5b, 125413-46-9; **5c**, 125541-79-9; **5d**, 125567-54-6; **5e**, 105595-28-6; **5f**, 107960-09-8; **5g**, 125541-80-2; **6**, 125541-75-5; **7**, 125541-76-6; chloral, 75-87-6; phosgene, 75-44-5; bromal, 115-17-3; cholesterol, 57-88-5; *N*-ethylpiperidine, 766-09-6; piperidine, 110-89-4; *N*-(2,2-dibromovinyloxycarbonyl)piperidine, 125541-78-8; neopentyl alcohol, 75-84-3; morpholine, 110-91-8; *N*-methylpiperidine, 626-67-5.

Structure of the IN_3 Adduct of 1-Phenylcyclohexene. Its Chemistry and CH Coupling as a Diagnostic Tool[1]

Alfred Hassner* and Wim Dehaen

Department of Chemistry, Bar-Ilan University, Ramat-Gan, 52100 Israel

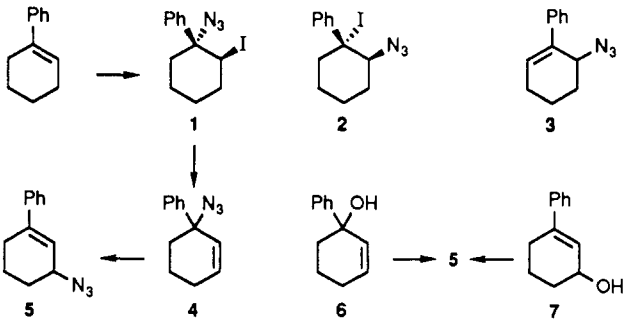
Received July 27, 1989

The addition of iodine azide to alkenes, discovered by Hassner et al.,[2] is by now a well-established method for stereo- and regiospecific introduction of nitrogen functional groups.[2] In a recent paper, Sivasubramanian et al.[3] claimed that the regiochemistry of the IN_3 addition to 1-aryl-1-cyclohexenes was the reverse of that usually observed for conjugated aromatic alkenes. Thus, the IN_3 adduct of 1-phenylcyclohexene, originally assigned structure **1** by Hassner et al.,[4] was claimed to be instead the tertiary iodide **2**.[3] The unsaturated azide obtained on dehydroiodination of the adduct with hot KOH in ethanol was assigned structure **3**.[3]

A tertiary benzylic iodide structure as in **2** is highly suspect, since it would be expected to be extremely unstable and to solvolyze at room temperature. Furthermore, it has been established[2,5,6] that IN_3 or INCO additions to arenes including styrene, indene, and 1,2-dihydronaphthalene proceed by opening of an iodonium ion intermediate at the benzylic carbon[7,8] to produce regiospecifically the benzylic azide.

We reinvestigated the reaction of IN_3 to 1-phenylcyclohexene and were able to confirm the originally assigned structure **1** on the following grounds.[8]

The high-resolution ^{13}C NMR spectrum of **1**[8] showed a $^1J_{CH}$ of 153 Hz for the methine carbon. As discussed below this is consistent with a CHI methine coupling (ca. 152 Hz)[9] but not with CHN_3 (ca. 142 Hz).

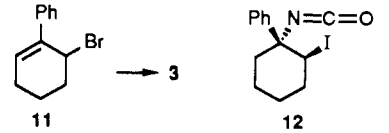


The adduct was found to be unchanged on standing in ethanol–water (4:1) for several hours, and no traces of iodide ions were detected by means of silver nitrate. Under these conditions *tert*-butyl iodide is solvolyzed almost completely. These results are inconsistent with a tertiary benzylic iodide structure **2**.

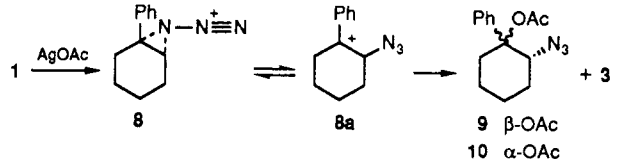
Elimination of HI from the IN_3 adduct **1** (heating with KOH in ethanol) gave an allylic azide, which proved to be 3-azido-1-phenylcyclohexene (**5**), rather than the postulated[3] 6-azido-1-phenylcyclohexene (**3**). This was clear from NMR data and decoupling experiments[8] as well as by an unequivocal synthesis of **5** via a Mitsunobu reaction[10] on allyl alcohol **7**.

