Synthesis of Succinimido[3,4-b]indane and 1,2,3,4,5,6-Hexahydro-1,5-methano-3-benzazocine-2,4-dione by Sequential Alkylation and Intramolecular Arylation of Enolates Derived from *N,N,N′N′*-Tetramethylbutanediamides and *N,N,N′N′*-Tetramethylpentanediamides

Sushama A. Dandekar, Stacey N. Greenwood, Thomas D. Greenwood, Stéphane Mabic, Joseph S. Merola, James M. Tanko, and James F. Wolfe*

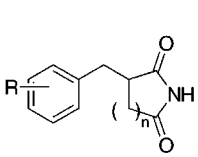
Department of Chemistry and the Harvey W. Peters Research Center for the Study of Parkinson's Disease and Disorders of the Central Nervous System, Virginia Polytechnic Institute and State University, Blacksburg, Virginia 24061-0212

Received October 5, 1998

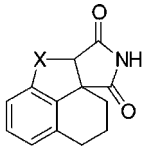
The tricyclic title compounds, **4** and **5**, were synthesized by initial alkylation of the lithium monoenolates of *N,N,N′,N′*-tetramethylbutanediamide (**6**) and *N,N,N′,N′*-tetramethylpentanediamide (**19**) with 2-iodobenzyl chloride in liquid NH_3 at −60 °C to afford 2-(2-iodobenzyl)-*N,N,N′,N′*-tetramethylbutanediamide (**9**) and 2-(2-iodobenzyl)-*N,N,N′,N′*-tetramethylpentanediamide (**20**) in yields of 88 and 87%, respectively. Treatment of **9** with KNH_2 in liquid NH_3 resulted in formation and intramolecular arylation of the less-substituted α-enolate to produce *trans*-1,2-bis(*N,N*-dimethylcarboxamido)indane (**10a**) in 60% yield. Selective hydrolysis of **10a** with aqueous Na_2O_2 gave *trans*-1-(*N,N*-dimethylcarboxamido)indane-2-carboxylic acid (**17**), which was then converted to bridged succinimide **4** by transformation to *trans*-1-(*N,N*-dimethylcarboxamido)indane-2-carboxamide (**10c**) followed by cyclization of this mixed primary/tertiary amide by means of NaH in refluxing THF. Treatment of **20** with KNH_2 in liquid NH_3 led to intramolecular arylation and accompanying ammonolysis to afford *trans*-1-(*N,N*-dimethylcarboxamido)-1,2,3,4-tetrahydronaphthalene-3-carboxamide (**21b**). Conversion of **21b** to **5** was similarly effected by means of NaH. Experiments designed to test the mechanistic aspects of the intramolecular arylations provided evidence for competing aryne and SET pathways.

Introduction

We recently reported on the preparation and anticonvulsant activity of a series of 2-benzylsuccinimides (**1a**)[1] and 2-benzylglutarimides (**1b**),[2] which blocked pentylenetetrazol-induced seizures in murine models. As part of a study of structural features which might contribute to and enhance this activity, we performed molecular mechanics calculations on **1a** (R = H) and **1b** (R = H).[3]



1a, n = 1
1b, n = 2



2

These calculations revealed that there are two important (nearly degenerate) conformations associated with these molecules, one in which the relatively bulky phenyl and cyclic imide moieties assumed a nearly face-to-face, gauche type conformation (Figure 1) and the other where these groups were *anti*. The face-to-face orientation of the phenyl and imidyl groups in the gauche conformation is reminiscent of π-stacking. It is conceivable that donor−acceptor interactions might be important in this conformation and thus that the orientation of these groups (i.e, the conformation) may affect the biological activity of these compounds. To address this issue, higher level, semiempirical MO calculations (AM1)[4] were performed and revealed that the gauche conformation was preferred for both compounds by ca. 1−2 kcal mol^{-1}. These calcula-

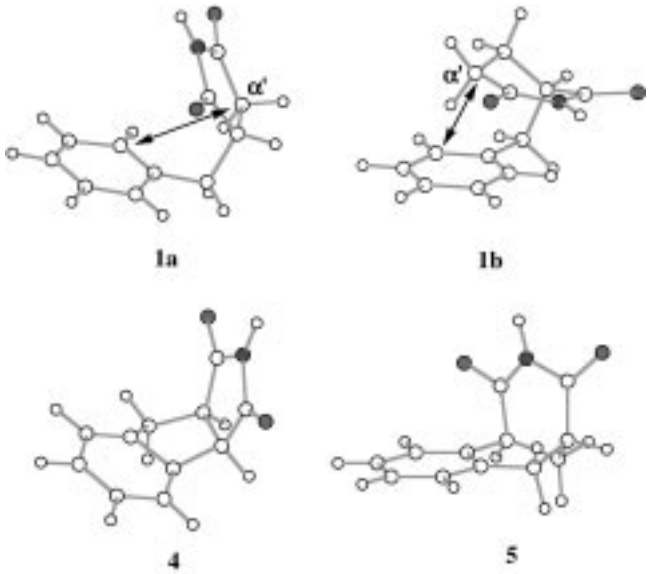


Figure 1.

* Corresponding author. Phone: (540) 231-8200. Fax: (540) 231-8890. E-mail: jwolfe@chemserver.chem.vt.edu.

(1) Goehring, R. R.; Greenwood, T. D.; Pisipati, J. S.; Wolfe, J. F. *J. Pharm. Sci.* **1991**, *80*, 790.

(2) Goehring, R. R.; Greenwood, T. D.; Nwokogu, G. C.; Pisipati, J. S.; Rogers, T. G.; Wolfe, J. F. *J. Med. Chem.* **1990**, *33*, 926.

(3) PCModel, v. 4.0, Serena Software, Box 3076, Bloomington, IN 47402. See Gajewski, J. J.; Gilbert, K. W. In *Advances in Molecular Modeling*; Liotta, D., Ed.; JAI Press Inc.: Greenwich, CT, 1990; Vol. 2, pp 65−92.

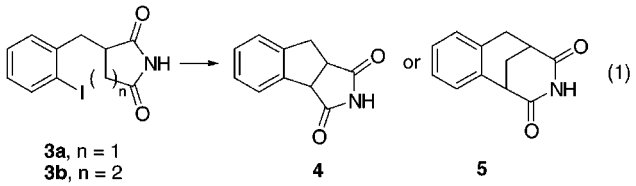
10.1021/jo982000b CCC: $18.00
Published on Web 02/09/1999

tions also suggested a slight shift distortion in electron density from the phenyl group into the imidyl, consistent with the notion that this donor−acceptor interaction stabilizes the gauche conformation.

If these conformational preferences are important to anticonvulsant activity, it seemed that establishment of a bond between the α′ position of the imide ring of **1a**,**b** (R = H) and the *ortho*-position of their phenyl substituents might enhance antiseizure efficacy in the resulting fused compounds, succinimido[3,4-*b*]indane (**4**) and 1,2,3,4,5,6-hexahydro-1,5-methano-3-benzazocine-2,4-dione (**5**), respectively (Figure 1). We were further encouraged to investigate the synthesis of these conformationally constrained analogues of **1a**,**b** (R = H) by an earlier report that several benzo-fused succinimides of type **2** exhibited anticonvulsant activity,[5] and by the fact that **5** had not been reported in the literature, while **4** had been reported once[6] but without complete structure elucidation or biological test data.

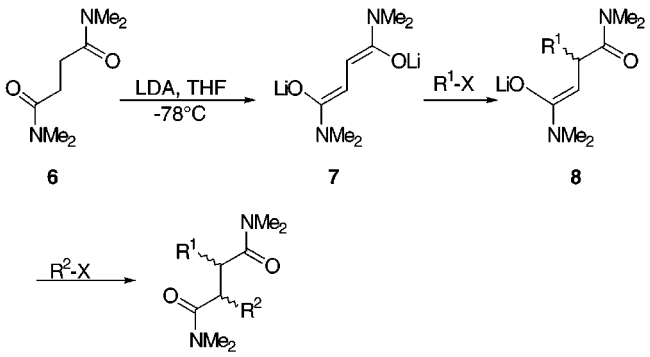
Results and Discussion

Initially we anticipated that **4** and **5** might be conveniently accessible by photoinduced intramolecular $S_{RN}1$[7] cyclization of the N,C(α′)-dianions of 2-iodobenzylimides **3a**−**b** (eq 1). Although the $S_{RN}1$ reactivity of N, C(α′)-dianions of imides had not been investigated, the participation of carboxamide monoenolates in both inter-[8] and intramolecular[9] photoassisted radical-chain aromatic substitution reactions encouraged us to test this approach.

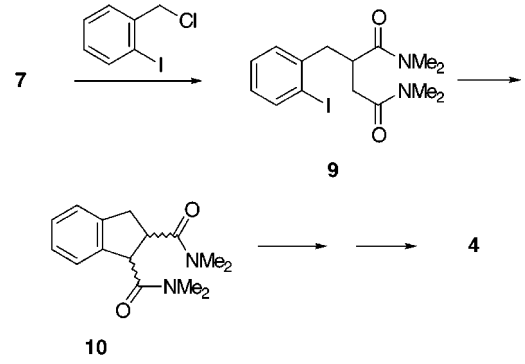


Irradiation of **3a** with near-UV light in the presence of 3 equiv of KNH_2 in liquid NH_3 resulted in rapid consumption of starting material to afford an inseparable 3:2 mixture of the desired cyclization product **4** and 2-benzylsuccinimide (**1a**, R = H), formed by reductive dehalogenation of **3a**. Similar treatment of glutarimide **3b** led only to slow production of 2-benzylglutarimide (**1b**, R = H) with no accompanying formation of the desired tricyclic product **5**. Attempts to induce possible aryne cyclization of **3a** with excess KNH_2 in liquid NH_3 without irradiation gave results essentially identical with those obtained under photostimulation (3:2 mixture of **4**:**1a** (R = H).

Scheme 1



Scheme 2



Preparation of Succinimido[3,4-*b*]indane (4). A report by Snieckus and co-workers,[10] describing the sequential α,α′-dialkylation of the dilithium salt, **7**, of *N*,*N*,*N*′,*N*′-tetramethylbutanediamide (**6**) (Scheme 1) appeared promising as a starting point for an alternative synthesis of **4**.

The success of this mixed dialkylation reaction is likely attributable to the greater reactivity of dianion **7** compared with the monoalkylated enolate **8**, which allows introduction of the first alkyl group without significant dialkylation until the second alkyl halide is added. Although the Snieckus group did not attempt to obtain monoalkylated products, it seemed possible that monalkylation might be achieved by treating dianion **7** with 1 equiv of an alkylating agent. Thus, our alternative synthetic strategy as outlined in Scheme 2 was based on monoalkylation of dianion **7** with 2-iodobenzyl chloride to give **9**, followed by cyclization, hydrolysis, and imidization. Although Rathke and Long[11] have accomplished the successful generation and monoalkylation of the lithium dienolate of diethyl succinate, we chose to use diamide **6**, anticipating that it would be less vulnerable

(4) Dewar, M. J. S.; Zoebisch, E. G.; Healy, E. F.; Stewart, J. J. P. *J. Am. Chem. Soc.* **1985**, *107*, 3902.

(5) (a) Campaigne, E.; Roelofs, W.; Weddleton, R. F. *J. Med Chem.* **1968**, *11*, 395. (b) Campaigne, E.; Yodice, R. *J. Heterocycl. Chem.* **1980**, *17*, 661. (c) Campaigne, E.; Yodice, R. *J. Heterocycl. Chem.* **1981**, *18*, 79. (d) Despite good anticonvulsant activity in clinical trials, **2** (X = carbonyl) caused undesirable psychological side effects see: Angrist, B. M., Gershon, S., Floyd, A. *Curr. Ther. Res.* **1968**, *10*, 237.

(6) Pathak, K. L.; Pathak, K. B. *J. Indian Chem. Soc.* **1961**, *38*, 253.

