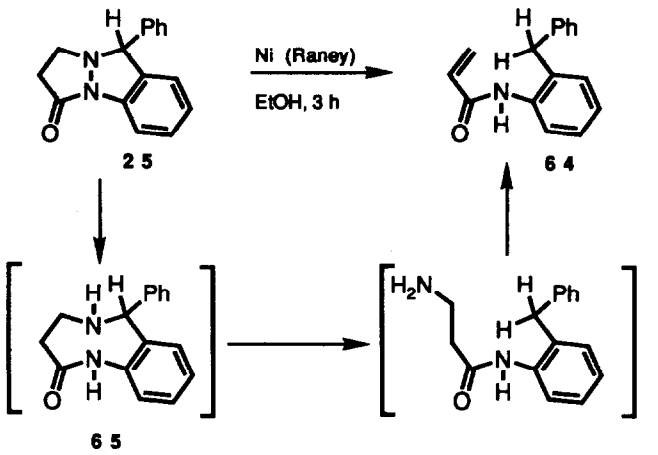
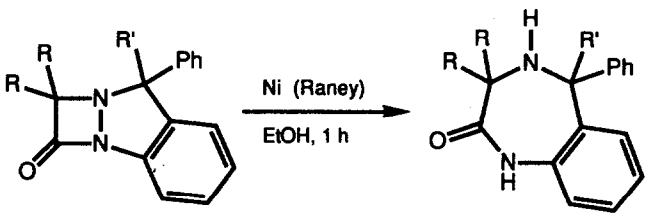


Figure 21

unsuccessful. Even treatment of these substrates under reflux in ethanol for 48 hours in the presence of fully active W-2 Raney nickel resulted in the recovery of unreacted starting material. The failure of these compounds to react appears to be due to steric constraints imposed by substitution at C-9. However, both **32** and **30** were successfully converted to the 1,4-benzodiazepinones **66** (36%) and **67** (6%) by heating under reflux in ethanol in the presence of fully active W-2 Raney nickel (Figure 22). Attempts to reduce **30** with hydrogen in the presence of Pd-C or $BaSO_4$ were unsuccessful.



32 (R = Me, R' = H)
30 (R = H, R' = Ph)

66 (R = Me, R' = H)
67 (R = H, R' = Ph)

Figure 22

Conclusions: Two routes to "bicycloaryldiazocinones" and one route to "bicyclobenzodiazepinones" have been described. Pyrazolidinone **18** undergoes base-catalyzed cyclization to **20**. Both 3-oxopyrazolidinium hydroxide, inner salts, and 3-oxo-1,2-diazetidinium hydroxide, inner salts, have been shown to undergo 1,3-dipolar cycloadditions with benzyne. Although the former adducts are stable, isolable compounds, the more highly strained latter "bicyclobenzodiazepinones" exhibit a tendency to decompose by extrusion of carbon monoxide. Attempts to effect base-catalyzed cleavage of the nitrogen-nitrogen bond of the "bicyclobenzodiazepinones" failed to effect ring expansion to 1,4-benzodiazepinones due to stereoelectronic constraints. However, reductive cleavage of the nitrogen-nitrogen bond of both of the above series of adducts is possible in some cases and provides a novel entry to 1,5-benzodiazocine and 1,4-benzodiazepine systems.

Experimental Section

(Z)-3-Oxo-1-(3-Pyridinylmethylene)pyrazolidinium Hydroxide, Inner Salt, N-Oxide (13). Pyrazolidin-3-one hydrochloride (245 mg, 2 mmol) was dissolved in water (1 mL). Potassium bicarbonate (200 mg, 2 mmol) was added and the reaction mixture was stirred at room temperature for 10 min.. Pyridine-3-carboxaldehyde N-oxide, (246 mg, 2 mmol) was added and the reaction solution was stirred at room temperature for 30 min. and then continuously extracted with dichloromethane for five days. Filtration of the dichloromethane solution gave 262 mg (68%) of product as a yellow solid, mp 240 °C. IR (KBr) 3130, 3070, 3020, 2975, 1680, 1660, 1600, 1572, 1445, 1415, 1125, 1280, 1215, 1157, 1105, 1010, 950, 895, 800, 780, 658 cm^{-1}. ^1H NMR (DMSO-d_6) δ 9.25 (s, 1 H, aromatic), 8.35-7.96 (m, 2 H, aromatic), 7.68-7.45 (m, 2 H, ^+N=CH-Ar and aromatic), 4.62 (t, 2 H, -CO-CH_2-CH_2-, J= 8.8 Hz), 2.62 (t, 2 H, -CO-CH_2-CH_2-, J= 8.8Hz). Anal. Calcd for $C_9H_9N_3O_2$: C, 56.54; H, 4.75; N, 21.98. Found: C, 56.70; H, 4.78; N, 22.01.

(Z)-1-[(2-Chloro-3-quinolinyl)methylene]-3-oxopyrazolidinium Hydroxide, Inner Salt (16). A mixture of pyrazolidin-3-one hydrochloride (2.45 g, 20 mmol) in methanol (20 mL) containing sodium methoxide (4.06 mL of 25% in methanol, 20 mmol) was stirred at room temperature for 10 min. and filtered through a pad of diatomaceous earth. The solution was diluted to 30 mL with methanol, 2-chloroquinoline-3-carboxaldehyde (1.92 g, 10 mmol) was added, and the reaction mixture was stirred at room temperature for 4 h. The resulting solid was then filtered and dried under reduced pressure to give 2.33 g (90%) of product as a yellow powder, mp 240 °C. IR (KBr) 3090, 3065, 1685, 1655, 1610, 1580, 1480, 1455, 1440, 1425, 1370, 1320, 1265, 1240, 1200, 1130, 1110, 1045, 1020, 960, 930, 810, 780, 755, 655, cm^{-1}. ^1H NMR (DMSO-d_6) δ 10.08 (s, 1 H, =CH-Ar), 8.20-7.70 (m, 5 H, aromatic), 4.78 (t, 2 H, -CO-CH_2-CH_2-, J= 7 Hz), 2,68 (t, 2 H, -CO-CH_2-CH_2-, J= 7 Hz). Anal. Calcd for $C_{13}H_{10}ClN_3O$: C, 60.13; H, 3.88; Cl, 13.65; N, 16.18. Found: C, 59.99; H, 4.15; Cl, 13.48; N, 15.98.