Apparently, the initially produced 1-azido-1-phenylcyclohexene (**4**) (formed by dehydroiodination of **1**) underwent a well-documented (3,3) allylic azide rearrangement.[11] Indeed, attempts to synthesize allyl azide **4** from allyl alcohol **6** with $TiCl_4$–HN_3[12] gave only rearranged azide **5**. The tertiary alcohol **6** was unreactive under Mitsunobu conditions.

Reaction of **1** under more severe solvolysis conditions with AgOAc in acetic acid at 60 °C led to formation of allyl azide **3** (10%) together with *E* (trans) and *Z* (cis) azido acetates **9** (37%) and **10** (31%). The structure of **3** was verified from its NMR spectra and its preparation from the allyl bromide **11**.[8]



The regiochemistry for **9** and **10** was evident from the chemical shift for CHN_3 both in ^1H NMR (3.88 and 3.09 ppm, respectively) and ^{13}C NMR (66.29 and 67.84 ppm), values at much higher field than expected for a regioisomeric CHOAc. The *Z* (cis) stereochemical assignment to **10** rests on the 11- and 5-Hz coupling of the CHN_3, indicative of an axial hydrogen geminal to an equatorial azide, vs J = 3 Hz for the corresponding proton in the *E* isomer **9** (this presumes anchoring of the chair cyclohexane ring by the larger phenyl group in an equatorial position).



Solvolysis of **1** apparently involved azide migration which may have proceeded via the intermediacy of a cyclic

(1) Stereochemistry. 77. For paper 76, see: Hassner, A.; Dehaen, W. *Tetrahedron Lett.*, in press.
(2) Hassner, A. *Acc. Chem. Res.* **1971**, *4*, 9.
(3) Sivasubramanian, S.; Aravind, S.; Kumarasingh, L. T.; Arumugam, N. *J. Org. Chem.* **1986**, *51*, 1985.
(4) Hassner, A.; Matthews, G. J.; Fowler, F. W. *J. Am. Chem. Soc.* **1969**, *91*, 5045.
(5) (a) Hassner, A.; Fowler, F. W. *J. Org. Chem.* **1968**, *33*, 2686. (b) Fowler, F. W.; Hassner, A.; Levy, L. A. *J. Am. Chem. Soc.* **1967**, *89*, 2077.
(6) (a) Hassner, A.; Lorber, M. E.; Heathcock, C. H. *J. Org. Chem.* **1967**, *32*, 540. (b) Anselmi, C.; Camici, G.; Macchia, F.; Monti, L. *Gazz. Chim. Ital.* **1972**, *102*, 1129.
(7) Sivasubramanian argued that formation of **2** was analogous to opening of an epoxide at the less hindered carbon. In fact, 1-arylcyclohexene oxides have been shown to open with nucleophilic attack at the benzylic carbon. Cecchi, P.; Pizzabiocca, A.; Renzi, G.; Chimi, M.; Crotti, P.; Macchia, F.; Speranza, M. *Tetrahedron* **1989**, *45*, 4227.
(8) After our paper had been submitted, Crotti, P.; Chimi, M.; Uccello-Barretta, G.; Macchia, F. *J. Org. Chem.* **1989**, *54*, 4525, published their independent conclusion regarding the incorrect structure assignment of **2** and **3**.[3] Hence, we have condensed our paper slightly and omitted some NMR data and discussion in order to minimize overlap.
(9) Watts, L. S.; Goldstein, J. H. *J. Phys. Chem.* **1966**, *70*, 3887.
(10) (a) Mitsunobu, O. *Synthesis* **1981**, 1. (b) Loibner, H.; Zbiral, E. *Helv. Chim. Acta* **1976**, *59*, 2100. (c) Schweng, J.; Zbiral, E. *Justus Liebigs Ann. Chem.* **1978**, 1089.
(11) (a) Gagneaux, A.; Winstein, S.; Young, W. G. *J. Am. Chem. Soc.* **1960**, *82*, 5956. (b) Hassner, A.; Teeter, J. S. *J. Org. Chem.* **1970**, *35*, 3397. (c) Hassner, A.; Keogh, J. *Ibid.* **1986**, *51*, 2767.
(12) Hassner, A.; Fibiger, R.; Andisik, D. *J. Org. Chem.* **1984**, *49*, 4237.