(7) For reviews on $S_{RN}1$ reactions see: (a) Rossi, R. A.; de Rossi, R. H. *Aromatic Substitution by the $S_{RN}1$ Mechanism*; ACS Monograph 178; American Chemical Society: Washington D. C., 1983. (b) Bowman, W. R. *Chem. Soc. Rev.* **1988**, *17*, 283. (c) Rossi, R. A.; Pierini, A. B.; Palacios, S. M. In *Advances in Free Radical Chemistry*; Tanner, D. D., Ed.; JAI Press: Greenwich, CT, 1990; Chapter 5, p 193. *J. Chem. Educ.* **1989**, *66*, 720. (d) Norris, R. K. In *Comprehensive Organic Synthesis*; Trost, B. M., Ed.; Pergammon: New York, 1991; Vol. 4, p 451. (e) Savéant, J.-M. *Tetrahedron* **1994**, *50*, 10117. (f) Rossi, R. A.; Pierini, A. B.; Penenory, A. B. In *The Chemistry of Functional Groups, Suppl. D, The Chemistry of Halides, Pseudo-halides and Azides*; Patai S., Rappoport, Z., Eds.; Wiley: New York, 1995; Chapter 24, p 1395.

(8) (a) Rossi, R. A.; Alonso, R. A. *J. Org. Chem.* **1980**, *45*, 1239. (b) Alonso, R. A.; Rodriguez, C. H.; Rossi, R. A. *J. Org. Chem.* **1989**, *54*, 5983. (c) Palacios, S. M.; Asis, S. E.; Rossi, R. A. *Bull. Soc. Chim. Fr.* **1993**, *130*, 111. (d) van Leeuwen, M.; McKillop, A. *J. Chem. Soc., Perkin Trans. 1* **1993**, 2433. (e) Wong, J.-W.; Natalie, K. J., Jr.; Nwokogu, G. C.; Pisipati, J. S.; Flaherty, P. T.; Greenwood, T. D.; Wolfe, J. F. *J. Org. Chem.* **1997**, *62*, 6152.

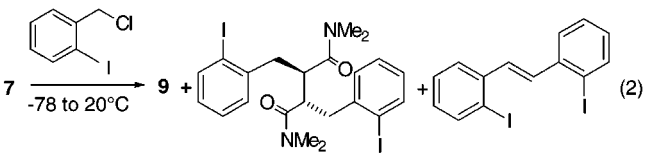
(9) (a) Wolfe, J. F.; Sleevi, M. C.; Goehring, R. R. *J. Am. Chem. Soc.* **1980**, *102*, 3646. (b) Goehring, R. R.; Sachdeva, Y. P.; Pisipati, J. S.; Sleevi, M. C.; Wolfe, J. F. *J. Am. Chem. Soc.* **1985**, *107*, 435. (c) Goehring, R. R. *Tetrahedron Lett.* **1992**, *33*, 6045.

(10) Mahalanabis, K. K.; Mumtaz, M.; Snieckus, V. *Tetrahedron Lett.* **1982**, *23*, 3971.

(11) Long, N. R.; Rathke, M. W. *Synth. Commun.* **1981**, *11*, 687.

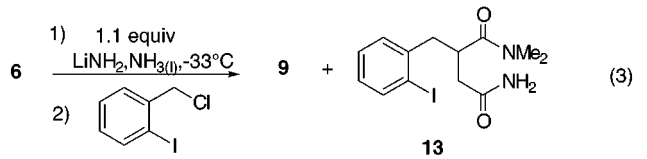
than the diester to side reactions during the subsequent cyclization step, which we planned to effect with an alkali metal amide in liquid NH_3.[9b]

When dianion **7**, generated from diamide **6** as described previously[10] (2.2 equiv of LDA in THF at −78 °C), was alkylated using 1 equiv of 2-iodobenzyl chloride at 0 °C, mostly dibenzylated *threo* product **11** (68%) was obtained along with lesser amounts of the desired **9** (12%) and stilbene derivative **12** (8%) (eq 2). By adding a cooled (−78 °C), dilute (6% w/v) THF solution of the halide slowly (30 min) to the dianion at −78 °C, the yield of **9** was improved to 34%, but dialkylation product **11** was still formed in 47% yield. When **6** was treated with 1 equiv of LDA in THF at −78 °C in an attempt to generate exclusively the monoenolate, subsequent alkylation afforded a mixture of **9** (38%), **11** (10%), and recovered halide (36%). Apparently, even under these conditions, proton exchange between the original monoenolate and newly formed **9** occurs competitively with alkylation of the original monoenolate. Owing to the chronic problem of dialkylation, the use of LDA as a base in the preparation of **9** was abandoned.



11 **12**

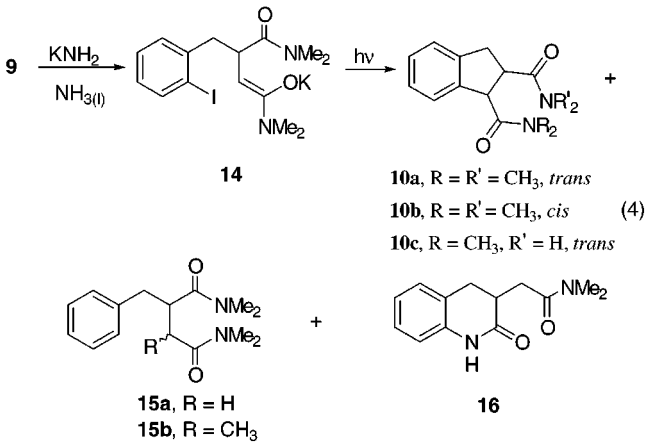
We then shifted our attention to finding a more satisfactory base/solvent system for the alkylation of diamide **6**. Since alkali metal amides in liquid NH_3 have been used successfully to generate the requisite enolates in alkylation reactions of certain *N*,*N*-disubstituted carboxamides,[12] we decided to investigate the feasibility of generating and alkylating the monoanion of **6** in this reaction system using $LiNH_2$ to suppress polyalkylation.[13] Thus, treatment of diamide **6** with 1.1 equiv of $LiNH_2$ in liquid NH_3 at −33 °C for 30 min, followed by the addition of 2-iodobenzyl chloride, afforded a mixture consisting of the desired **9** (46%), monoalkylated ammonolysis product **13**[14] (22%) and unreacted **6** (14%) (eq 3). When the deprotonation-alkylation sequence was carried out at lower temperature (−60 °C), an 88% yield of **9** was obtained virtually free of ammonolysis product **13**.[15]



13

With a satisfactory synthesis of **9** in hand, we next investigated its conversion to indane **10** (eq 4), which we anticipated might occur via an intramolecular $S_{RN}1$ reaction involving enolate **14**, formed by means of KNH_2 in liquid NH_3. To determine if synthetically useful concentrations of the required enolate **14**[16] could be prepared from **9** in this reaction system, preliminary methylation studies were carried out using 2-benzylbutanediamide **15a** as a model substrate.[17] When **15a** was treated with 1.1 equiv of KNH_2 in liquid NH_3 and the resulting solution quenched with methyl iodide, a mixture of *threo* and *erythro* methylation products **15b**[18] were obtained in 76% yield along with 23% of recovered **15a**. This regiospecificity implies selective formation of the less-substituted enolate.

Having established the efficacy of KNH_2 as a base for the generation of the required enolate, diamide **9** was treated with 3 equiv of KNH_2 in liquid NH_3 under photostimulation (eq 4). After 30 min of irradiation, **9** was completely consumed and the desired *trans*-cyclized product **10a** was isolated in 60% yield by MPLC. Also obtained were minor amounts of the corresponding *cis*-cyclized product **10b** (7%), *trans*-cyclized ammonolysis product **10c** (2%), hydrogenolysis compound **15a** (9%) and N-cyclized compound **16** (9%). Surprisingly, the cyclization reaction proceeded equally well with 3 equiv of KNH_2 in the absence of photostimulation to afford a 70% yield of indanes **10a**,**b** along with minor amounts of **10c** (3%), **15a** (2%), and **16** (13%) after only 5 min. Employment of as much as 8 equiv of KNH_2 had a negligible effect on the product distribution in either photostimulated or dark reactions. Attempts to avoid amide ion-derived products **10c** and **16** through the use of other bases were unsuccessful. Thus, attempted photocyclization of **9** with 3 equiv of t-BuOK in liquid NH_3 failed, presumably due to the inability of t-BuOK to generate the required enolate.[8a] The photostimulated reaction of **9** in the presence of 4 equiv of LDA in THF at −30 °C gave mostly unreacted **9** (72%) and only 10% of **10a** after 3 h of irradiation.



14

10a, R = R' = CH_3, *trans*
10b, R = R' = CH_3, *cis*
10c, R = CH_3, R' = H, *trans*

15a, R = H
15b, R = CH_3

16

The next step in the synthetic sequence leading to succinimide **4**, involved the hydrolysis of **10a**. By utilizing the mild procedure developed by Vaughn and Robbins,[19] and through careful choice of reaction conditions (1.1 equiv of Na_2O_2, 50 °C, 12 h), selective hydrolysis of the less-hindered carboxamido group of **10a** was achieved to afford a 77% yield of monoacid **17**[20] along with 5% of

(12) (a) Gassman, P. G.; Fox, B. L. *J. Org. Chem.* **1966**, *31*, 982. (b) Needles, H. L.; Whitfield, R. E. *J. Org. Chem.* **1966**, *31*, 989.

(13) Hampton, K. G.; Harris, T. M.; Hauser, C. R. *J. Org. Chem.* **1965**, *30*, 61.

(14) The regiochemistry for **13** was established from its ^1H NMR spectrum, mass spectral fragmentation pattern, and by X-ray crystallographic structure determination.

(15) In contrast, attempted alkylation of the monoanion of dimethyl succinate under identical conditions gave only Claisen condensation products and unreacted starting materials.

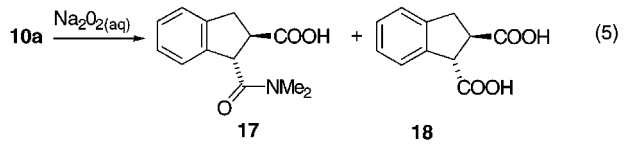
(16) The enolate structure is shown in the preferred *Z*-configuration based on stability studies of lithium *N*,*N*-dialkylcarboxamide enolates see: Heathcock, C. H.; Buse, C. T.; Kleschick, W. A.; Pirrung, M. C.; Sohn, J. E.; Lampe, J. *J. Org. Chem.* **1980**, *45*, 1066.

(17) Compound **15a** was prepared by alkylation of the enolate of **6** with benzyl chloride in a manner analogous to the preparation of **9**.

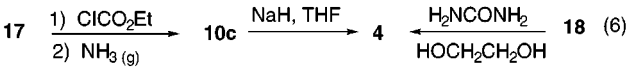
(18) The *threo*:*erythro* ratio of **15b** was ca. 12:1 and is very similar to that reported[10] for the dibenzylation of **6**.

(19) Vaughn, H. L.; Robbins, M. D. *J. Org. Chem.* **1975**, *40*, 1187.

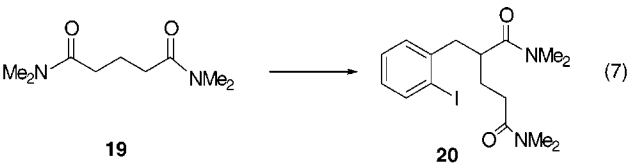
diacid **18** (eq 5). By comparison, complete hydrolytic conversion of **10a** to diacid **18** (88% isolated yield) was accomplished by heating an aqueous solution of **10a** in the presence of 3 equiv of Na_2O_2 at 70−75 °C for 24 h.