(Z)-1-[(2-Iodo-3-quinolinyl)methylene]-3-oxopyrazolidinium Hydroxide, Inner Salt (17). A mixture of pyrazolidin-3-one hydrochloride (2.20 g, 18 mmol) in methanol (10 mL) containing sodium methoxide (3.65 mL of 25 % in methanol, 18 mmol) was stirred at room temperature for 10 min. and filtered through a pad of diatomaceous earth. The solution was diluted to 19 mL with methanol, 2-iodoquinoline-3-carboxaldehyde (2.55 g, 9 mmol) was added, and the reaction mixture was stirred at room temperature until the 2-iodoquinoline-3-carboxaldehyde dissolved (ca. 10 min). The reaction solution was then heated under reflux for 40 min. after which it was cooled to room temperature and filtered to give 2.75 g (83%) of product as a solid, mp 170-180 °C (dec). IR (KBr) 3060, 3000, 1678, 1656, 1608, 1572, 1550, 1478, 1430, 1370, 1196, 1128, 1105, 1005, 965, 920, 748, 660 cm^{-1}. ^1H NMR (DMSO-d_6) δ 10.03 (s, 1 H, -N^+=CH-Ar), 8.07-7.58 (m, 5 H, aromatic), 4.70 (t, 2 H, -CO-CH_2CH_2-, J = 8.8 Hz), 2.90 (t, 2 H, -$COCH_2CH_2$-, J = 8.8 Hz). Anal. Calcd for $C_{13}H_{10}IN_3O.H_2O$: C, 42.30; H, 3.38; N, 11.38. Found: C, 42.13; H, 3.05; N, 11.40.

1-[(2-Chloro-3-quinolinyl)methyl]pyrazolidin-3-one (18). To a solution of (Z)-1-[(2-chloro-3-quinolinyl)methylene]-3-oxopyrazolidinium hydroxide, inner salt, (2.33 g, 9 mmol) in methanol (30 mL), cooled in an ice bath to 0 °C, was added sodium borohydride (340 mg, 9 mmol). The reaction mixture

spontaneously warmed to 20 °C with gas evolution. After 30 min. the reaction mixture was poured into ice water (60 mL), and the solution was saturated with sodium chloride and extracted with dichloromethane (1 x 70 mL, then 2 x 15 mL). The organic extracts were combined, dried (Na_2SO_4), and filtered. The solvent was removed under reduced pressure and the resulting solid residue was recrystallized from isopropanol (ca. 40 mL) to give 1.95 g (83%) of product as a white crystalline solid, mp 176-177 °C. IR (KBr) 3140, 3060, 3040, 2840, 1690, 1618, 1590, 1560, 1485, 1435, 1405, 1345, 1330, 1300, 1200, 1170, 1130, 1040, 1005, 995, 745 cm^{-1}. ^1H NMR ($CDCl_3$) δ 8.22-7.45 (m, 6 H, aromatic and NH), 4.14 (s, 2 H, N-CH_2-Ar), 3.45 (t, 2 H, -CO-CH_2-CH_2-N, J = 8 Hz), 2.56 (t, 2 H, -CO-CH_2-CH_2-N, J = 8 Hz). Anal. Calcd for $C_{13}H_{12}ClN_3O$: C, 59.66; H, 4.62; Cl, 13.55; N, 16.06. Found: C, 59.47; H, 4.48; Cl, 13.67; N, 16.24.

1-[(2-Iodo-3-quinolinyl)methyl]pyrazolidin-3-one (19): To a solution of (Z)-1-[(2-iodo-3-quinolinyl)methylene]-3-oxopyrazolidinium hydroxide, inner salt, (1.40 g, 4 mmol) in ethanol (12 mL), cooled to 0 °C, was added (portionwise) sodium borohydride (152 mg, 4 mmol), and the reaction mixture was stirred at 0 °C for 30 min. The reaction mixture was poured into water (20 mL), and the resulting aqueous solution was saturated with sodium chloride and extracted with dichloromethane (3 x 33 mL). The organic extracts were combined, dried (Na_2SO_4), and filtered. The solvent was removed under reduced pressure and the residue was recrystallized from isopropanol to give 1.11 g (79%) of a crystalline colorless solid, mp 159-163 °C. IR (KBr) 3155, 3050, 1690, 1615, 1585, 1558, 1485, 1395, 1350, 1330, 1310, 1165, 1175, 1023, 990, 748 cm^{-1}. ^1H NMR ($CDCl_3$) δ 8.10-7.55 (m, 6 H, aromatic and NH), 4.08 (s, 2 H, N-CH_2N), 3.45 (t, 2 H, -$COCH_2CH_2$-N, J = 8 Hz), 2.58 (t, 2 H, -CO-CH_2-CH_2-N, J = 8 Hz). Anal. Calcd for $C_{13}H_{12}IN_3O$: C, 44.21; H, 3.43; I, 35.93; N, 11.90. Found: C, 44.10; H, 3.22; I, 36.04; N, 11.64.