0022-3263/90/1955-2243$02.50/0

Table I. $^1J_{CH}$ Values (Hz) for CH-N_3 versus CH-I Compounds

	$^1J_{CH-N_3}$	$^1J_{CH-I}$
n-hexyl azide	141.5	
cyclohexyl azide	141	
1-azido-2-iodocyclohexane	142	150
1-methyl-1-azido-2-iodocyclohexane		153
1		153
3	144	
5	143	
9	145	
10	145	
12		154

azidonium ion **8**.[13] The formation of both cis and trans azido acetates suggests that azide migration produced a benzylic cation **8a**, which is trapped by acetate ion.

During the course of this work, we discovered that ^{13}C–H coupling serves as a diagnostic tool to differentiate between a proton geminal to an azido and one geminal to an iodo function. It is well recognized that $^1J_{CH}$ values are quite characteristic of the polar substituent on the CH but rather insensitive to groups present on adjacent carbons;[9] nevertheless, this technique has remained rather underutilized. For CH-I a ^{13}C–H coupling constant of ca. 152 Hz had been reported;[9] however, no values for CH-N_3 were known. On the basis of several examples (see Table I), we are now able to assign a $^1J_{CH}$ value of 142 ± 3 Hz for a CHN_3 group which clearly differentiates it from a CHI or CH-halogen group.

In analogy to IN_3 addition to 1-phenylcyclohexene, the addition of INCO[6] to the same olefin led to an adduct for which the assigned structure **12** (opening of the iodonium ion intermediate at the benzylic carbon) is consistent with the $^1J_{CH-I}$ at 154 Hz.

It stands to reason that all the structures assigned as tertiary benzylic iodides by Sivasubramanian[3] to the IN_3 addition products of 1-arylcyclohexenes should be revised as benzylic azides (e.g. **1**) and their dehydroiodination products should be reassigned as 3-azido-1-arylcyclohexenes (e.g. **5**).

Experimental Section

Melting points were determined on a Fisher-Johns apparatus and are uncorrected. IR spectra were taken with a Perkin-Elmer 177 spectrometer. ^1H NMR (300 MHz) and ^{13}C NMR (75 MHz) spectra were measured on a Bruker 300 AM FT spectrometer using deuteriochloroform solutions and are reported in ppm from internal tetramethylsilane (^1H) or deuteriochloroform (^{13}C) on the δ scale. The ^1H NMR spectra are reported as follows: chemical shift (multiplicity, coupling constant(s) in hertz, integration, interpretation). All the ^1H and ^{13}C spectra were correlated with decoupling or off-resonance experiments. Abbreviations: s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet; br, broad. Mass spectra were obtained on a Finnigan 4021 mass spectrometer. Elementary analysis was performed at the Hebrew University, Jerusalem.

1-Azido-2-iodo-1-phenylcyclohexane (1). Iodo azide **1** was prepared as earlier reported[4] in 91% yield: mp 75 °C; IR (cm^{-1}, $CHCl_3$) 2100 (N_3); ^1H NMR 1.69 (m, 1 H, H_{eq}), 1.74–1.87 (m, 3 H), 2.04 (dm, J = 14, 1 H, $H3_{eq}$), 2.17 (dm, J = 14, 1 H, $H6_{eq}$), 2.24 (ddt, J = 14, 8, 3, 1 H, $H3_{ax}$), 2.62 (ddd, J = 14, 7, 6, 1 H, $H6_{ax}$), 4.69 (dd, J = 3, 1, 1 H, CHI), 7.31–7.42 (m, 5 H, Ph); ^{13}C NMR 21.32 (t, 4- and 5-CH_2), 28.00 (t, 6-CH_2), 31.41 (t, 3-CH_2), 41.13 (d, $^1J_{CH}$ = 153 Hz, CHI), 68.09 (s, C-N_3), 125.67, 128.38 and 128.48 (d, Ph C-H), 143.24 (s, Ph C-1).