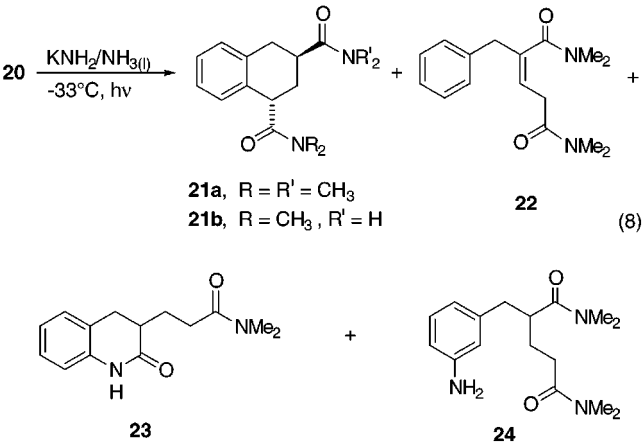
The target succinimide **4** was then prepared from **17** in 91% yield, as shown in eq 6. Conversion of **17** to the mixed primary/tertiary amide **10c**[21] was achieved by reaction with ethyl chloroformate at 0 °C and subsequent treatment of the intermediate mixed anhydride with gaseous NH_3 in situ. Refluxing a solution of **10c** with 2.5 equiv of NaH in THF for 1 h then afforded a nearly quantitative yield of **4**. More directly, but less satisfactorily, **4** was prepared by the reaction of diacid **18** with urea in refluxing ethylene glycol.[22]



Preparation of 1,2,3,4,5,6-Hexahydro-1,5-methano-3-benzazocine-2,4-dione (5). The successful preparation of succinimide **4** via the synthetic route just described prompted us to apply similar methodology to the synthesis of glutarimide **5**. Thus, alkylation of the lithium monoenolate of *N*,*N*,*N*′,*N*′-tetramethylpentanediamide (**19**), prepared by means of 1.1 equiv of $LiNH_2$ in liquid NH_3 with 2-iodobenzyl chloride, proceeded smoothly to afford monobenzylation product **20** in 87% yield (eq 7).



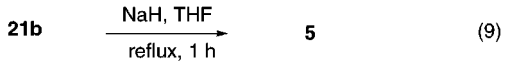
Treatment of **20** with 3 equiv of KNH_2 in liquid NH_3 and irradiation for 30 min led to formation of the product mixture shown in eq 8. As in the analogous cyclization of diamide **9** (eq 4), the corresponding trans C-cyclized



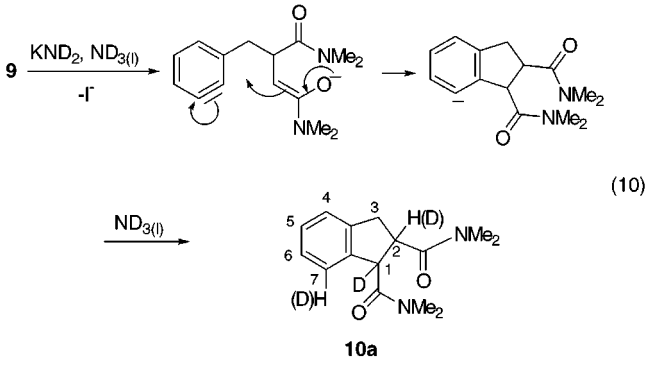
products **21a** (39%) and **21b**[20] (2%) and N-cyclized compound **23** (12%) were obtained, along with α,β-unsaturated diamide **22** (31%) and ring amination product **24** (3%).[23] The *trans* stereochemical assignment for **21a** was based on the results of an NOE experiment. Irradiation of the tertiary benzylic proton at C-1 produced enhancements in the intensities of the signals of the *N*-methyl protons of the carboxamido group at C-1 (4.4% and 2.3%), the C-2 methylene protons (6.7%), and the C-8 aryl proton (8.2%); however, the C-3 methine proton was completely unaffected.

When the cylization of **20** was carried out in the dark using 4 equiv of KNH_2 in liquid NH_3, complete consumption of **20** occurred within 5 min to afford **21a** (43%), **21b** (14%), **22** (12%), **23** (14%), and **24** (6%). Complete, in situ conversion of **21a** to the key synthetic intermediate, mixed amide **21b,** was accomplished by extending the cyclization reaction time from 5 to 45 min, in the dark, after which **21b** was isolated in 53% yield. It is interesting to note here that similar attempts to produce the penultimate intermediate, **10c**, for the synthesis of target succinimide **4** by treating indane derivative **10a** or its precursor, **9**, with excess KNH_2 in liquid NH_3 for several hours failed to produce synthetically useful amounts of **10c**.

Conversion of **21b** to glutarimide **5** proceeded in high yield (88%) under the same conditions employed for the preparation of **4** from **10c** (eq 9). Thus, the synthesis of **5** was accomplished in just three steps from starting diamide **19**.



Mechanistic Aspects of the Cyclization Reactions of 9 and 20. We have found evidence for the existence of competing and occasionally divergent mechanisms in the cyclization reactions of diamides **9** and **20**. These efficient processes proceed rapidly (2−5 min) in the dark at −33 °C with 3−4 equiv of KNH_2 and are not affected by up to 40 mol % of the radical scavenger, di-*tert*-butylnitroxide (DTBN),[24] thereby seeming to implicate mainly an aryne pathway.[25] To test this hypothesis, the cyclization of **9** was carried out in liquid ND_3 using 3 equiv of KND_2 (eq 10). Following isolation of deuterated



(20) The regiochemical and stereochemical assignments were unambiguously confirmed by X-ray crystallographic analysis.

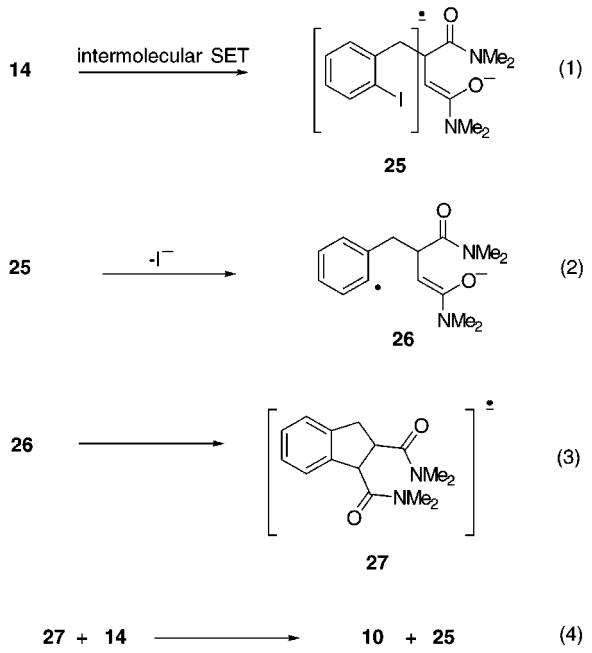
(21) This compound was identical in all respects with that obtained previously in the cyclization reaction of **9**.

(22) Kondrat′eva, G. Y.; Huang, C. H. *Zh. Priklad. Khim.* **1962**, *35*, 199.

(23) Although the corresponding ring amination product was never isolated from cyclization reactions of **9**, evidence for its presence in trace amounts was obtained by ^{1}H NMR.

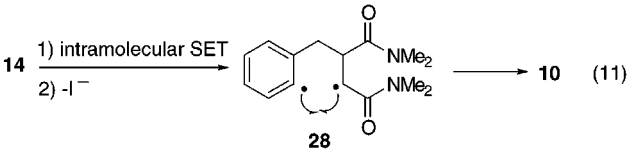
(24) (a) Hoffmann, A. K.; Feldman, A. M.; Gelblum, E.; Hodgson, W. G. *J. Am. Chem. Soc.* **1964**, *86*, 639. (b) Nelsen, S. F.; Bartlett, P. D. *J. Am. Chem. Soc.* **1966**, *88*, 143.

Scheme 3

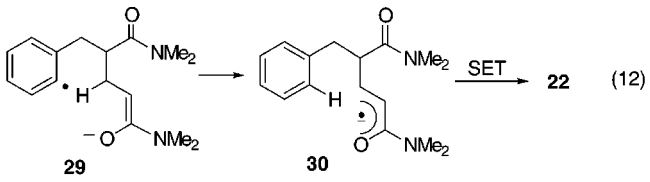


10a by MPLC, its ^{1}H NMR spectrum indicated the absence of the H-1 resonance at 5.01δ and integrated intensities of the H-2 and H-7 resonances at δ 4.18 and δ 7.01 corresponding to 0.5 and 0.4 deuteruim atom, respectively. These results strongly support the intermediacy of aryne in the cyclization reaction, but also allow for the operation of nonaryne processes.[9,26] Indeed, evidence for single electron transfer (SET) pathways may be found in the cyclization reactions of both **9** and **20**. For example, the presence of reduction product **15a** in the reaction of diamide **9** is indicative of the participation of a radical-chain $S_{RN}1$ process[27] (Scheme 3). Compound **15a** may result when intermediate aryl radical anion **26** reacts by hydrogen atom acquisition or when **26** undergoes further reduction to the corresponding phenyl anion followed by protonation.[27]

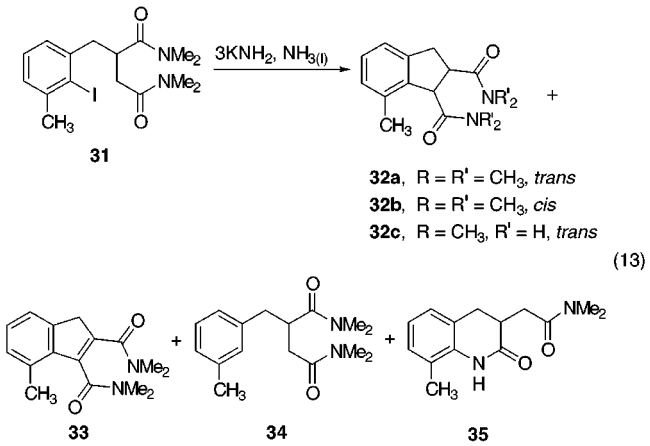
An alternative, nonchain SET mechanism initiated by intramolecular electron transfer may also play a part in the cyclization process (eq 11). Transfer of an electron from the carboxamide enolate to the aromatic ring in **14** would be facilitated by their close proximity. Subsequent fragmentation of the C−I bond would then yield diradical **28,** which would undergo ring closure via a radical coupling reaction. Evidence for similar competing nonchain radical coupling mechanisms in $S_{RN}1$ reactions has been previously observed.[28,29]



The production of α,*β*-unsaturated diamide **22** from diamide **20** provides indirect evidence for the presence of a radical-chain component in the cyclization milieu. In an analogous reaction, Semmelhack and Bargar[30] reported formation of α,*β*-unsaturated ketones in photoinduced $S_{RN}1$ cyclization reactions of certain haloaryl ketone enolates. Based on their study, it seems likely that **22** arises through a divergent, chain propagating pathway within the traditional $S_{RN}1$ mechanism. Thus, intermediate radical anion **29**, which is analogous to radical anion **26** formed in step 2 of Scheme 3, undergoes an intramolecular hydrogen atom transfer from the *β*-position of the enolate to the sp^2 radical site on the phenyl ring rather than an intramolecular cyclization reaction. Oxidation of the resulting radical anion, **30**, possibly by electron transfer to the aryl system of the enolate derived from **20**, would yield **22** and at the same time effect propagation of the chain (eq 12).



Additional evidence for operation of SET mechanisms in the cyclization processes was obtained from the successful cyclization of aryne-blocked diamide substrate, **31**, which occurred without the need for photostimulation to give the products shown in eq 13. Furthermore, this reaction, which would not be expected to proceed by the addition−elimination route of the S_NAr mechanism, was strongly inhibited by the addition of 40 mol % of DTBN. These findings make a compelling argument for a thermally initiated electron transfer cyclization and may imply[28] a preponderance of the typical radical-chain $S_{RN}1$ mechanism over radical coupling. The different responses to inhibition by DTBN in the reactions of unblocked **9** and blocked **31** may be accounted for by the fact that in the presence of inhibitor, cyclization of **9**, but not **31**, may divert entirely to a facile aryne pathway. The presence of α,*β*-unsaturated diamide **33** and the absence of its desmethyl analogue in the corresponding reaction of **9** may also be attributable to the difference in mechanistic



(25) Other indications of aryne participation in the cyclization reactions of **9** and **20** include the formation of ring amination product **24** and N-cyclized compounds **16** and **23**.

(26) Scamehorn, R. G.; Bunnett, J. F. *J. Org. Chem.* **1977**, *42*, 1449.