1,2-Dihydro-3H,11H-pyrazole[1',2':1,2]pyrazolo[3,4-b]-quinolin-3-one (20). 1-[(2-Chloro-3-quinolinyl)methyl]-pyrazolidin-3-one (18) (262 mg, 1 mmol) was dissolved in DMF (5 mL) and sodium hydride (48 mg of 60% in mineral oil, 1 mmol) was added. The reaction mixture was heated under reflux for 21 h, poured into ice water (10 mL) and extracted with dichloromethane (2 x 15 mL). The organic extracts were combined, dried (Na_2SO_4), and filtered. The solvent was removed under reduced pressure and the residue was recrystallized from isopropanol to give 50 mg (22%) of a yellow-orange solid, mp 208-212 °C. IR (KBr) 3065, 2980, 2925, 2830, 1710, 1635, 1465, 1425, 1400, 1360, 1335, 1115, 1080, 1010, 755 cm^{-1}. ^1H NMR ($CDCl_3$) δ 8.14-7.25 (m, 5H, aromatic), 4.33 (s, 2 H, N-CH_2Ar), 3.45 (t, 2 H, N-CH_2CH_2-, J = 7.2 Hz), 2.98 (t, CH_2CH_2CO-, J = 7.2 Hz). Mass spectrum, m/z (relative intensity) 225 (M^+, 100), 197 (20), 183 (77), 170 (27), 169 (18), 141 (96), 140 (46), 114 (27), 55 (22). Anal. Calcd for $C_{13}H_{11}N_3O$: C, 69.32; H, 4.92; N, 18.66. Found: C, 69.06; H, 5.14; N, 18.40.

N-(2-Chlorophenylmethylene)methanamine. 2-Chlorobenzaldehyde (3.51 g, 0.025 mol) was dissolved in dry benzene (25 mL). The solution was saturated with methylamine and heated under reflux with azeotropic removal of water for 1 h. The solvent was removed by distillation and the residue was distilled under reduced pressure to give 3.32 g (86%) of product as a colorless liquid, bp 53-54 °C (0.70 mm Hg). IR (neat) 3070, 2940, 2895, 2850, 2835, 2770, 1642, 1593, 1470, 1445, 1435, 1403, 1368, 1275, 1053, 1030, 1002, 957, 752, 708 cm^{-1}. ^1H NMR ($CDCl_3$) d 8.72 (d, 1 H, ArCH=N-, J = 1.8 Hz), 8.02-7.90 (m, 1 H, aromatic),

7.38-7.21 (m, 3 H, aromatic), 3.56 (d, 3 H, -CH3, J = 1.8 Hz). Anal. Calcd for C8H8ClN: C, 62.55; H, 5.25; Cl, 23.08; N, 9.12. Found: C, 62.75; H, 5.46; Cl, 23.19; N, 9.23.

(Z)-1-(2-Chlorophenylmethylene)-3-oxopyrazolidinium Hydroxide, Inner Salt (23). N-(2-Chlorophenylmethylene)-methanamine (460 mg, 3 mmol) was dissolved in dichloromethane (30 mL), pyrazolidin-3-one hydrochloride (368 mg, 3 mmol) was added, and the reaction mixture was refluxed for 3 h, filtered and the solvent removed under reduced pressure. The residue was recrystallized from isopropanol (ca. 8 mL) to give 370 mg (59%) of a white crystalline solid, mp 196-198°C. IR (KBr) 3098, 3080, 3065, 3005, 1675, 1655, 1590, 1460, 1448, 1436, 1328, 1299, 1279, 1253, 1102, 958, 788, 762, 610 cm^{-1}. ^1H NMR (DMSO-d_6) δ 9.16-9.05 (m, 1 H, aromatic), 7.74-7.45 (m, 4 H, ^+N=CH- and aromatic), 4.67 (t, 2H, -CO-CH_2-CH_2-N^+, J = 9 Hz), 2.61 (t, 2 H, OC-CH_2-, J = 9 Hz). Anal. Calcd for $C_{10}H_9ClN_2O$: C, 57.57; H, 4.35; Cl, 16.99; N, 13.43. Found: C, 57.81; H, 4.45; Cl, 17.05; N, 13.61.

9,9-Diphenyl-1,2-dihydro-3H, 9H-pyrazolo[1,2-a]indazol-3-one (24). To a solution of 1-(diphenylmethylene)-3-oxopyrazolidinium hydroxide, inner salt,[2c] (7.75 g, 31 mmol) in THF (300 mL) was added solvent-moist benzenediazonium-2-carboxylate[15] (37.2 mmol), and the reaction mixture was heated to 60 °C with stirring for 2 1/2h. The solvent was removed under reduced pressure and the residue was triturated with boiling ethanol (100 mL). The cooled solution was filtered to give 7.93 g (78%) of a white crystalline solid, mp 211-212 °C. IR (KBr) 3050, 3022, 2922, 2850, 1690, 1601, 1591, 1480, 1410, 1312, 1290, 1112, 919, 745, 700 cm^{-1}. ^1H NMR ($CDCl_3$) δ 7.80-7.65 (m, 1 H, aromatic), 7.55-7.03 (m, 13 H, aromatic), 2.78 (s, 4 H, -CO-CH_2-CH_2-N). ^1H NMR (trifluororacetic acid) d 7.95-7.32 (m, 14 H, aromatic), 4.25 (t, 2 H, -CH_2-N, J = 7 Hz), 3.15 (t, 2 H, -COCH_2-, J = 7 Hz). ^{13}C NMR ($CDCl_3$) δ 163.0, 140.5, 137.2, 133.2, 128.8, 128.6, 128.1, 127.7, 124.8, 112.4, 76.0, 45.3, 36.3. Anal. Calcd for $C_{22}H_{18}N_2O$: C, 80.97; H, 5.56; N, 8.58. Found: C, 81.17; H, 5.45; N, 8.52.