3-Azido-1-phenyl-1-cyclohexene (5). A. From 1-Phenyl-1-cyclohexen-3-ol (7).[14] A stirred solution of 0.350 g (2 mmol) of allylic alcohol **7** and 0.58 g (2.2 mmol) of PPh_3 in 10 mL of dry benzene was treated with 2 mL (2.3 mmol) of a 5% HN_3 solution in benzene,[14] immediately followed by addition of 0.383 g (2.2 mmol) of diethyl azodicarboxylate. The stirring was continued at room temperature for 24 h. The mixture was filtered, the filtrate was concentrated, and the resulting oil was chromatographed. This gave a 52% yield of azide **5**, identical with the azide previously reported.[3,8] Tertiary alcohol **6** did not react under these conditions.

B. From 3-Phenyl-1-cyclohexene-3-ol (6).[14] Tertiary alcohol **6** (0.350 g, 2 mmol) was mixed with 6 mL (10 mmol) of a 1.7 N solution of HN_3 in ethanol-free chloroform.[15] A solution of 1 mmol of $TiCl_4$ in 2 mL of chloroform was added dropwise. The resulting mixture was stirred for 2 h at 20 °C. Filtration over basic alumina and evaporation afforded an oil, which gave pure azide **5** in 85% yield after chromatography: IR (neat, cm^{-1}) 2105 (N_3); ^1H NMR 1.74–1.84 (m, 2 H, 5-CH_2), 1.87–2.02 (m, 2 H, 6-CH_2), 2.35–2.56 (m, 2 H, 4-CH_2), 4.09 (m, 1 H, CHN_3), 6.07 (dt, J = 4, 2, 1 H, olefinic C-H), 7.24–7.43 (m, 5 H, Ph); ^{13}C NMR 19.71 (t, C-5), 27.36 (t, C-4), 28.29 (t, C-6), 58.86 (d, J_{CH} = 143, CHN_3), 121.35 (d, olefin C-H), 125.42, 127.68 and 128.29 (d, Ph C-H), 140.96 and 142.45 (s, Ph C-1 and cyclohexyl C-1); MS (*m/z*, relative intensity, electron impact) 199 (M^+, 1), 171 ($M^+ - N_2$, 9), 157 ($M^+ - N_3$, 100), 143 (171 – $H_2C{=}N$, 8), 129 (157 – C_2H_4, 14), 118 (171 – C_3H_3N, 22), 115 (157 – C_3H_6, 19), 91 ($C_7H_7^+$, 21).

Solvolysis of Iodo Azide 1. To a solution of 0.5 g (1.54 mmol) of iodo azide **1** in glacial acetic acid (10 mL) was added 0.28 g (1.7 mmol) AgOAc, and the suspension was stirred at 60 °C for 4 h. Silver iodide was filtered off, and the product extracted into ether. The extract was washed with water and saturated $NaHCO_3$ solution, dried over $MgSO_4$, and concentrated. The resulting oil was chromatographed over silica gel with 4:1 petroleum ether–ether as the eluent. This gave three products: **3**, **9**, **10**.

(A) 6-Azido-1-phenyl-1-cyclohexene (3) was obtained as a colorless oil in 10% yield: IR (neat, cm^{-1}) 2100 (N_3); ^1H NMR 1.67–1.87 (m, 2 H, $H4_{eq}$ + $H5_{eq}$), 1.97 (dm, J = 19, 1 H, $H4_{ax}$), 2.19 (dqd, J = 13, 4, 1, 1 H, $H5_{ax}$), 2.29 (dddd, J = 7.5, 6.5, 4, 1.5, 1 H, $H3_{eq}$), 2.38 (dq, J = 19, 4.5, $H3_{ax}$), 4.36 (br t, J = 4, 1 H, $CH_{eq}N_3$), 6.39 (dd, J = 5, 3.5), 7.24–7.43 (m, 5 H, Ph); ^{13}C NMR 17.59 (t, 4-CH_2), 25.69 (t, 3-CH_2), 29.59 (t, 5-CH_2), 56.98 (d, $^1J_{CH}$ = 144, CHN_3), 125.87, 127.41 and 128.53 (d, Ph C-H), 130.46 (d, olefinic C-H), 134.97 and 140.20 (s, Ph and cyclohexane C-1); MS (*m/z*, relative intensity, chemical ionization, CH_4) 199 (M^+, not obtained), 172 ($MH^+ - N_2$, 23), 157 ($M^+ - N_3$, 100). Anal. Calcd for $C_{12}H_{13}N_3$: C, 72.36; H, 6.53; N, 21.10. Found: C, 71.99; H, 6.73; N, 20.49.

