

Synthesis of Tetrahydropyrimidines with 2-Oxoalkyl Groups using Pyrimidinium Salts and Enol Silyl Ethers: Formation of Diazabicyclo[3.3.1]nona-3,6-diene Derivatives¹

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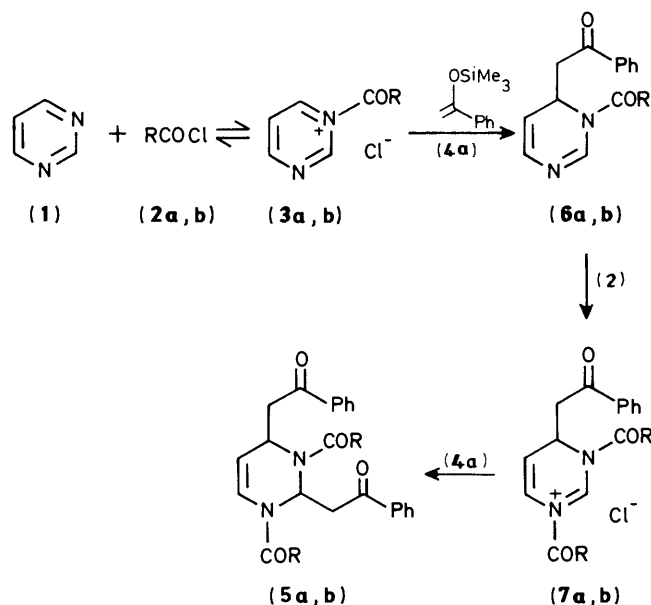
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Reactions of *N*-silyl- or *N*-acyl-pyrimidinium salts with enol trimethylsilyl ethers were carried out to afford the adducts with a 2-oxoalkyl group, that is, 2-hydroxy-4-(2-oxoalkyl)-1,2,3,4-tetrahydropyrimidines (**9**) or the 3-acyl derivatives (**8**), respectively. Monoacylation of compounds (**9**) gave monoamides (**8**) in high yields. Exhaustive acylation of diamines (**9**) with a large excess of 2,2,2-trichloroethyl chloroformate in the presence of pyridine gave bicyclic compounds, 2-oxa-8,9-diazabicyclo[3.3.1]nona-3,6-dienes (**14**). By addition of trifluoroacetic acid, compounds (**14**) were reopened to afford 3,4-dihydropyrimidinium salts (**11'**), which were subjected to nucleophilic attack to give 1,2,3,4-tetrahydropyrimidines (**16**) in high yield.

Pyrimidines form part of the skeleton of the nucleic acids and much research has been carried out on pyrimidines with oxygen and nitrogen substituents at the 2- and/or 4-position.² The chemistry of dihydropyrimidines has attracted increasing interest especially in respect of their amidinic tautomerism,³ but on the whole it can be said that relatively little attention has been focussed on hydropyrimidines, irrespective of the reported biological activities of simple di- and tetra-hydropyrimidines.⁴ Synthesis of hydropyrimidines has been achieved by the direct cyclization and nucleophilic addition of organolithium reagents to the pyrimidine ring.⁵ However, the synthetic possibility of obtaining hydropyrimidines *via* pyrimidinium salts has been neglected, although van der Plas reported the ring transformation of pyrimidine by the reaction of pyrimidinium salts with nucleophiles.⁶ This method is attractively based on the expected mild reaction conditions and chemoselectivity, and in addition a variety of hydropyrimidines may be synthesized.

Recently we have developed the reaction of heteroatomic cations such as pyridinium, quinolinium, and isoquinolinium salts with soft nucleophiles, *e.g.*, enol silyl ethers,⁷ boron enolates,⁸ trialkyl phosphite,⁹ and alkylcopper,¹⁰ and have discovered novel methods for introducing a variety of substituents regioselectivity into parent heteroaromatics. We have now extended the scope of the reaction to pyrimidinium salts. Enol silyl ethers (**4**) were employed here because of their high chemoselectivity, and ready availability from ketones and esters, and also because of the usefulness of the resulting 2-oxoalkyl group for further transformation.