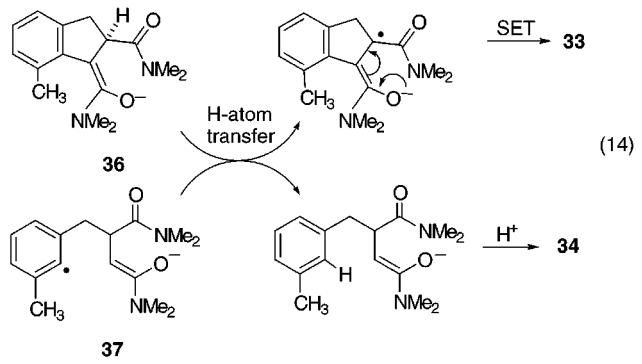
(27) Reductive dehalogenation of the substrate is a common side reaction which competes with substitution in $S_{RN}1$ reactions see: Santiago, A. N.; Stahl, A. E.; Rodriguez, G. L.; Rossi, R. A. *J. Org. Chem.* **1997**, *62*, 4406.

(28) Galli, C. *Tetrahedron* **1988**, *44*, 5205 and references therein.

(29) Ahbala, M.; Hapiot, P.; Houmam, A.; Jouini, M.; Pinson, J.; Savéant, J.-M. *J. Am. Chem. Soc.* **1995**, *117*, 11488.

(30) (a) Semmelhack, M. F.; Bargar, T. M. *J. Org. Chem.* **1977**, *42*, 1481. (b) Semmelhack, M. F.; Bargar, T. M. *J. Am. Chem. Soc.* **1980**, *102*, 7765.

options available in these two reactions. The greater involvement of SET pathways in the case of **31** would favor the formation of **33**, since it is likely formed by a SET process. Furthermore, since **33** and hydrogenolysis product **34** were obtained in comparable yields (11% and 16%, repectively), it seems reasonable to assume that these compounds may arise via a redox reaction involving enolate **36** and intermediate radical-anion **37**, as illustrated in eq 14. Finally, in the absence of aryne possibilities, the genesis of N-cyclized product **35** may be rationalized in terms of a SET mechanism for ring amination of **37** with amide ion,[31] followed by cyclization involving the nonenolized *N*,*N*-dimethyl carboxamide function.



(14)

Conclusions

In the present study, we have developed efficient routes to target compounds **4** and **5** based on several new discoveries concerning the chemistry of carboxamide enolates. For example, we have found a high-yield, general method for clean α-monoalkylation of tertiary amides derived from dicarboxylic acids which compares very favorably with similar alkylations of other dicarboxylic acid derivatives.[11,15,32] In addition, such amides have the potential of being superior to these other derivatives as synthetic intermediates because they are less susceptible to side reactions with strongly nucleophilic bases. The high reactivity of the enolates derived from carboxamides **9**, **20**, and **31** in intramolecular aromatic nucleophilic substitutions observed in this study, even in the absence of photostimulation, bring to such intermediates a previously unrecognized synthetic utility. In fact, the present cyclization of **20** to produce 1,2,3,4-tetrahydronaphthalene-1,3-dicarboxylic acid derivatives **21a**,**b** represents a rare synthesis of such 1,3-disubstituted tetralins.[33]

Experimental Section

General. Photostimulated reactions were carried out in a 36 mm × 420 mm double-jacketed cylindrical reaction vessel under N_2 using either a Rayonet RPR-100 or Rayonet RPR-240 photochemical reactor equipped with lamps emitting maximally at 350 nm. Dark reactions were performed in a 500 mL three-neck round-bottomed flask wrapped in a black cloth. Commercial anhydrous $NH_{3(l)}$ (Matheson) and $ND_{3(l)}$ (Cambridge Isotope Laboratories) were used directly from the tanks. *N*,*N*,*N*′,*N*′-Tetramethylbutanediamide (**6**) and *N*,*N*,*N*′,*N*′-tetramethylpentanediamide (**19**) were obtained via the reactions of the corresponding diacids with HMPA.[34] 2-Iodo-3-methylbenzyl bromide was prepared from 2,6-dimethyliodobenzene[35] according to the procedure of Bacon and Lindsay.[36] All other reagents were obtained commercially from Aldrich Chemical. ^{1}H NMR and ^{13}C NMR spectra were determined on either a Varian EM-390 or a Bruker WP 270 spectrophotometer using $CDCl_3$ as the solvent, unless otherwise indicated. Elemental analyses were performed by Atlantic Microlab, Inc., Norcross, GA. Medium-pressure liquid chromatography (MPLC) was carried out using Kiesel gel 60 (230−400 mesh) silica gel. Melting points are uncorrected.

2-(2-Iodobenzyl)succinimide (3a). This compound was prepared by a modification of the procedure described by Wolfe and Rogers.[37] Succinimide (0.50 g, 5 mmol) was added to a slurry of $LiNH_2$ prepared from lithium wire (0.43 g, 11 mmol) in 250 mL of liquid NH_3. The mixture was stirred while cooling to −60 °C in a dry ice−$CHCl_3$ bath over a period of 40 min. A solution of 2-iodobenzyl chloride (1.26 g, 5.0 mmol) in 30 mL of ether was then added dropwise over a period of 15 min. After stirring for an additional 30 min at −55 °C, standard workup followed by evaporation of the solvent gave a viscous oil from which *trans*-2,2′-diiodostilbene (**12**) (0.19 g, 18%), mp 127−128.5 °C, lit.[38] mp 128−128.5 °C, and **3a** (0.79 g, 50%), mp 132−133 °C, were obtained following MPLC with 2% MeOH in CH_2Cl_2; ^{1}H NMR: δ 2.55 (dd, 1H, J = 5.4, 18 Hz), 2.73 (dd, 1H, J = 8.8, 18 Hz), 2.94 (dd, 1H, J = 9.5, 14 Hz), 3.33 (m, 1H), 3.44 (dd, 1H, J = 5.0, 14 Hz), 6.96 (t, 1H, J = 7.6 Hz), 7.21 (d, 1H, J = 7.6 Hz), 7.32 (t, 1H, J = 7.5 Hz), 7.86 (d, 1H, J = 7.9 Hz), 8.63 (bs, 1H); ^{13}C NMR: δ 34.9, 41.0, 41.9, 100.9, 128.8, 129.0, 130.0, 140.0, 140.1, 176.5, 179.1. Anal. Calcd for $C_{11}H_{10}INO_2$: C, 41.90; H, 3.17; N, 4.44. Found: C, 42.01; H, 3.26; N, 4.52.

2-(2-Iodobenzyl)glutarimide (3b). Compound **3b** was prepared in 42% yield by a reported procedure,[37] mp 109−110 °C; ^{1}H NMR (DMSO-d_6): δ 1.69 (m, 2H), 2.08 (m, 1H), 2.19 (m, 1H), 2.61 (m, 1H), 2.73 (m, 1H), 2.92 (m, 1H), 6.97 (t, 1H, J = 7.0 Hz), 7.27 (m, 2H), 7.81 (d, 1H, J = 7.8 Hz), 8.42 (br s, 1H); MS: *m*/*z* (relative intensity) $(M + 1)^+$, 330 (100), 204 (70), 176 (18), 130 (45), 112 (25), 85 (15). Anal. Calcd for $C_{12}H_{12}INO_2$: C, 43.77; H, 3.65; N, 4.25. Found: C, 43.66; H, 3.68; N, 4.32.

Attempted Photocyclization of 3a and 3b with $KNH_2/NH_{3(l)}$. To a solution of KNH_2 prepared from potassium metal (0.47 g, 12 mmol) in 300 mL of liquid NH_3 was added succinimide **3a** (0.95 g, 3 mmol) as a solid, and the resulting slurry was stirred under irradiation for 1 h. The reaction mixture was poured onto excess solid NH_4Cl in a beaker, combined with a 50 mL ether rinse of the reaction of flask, and allowed to evaporate overnight. The yellow solid residue was dissolved in 50 mL of water, made acidic (pH = 1) by the addition of 2 M HCl, and extracted twice with 100 mL portions of CH_2Cl_2. The organic extracts were combined, extracted once with 50 mL of a saturated NaCl solution, dried, and concentrated to a light orange oil, 0.47 g. ^{1}H NMR analysis indicated that the oil mainly consisted of a 4:3

(31) Kim, J. K.; Bunnett, J. F. *J. Am. Chem. Soc.* **1970**, *92*, 7463.
(32) Kofron, W. G.; Wideman, L. G. *J. Org. Chem.* **1972**, *37*, 555.
(33) Araneo, S.; Fontana, F.; Minisci, F.; Recupero, F.; Serri, A. *Tetrahedron Lett.* **1995**, *36*, 4307.
(34) Kopecky, J.; Smejkal, J. *Chem. Ind.* **1966**, *36*, 1529.
(35) Jacobs, T. L.; Reed, R.; Pacovska, E. *J. Am. Chem. Soc.* **1951**, *73*, 4505.
(36) Bacon, R. G. R.; Lindsay, W. S. *J. Chem. Soc.* **1958**, 1375.
(37) Wolfe, J. F.; Rogers, T. G. *J. Org. Chem.* **1970**, *35*, 3600.
(38) Kelly, T. R.; Li, Q.; Bhushan, V. *Tetrahedron Lett.* **1990**, *31*, 161.

mixture of succinimido[3,4-*b*]indane (**4**) and 2-benzylsuccinimide (**1a**, R = H), respectively. Attempted separation of this mixture by TLC using a variety of solvents and solvent mixtures was unsuccessful. MPLC using 2% MeOH−CH_2Cl_2 resulted in the isolation of the pure 4:3 mixture of **4** and (**1a**, R = H) respectively, as a pale yellow semisolid, 0.39 g, which leads to calculated yields of 0.22 g (40%) for **4** and 0.17 g (30%) for **1a** (R = H). The analogous cyclization reaction of glutarimide **3b** (0.99 g, 3 mmol) returned only unreacted **3b** (0.79 g, 80%) isolated as a light brown solid which was insoluble in the aqueous or CH_2Cl_2 layers during the usual workup and 2-benzylglutarimide (**1b**, R = H) (0.05 g, 8%) from concentration of the CH_2Cl_2 layer, mp 136−140 °C, lit.[37] mp 142−144 °C.

2-(2-Iodobenzyl)-*N,N,N′,N′*-tetramethylbutanediamide (9). A. Via Alkylation of *N,N,N′,N′*-Tetramethylbutanediamide (6) Using LDA in THF at −78 °C. LDA was prepared by the slow addition of *n*-BuLi (9.8 mL of a 2.25 M solution in hexane, 22 mmol) to a solution of diisopropylamine (2.22 g, 22 mmol) in 60 mL of dry THF under N_2 at 0 °C. After stirring for 15 min, the pale yellow solution was cooled to −78 °C in a dry ice−acetone bath. A solution of **6** (1.72 g, 10 mmol) in 40 mL of THF was then added, and the resulting yellow solution of the dianion was stirred for 30 min. 2-Iodobenzyl chloride (2.53 g, 10 mmol) dissolved in 40 mL of THF and cooled to −78 °C in a jacketed pressure equalizing funnel with dry ice−acetone was added dropwise over a period of 30 min. The resulting solution was stirred for an additional 20 min at −78 °C and then slowly warmed to room temperature. The reaction mixture, now containing precipitated LiCl, was quenched by the addition of 10 mL of a saturated solution of NH_4Cl. The organic layer was separated and the aqueous layer extracted with 2 × 50 mL portions of ether. The combined organic layers were dried ($MgSO_4$) and concentrated to yield a viscous brown oil, which was chromatographed initially with CH_2Cl_2 as the eluent to remove stilbene derivative **12** (0.12 g, 10%) and then with 2% MeOH in CH_2Cl_2 to yield first *threo*-2,3-bis(2-iodobenzyl-*N,N,N′,N′*-tetramethylbutanediamide) (**11**) (1.49 g, 47%), as a colorless solid, mp 150−152 °C, which was recrystallized from ether/hexane, mp 159−160 °C. Further elution gave **9** (1.32 g, 34%) as a viscous, pale yellow oil which crystallized when triturated with ether. Recrystallization from ether in the cold afforded pure **9**, mp 82−83 °C. ^{1}H NMR for **11**: δ 2.38 (s, 6H), 2.64 (s, 6H), 3.10 (m, 4H), 3.56 (m, 2H), 6.92 (t, 2H, J = 7.5 Hz), 7.15 (d, 2H, J = 7.6 Hz), 7.23 (t, 2H, J = 7.5 Hz), 7.82 (d, 2H, J = 7.8 Hz);^{13} C NMR: δ 35.1, 37.0, 42.2, 44.0, 100.7, 127.9, 128.2, 130.7, 139.1, 141.8, 173.9; MS: *m/z* (relative intensity) M^+, 604 (1.2), 559 (6), 547 (10), 314 (25), 259 (85), 214 (20), 128 (20), 115 (25), 91 (20), 72 (100). Anal. Calcd for $C_{22}H_{26}I_2N_2O_2$: C, 41.51; H, 4.09; N, 4.40. Found: C, 41.55; H, 4.17; N, 4.46. ^{1}H NMR for **9**: δ 2.32 (dd,1H, J = 3.2, 16 Hz), 2.76 (s, 3H), 2.88 (s, 3H), 2.92 (s, 3H), 2.93 (m, 2H), 3.06 (s, 3H), 3.10 (dd, 1H, J = 11, 16 Hz), 3.65 (m, 1H), 6.90 (t, 1H, J = 7.5 Hz), 7.15 (d, 1H, J = 7.6 Hz), 7.22 (t, 1H, J = 7.5 Hz), 7.80 (d, 1H, 7.6 Hz); ^{13}C NMR: δ 35.1, 35.5, 36.9, 37.0, 37.1, 37.2, 43.5, 100.5, 128.0, 128.5, 130.5, 139.5, 141.5, 171.0, 174.3; MS: *m/z* (relative intensity) M^+, 388 (3), 344 (20), 316 (35), 302 (40), 272 (15), 261 (100), 217 (30), 188 (40), 174 (20), 144 (18), 115 (33), 84 (48), 72 (70). Anal. Calcd for $C_{15}H_{21}IN_2O_2$: C, 46.39; H, 5.41: I, 32.73; N, 7.22. Found: C, 46.49; H, 5.47; I, 32.65; N, 7.19.