This azide is identical with **3** obtained by reaction of 6-bromo-1-phenylcyclohexene (**11**) with sodium azide in acetone.[8]

(B) (*E*)-*trans*-1-Acetoxy-2-azido-1-phenylcyclohexane (9) was crystallized from ether/hexane: mp 48–9 °C in 37% yield; IR ($CHCl_3$, cm^{-1}) 2100 (N_3), 1745 (C=O); ^1H NMR 1.15–1.60 (m, 3 H, 4-CH_2 + $H5_{ax}$), 1.70 (dm, J = 13, $H5_{eq}$), 1.86 (dm, J = 14, 1 H, $H3_{eq}$), 2.04 (s, 3 H, CH_3CO), 2.13 (dddd, J = 14, 11, 5, 3, 1 H, $H3_{ax}$), 2.6 (ddd, J = 14, 13, 4, 1 H, $H6_{ax}$), 2.80 (dm, J = 14, 1 H, $H6_{eq}$), 3.88 (br q, J = 3, 1 H, CHN_3), 7.28–7.39 (m, 5 H, Ph); ^{13}C NMR 19.45 and 20.84 (t, 4- and 5-CH_2), 22.00 (q, CH_3CO), 25.95 (dd, 6-CH_2), 26.76 (t, 3-CH_2), 66.29 (d, $^1J_{CH}$ = 145, CHN_3), 82.47 (s, C-OAc), 125.35, 127.82 and 128.40 (d, Ph C-H), 142.25 (s, Ph C-1), 168.35 (s, C=O); MS (*m/z*, relative intensity, electron impact) 259 (M^+, not observed), 188 ($M^+ - C_2H_5N_3$, 42), 172 ($M^+ - N_2 - OAc$, 18), 105 ($C_7H_7N_+$, 100); (chemical ionization, NH_3), 277 (MNH_4^+, 12), 260 (MH^+, 2), 2.49 ($MNH_4 - N_2$, 2), 232 ($MH^+ - N_2$, 6), 217 ($M^+ - N_3$, 34), 172 ($M^+ - N_2 - OAc$, 100). Anal. Calcd for $C_{14}H_{17}N_3O_2$: C, 64.86; H, 6.56; N, 16.22. Found: C, 64.58; H, 6.60; N, 15.84.

(C) (*Z*)-*cis*-1-Acetoxy-2-azido-1-phenylcyclohexane (10) was obtained as a colorless oil in 31% yield: IR (neat, cm^{-1}) 2100 (N_3), 1745 (C=O); ^1H NMR 1.38–1.50 (m, 3 H, 4-CH_2 + $H5_{ax}$), 1.63–1.71 (m, 1 H, $H5_{eq}$), 1.88–2.03 (m, 2 H, 3-CH_2), 2.05 (ddd, J = 14, 11, 3, 1 H, $H6_{ax}$), 2.19 (s, 3 H, CH_3CO), 2.98 (dm, J = 14, 1 H, $H6_{eq}$), 3.09 (dd, J = 11, 5, 1 H, CHN_3), 7.22–7.38 (m, 5 H, Ph); ^{13}C NMR 21.15 (t, 5-CH_2), 22.19 (q, CH_3CO), 24.41 (t, 4-CH_2), 27.52 (t, 3-CH_2), 32.11 (t, 6-CH_2), 67.84 (d, $^1J_{CH}$ = 145, CHN_3), 85.45 (s, C-OAc), 125.53, 127.89 and 128.50 (d, Ar C-H), 142.08

(13) Streitweiser, A.; Pulver, S. *J. Am. Chem. Soc.* **1964**, *86*, 1587.
(14) Reich, H. J.; Wollowitz, S. *J. Am. Chem. Soc.* **1982**, *104*, 7051.
(15) Wolff, H. *Org. React.* **1946**, 327.

(s, Ar C-1), 169.33 (s, C=O); MS (*m/z*, relative intensity, chemical ionization, NH_3) 277 (MNH_4^+, 32), 260 (MH^+, 3), 249 ($MNH_4^+ - N_2$, 3), 232 ($MH^+ - N_2$, 6), 217 ($M^+ - N_3$, 80), 172 ($M^+ - N_2 -$ OAc, 100).