According to the reported method for pyridine,⁷ we attempted to quaternize pyrimidine (**1**) with acetyl chloride (1 mol equiv.) (**2a**) and then to treat the product with the trimethylsilyl ether of enolic acetophenone (**4a**) (1 mol equiv.). To our surprise, a 1,2,3,4-tetrahydropyrimidine with two phenacyl groups (**5a**) was obtained as a mixture of diastereoisomers, which were assigned by ¹H n.m.r., mass spectra, and elemental analyses. No 1:1 adduct (**6a**) was observed even for a prolonged reaction of (**2a**) and pyrimidine (**1**) before the addition of enol (**4a**). This result indicated that equilibrium was present between (**1**) and its salt (**3a**) during the quaternization of pyrimidine, and the 1,6-dihydropyrimidine (**6**) once formed was further acetylated by the remaining acetyl chloride to give the dihydropyrimidinium salt (**7a**), which was more reactive than (**3a**) towards (**4a**), resulting in the formation of (**5a**) (Scheme 1). Similar results were obtained when ethyl chloroformate (**2b**) (1 mol equiv.) was used as a quaternizing

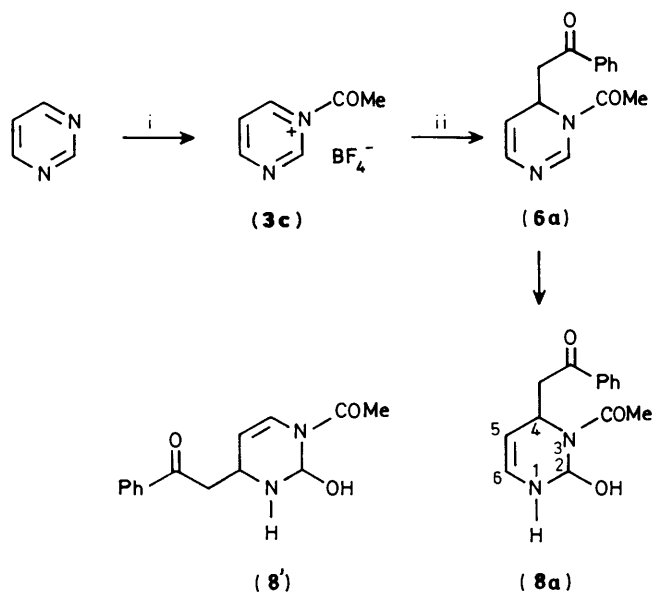


Scheme 1. a; R = Me, b; R = EtO

reagent, thus affording product (**5b**) in 44% yield. We tried in vain to isolate the *N*-acetylpyrimidinium salt (**7**), although it is known that *N*-acetylpyrimidinium salts can be isolated.¹¹ This difference is probably due to the lower nucleophilicity of pyrimidine; the basicity of pyrimidine ($\text{p}K_{\text{a}}$, 1.30) is *ca.* 10⁴-times smaller than that of pyridine ($\text{p}K_{\text{a}}$, 5.20).^{5c,12}

Replacement of the chloride ion by a less nucleophilic anion may avoid the equilibration. In the presence of silver tetrafluoroborate, 3-acetyl-2-hydroxy-4-phenacyl-1,2,3,4-tetrahydropyrimidine (**8a**) was obtained in at most 32% yield, accompanied by precipitation of AgCl. The structure of compound (**8a**) was assigned by the m.s., elemental analysis, and the ¹H n.m.r. spectrum. By the addition of D₂O to a deuteriochloroform solution of (**8a**), the signal at δ 9.34 (d, *J* 11 Hz, 1 H) disappeared and the integrated area of the multiplet at δ 7.34–8.24 (m, 7 H) decreased to 6 protons [Ph + 2-H]. It is interesting that the peak at δ 6.77 (dd, *J* 11, 8 Hz, 1 H, 6-H) simplified to a doublet (*J* 8 Hz), thus the signal was also coupled with the NH at the 1-position. Consequently the 2-oxoalkyl

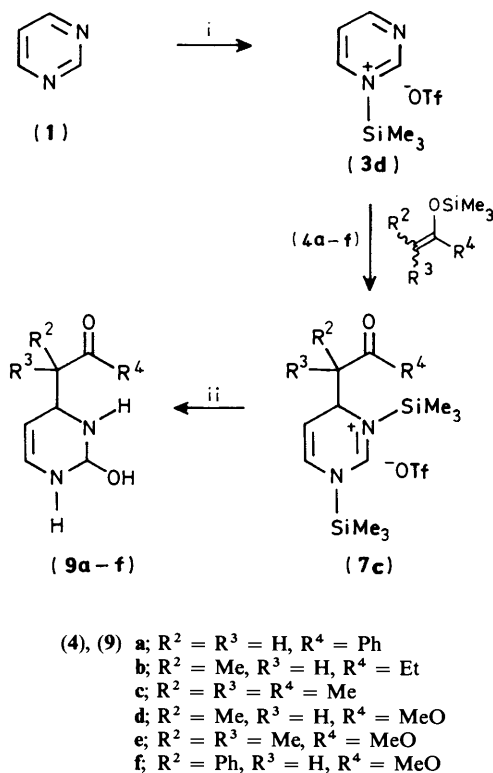
group had been introduced not γ but α to the acetyl group. Any other isomer such as (8') was not observed. The ^1H n.m.r. spectrum of the crude reaction mixture showed the presence of the 1,6-dihydropyrimidine (6a), which was hydrated to (8a) in the purification process. The reaction sequence is illustrated in Scheme 2.