B. Via Alkylation of 6 Using $LiNH_2$ in $NH_{3(l)}$ at −60 °C. To a slurry of $LiNH_2$ prepared from lithium wire (0.15 g, 22 mmol) in 300 mL of liquid NH_3 at −65 °C was added rapidly a solution of **6** (3.44 g, 20 mmol) in 30 mL of THF under N_2. The reaction temperature rose to ca. −60 °C and was maintained at that temperature with a dry ice−acetone bath as the mixture was stirred for 30 min. A solution of 2-iodobenzyl chloride (5.05 g, 20 mmol) in 30 mL of THF was then added dropwise over a period of 15 min, and the reaction mixture became clear. The solution was allowed to warm to −33 °C and then poured slowly onto solid excess NH_4Cl in a beaker. The NH_3 was evaporated, and the remaining THF solution was decanted from the solid residue, which was dissolved in 50 mL of water. The aqueous solution was extracted with 2 × 100 mL portions of ether, and the combined organic solutions were dried ($MgSO_4$) and concentrated on a rotary evaporator to give 7.25 g of a pale yellow viscous oil. MPLC using CH_2Cl_2 as the eluent resulted in the recovery of 0.35 g (7%) of unreacted halide. The eluent was then changed to 5% MeOH in CH_2Cl_2, and **9** (6.82 g, 88%) was eluted as a nearly colorless oil which crystallized on standing, mp 80−82 °C.

When the above reaction was carried out at −33 °C, an oily brown residue was obtained following concentration of 2 × 100 mL CH_2Cl_2 extracts of the reaction mixture. Upon trituration of this oil with ether, a white solid separated which after recrystallization from CH_2Cl_2/hexane gave 1.58 g (22%) of 3-(*N,N*-dimethylcarboxamido)-4-(2-iodophenyl)butanamide (**13**) as white crystals, mp 163−164 °C; ^{1}H NMR: δ 2.35 (dd, 1H, J = 4.0, 15 Hz), 2.71 (s, 3H), 2.78 (m, 1H), 2.82 (s, 3H), 2.92 (m, 2H), 3.67 (m, 1H), 5.55 (br s, 1H), 6.10 (br s, 1H), 6.92 (t, 1H, J = 7.5 Hz), 7.14 (d, 1H, J = 7.6 Hz), 7.24 (t, 1H, J = 7.5 Hz), 7.81 (d, 1H, J = 7.8 Hz); ^{13}C NMR: δ 35.5, 37.1, 37.5, 38.6, 43.6, 100.5, 128.1, 128.4, 130.4, 139.7, 141.3, 174.0, 174.3; MS: *m/z* (relative intensity) M^+ 360 (0.9), 302 (55), 233 (100), 217 (30), 188 (40), 174 (25), 144 (20), 115 (35), 84 (45), 72 (70). Anal. Calcd for $C_{13}H_{17}IN_2O_2$: C, 43.33; H, 4.72; I, 35.28; N, 7.78. Found: C, 43.40; H, 4.78; I, 35.20; N, 7.70. Evaporation of the ethereal solution gave an oil whose ^{1}H NMR spectrum indicated it to be a mixture of mostly **9** along with unreacted **6**. Separation by MPLC using 5% MeOH in CH_2Cl_2 afforded initially **9** (3.57 g, 46%) followed by **6** as a colorless liquid which solidified after drying in vacuo, 0.49 g (14%).

2-Benzyl-*N,N,N′,N′*-tetramethylbutanediamide (15a). This compound was prepared by a procedure strictly analogous to that described previously for the preparation of **9** from **6** using 1.1 equiv of $LiNH_2$ in $NH_{3(l)}$ at −60 °C. The reaction of $LiNH_2$, prepared from lithium wire (0.15 g, 22 mmol) in 300 mL of liquid NH_3, **6** (3.44 g, 20 mmol), and benzyl chloride (2.53 g, 20 mmol) at −60 °C gave 5.22 g of a viscous yellow oil which after MPLC with EtOAc afforded 0.31 g (12%) of unreacted benzyl chloride followed by 4.36 g (83%) of essentially pure **15a** as a nearly colorless oil. An analytical sample was prepared by distillation at 130−132 °C/0.04 mm. ^{1}H NMR: δ 2.29 (dd, 1H, J = 3.7, 14 Hz), 2.68 (dd, 1H, J = 7.1, 14 Hz), 2.78 (s, 3H), 2.85 (s, 3H), 2.87 (s, 3H), 2.98 (s, 3H), 2.98 (m, 2H), 3.51 (m, 1H), 7.22 (m, 5H); ^{13} C NMR: δ 35.6, 35.7, 36.2, 36.6, 36.9, 38.7, 40.1, 124.3, 127.1, 127.9, 128.8, 129.6, 141.3, 172.8, 173.8; MS: *m/z* (relative intensity) M^+, 262 (25), 218 (22), 190 (15), 176 (83), 145 (28), 131 (19), 117 (14), 91 (22), 72 (100). Anal. Calcd for $C_{15}H_{22}N_2O_2$: C, 68.70; H, 8.40; N, 10.69. Found: C, 68.73; H, 8.45; N, 10.76.

2-Benzyl-3-methyl-*N,N,N′,N′*-tetramethylbutanediamide (15b). A solution of **15a** (1.31 g, 5.0 mmol) in 15 mL of THF was added rapidly via syringe to a KNH_2 solution prepared from potassium (0.22 g, 5.5 mmol) in 150 mL of liquid NH_3. After stirring for 15 min, a solution of CH_3I (0.78 g, 5.5 mmol) in 15 mL of THF was added, and the resulting solution was stirred for 15 min. The reaction mixture was then poured onto excess NH_4Cl in a beaker, and the NH_3 and THF were evaporated on a steam bath. The solid residue was partitioned between water (20 mL) and ether (100 mL), and the ethereal layer was separated, dried over $MgSO_4$, and concentrated to a yellow oil. TLC analysis using ether as the eluent indicated the oil to be a mixture of mainly one product along with some unreacted **15a**. Column chromatography with ether gave 0.97 g (70%) of the *threo* isomer of **15b** as a pale yellow oil which solidified on standing, mp 70−72 °C. Recrystallization from ether−hexane gave pure **15b** as colorless crystals, mp 73−74 °C. Further elution with EtOAc afforded 0.38 g of a yellow oil which was a 4:1 mixture of **15a**:*erythro* isomer of **15b** by ^{1}H NMR analysis. The calculated yield of **15a** was 0.30 g (23%) and for the *erythro* isomer of **15b**, 0.08 g (6%). Upon rechromatography with ether, a pure sample of the *erythro* isomer as a colorless oil was obtained for ^{1}H NMR characterization. ^{1}H NMR for *threo*-**15b**: δ 1.03 (d, 3H, J = 6.7 Hz), 2.45 (s, 3H), 2.73 (d, 2H, J = 7.3 Hz), 2.79 (s, 3H), 3.02 (s, 3H), 3.13 (s, 3H), 3.21 (m, 1H), 3.39 (m, 1H), 7.18 (m, 5H). Anal. Calcd for $C_{16}H_{24}N_2O_2$: C, 69.53; H, 8.75; N, 10.14. Found: C, 69.43; H, 8.78; N, 10.10. ^{1}H NMR for *erythro*-**15b**: δ 1.26 (d, 3H, J = 6.5 Hz), 2.40 (s, 3H), 2.68 (s, 3H), 2.83 (d, 2H, J = 7.2 Hz), 2.99 (s, 3H), 3.10 (s, 3H), 3.20 (m, 2H), 7.17 (m, 5H).