1,2-Dihydro-9-phenyl-3H,9H-pyrazolo[1,2-a]indazol-3-one (25). To a solution of (Z)-3-oxo-1-(phenylmethylene)pyrazolidinium hydroxide, inner salt,[2c] (3.14 g, 18 mmol) in THF (200 mL) was added solvent-moist benzenediazonium-2-carboxylate (19.8 mmol), and the mixture was heated to 40°C with stirring for 4 h. The solvent was removed under reduced pressure and the residue was recrystallized from isopropanol to give 2.46 g (55%) of a white crystalline solid, mp 152-155°C. IR (KBr) 3060, 3030, 2990, 2865, 2830, 1690, 1603, 1480, 1460, 1404, 1310, 1280, 1060, 750, 690 cm^{-1}. ^1H NMR ($CDCl_3$) δ 7.66-6.79 (m, 9 H, aromatic), 5.09 (s, 1 H, N-CH(Ph)-), 3.67-3.53 (m, 1 H, alkyl), 3.18-2.72 (m, 3 H, alkyl). Anal. Calcd for $C_{16}H_{14}N_2O$: C, 76.78; H, 5.64; N, 11.19. Found: C, 76.86; H, 5.80; N, 11.23.

9-(2-Chlorophenyl)-1,2-dihydro-3H,9H-pyrazolo[1,2-a]-indazol-3-one (26). To a solution of 1-(2-chlorophenylmethylene)-3-oxopyrazolidinium hydroxide, inner salt,[2c] (1.46 g, 7 mmol) in THF (200 mL) was added solvent-moist benzenediazonium-2-carboxylate (8.4 mmol), and the reaction mixture was heated to 60 °C for 4 h, filtered, and the solvent removed under reduced pressure. The residue was then dissolved in diethyl ether (ca. 200 mL) and filtered. The solvent was removed under reduced pressure to give an oil which solidified upon cooling. The solid residue was triturated with hexanes and filtered to give 1.46 g of a yellow

solid, mp 95-104 °C. Recrystallization of the solid from ethanol (ca. 2 mL) gave 1.20 g (60%) of 26 as a white crystalline solid, mp 110-112 °C. IR (KBr) 3105, 3028, 2990, 2984, 1870, 1690, 1603, 1483, 1460, 1407, 1315, 1065, 1055, 1038, 772, 747 cm^{-1}. ^1H NMR ($CDCl_3$) δ 7.68-6.98 (m, 8 H, aromatic), 5.79 (s, 1 H, benzhydryl), 3.70-2.60 (m, 4 H, -CO-CH_2-CH_2-). Anal. Calcd for $C_{16}H_{13}ClN_2O$: C, 67.49; H, 4.61; Cl, 12.45; N, 9.84. Found: C, 67.60; H, 4.79; Cl, 12.42; N, 9.85.

8,8-Diphenyl-8H-[1,2]diazeto[1,2-a]indazol-2(1H)-one (30). To a solution of 1-(diphenylmethylene)-3-oxo-1,2-diazetidinium hydroxide, inner salt[2c] (27) (4.25 g, 18 mmol) in THF (150 mL) was added solvent-moist benzenediazonium-2-carboxylate (19.8 mmol), and the reaction mixture was heated to 38 °C for 12 h, the solvent removed under reduced pressure, and the residue recrystallized from ethanol:THF to give 4.19 g (74%) of 30 as a colorless crystalline solid, mp 163°C (dec.). IR (KBr) 3050, 1785, 1475, 1455, 1270, 750, 730, 700 cm^{-1}. ^1H NMR ($CDCl_3$) δ 7.78-7.62 (m, 2 H, aromatic), 7.40-7.00 (m, 12 H, aromatic), 4.24 (d, 1 H, -HCH-, J = 16 Hz), 3.63 (d, 1 H, -HCH-, J = 16 Hz). ^{13}C NMR ($CDCl_3$) δ 173.9, 147.2, 139.9, 139.1, 136.8, 129.0, 128.8, 128.4, 128.2, 127.3, 127.0, 126.4, 125.9, 114.3, 79.2, 64.1. Anal. Calcd for $C_{21}H_{16}N_2O$: C, 80.75; H, 5.16; N, 8.97. Found: C, 80.97; H, 5.16; N, 8.72.

8,8-Diphenyl-1-methyl-8H-[1,2]diazeto[1,2-a]indazol-2(1H)-one (31). To a solution of 1-(diphenylmethylene)-4-methyl-3-oxo-1,2-diazetidinium hydroxide, inner salt[2c] (28) (1.44 g, 5.77 mmol) in THF (75 mL) was added solvent-moist benzenediazonium-2-carboxylate (6.35 mmol), and the reaction mixture was heated to 35-40 °C for 6 h, the solvent removed under reduced pressure, and the residue (1.9 g) dissolved in dichloromethane:hexanes (3:1, 100 mL). The solvent was allowed to evaporate to approximately one-third of its original volume. The resulting crystals were collected by suction filtration and washed with diethyl ether to give 1.03 g (55%) of product as a crystalline solid, mp 168 °C with decomposition. IR (KBr) 3060, 2980, 1820, 1218, 1118, 1087, 746, 730, 700 cm^{-1}. ^1H NMR ($CDCl_3$) δ 7.70-7.67 (m, 2 H, aromatic), 7.38-7.08 (m, 12 H, aromatic), 3.91 (q, 1 H, CH_3-CH(CO-), J = 7 Hz), 1.25 (d, 3 H, CH_3-CH(CO-), J = 7 Hz). ^{13}C NMR ($CDCl_3$) δ 177.5, 147.8, 139.9, 135.6, 129.4, 128.9, 128.6, 128.3, 128.1, 127.1, 126.8, 126.4, 125.5, 114.1, 78.7, 72.3, 15.5. Anal. Calcd for $C_{22}H_{18}N_2O$: C, 80.96; H, 5.56; N, 8.58. Found: C, 80.77; H, 5.81; N, 8.80.