Scheme 2. Reagents: i, MeCOCl , AgBF_4 ; ii, (4a)

We examined the effect of molar ratio of the reagents, reaction temperature, the reaction time of the quaternization and of the addition of (4a), but could not improve the yield of (8a). The by-products were the tetrahydropyrimidine (5a) and some unidentified ring-opened products. Therefore the low yield of compound (8a) may be due to the inefficiency of the counter-anion exchange or to dication formation in the quaternization step.

Reaction of *N*-Trimethylsilylpyrimidinium Trifluoromethanesulphonate (Triflate) with Silyl Enol Ethers.—Pyrimidinium salts quaternized with an alkyl or trimethylsilyl group did not react with enol silyl ethers (4).¹³ In contrast, *N*-trimethylsilylpyrimidinium salt, which could be readily formed by the reaction of pyrimidine (1) with trimethylsilyl triflate, reacted with enol (4a) to give 2-hydroxy-4-phenacyl-1,2,3,4-tetrahydropyrimidine (9a) in ca. 50% yield. The success of the reaction is explained by the stronger electrophilicity of the pyrimidinium salt. The reaction sequence is illustrated in Scheme 3. Further nucleophilic attack by (4a) on (7c) did not occur due to the large steric hindrance in the intermediate (7c). Although compound (9a) was unstable to acid and base and did not give correct elemental analysis (may be contaminated with sodium trifluoromethanesulphonate), it showed a sharp m.p. (175.5–177.5 °C) and a clear ^1H n.m.r. spectrum. By the addition of D_2O to a $(\text{CD}_3)_2\text{SO}$ ($[\text{2H}_6]$ DMSO) solution of (9a), two peaks, at δ 10.09 (s, 1 H) and 10.87 (s, 1 H), disappeared and the integrated area of the multiplet at δ 7.33–8.33 (m, 7 H) decreased to 6 protons. Therefore 3 labile hydrogens are indicated. The purity of the crystals of compound (9a) was determined by ^1H n.m.r. spectroscopy with 4-dimethylaminopyridine (DMAP) as a reference. Thus measured amounts of (9a) and DMAP were dissolved in $[\text{2H}_6]$ DMSO and the purity of compound (9a) was calculated to be in the range 60–70% for each sample by comparison of the integral ratio of the specified peaks of the two compounds.



Scheme 3. Reagents: i, TMSOTf; ii, water

In order to confirm the structure (9a) and to lead to other useful compounds, the acylation of compound (9a) was attempted. Acetic anhydride and (9a) (1:1 molar ratio) were treated to give compound (8a) in high yield (ca. 80%), which was identical with the compound formed in the reaction of (3c) and (4a) (*vide supra*). This result supported the structure (9a) and indicated that the acylation took place selectively at the 3-position, probably due to the higher nucleophilicity of the amino nitrogen than that of the enamino nitrogen. The overall yields of compounds (8a–i) from pyrimidine itself are summarized in Table 1.