Photoinduced Cyclization of 9. A solution of KNH_2 was prepared from potassium metal (2.05 g, 52.5 mmol) in 250 mL of liquid NH_3. This solution was irradiated as a solution of **9** (6.80 g, 17.5 mmol) in 50 mL of THF was added via syringe, and irradiation was continued for a period of 30 min. The dark red reaction mixture was then quenched by pouring onto excess solid NH_4Cl in a beaker, and the NH_3 and THF were evaporated on a steam bath. The resulting solid-gummy mixture was partitioned between CH_2Cl_2 (100 mL) and water (50 mL) and transferred to a separatory funnel. The organic layer was separated and the aqueous layer extracted with 2 × 100 mL portions of CH_2Cl_2. The combined organic layers were dried ($MgSO_4$) and concentrated to give 4.49 g of a dark orange viscous oil which was subjected to flash chromatographic separation. A mixture of *trans*-1,2-bis(*N*,*N*-dimethylcarboxamido)indane (**10a**) and 3-(*N*,*N*-dimethylacetamido)-3,4-dihydro-2(1*H*)-quinolone (**16**) was eluted first with 1:1 CH_2Cl_2−EtOAc as a pale yellow oil. Trituration with ether caused **16** to crystallize as a nearly colorless solid, 0.37 g (9%), mp 172−73 °C, which after recrystallization from EtOAc afforded colorless crystals, mp 173−174 °C. Evaporation of the ether gave 2.73 g (60%) of essentially pure **10a**, by ^{1}H NMR, which solidified on cooling. Recrystallization from ether−hexane gave colorless crystals of **10a**, mp 96−97 °C. The eluent was changed to EtOAc, and **15a**, contaminated with a small amount of *trans*-1-(*N*,*N*-dimethylcarboxamido)indane-2-carboxamide (**10c**), was eluted next. Kugelrohr distillation of this pale yellow oil at 140 °C/0.1 mm afforded 0.40 g (9%) of pure **15a** as a colorless oil. Further gradient elution with 5−10% MeOH−EtOAc gave 0.08 g (2%) of **10c** as a tan solid followed by 0.32 g (7%) of *cis*-1,2-bis(*N*,*N*-dimethylcarboxamido)indane (**10b**), mp 145−148 °C. Analytically pure samples of **10c** and **10b** were prepared by recrystallization from EtOAc and ether−EtOAc, respectively; **10c** was obtained as fine colorless needles, mp 166−167 °C, and **10b** as pale yellow plates, mp 149−150 °C. ^{1}H NMR for **10a**: δ 2.98 (s, 3H), 3.05 (dd, 1H, J = 8.2, 14 Hz), 3.07 (s, 3H), 3.16 (s, 3H), 3.28 (dd, 1H, J = 10,14 Hz), 3.31 (s, 3H), 4.18 (ddd, 1H, J = 8.2, 9.2, 10 Hz), 5.01 (d, 1H, J = 9.2 Hz), 7.01 (m, 1H), 7.18 (m, 3H); ^{13}C NMR: δ 35.6, 35.7, 35.8, 37.2, 37.6, 46.6, 50.4, 122.8, 124.3, 126.8, 127.3, 141.2, 141.4, 172.7, 173.4; MS: *m*/*z* (relative intensity) M^+, 260 (5), 215 (85), 188 (20), 143 (13), 115 (33), 72 (100). Anal. Calcd for $C_{15}H_{20}N_2O_2$: C, 69.20; H, 7.74; N, 10.76. Found: C, 69.26; H, 7.74; N, 10.71. ^{1}H NMR for **10b**: δ 2.92 (s, 3H), 2.96 (s, 3H), 3.08 (s, 3H), 3.10 (dd, 1H, J = 8, 15 Hz), 3.13 (s, 3H), 3.73 (m, 1H), 3.88 (dd, 1H, J = 10, 15 Hz), 4.63 (d, 1H, J = 8.4 Hz), 7.22 (m, 4H); ^{13}C NMR: δ 35.9, 36.2, 36.9, 37.6, 37.9, 47.5, 50.7, 123.7, 124.8, 126.6, 127.5, 141.3, 143.5, 171.8, 172.6; MS: *m*/*z* (relative intensity) M^+, 260 (3), 215 (28), 188 (6), 143 (4), 115 (31), 72 (100). Anal. Calcd for $C_{15}H_{20}N_2O_2$: C, 69.20; H, 7.74; N, 10.76. Found: C, 69.07; H, 7.70; N, 10.66. ^{1}H NMR for **10c**: δ 3.10 (s, 3H), 3.13 (dd, 1H, J = 8.5, 14 Hz), 3.27 (s, 3H), 3.31 (dd, 1H, J = 10, 14 Hz), 3.85 (ddd, 1H, J = 8.5, 10, 10 Hz), 4.59 (d, 1H, J = 10 Hz), 5.48 (br s, 1H), 6.20 (br s, 1H), 7.00 (m, 1H), 7.19 (m, 3H); ^{13}C NMR: δ 35.2, 36.1, 37.7, 49.4, 51.0, 122.9, 124.7, 126.7, 127.5, 140.4, 142.1, 172.4, 175.7; MS: *m*/*z* (relative intensity) M^+, 232 (23), 215 (20), 188 (49), 160 (29), 115 (92), 91 (21), 72 (100). Anal. Calcd for $C_{13}H_{16}N_2O_2$: C, 67.22; H, 6.94; N, 12.06. Found: C, 66.98; H, 6.92; N, 11.93. ^{1}H NMR for **16**: δ 2.40 (dd, 1H, J = 8,16 Hz), 2.86 (m, 1H), 2.98 (s, 3H), 3.05 (s, 3H), 3.15 (m, 3H), 6.73 (d, 1H, J = 7.8 Hz), 6.95 (t, 1H, J = 7.5 Hz), 7.17 (m, 2H), 7.95 (br s, 1H); ^{13}C NMR: δ 31.4, 33.1, 35.6, 36.8, 37.2, 115.1, 122.9, 123.7, 127.3, 128.1, 137.1, 170.9, 173.4; MS: *m*/*z* (relative intensity) M^+, 232 (7), 188 (5), 158 (8) 146 (100), 130 (18), 87 (53), 72 (22). Anal. Calcd for $C_{13}H_{16}N_2O_2$: C, 67.22; H, 6.94; N, 12.06. Found: C, 67.13; H, 6.97; N, 12.10.

Hydrolysis of 10a with Aqueous Na_2O_2. A. *trans*-1-(*N*,*N*-Dimethylcarboxamido)indane-2-carboxylic acid (17). Solid sodium peroxide (0.88 g of 93%, 10.5 mmol) was added portionwise to a solution of **10a** (2.48 g, 9.52 mmol) in 35 mL of water with stirring. After the peroxide had dissolved, the solution was heated in a water bath at 50 °C for 12 h and then cooled and extracted twice with 20 mL portions of ether by vigorous stirring to remove unreacted **10a**, 0.20 g (8%). The aqueous solution was then cooled in an ice bath and acidified to pH = 1 with 2 M HCl causing a yellow gummy solid to precipitate. Addition of 40 mL of CH_2Cl_2 resulted in the dissolution of the gum, leaving a solid which was insoluble in either layer. The solid was collected by filtration and determined to be *trans*-indane-1,2-dicarboxylic acid (**18**),[39] 0.10 g (5%), mp 222−226 °C. The organic and aqueous layers were separated, and the organic layer was combined with 2 × 50 mL CH_2Cl_2 extractions of the aqueous layer. The combined organic extracts were dried ($MgSO_4$), and the CH_2Cl_2 was removed at the rotary evaporator to give 1.71 g (77%) of **17** as a white solid, mp 198−202 °C. Recrystallization from CH_2Cl_2−ether afforded tiny, colorless crystals of **17**, mp 201−202 °C; ^{1}H NMR: δ 3.11 (s, 3H), 3.20 (dd, 1H,

(39) Cook, J. W.; Preston, R. W. G. *J. Chem. Soc.* **1944**, 553.

J = 9.2, 16 Hz), 3.31 (s, 3H), 3.41 (dd, 1H, J = 9.0, 16 Hz), 4.01 (ddd, 1H, J = 8.8, 9.0, 9.2 Hz), 4.70 (d, 1H, J = 8.8 Hz), 7.04 (d, 1H, J = 6.7 Hz), 7.20 (m, 3H); ^{13}C NMR: δ 35.6, 35.8, 36.2, 46.8, 50.7, 124.9, 125.1, 126.7, 127.4, 140.6, 141.5, 173.6, 174.1; MS: *m/z* (relative intensity) M^+, 233 (12), 188 (9), 161 (2), 115 (30), 72 (100). Anal. Calcd for $C_{13}H_{15}NO_3$: C, 66.95; H, 6.44; N, 6.01. Found: C, 66.87; H, 6.39; N, 5.92.

B. *trans*-Indane-1,2-dicarboxylic Acid (18). A solution containing **10a** (0.32 g, 1.23 mmol) and sodium peroxide (0.31 g of 93%, 3.69 mmol) in 10 mL of water was heated at 70−75 °C for 24 h, cooled to room temperature, and poured onto 10 mL of ice-cold 2 M HCL with stirring. The precipitated white solid was filtered, washed twice with 20 mL portions of ice−water, and air-dried to yield 0.22 g (88%) of pure trans diacid **18**, mp 227−228 °C, lit.[39] mp 228 °C; ^{1}H NMR (acetone-d_6): δ 3.20 (dd, 1H, J = 8.2, 16 Hz), 3.39 (dd, 1H, J = 9.3, 16 Hz), 3.78 (ddd, 1H, J = 8.2, 9.3, 16 Hz), 4.23 (d, 1H, J = 7.8 Hz), 7.25 (m, 3H), 7.47 (m, 1H); ^{13}C NMR: δ 35.9, 46.9, 53.7, 125.0, 125.1, 127.7, 128.4, 140.2, 142.5, 173.6, 175.1; MS: *m/z* (relative intensity) M^+, 206 (1), 188 (16), 160 (50), 133 (10), 116 (100), 91 (14), 77 (12), 63 (15).

Preparation of 10c from 17. To a solution of ethyl chloroformate (0.69 g, 6.39 mmol) in 20 mL of CH_2Cl_2 cooled to 0 °C in an ice bath was added dropwise a solution of **17** (1.49 g, 6.39 mmol) and triethylamine (0.71 g, 7.03 mmol) in 100 mL of CH_2Cl_2. Triethylamine hydrochloride precipitated immediately, and the mixture was stirred at 0 °C for 1 h. Anhydrous NH_3 was then bubbled through the reaction mixture for 15 min. The cooling bath was removed, and 2 M HCl was added with vigorous stirring until pH = 1 was reached. The CH_2Cl_2 layer was separated and combined with a 50 mL of CH_2Cl_2 extract of the aqueous layer. The combined CH_2Cl_2 solutions were dried ($MgSO_4$), and the CH_2Cl_2 was removed at the rotary evaporator to yield a light tan oil which solidified when triturated with ether. The solid was filtered and washed twice with 10 mL portions of cold ether to give 1.45 g of a pale tan solid, the ^{1}H NMR of which indicated it to be **10c** containing a small amount of urethane, which was removed by heating at 70 °C/0.05 mm in a sublimator. The urethane which condensed on the coldfinger as a white solid amounted to 0.05 g leaving 1.40 g (95%) of pure **10c**. The ^{1}H NMR of this material was identical with that obtained in the cyclization reaction of **9**.

Succinimido[3,4-*b*]indane (4). A. From 10c. Sodium hydride (0.60 g of a 60% dispersion in mineral oil, 15.1 mmol) was weighed into a 200 mL round-bottomed flask, and the mineral oil was removed by washing twice with 20 mL of hexane followed by decantation. The hydride was covered with 20 mL of dry THF, a THF solution of **10c** (1.40 g, 6.03 mmol) was added in a slow stream, and the mixture was heated slowly to reflux under N_2. Hydrogen gas evolution became vigorous on heating, and refluxing was continued for 1 h. The flask was then cooled in an ice bath, the excess hydride was quenched with a few drops of isopropyl alcohol, and the reaction mixture was brought to pH = 1 by the dropwise addition of 2 M HCl. The THF solution was separated, and the aqueous layer was extracted twice with 50 mL portions of CH_2Cl_2. The combined organic layers were dried ($MgSO_4$) and concentrated on a rotary evaporator to a yellow, viscous oil, which when triturated with 5 mL of ether, gave 1.08 g (96%) of **4** as a white solid, mp 140−141 °C, lit.[6] mp 170−172 °C; ^{1}H NMR: δ 3.42 (m, 2H), 3.67 (m, 1H), 4.36 (d, 1H, J = 7.9 Hz), 7.28 (m, 3H), 7.55 (d, 1H, J = 6.2 Hz), 7.99 (br s, 1H); ^{13}C NMR: δ 34.4, 45.0, 53.0, 125.1, 127.6, 128.8, 130.2, 136.9, 141.1, 177.5, 180.2; MS: *m/z* (relative intensity) M^+, 187 (45), 116 (100), 115 (35), 84 (25), 63 (10), 58 (12). Anal. Calcd for $C_{11}H_9NO_2$: C, 70.58; H, 4.81; N, 7.49. Found: C, 70.63; H, 4.89; N, 7.53. **B. From 18.** Urea (0.18 g, 3.0 mmol) and diacid **18** (0.20 g, 0.97 mmol) were weighed in a 25 mL round-bottomed flask followed by the addition of 5 mL of ethylene glycol. The mixture was stirred and heated at 190−195 °C in an oil bath for 30 min and cooled, and the ethylene glycol was Kugelrohr distilled at 90 °C/0.10 mm. The brown residue was chromatographed with ether, and the first fraction off the column was collected and concentrated to a pale yellow oil which solidified on standing to give 0.09 g (50%) of **4**, mp 138−140 °C.