1,1-Dimethyl-8-phenyl-8H-[1,2]diazeto[1,2-a]indazol-2(1H)-one (32). To a solution of (Z)-4,4-dimethyl-3-oxo-1-(phenylmethylene)-1,2-diazetidinium hydroxide, inner salt,[2c] (29) (500 mg, 2.66 mmol) in THF (20 mL) was added solvent-moist benzenediazonium-2-carboxylate (2.92 mmol), and the reaction mixture was heated to 40 °C with stirring for 4h. The solvent was removed under reduced pressure (40 °C) and the residue was recrystallized from diethyl ether to give 290 mg (41%) of 32 as a white crystalline solid, mp 130-131 °C. Concentration of the mother liquor afforded an additional 50 mg (7%) of product, mp 129-130 °C. IR (KBr) 2980, 1800, 1460, 1260, 1180, 1155, 1082, 752 cm^{-1}. ^1H NMR ($CDCl_3$) δ 7.37-6.98 (m, 9 H, aromatic), 5.73 (s, 1 H, N-CH(Ar)Ar'), 1.64 (s, 3 H, -CH_3, exhibits no nuclear Overhauser enhancement upon irradiation at 5.73 d), 1.52 (s, 3H, -CH_3, exhibits a nuclear Overhauser enhancement upon irradiation at 5.73 d). ^{13}C NMR ($CDCl_3$) δ 177.9, 142.3, 138.5, 137.0, 128.6, 127.7, 125.5, 124.5, 114.1, 77.9, 67.1, 25.2, 17.8. Anal. Calcd: for C $_{17}H_{16}N_2O$: C, 77.25; H, 6.10; N, 10.60. Found: C, 77.05; H, 6.39; N, 10.49.

8,8-(4,4'-Dichlorodiphenyl)-8H-[1,2]diazeto[1,2-a]-indazol-2(1H)-one (44). To a solution of 1-(4,4'-dichlorodiphenylmethylene)-3-oxo-1,2-diazetidinium hydroxide, inner salt[2c] (39) (500 mg, 1.64 mmol) in THF (20 mL) was added solvent-moist benzenediazonium-2-carboxylate (1.94 mmol), and the reaction mixture was heated to 40 °C with stirring for 4h. The solvent was removed under reduced pressure and the residue was recrystallized from ethanol:THF to give 50 mg (8%) of 44, mp 150-153 °C. Alternatively, in place of recrystallization, trituration of the residue with boiling hexanes gave a black tar and 50 mg (8%) of product which crystallized from the hexanes upon cooling, mp 150-153 °C. IR (KBr) 3065, 2935, 1817, 1590, 1478, 1460, 1402, 1253, 1228, 1095, 1050, 1016, 820, 750 cm^{-1}. ^1H NMR ($CDCl_3$) d 7.65-7.52 (m, 2 H, aromatic), 7.40-7.10 (m, 8 H, aromatic), 6.98-6.85 (m, 2 H, aromatic), 4.27 (d, 1H, -HCH-, J= 16 Hz), 3.65 (d, 1 H, -HCH-, J= 16 Hz). Anal. Calcd for $C_{21}H_{14}Cl_2N_2O$: C, 66.16; H, 3.70; Cl, 18.60; N, 7.35. Found: C, 65.91; H, 3.93; Cl, 18.64; N, 7.21.

8,8-(4,4'-Dimethoxydiphenyl)-8H-[1,2]diazeto[1,2-a]indazol-2(1H)-one (45). To a solution of 1-(4,4'-dimethoxydiphenylmethylene)-3-oxo-1,2-diazetidinium hydroxide, inner salt[2c] (40) (486 mg, 1.64 mmol) in THF (10 mL) was added solvent-moist benzenediazonium-2-carboxylate (1.97 mmol), and the mixture was heated to 40 °C with stirring for 4 h. The solvent was then removed under reduced pressure and the residue was recrystallized from isopropanol to give 310 mg (51%) of 45, mp 142-145 °C. IR (KBr) 2940, 2845, 1792, 1610, 1508, 1460, 1302, 1252, 1180, 1030, 828 cm^{-1}. ^1H NMR ($CDCl_3$) δ 7.65-7.55 (m, 2 H, aromatic), 7.26-7.16 (m, 4 H, aromatic), 6.88-6.80 (m, 6 H, aromatic), 4.15 (d, 1H, -HCH-, J=16 Hz), 3.80 (s, 3 H, -OCH_3), 3.78 (s, 3 H, -OCH_3), 3.62 (d, 1H, -HCH-, J= 16 Hz). Anal. Calcd for $C_{23}H_{20}N_2O_3$: C, 74.18; H, 5.41; N, 7.52. Found: C, 73.89; H, 5.51; N, 7.49.