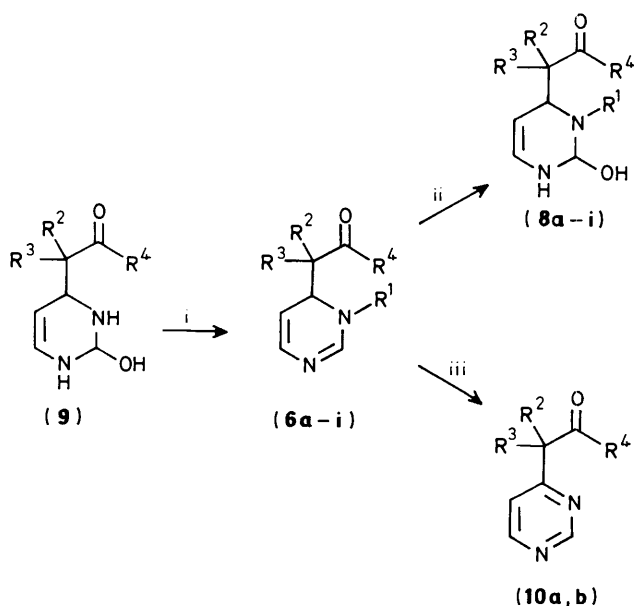
By inspection of ^1H n.m.r. spectrum of the crude reaction mixture of compounds (9) and acetyl chloride (or ethyl chloroformate), dihydropyrimidines (6) were found to be the initial products. Thus the proton at the 6-position in compounds (6) appeared as δ 6.4–6.8 as only a doublet (no coupling with NH). The mechanism of the dehydration may be an acid–base-catalysed reaction by triethylamine and its hydrochloride. Compounds (6) were hydrated to give (8) during isolation. The rate of hydration was slower in the ethoxycarbonyl series (6b), (6d–g), (6i) than in the acetyl ones (6a), (6c), (6h), also slower in esters (6f–i) than in ketones (6a–e). In fact, compounds (6g) and (6i) were isolated in almost pure form by t.l.c. on Kieselguhr (Merck Art 8129). We then attempted to oxidize crude (6) to the corresponding pyrimidine. By the use of 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (DDQ), compounds (6f) and (6i) could be oxidized to pyrimidine derivatives (10a) and (10b) in 15 and 47% yield from parent pyrimidine, respectively (Scheme 4). However, in the ketone series, these compounds could not be oxidized to pyrimidines and gave a mixture of decomposed products.

When a large excess of the acylating agent was used in the acylation of compounds (9), the ring-opened product (13) was the main product. For example, when ethyl chloroformate (8 mol equiv.) in pyridine was treated with compound (9a), the

Table 1. Synthesis of 4-(2-oxoalkyl)-1,2,3,4-tetrahydropyrimidines (**8**)

Entry	(8)	COR	R ²	R ³	R ⁴	Yield ^a (%)	Reaction conditions ^b	
							1st step	2nd step
1	(8a)	COMe	H	H	Ph	43	rt, 4 days	rt, 2.6 h ^c
2	(8b)	CO ₂ Et	H	H	Ph	43	0 °C, 4.8 days	0 °C, 10 min
3	(8c)	COMe	Me	H	Et	40	0 °C, 7 days	0 °C, 10 min
4	(8d)	CO ₂ Et	Me	H	Et	30	10 °C, 5.7 days	0 °C, 10 min
5	(8e)	CO ₂ Et	Me	Me	Me	43	0 °C, 9 days	0 °C, 10 min
6	(8f)	CO ₂ Et	Me	H	OMe	22	0 °C, 3.6 days	0 °C, 10 min
7	(8g)	CO ₂ Et	Me	Me	OMe	32 ^d	rt, 4 days	0 °C, 10 min
8	(8h)	COMe	Ph	H	OMe	63	rt, 2 days	rt, 2.5 h ^c
9	(8i)	CO ₂ Et	Ph	H	OMe	68	10 °C, 2.6 days	0 °C, 10 min

^a Isolated yield from pyrimidine by flash column chromatography. A mixture of diastereoisomers. ^b rt = Room temperature. ^c Catalytic amount of 4-dimethylaminopyridine was used. ^d In this experiment (**6g**) was the main product, and (**8g**) was a by-product (ratio 9:1).



- (6), (8) **a**; R¹ = MeCO, R² = R³ = H, R⁴ = Ph
b; R¹ = EtO₂C, R² = R³ = H, R⁴ = Ph
c; R¹ = MeCO, R² = Me, R³ = H, R⁴ = Et
d; R¹ = EtO₂C, R² = Me, R³ = H, R⁴ = Et
e; R¹ = EtO₂C, R² = R³ = R⁴ = Me
f; R¹ = EtO₂C, R² = Me, R³ = H, R⁴ = MeO
g; R¹ = EtO₂C, R² = R³ = Me, R⁴ = MeO
h; R¹ = MeCO, R² = Ph, R³ = H, R⁴ = MeO
i; R¹ = EtO₂C, R² = Ph, R³ = H, R⁴ = MeO
(10) a; R² = Me, R³ = H, R⁴ = MeO
b; R² = Ph, R³ = H, R⁴ = MeO