2-Iodo-1-isocyanato-1-phenylcyclohexane (12). The adduct **12** was prepared, following the published procedure,[6] from 1-phenyl-1-cyclohexene in 82% yield as an unstable oil: IR (neat, cm^{-1}) 2240 (N=C=O); ^1H NMR 1.60–1.98 (m, 5 H, 4- and 5-CH_2, 6-H_{eq}), 2.12 (dm, J = 15, 1 H, 3-H_{eq}), 2.35 (ddt, J = 15, 11, 4, 1 H, 3-H_{ax}), 2.71 (ddd, J = 14, 12, 5, 1 H, 6-H_{ax}), 4.68 (brt, J = 4, 1 H, CHN_3), 7.26–7.50 (m, 5 H, Ph); ^{13}C NMR 21.24 and 22.36 (t, 4-CH_2 and 5-CH_2), 32.06 (dd, 6-CH_2), 33.16 (t, 3-CH_2), 43.60 (d, J_{CH} = 154, CHI), 74.31 (s, CN=C=O), 125.33, 127.82 and 128.21 (d, Ph C-H), 128.69 (s, Ph C-1), 147.41 (s, N=C=O).

Acknowledgment. Support of this research by Grant 87-00299 from the US–Israel Binational Science Foundation is gratefully acknowledged. We thank Dr. H. E. Gottlieb for valuable help with NMR spectra.

Supplementary Material Available: ^{13}C NMR spectra for compounds **3**, **5**, **9**, and **10** (4 pages). Ordering information is given on any current masthead page.

Synthesis of Des-*N*-methylacronycine and Acronycine[1]

David G. Loughhead

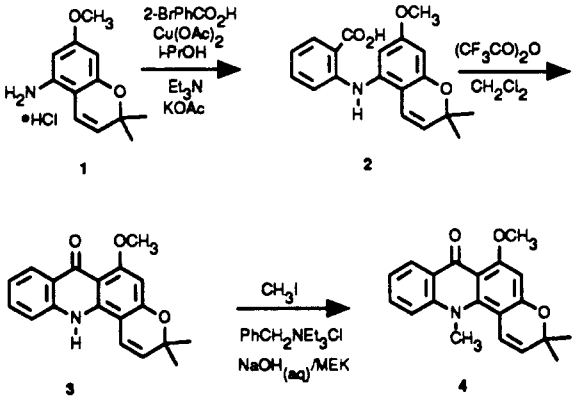
Syntex Research, Institute of Organic Chemistry, 3401 Hillview Ave., Palo Alto, California 94304

Received August 17, 1989

Des-*N*-methylacronycine (**3**) and acronycine (**4**) are closely related acridine alkaloids which have been isolated from a variety of plant sources.[2,3] Acronycine in particular has attracted attention because it has demonstrated antitumor activity in experimental animals[4] and has been evaluated in human patients with multiple myeloma.[5] We had interest in preparing des-*N*-methylacronycine since this compound could serve as an intermediate for the preparation of several N-substituted analogues, including acronycine itself.[6]

Des-*N*-methylacronycine has been prepared before. Adams et al.[6d] offer three related syntheses of this material. The most efficient of these three routes provides **3** in three steps from 3,5-dimethoxyphenol, but in an overall yield of less than 2%. Blechert et al.,[7] whose aim was to design a synthesis which would have the flexibility to allow preparation of acronycine metabolites, describe an eight-step synthesis of des-*N*-methylacronycine from aminochromene **1**. Since the yield of one step in this sequence is not reported, it is possible to say only that the overall yield must be less than 9%.

For the present work, a direct, two-step synthesis of des-*N*-methylacronycine from the previously described aminochromene **1**[7,8] was planned. Ullmann coupling of **1** with 2-bromobenzoic acid efficiently provided the substituted anthranilic acid **2**. A simple workup of this reaction afforded a 97% yield of crude product; then chromatography and recrystallization provided a 58% yield of analytical material. Conversion of **2** to des-*N*-methylacronycine required only an electrophilic cyclization. This turned out to be more difficult than anticipated since **2** decomposed under a variety of acid conditions (H_2SO_4, polyphosphoric acid, trifluoroacetic acid in CH_2Cl_2, $POCl_3$ followed by $HCl_{(aq)}$, or polyphosphate ester in $CHCl_3$) used to try to effect this ring closure. This problem was overcome when it was discovered that trifluoroacetic anhydride efficiently induced the desired cyclization to occur. When a recrystallized sample of **2** was allowed to stir for 3 days at room temperature with 5 equiv of trifluoroacetic anhydride in methylene chloride, workup and chromatography provided a 62% yield of an analytical sample of the desired product. Thus, this process provided des-*N*-methylacronycine in 36% yield from aminochromene **1**. Purification of the anthranilic acid **2** was not necessary to successfully achieve the preparation of **3**. In fact, a slightly higher overall conversion of aminochromene **1** to the desired **3** was achieved when the crude intermediate anthranilic acid **2** was subjected to the cyclization conditions described above. Using this procedure, des-*N*-methylacronycine was provided in 40% yield from aminochromene **1**.