2-(2-Iodobenzyl)-*N,N,N′,N′*-tetramethylpentanediamide (20). This compound was prepared in the same manner as that described previously for the alkylation of **6** using 1.1 equiv of $LiNH_2$ in liquid NH_3 at −60 °C. Thus, reaction of **19** (7.45 g, 40.0 mmol) with 2-iodobenzyl chloride (10.10 g, 40.0 mmol) gave 15.7 g of a viscous, orange oil, which after removal of unreacted halide (0.84 g, 8%) by MPLC with 1:1 hexanes−EtOAc afforded, upon subsequent elution with 10% MeOH−EtOAc, 14.05 g (87%) of **20** as a nearly colorless, viscous oil; ^{1}H NMR: δ 1.85 (m, 1H), 2.04 (m, 1H), 2.21 (m, 1H), 2.45 (m, 1H), 2.62 (s, 3H), 2.80 (s, 3H), 2.91 (s, 3H), 2.93 (m, 2H), 2.98 (s, 3H), 3.28 (m, 1H), 6.87 (m, 1H), 7.19 (m, 2H), 7.78 (dd, 1H, J = 1.0, 7.8 Hz); ^{13}C NMR: δ 27.7, 30.6, 35.5, 37.0, 37.2, 40.0, 43.5, 100.9, 128.0. 128.1, 130.5, 139.5, 142.0, 172.5, 174.6; MS: *m/z* (relative intensity) M^+, 402 (7), 358 (8), 329 (20), 316 (18), 302 (32), 275 (40), 230 (15), 217 (15), 188 (22), 176 (20), 149 (15), 140 (22), 131 (10), 116 (15), 100 (12), 84 (100), 72 (90), 55 (20). Anal. Calcd for $C_{16}H_{23}IN_2O_2$: C, 47.76; H, 5.72; N, 6.96. Found: C, 47.83; H, 5.77; N, 6.90.

Photoinduced Cyclization of 20. To an irradiated solution of KNH_2 prepared from potassium (1.17 g, 30 mmol) in 250 mL of liquid NH_3 was added a solution of **20** (4.02 g, 10 mmol) in 40 mL of THF via syringe. Irradiation was continued for 30 min, and the resulting orange solution was poured onto excess solid NH_4Cl in a beaker. A 100 mL ether rinse of the reaction vessel was added to the reaction solution, and the NH_3 was evaporated on a steam bath. The resulting ethereal solution was decanted from the solid residue which was then dissolved in 50 mL of water and extracted with 2 × 100 mL portions of CH_2Cl_2. The combined organic solutions were extracted with 25 mL of 2 M $NaHSO_3$ to remove I_2 and 50 mL of water, dried ($MgSO_4$), and concentrated to a pale yellow oil, 2.78 g, which was subjected to flash chromatography. The first and major fraction, eluted with 1:1 ether−EtOAc, was obtained as a pale yellow oil (1.70 g) and was identified by ^{1}H NMR as a 1:1 molar mixture of *trans*-1,3-bis(*N*,*N*-dimethylcarboxamido)-1,2,3,4-tetrahydronaphthalene (**21a**) and 1,3-bis(*N*,*N*-dimethylcarboxamido)-4-phenyl-2-butene (**22**), respectively. A second fraction was eluted next with EtOAc as a nearly colorless oil (0.52 g), which when triturated with ether gave 0.29 g (12%) of 3-(*N*,*N*-dimethyl-β-propanamido)-3,4-dihydro-2(1*H*)-quinolone (**23**) as a white solid, mp 143−144 °C after recrystallization from EtOAc. Concentration of the ether solution gave 0.22 g of nearly pure **21a**. Further elution with 5% MeOH−EtOAc afforded *trans*-1-(*N*,*N*-dimethylcarboxamido)-1,2,3,4-tetrahydronaphthalene-3-

carboxamide (**21b**), 0.06 g (2%), mp 181−183 °C. After recrystallization from EtOAc, pale yellow crystals of **21b** were obtained, mp 184−185 °C. A final fraction was collected as an orange oil, 0.12 g, when the eluent was changed to 15% MeOH−EtOAc. After Kugelrohr distillation at 185 °C/0.10 mm, 0.10 g (3%) of 2-(3-aminobenzyl)-*N*,*N*,*N*′,*N*′-tetramethylpentanediamide (**24**) was obtained as a yellow oil. Partial separation of the mixture of **21a** and **22** was achieved by rechromatography with ether. Pure **21a**, 0.30 g, obtained in the first chromatographic fractions, crystallized from ether−hexane in fan shaped crystals, mp 83−84 °C. Intermediate fractions contained a mixture of **21a** and **22**, 1.08 g. Compound **22**, 0.24 g, was isolated from latter fractions as a pale yellow oil, which was Kugelrohr distilled at 150 °C/0.10 mm. ^{1}H NMR for **21a**: δ 2.10 (m, 2H), 2.96 (m, 2H), 2.97 (s, 3H), 3.01 (s, 3H), 3.08 (s, 3H), 3.22 (s, 3H), 3.48 (m, 1H), 4.24 (dd, 1H, J = 3.7, 6.2 Hz), 6.96 (d, 1H, J = 6.9 Hz), 7.13 (m, 3H); ^{13}C NMR: δ 29.2, 32.0, 33.5, 35.7, 35.9, 37.2, 38.0, 39.5, 126.1, 126.7, 128.1, 129.4, 135.0, 137.1, 175.8, 176.5; MS: *m*/*z* (relative intensity) M^+, 274 (12), 229 (4), 201 (14), 157 (3), 129 (26), 102 (3), 72 (100). Anal. Calcd for $C_{16}H_{22}N_2O_2$: C, 70.04; H, 8.08; N, 10.21. Found: C, 69.95; H, 8.06; N, 10.28. ^{1}H NMR for **21b**: δ 2.15 (m, 2H), 3.00 (s, 3H), 3.02 (m, 3H), 3.22 (s, 3H), 4.24 (t, 1H, J = 5.0 Hz), 5.42 (br s, 1H), 5.86 (br s, 1H), 6.94 (d,1H, J = 7.7 Hz), 7.14 (m, 3H); ^{13}C NMR: δ 29.2, 32.4, 35.9, 37.1, 37.8, 39.7, 126.2, 126.8, 128.3, 129.2, 134.4, 136.2, 174.7, 177.6; MS: *m*/*z* (relative intensity) M^+, 246 (36), 201 (58), 174 (11), 129 (75), 115 (22), 91 (19), 72 (100). Anal. Calcd for $C_{14}H_{18}N_2O_2$: C, 68.27; H, 7.37; N, 11.37. Found: C, 68.02; H, 7.41; N, 11.35. ^{1}H NMR for **22**: δ 2.83 (s, 6H), 2.96 (s, 3H), 3.00 (s, 3H), 3.26 (d, 2H, J = 7.0 Hz), 3.66 (s, 2H), 5.80 (t, 1H, J = 7.0 Hz), 7.22 (m, 5H); ^{13}C NMR: δ 32.4, 35.2, 35.5, 37.0, 37.2, 42.5, 124.2, 126.4, 128.3, 128.4, 128.8, 128.9, 136.8, 138.0, 170.3, 172.1; MS: *m*/*z* (relative intensity) M^+, 274 (3), 229 (12), 202 (8), 188 (4), 157 (8), 128 (10), 91 (13), 72 (100). HRMS: Calcd 274.1681. Found 274.1685. ^{1}H NMR for **23**: δ 1.95 (m, 1H), 2.03 (m, 1H), 2.56 (m, 2H), 2.64 (m, 1H), 2.80 (dd, 1H, J = 9.6, 15 Hz), 2.93 (s, 3H), 3.01 (s, 3H), 3.07 (dd, 1H, J = 5.8, 15 Hz), 6.71 (d, 1H, J = 8.2), 6.97 (t, 1H, J = 7.5), 7.17 (m, 2H), 7.79 (br s, 1H); ^{13}C NMR: δ 25.7, 31.0, 31.6, 35.4, 37.2, 39.5, 115.0, 123.0, 123.4, 127.4, 128.2, 136.9, 172.5, 173.7; MS: *m*/*z* (relative intensity) M^+, 246 (3), 202 (3), 172 (4), 146 (100), 128 (14), 101 (17), 72 (15). Anal. Calcd for $C_{14}H_{18}N_2O_2$: C, 68.27; H, 7.37; N, 11.37. Found: C, 68.42; H, 7.40; N, 11.27. ^{1}H NMR for **24**: δ 1.86 (m, 1H), 2.00 (m, 1H), 2.16 (m, 1H), 2.35 (m, 1H), 2.58 (dd, 1H, J = 5.9, 13 Hz), 2.69 (s, 3H), 2.80 (dd, 1H, J = 8.9, 13 Hz), 2.86 (s, 3H), 2.90 (s, 3H), 2.95 (s, 3H), 3.14 (m, 1H), 3.54 (br s, 2H), 6.49 (s, 1H), 6.52 (m, 2H), 7.01 (t, 1H, J = 7.6 Hz); MS: *m*/*z* (relative intensity) M^+, 291 (24), 219 (8), 191 (76), 174 (27), 146 (54), 132 (28), 106 (37), 72 (100); HRMS: Calcd 291.1947. Found 291.1957.

Cyclization of 20 in the Dark. To a solution of KNH_2 prepared from potassium (1.57 g, 40 mmol) in 250 mL of liquid NH_3 contained in a 500 mL three-neck round-bottomed flask covered with a black cloth was introduced a solution of **20** (4.02 g, 10 mmol) in 40 mL of THF. The resulting solution was stirred under N_2 for 45 min and then quenched on excess solid NH_4Cl in a beaker. Following the workup procedure previously described for the photostimulated cyclization of **20**, 2.12 g of a viscous orange oil was obtained, which was then dissolved in 25 mL of EtOAc. On standing, 0.92 g of **21b** crystallized as a nearly colorless solid, mp 183−184 °C. The mother liquor was concentrated and chromatographed with EtOAc. The first fraction was obtained as a yellow oil which on trituration with ether gave 0.68 g of **23** as a nearly colorless solid. The mother liquor, which contained mostly **22** was concentrated and combined with a second fraction eluted with 5% MeOH−EtOAc to give 0.25 g of an ether soluble yellow oil, ^{1}H NMR analysis of which indicated a 4:1 mixture of **22**:**23**. Thus, the yield of **22** calculated from its molar fraction was 0.20 g (7%), and the total yield of **23** was 0.73 g (30%). Further elution with 15% MeOH−EtOAc gave 0.38 g of additional **21b**; total yield 1.30 g (53%).

1,2,3,4,5,6-Hexahydro-1,5-methano-3-benzazocine-2,4-dione (5). Compound **5** was prepared by the same procedure used in the synthesis of indane **4** from **10c**. Thus, a solution of **21b** (2.71 g, 11 mmol) in 150 mL of THF was refluxed in the presence of sodium hydride (1.10 g of a 60% dispersion in mineral oil, 27.5 mmol) for 1 h to afford a tan-colored solid which after chromatography with EtOAc gave **5**, 1.94 g (88%), as a white solid, mp 201−202 °C; ^{1}H NMR: δ 2.15 (m, 1H), 2.49 (m, 1H), 3.12 (d, 1H, J = 17 Hz), 3.20 (m, 1H), 3.31 (dd, 1H, J = 6.5, 17 Hz), 3.82 (s, 1H), 7.13 (d, 1H, J = 5.2 Hz), 7.22 (m, 2H), 7.33 (d, 1H, J = 5.4 Hz), 7.92 (br s, 1H); ^{13}C NMR: δ 25.6, 31.8, 36.1, 42.5, 127.0, 128.4, 129.4, 129.6, 132.0, 133.1, 173.8, 175.3; MS: *m*/*z* (relative intensity) M^+, 201 (63), 158 (14), 130 (100), 115 (57), 102 (13), 77 (16), 64 (39). Anal. Calcd for $C_{12}H_{11}NO_2$: C, 71.63; H, 5.51; N, 6.96. Found: C, 71.43; H, 5.56; N, 6.90.

Cyclization of 9 with KND_2 in ND_3. To a solution of KND_2 prepared from potassium (0.12 g, 3 mmol) in 20 mL of ND_3 contained in a three-neck round-bottomed flask draped with a black cloth was added a solution of **9** (0.39 g, 1.0 mmol) in 3 mL of THF under N_2. After stirring for 15 min, the reaction was quenched by the addition of solid, anhydrous ND_4Cl (0.25 g, 4.3 mmol). The ammonia and THF were evaporated under a stream of N_2 to give a tan solid, which was extracted twice with 25 mL portions of CH_2Cl_2. The combined extracts were concentrated to a tan-colored viscous oil, 0.25 g, which was chromatographed with EtOAc to obtain 0.13 g of deuterated **10a** as a yellow, viscous oil and 0.03 g of deuterated **16** as a pale yellow solid. The ^{1}H NMR spectrum of indane **10a** showed the absence of the H-1 benzylic proton resonance at δ 5.01 and integration of the H-2 (δ 4.18) and H-7 (δ 7.01) resonances indicated 0.5 D atom at C-2 and 0.4 D atom at C-7. The integrated ^{1}H NMR spectrum of quinolone **16** was consistent with 0.35 D atom incorporation at C-8.