2-Isopropyl-3-phenyl-2H-indazole (49). A solution of 1,1-dimethyl-8-phenyl-8H-[1,2]diazeto[1,2-a]indazol-2(1H)-one (32) (150 mg, 0.57 mmol) in 10 mL of CCl_4 was heated under reflux for 20 h, the solvent was removed under reduced pressure, and the residue was chromatographed over silica gel (10:1 petroleum ether (bp 30-60 °C):diethyl ether) to give 90 mg (67%) of 49, mp 102-105 °C (R_f 0.31, silica gel, 3:1 petroleum ether (bp 30-60 °C):diethyl ether). IR (KBr) 3055, 3040, 2990, 2975, 2930, 1601, 1490, 1460, 1445, 1365, 1350, 1265, 1218, 1070, 1005, 982, 895, 830, 745, 695, 635 cm^{-1}. ^1H NMR ($CDCl_3$) δ 7.82-7.04 (m, 9 H, aromatic), 4.88 (septet, 1 H, $(CH_3)_2CH$-, J = 6.6 Hz), 1.63 (d, 6 H, 2 CH_3, J = 6.6 Hz). ^{13}C NMR ($CDCl_3$) δ 148.0, 134.8, 130.1, 129.8, 129.0, 125.9, 121.4, 120.1, 117.4, 51.3, 23.3. Mass spectrum, m/z (relative intensity) 237 (7), 236 (M^+, 39), 221 (7), 195 (13), 194 (100), 193 (9), 167 (7), 165 (9), 77 (20), 76 (6), 66 (8), 63 (11), 51 (15), 50 (6). Anal. Calcd. for $C_{16}H_{16}N_2$: C, 81.32; H, 6.82; N, 11.85. Found: C, 81.47; H, 6.83; N, 12.09.

N,a,a-Trimethyl-3-phenyl-2H-indazole-2-acetamide (36). 1,1-Dimethyl-8-phenyl-8H-[1,2]diazeto[1,2-a]indazol-2(1H)-one (32) (1.00 g, 3.8 mmol) was added to a mixture of ethanol (8 mL) and methylamine (1.1 g) at 0 °C, the resulting solution was allowed to warm to room temperature, and the solvent was removed under reduced pressure. The residue was dissolved in chloroform (15 mL) and stirred at room temperature with exposure to air for 3 days. The solvent was removed under reduced pressure and the residue

was chromatographed over silica gel (20 g, 1:1 diethyl ether:petroleum ether, bp 30-60 °C). Fractions 9-13 (20 mL fractions) were combined and the solvent was removed under reduced pressure to yield 0.90 g (81%) of 32 as a colorless solid, mp 153-156 °C (Rf. 0.43, silica gel, diethyl ether). IR (KBr) 3300, 3060, 2990, 2940, 1663, 1525, 1460, 1408, 1350, 1260, 1230, 1160, 1000, 915, 745 cm^{-1}. ^1H NMR ($CDCl_3$) δ 7.76-6.92 (m, 9 H, aromatic), 5.81 (s broad, 1 H, CO-NH-), 2.70 (d, 3 H, -NH-CH_3, J= 4.8 Hz), 1.79 (s, 6 H, $2CH_3$). ^{13}C NMR ($CDCl_3$) δ 173.5, 146.7, 136.2, 130.7, 129.8, 128.7, 128.3, 126.3, 123.5, 121.8, 120.0, 116.9, 67.5, 27.3, 26.2. Anal. Calcd for $C_{18}H_{19}N_3O$: C, 73.69; H, 6.53; N, 14.32. Found: C, 73.40; H, 6.36; N, 14.40.

3-Phenyl-2H-indazole-2-propionic Acid (53). 1,2-Dihydro-9-phenyl-3H, 9H-pyrazolo[1,2-a]indazol-3-one (25) (200 mg, 0.80 mmol) was dissolved in isopropanol (6 mL) and hydrogen peroxide (3 mL, 30% in water) was added. The solution was heated under reflux for 24 h, the solvent was removed under reduced pressure, and the resulting residue was recrystallized from ethyl acetate to give 85 mg (40%) of 53, mp 181-183 °C. IR (KBr) 2900 (very broad), 1720, 1625, 1500, 1470, 1442, 1410, 1380, 1365, 1298, 1230, 1200, 1150, 1102, 705, 698 cm^{-1}. ^1H NMR ($CDCl_3$) δ 7.72-6.98 (m, 9 H, aromatic), 4.68 (t, 2 H, Ar-CH_2-CH_2-, J= 7.2 Hz), 3.03 (t, 2 H, HOOC-CH_2-CH_2-, J= 7.2 Hz). Anal. Calcd for $C_{16}H_{14}N_2O_2$: C, 72.17; H, 5.30; N, 10.52. Found: C, 71.95; N, 5.19; N, 10.51.

Methyl 3,3-Diphenyl-2H-indazoline-2-acetate (62). To a refluxing solution of 8,8-diphenyl-8H-[1,2]diazeto[1,2-a]indazol-2(1H)-one (30) (0.31 g, 1 mmol) in methanol (3 mL) was added slowly sodium methoxide in methanol (1.1 mmol, 0.25 mL of 4.4 M), and the reaction mixture was heated under reflux for 5 min. During this time a precipitate formed. The reaction mixture was allowed to cool for 10 min. and then filtered to give 0.29 g (85%) of product as a crystalline solid, mp 158-160 °C. IR (KBr) 3290, 3065, 3020, 2955, 2870, 1735, 1599, 1483, 1460, 1440, 1402, 1380, 1315, 1282, 1212, 1175, 1158, 983, 918, 794, 750, 700 cm^{-1}. ^1H NMR ($CDCl_3$) δ 7.47-6.80 (m, 15 H, aromatic, and N-H), 3.68 (s, 3 H, $COOCH_3$), 3.04 (s, 2H, N-CH_2-$COOCH_3$). ^{13}C NMR ($CDCl_3$) δ 171.3, 147.4, 142.1, 135.3, 128.8, 128.1, 127.9, 127.3, 124.5, 122.1, 111.8, 79.1, 55.2, 51.3. Mas spectrum, m/z (relative intensity) 344 (M^+, 15), 168 (18), 267 (100), 256 (19), 241 (15), 239 (14), 207 (40), 180 (13), 165 (32), 77 (23). Anal. Calcd for $C_{22}H_{20}N_2O_2$: C, 76.72; H, 5.85; N, 8.13. Found: C, 76.50; H, 5.62; N, 8.03.