Des-*N*-methylacronycine is a versatile compound which can be N-alkylated to give materials related to acronycine. Conversion to acronycine (**4**) itself was achieved in 96% yield by alkylation with methyl iodide under phase-transfer conditions.[9] Thus efficient preparations of both des-*N*-methylacronycine and acronycine have been realized.

Experimental Section

Melting points are uncorrected. IR, NMR, and mass spectra of all compounds were consistent with the assigned structures. IR spectra were measured as dispersions in KBr on a Nicolet 5 PC FT infrared spectraphotometer. ^1H NMR spectra were ob-

(1) Contribution Number 774 from the Syntex Institute of Organic Chemistry.

(2) For isolation and structure determination of des-*N*-methylacronycine, see: (a) Govindachari, T. R.; Pai, B. R.; Subramaniam, P. S. *Tetrahedron* **1966**, *22*, 3245. (b) Fauvel, M. T.; Gleye, J.; Moulis, C.; Fouraste, I. *Plant. Med. Phytother.* **1978**, *12*, 207. (c) Wu, T. S.; Furukawa, H.; Kuoh, C. S.; Hsu, K. S. *J. Chem. Soc., Perkin Trans. 1* **1983**, 1681. (d) Funayama, S.; Cordell, G. A. *J. Nat. Prod.* **1984**, *47*, 285.

(3) For isolation and structure determination of acronycine, see: (a) Lahey, F. N.; Thomas, W. C. *Aust. J. Sci. Res. A* **1949**, *2*, 423. (b) Brown, R. D.; Drummond, L. J.; Lahey, F. N.; Thomas, W. C. *Ibid.* **1949**, *2*, 622. (c) Drummond, L. J.; Lahey, F. N. *Ibid.* **1949**, *2*, 630. (d) Macdonald, P. L.; Robertson, A. V. *Aust. J. Chem.* **1966**, *19*, 275. Also see ref 2a.

(4) Svoboda, G. H.; Poore, G. A.; Simpson, P. J.; Boder, G. B. *J. Pharm. Sci.* **1966**, *55*, 758.

(5) Scarffe, J. H.; Beaumont, A. R.; Crowther, D. *Cancer Treat. Rep.* **1983**, *67*, 93.

(6) For other syntheses of acronycine, see: (a) Beck, J. R.; Kwok, R.; Booher, R. N.; Brown, A. C.; Patterson, L. E.; Pranc, P.; Rockey, B.; Pohland, A. *J. Am. Chem. Soc.* **1968**, *90*, 4706. (b) Hlubucek, J. R.; Ritchie, E.; Taylor, W. C. *Aust. J. Chem.* **1970**, *23*, 1881. (c) Bandaranayake, W. M.; Begley, M. J.; Brown, B. O.; Clarke, D. G.; Crombie, L.; Whiting, D. A. *J. Chem. Soc., Perkin Trans. 1* **1974**, 998. (d) Adams, J. H.; Brown, P. M.; Gupta, P.; Khan, M. S.; Lewis, J. R. *Tetrahedron* **1981**, *37*, 209. (e) Watanabe, M.; Kurosaki, A.; Furukawa, S. *Chem. Pharm. Bull.* **1984**, *32*, 1264.

(7) Blechert, S.; Fichter, K.; Winterfeldt, E. *Chem. Ber.* **1978**, *111*, 439.

(8) For the present work, aminochromene **1** was obtained in 65% yield in four steps from the commercially available 2,2-dimethyl-7-methoxychromanone using minor variations of the procedures described in ref 7.

(9) Nishi, H.; Kohno, H.; Kano, T. *Bull. Chem. Soc. Jpn.* **1981**, *54*, 1897.

0022-3263/90/1955-2245$02.50/0