2-(2-Iodo-3-methylbenzyl)-*N*,*N*,*N*′,*N*′-tetramethylbutanediamide (31). The procedure for the preparation of **31** was the same as that described previously for the analogous synthesis of **9** from **6** with 1.1 equiv of $LiNH_2$ in liquid NH_3 at −60 °C. Reaction of 2-iodo-3-methylbenzyl bromide (9.33 g, 30 mmol) and the lithium enolate of **6** (5.16 g, 30 mmol) at −60 °C for 45 min gave 9.85 g of a yellow solid. After two recrystallizations from CH_2Cl_2−hexane, 7.65 g (63%) of pure **31** was obtained as colorless crystals, mp 128−129 °C; ^{1}H NMR: δ 2.33 (dd, 1H, J = 3.0, 16 Hz), 2.47 (s, 3H), 2.72 (s, 3H), 2.82 (s, 3H), 2.88 (s, 3H), 2.94 (m, 2H), 3.00 (s, 3H), 3.09 (dd, 1H, J = 11, 16 Hz), 3.68 (m, 1H), 6.95 (dd, 1H, J = 5.4, 5.6 Hz), 7.23 (two overlapping d, 2H, J = 5.4, 5.6 Hz); ^{13}C NMR: δ 30.0, 35.2, 35.3, 35.7, 35.8, 36.7, 37.2, 45.2,

108.0, 127.3, 127.7, 128.0, 142.2, 142.3, 171.1, 174.7; MS: *m/z* (relative intensity) M^+, 402 (4), 358 (18), 316 (44), 275 (65), 202 (34), 126 (48), 87 (67), 72 (100). Anal. Calcd for $C_{16}H_{23}IN_2O_2$: C, 47.76; H, 5.72; N, 6.97. Found: C, 47.87; H, 5.77; N, 6.91.

Cyclization of 31 in the Dark. A solution of KNH_2 was prepared from potassium (0.59 g, 15 mmol) in 150 mL of liquid NH_3. The reaction flask was covered with a black cloth, and **31** (2.02 g, 5 mmol) was added as a solid. After stirring for 5 min, the deep red solution was poured onto excess NH_4Cl in a beaker. A 50 mL ether rinse of the flask was added cautiously to the NH_3 solution, and the NH_3 and ether were evaporated. The orange solid residue was dissolved in water (20 mL) and CH_2Cl_2 (100 mL). The aqueous layer was separated and extracted with additional 100 mL of CH_2Cl_2, and the combined CH_2Cl_2 solutions were dried ($MgSO_4$) and concentrated. The resulting orange-brown viscous oil was chromatographed using EtOAc as the eluent, and 3-(*N*,*N*-dimethylacetamido)-3,4-dihydro-8-methyl-2(1*H*)-quinolone (**35**) was eluted as a pale yellow oil which upon trituration with ether crystallized, mp 142−143.5 °C, 0.06 g (5%). Recrystallization from ether afforded an analytical sample as colorless crystals, mp 143−143.5 °C. A 0.54 g mixture of *trans*-1,2-bis-(*N*,*N*-dimethylcarboxamido)-7-methylindane (**32a**) and 1,2-bis-(*N*,*N*-dimethylcarboxamido)-7-methyl-1-indene (**33**) was eluted next. This mixture was rechromatographed by gradient elution with 0−4% MeOH in CH_2Cl_2, and indane **32a** was eluted first as a pale yellow oil which crystallized when triturated with ether, 0.27 g (20%). Recrystallization from ether−hexane gave pure **32a** as colorless crystals, mp 87−88 °C. Indene **33** was then eluted as a yellow oil which crystallized on standing, mp 120−122 °C, 0.15 g (11%). After recrystallization from ether−hexane, pale yellow plates of pure **33**, mp 122.5−123 °C, were obtained. The eluent from the initial chromatography was changed from EtOAc to 10% MeOH−EtOAc, and a third fraction was eluted as a light yellow oil, 0.27 g. Trituration with ether resulted in the crystallization of 0.05 g (4%) of *trans*-1-(*N*,*N*-dimethylcarboxamido)-7-methylindane-2-carboxamide (**32c**) as a light tan solid, mp 210−212 °C. Recrystallization from EtOAc−ether afforded nearly colorless, pure **32c**, mp 213−214 °C. Evaporation of the ether gave a pale yellow oil whose ^{1}H NMR spectrum indicated it to be essentially pure 2-(3-methylbenzyl)-*N*,*N*,*N*′,*N*′-tetramethylbutanediamide (**34**), 0.22 g (16%). A final fraction was then eluted which crystallized to a tan solid, 0.38 g, which was rechromatographed with 2% MeOH−CH_2Cl_2 to give 0.31 g (23%) of pure *cis*-1,2-bis-(*N*,*N*-dimethylcarboxamido)-7-methylindane (**32b**) as colorless crystals, mp 185−186 °C. ^{1}H NMR for **32a**: δ 2.13 (s, 3H), 2.99 (s, 3H), 3.00 (dd, 1H, J = 8.2, 15 Hz), 3.03 (s, 3H), 3.10 (s, 3H), 3.32 (s, 3H), 3.39 (dd, 1H, J = 9.2, 15 Hz), 3.83 (ddd, 1H, J = 8.0, 8.2, 9.2 Hz), 5.07 (d, 1H, J = 8.0 Hz), 6.95 (d, 1H, J = 7.4 Hz), 7.01 (d, 1H, J = 7.4 Hz), 7.09 (t, 1H, J = 7.4 Hz); ^{13}C NMR: δ 18.6, 35.9, 36.1, 36.7, 37.4, 38.2, 48.1, 49.1, 121.6, 127.5, 128.6, 133.6, 140.8, 141.3, 173.3, 174.5; MS: *m/z* (relative intensity) M^+, 274 (3), 229 (18), 202 (26), 157 (20), 128 (76), 115 (46), 72 (100). Anal. Calcd for $C_{16}H_{22}N_2O_2$: C, 70.04; H, 8.08; N, 10.21. Found: C, 69.93; H, 8.12; N, 10.17. ^{1}H NMR for **32b**: δ 2.22 (s, 3H), 2.93 (s, 3H), 2.98 (s, 3H), 3.01 (s, 3H), 3.12 (m, 1H), 3.15 (s, 3H), 3.78 (m, 2H), 4.53 (m, 1H), 6.96 (m, 1H), 7.11 (m, 2H); ^{13}C NMR: δ 18.9, 36.0, 36.1, 36.3, 37.3, 37.7, 47.3, 49.4, 122.0, 127.7, 127.8, 133.4, 140.6, 143.4, 171.7, 172.5; MS: *m/z* (relative intensity) M^+, 274 (1), 229 (33), 201 (8), 157 (7), 128 (93), 115 (72), 72 (100). Anal. Calcd for $C_{16}H_{22}N_2O_2$: C, 70.04; H, 8.08; N, 10.21. Found: C, 70.10; H, 8.15; N, 10.29. ^{1}H NMR for **32c**: δ 2.11 (s, 3H), 3.03 (s, 3H), 3.11 (dd, 1H, J = 9.1, 15 Hz), 3.25 (s, 3H), 3.27 (dd, 1H, J = 8.8, 15 Hz), 3.44 (ddd, 1H, J = 8.2, 8.8, 9.1 Hz), 4.81 (d, 1H, J = 8.2 Hz), 5.39 (br s, 1H), 6.45 (br s, 1H), 6.96 (d, 1H, J = 7.3 Hz), 7.02 (d, 1H, J = 7.5 Hz), 7.11 (t, 1H, J = 7.4 Hz); ^{13}C NMR: δ 18.7, 36.2, 36.9, 38.1, 49.6, 50.3, 121.9, 127.8, 128.6, 133.7, 140.3, 141.9, 174.3, 175.9; MS: *m/z* (relative intensity) M^+, 246 (2), 202 (4), 129 (24), 115 (25), 91 (53), 72 (100). Anal. Calcd for $C_{14}H_{18}N_2O_2$: C, 68.27; H, 7.37; N, 11.37. Found: C, 68.14; H, 7.44; N, 11.43. ^{1}H NMR for **33**: δ 2.32 (s, 3H), 2.96 (s, 3H), 3.04 (s, 6H), 3.08 (s, 3H), 3.59 (d, 1H, J = 23 Hz), 3.81 (d, 1H, J = 23 Hz), 7.09 (d, 1H, J = 7.4), 7.18 (t, 1H, J = 7.4 Hz), 7.32 (d, 1H, J = 7.4 Hz); ^{13}C NMR: δ 18.0, 34.4, 36.6, 38.1, 38.7, 39.8, 121.6, 126.4, 129.1, 131.8, 137.0, 137.7, 139.5, 142.5, 168.2; MS: *m/z* (relative intensity) M^+, 272 (1), 229 (4), 200 (3), 184 (6), 156 (8), 127 (38), 72 (100). Anal. Calcd for $C_{16}H_{20}N_2O_2$: C, 70.56; H, 7.40; N, 10.29. Found: C, 70.48; H, 7.37; N, 10.27. ^{1}H NMR for **34**: δ 2.28 (dd, 1H, J = 3.6, 13 Hz), 2.32 (s, 3H), 2.64 (dd, 1H, J = 7.2, 13 Hz), 2.82 (s, 3H), 2.85 (m, 1H), 2.87 (s, 3H), 2.88 (s, 3H), 2.99 (s, 3H), 3.01 (m, 1H), 3.52 (m, 1H), 7.02 (m, 3H), 7.14 (m, 1H); ^{13}C NMR; δ 21.2, 35.3, 35.6, 36.0, 36.2, 37.0, 39.0, 39.6, 126.0, 127.1, 128.1, 129.6, 137.8, 139.0, 171.4, 175.0; MS: *m/z* (relative intensity) M^+, 276 (27), 232 (12), 190 (100), 159 (31), 145 (18), 126 (21), 105 (17), 72 (95). HRMS: Calcd for $C_{16}H_{24}N_2O_2$: 276.1838. Found: 276.1846. ^{1}H NMR for **35**: δ 2.24 (s, 3H), 2.40 (dd, 1H, J = 8.2, 16 Hz), 2.84 (m, 1H), 2.99 (s, 3H), 3.06 (s, 3H), 3.14 (m, 3H), 6.89 (t, 1H, J = 7.5 Hz), 7.03 (d, 2H, J = 7.5 Hz), 7.72 (br s, 1H); ^{13}C NMR: δ 16.6, 31.8, 33.0, 35.4, 36.8, 37.1, 122.4, 122.6, 123.9, 125.9, 128.9, 135.3, 170.8, 172.9; MS: *m/z* (relative intensity) M^+, 246 (4), 202 (2), 172 (8), 160 (87), 130 (32), 87 (31), 72 (100). Anal. Calcd for $C_{14}H_{18}N_2O_2$: C, 68.27; H, 7.37; N, 11.37. Found: C, 68.21; H, 7.41; N, 11.43.

When a similar dark reaction was carried out in the presence of 40 mol % of DTBN, ^{1}H NMR analysis of the reaction mixture indicated a 6:1 ratio of unreacted **31** to **32a**,**b**.

Xray Crystallographic Analysis of 4, 13, 17, and 21b.[40] X-ray data were collected at 25 °C on a Siemens R_3m/v diffractometer with Mo Kα radiation using a graphite monochromator. Other relevant experimental details are included in Supporting Information. The structures were solved by direct methods and refined using the SHELXTL-PLUS suite of programs.

Acknowledgment. We are pleased to acknowledge generous financial support from the Harvey W. Peters Research Center for Parkinson's Disease and Disorders of the Central Nervous System Foundation and from the National Science Foundation through Grant CHE-8513216.

JO982000B

(40) The author has deposited atomic coordinates for structures **4, 13**, **17**, and **21b** with the Cambridge Crystallographic Data Centre. The coordinates can be obtained, on request, from the Director, Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge, CB2 1EZ, U.K.