3-Phenyl-1H-indazole (63). Diisopropylamine (0.292 mL, 2.08 mmol) was dissolved in dry THF (4 mL) and cooled to -78°C. n-Butyllithium (2.08 mmol, 0.95 mL of 2.2 M in hexane) was added and the solution was stirred for 15 min. 1,1-Dimethyl-8-phenyl-8H-[1,2]diazeto[1,2-a]indazol-2(1H)-one (32) (500 mg, 1.89 mmol) in THF (5 mL) was then added dropwise over a period of 15 min. During the addition the reaction solution became deep red in color. The solution was stirred at -78 °C for 10 additional min. and then allowed to warm to 0 °C. The solution was stirred at 0 °C for 2 h, and a saturated solution of aqueous ammonium chloride (50 mL) was added. The color of the reaction solution changed from deep red to pale yellow. The aqueous and organic layers were separated and the aqueous layer was extracted with diethyl ether (2 x 40 mL). The organic layers were combined, dried (Na_2SO_4), filtered, and the solvent removed under reduced pressure to give 0.46 g of a thick yellow oil. Chromatography of the residue over silica gel (10 g, 20:1 petroleum ether (bp 30-60

°C):diethyl ether) gave a fraction which upon evaporation of the solvent under reduced pressure yielded a white solid (R_f 0.23, silica gel, 3:1 petroleum ether (bp 30-60 °C):diethyl ether). Recrystallization of the white solid from hexanes gave 111 mg (30%) of 3-phenyl-1H-indazole as a white crystalline solid, mp 114-115 °C (lit.[16] mp 114-115°C). IR (KBr) 3160 (very broad), 2990, 2940, 1620, 1610, 1500, 1480, 1345, 1310, 1255, 1135, 1105, 1075, 1030, 1010, 990, 905, 775, 740, 700 cm^{-1}. ^1H NMR ($CDCl_3$) δ 8.05-7.90 (m, 3 H, aromatic and N-H), 7.55-7.00 (m, 7 H, aromatic). Mass spectrum, m/z (relative intensity) 195 (17), 194 (M^+, 100), 193 (17), 168 (7), 97 (9), 77 (16), 71 (9), 69 (10), 56 (9), 55 (13), 51 (8).

N-[2-(Phenylmethyl)phenyl]-2-propenamide (64). A mixture of 1,2-dihydro-9-phenyl-3H,9H-pyrazolo[1,2-a]indazol-3-one (25) (250 mg, 1 mmol) and W-2 Raney nickel (2.5 g) in ethanol (10 mL) was heated under reflux for 3 h and then filtered. Evaporation of the solvent under reduced pressure followed by chromatography of the residue over silica gel (2:1 hexanes:diethyl ether) gave 55 mg (27%) of 64 as a white solid, mp 119-122 °C. IR (KBr) 3290, 3025, 1660, 1630, 1527, 1452, 1405, 1315, 1250, 1202, 755, 732 cm^{-1}. ^1H NMR ($CDCl_3$) δ 7.90 (s, 1 H, N-H), 7.40-7.08 (m, 9 H, aromatic), 6.12-5.56 (m, 3 H, -CO-CH=CH_2), 4.00 (s, 2 H, Ar-CH_2-Ar'). Anal. Calcd for $C_{16}H_{15}NO$: C, 80.98; H, 6.37; N, 5.90. Found: C, 80.72; H, 6.51; N, 5.69.

6-Phenyl-3,4,5,6-tetrahydro-1,5-benzodiazocin-2(1H)-one (65). A mixture of 1,2-dihydro-9-phenyl-3H,9H-pyrazolo[1,2-a]indazol-3-one (25) (200 mg, 0.8 mmol) and W-2 Raney nickel (2 g) in ethanol (8 mL) was heated under reflux with stirring for 1 h. The reaction mixture was then filtered through a pad of diatomaceous earth and the solvent was removed under reduced prssure. The residue was chromatographed over silica gel (with ether) to give 75 mg (37%) of 65 as a white solid, mp 189-192 °C (lit.[17] mp 187-189 °C). IR (KBr) 3310, 3260, 3160, 3020, 2940, 1650, 1480, 1380, 1295, 1245, 1175, 1100, 890, 745, 725, 695 cm^{-1}. ^1H NMR ($CDCl_3$) δ 8.72 (s, 1 H, -CONHAr), 7.37-6.95 (m, 9 H, aromatic), 4.96 (s, 1 H, NCH(Ar)-), 3.45-3.02 (m, 2 H, NCH_2CH_2-), 2.67-2.02 (m, 3 H, CH_2NH and $COCH_2$). Anal. Calcd for $C_{16}H_{16}N_2O$: C, 76.17; H, 6.39; N, 11.10. Found: C, 75.98; H, 6.36; N, 10.95.

3,3-Dimethyl-5-phenyl-1,3,4,5-tetrahydro-2H-1,4-benzodiaze-pin-2-one (66). A mixture of 1,1-dimethyl-8-phenyl-8H-[1,2]diazeto[1,2-a]indazol-2(1H)-one (32) (400 mg, 1.51 mmol) and W-2 Raney nickel (4 g) in ethanol (20 mL) was heated under reflux for 2 h. The reaction mixture was filtered through a pad of diatomaceous earth and the solvent was removed under reduced pressure. The residue was then triturated with petroleum ether (bp 30-60 °C) and filtered to give 145 mg (36%) of 66 as a white solid, mp 173-175 °C. IR (KBr) 3330, 3185, 3055, 2975, 2933, 1654, 1586, 1484, 1437, 1383, 1364, 1225, 1175, 1155, 876, 862, 749, 683 cm^{-1}. ^1H NMR ($CDCl_3$) δ 8.23 (s, 1 H, -CO-NH-), 7.40-6.50 (m, 9 H, aromatic), 5.21 (s, 1 H, benzhydryl), 1.85 (s, 1 H, -$C(CH_3)_2$-NH-), 1.51 (s, 3 H, -CH_3), 1.38 (s, 3 H, -CH_3). Mass spectrum, m/z (relative intensity) 266 (M^+, 44), 224, (21), 223 (96), 182 (59), 180 (100), 165 (21), 152 (18), 91 (19), 87 (27), 77 (27), 74 (47), 69 (22), 59 (97), 58 (38), 57 (19), 55 (24), 50 (19). Anal. Calcd for $C_{16}H_{18}N_2O$: C, 76.66; H, 6.81; N, 10.52. Found: C, 76.46; H, 6.81; N, 10.44.

5,5-Diphenyl-1,3,4,5-tetrahydro-2H-1,4-benzodiazepin-2-one (67). A mixture of 8,8-diphenyl-8H-[1,2]diazeto[1,2-a]indazol-2(1H)-one (30) (250 mg, 0.80 mmol) and W-2 Raney nickel (2.5 g) in ethanol (10 mL) was heated under reflux with stirring for 3 h, filtered and the solvent removed under reduced pressure. The resulting emerald green oil was triturated with diethyl ether:hexanes to give 20 mg of a light green solid. Chromatography of the crude product over silica gel (gradient 1:2 hexanes:diethyl ether going to 1:1 hexanes:diethyl ether) gave 15 mg (6%) of 67 as a solid, mp 235-239 °C. IR (KBr) 3350, 3210, 3080, 3060, 3030, 2990, 1670, 1585, 1490, 1445, 1435, 1400, 1215, 1180, 1165, 1035, 880, 760, 700 cm^{-1}. ^1H NMR ($CDCl_3$) δ 7.60 (s, 1 H, -CO-NH-), 7.35-6.60 (m, 14 H, aromatic), 3.64 (s, 2 H, -CO-CH_2-N), 2.58 (s, 1 H, -CH_2-NH-). Mass spectrum, m/z (relative intensity) 314 (M^+, 16), 255 (10), 237 (19), 236 (100), 195 (7), 180 (9), 165 (9), 127 (6), 91 (8), 77 (11), 55 (5), 51 (10). HRMS. Calcd for $C_{21}H_{18}N_2O$: 314.1419. Found: 314.1411 ± 0.003.

References and Footnotes

1. a) Hegedus, L. S.; Kramer, A. *Organometallics*, **1984**, *3*, 1263. b) Lawton, G.; Moody, C. J.; Pearson, C. J. *J. Chem. Soc. Chem. Comm.* **1984**, 754. c) Moody, C. J.; Pearson, C. J.; Lawton, G. *Tetrahedron Lett.* **1985**, *26*, 3167. d) Taylor, E.C.; Davies, H. M. L. *J. Org. Chem.* **1986**, *51*, 1537. e) Taylor, E. C.; Davies, H. M. L.; Hinkle, J. S. *J. Org. Chem.* **1986**, *51*, 1550.

2. a) Greenwald, R. B.; Taylor, E. C. *J. Am. Chem. Soc.*, **1968**, *90*, 5272. b) Taylor, E. C.; Davies, H. M. L.; Clemens, R. J.; Yanagisawa, H.; Haley, N. F. *J. Am. Chem. Soc.*, **1981**, *103*, 7659. c) Taylor, E. C.; Haley, N. F.; Clemens, R. J. *J. Am. Chem. Soc.*, **1981**, *103*, 7743. d) Ip, P.C.; Ramakrishnan, K.; Warkentin, J. *Can. J. Chem.*, **1974**, *52*, 3671.

3. Dorn, H.; Otto, A. *Chem. Ber.* **1968**, *101*, 3287. See also refs 2a) and 2b).

4. Hoffmann, R. W. "Dehydrobenzene and Cycloalkynes"; Academic Press; New York, **1967**.

5. Huisgen, R.; Knorr, R. *Naturwissenschaften*, **1961**, *48*, 716.

6. Hinkle, J. S. "The Synthesis and Elaboration of Diazetidinones as an Entry into Potential Aza-β-lactam Antibiotics"; Ph.D. Dissertation, Princeton University, **1985** and references therein.

7. Huisgen, R.; Reissig, H.-U. *J. Chem. Soc. Chem. Commun.*, **1979**, 568.

8. Dorn, H.; Zubek, A. *Z. Chem.*, **1967**, *7*, 150.

9. a) Wittig, G.; Hoffman, R. W. *Chem. Ber.*, **1962**, *95*, 2729. b) Friedman, L.; Logullo, F. M. *J. Org. Chem.*, **1969**, *34*, 3089. c) Base, C. W.; Kobayashi, R. *Tetrahedron Lett.*, **1984**, 2827. See also ref. 4.

10. Clemens, R. J. Ph.D. Dissertation, Princeton University, **1982**.

11. Jones, N. D., private communication.

12. Bouchet, P.; Frucheir, A.; Joncheray, G. *Org. Magn. Reson.*, **1977**, *9*, 716.

13. Fahr, E; Fischer, W. *Tetrahedron Lett.*, **1967**, 3291.

14. Schenck, G. O.; Engelhard, N. *Angew. Chem.*, **1956**, *68*, 71.

15. Logullo, F. M.; Seitz, A. H.; Friedman, L. *Org. Synthesis*, **1973**, *Col. Vol. 5*, 54.

16. Auwers, K. v.; Huge, R.; Ungemach, O. *Liebigs Ann.*, **1937**, *527*, 291.

17. Denzer, M.; Ott, H. *J. Org. Chem.*, **1969**, *34*, 183.