Scheme 4. Reagent: **i**, Ac₂O or EtO₂CCl; **ii**, water; **iii**, DDQ

acyclic dicarbamate (**13a**) was obtained in 19% yield. The ¹H n.m.r. spectrum of (**13a**) has a characteristic signal at δ 9.12 for an aldehyde proton. On addition of D₂O to a deuteriochloroform solution of compound (**13a**), the signal at δ 6.75 (dd, *J* 9, 8 Hz) changed to a doublet (*J* 9 Hz) and the integrated area of the multiplet (δ 7.31–8.10, 6 H) decreased to 5 protons, thus showing the presence of an enamino group. Interestingly, when 2,2,2-trichloroethyl chloroformate was used instead of ethyl chloroformate, the bicyclo[3.3.1]nonadiene derivatives (**14a**) was obtained as well as the ring-opened product (**13b**). The ¹H n.m.r. spectrum of compound (**14a**) shows that there are two

Table 2. Synthesis of 2-oxa-8,9-diazabicyclo[3.3.1]nona-3,6-dienes (**14**) or -6-ene (**15a**)

Entry (14), (15)	R ²	R ³	R ⁴	Yield ^a (%)	Reaction conditions ^d	
					1st step ^b	2nd step ^c
1 (14a)		H	Ph	29	rt, 3 days	rt, 18 h
2 (14b)		Me	Et	27	rt, 4 days	rt, 18 h
3 (15a)	Me	Me		37	0 °C, 9 days	rt, 17 h

^a Isolated yield from pyrimidine. ^b Acetonitrile was used as solvent. ^c Pyridine was used as solvent. ^d rt = Room temperature.

Table 3. Synthesis of 1,2,3,4-tetrahydropyrimidines (**16**) from compound (**14a**)

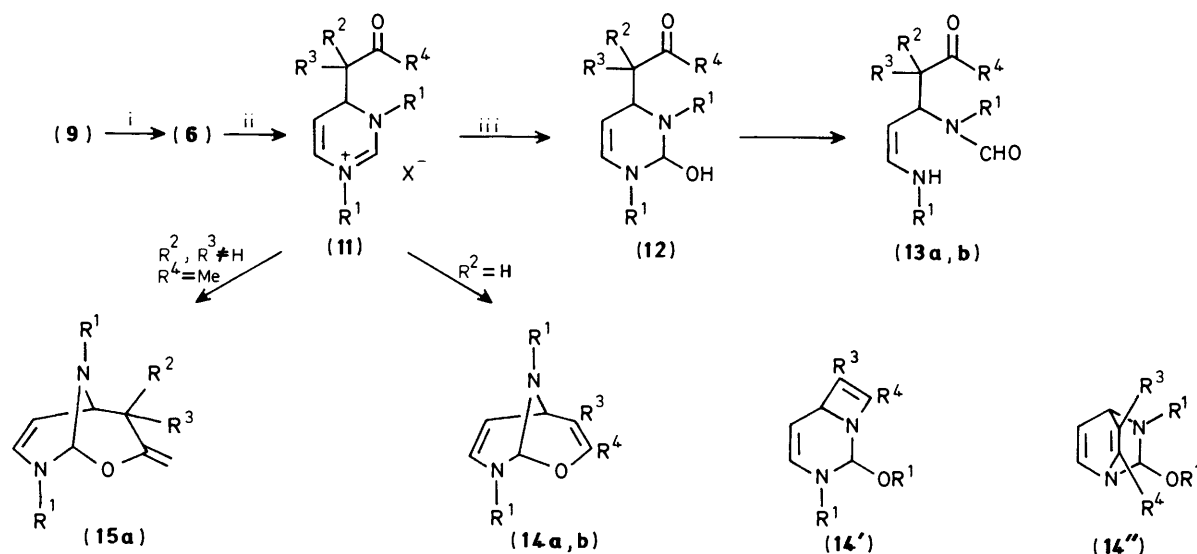
Entry	(16)	Nucleophile	Nu	Yield ^a (%)	Reaction conditions ^b
1	(16a)	PhSH	SPh	98	rt, 10 min
2	(16b)	MeOH	OMe	90	rt, 10 min
3	(16c)	EtOH	OEt	88	rt, 10 min
4	(16d)	(4c)	CMe ₂ COMe	9	rt, 5 h
5	(16e)	(4e)	CMe ₂ CO ₂ Me	67	rt, 5.5 h

^a Isolated yield by t.l.c. ^b Dichloromethane was used as solvent. rt = Room temperature.

sets of singlets for the OCH₂CCl₃ group, and the methylene proton of the phenacyl group is not present. The mass spectrum showed the molecular ion peak at *m/z* 548 containing six chlorine atoms, indicating that two CO₂CH₂CCl₃ groups were introduced and that deprotonation occurred at the phenacyl group. Elemental analysis of the white crystals supported the molecular formula of compound (**14a**).

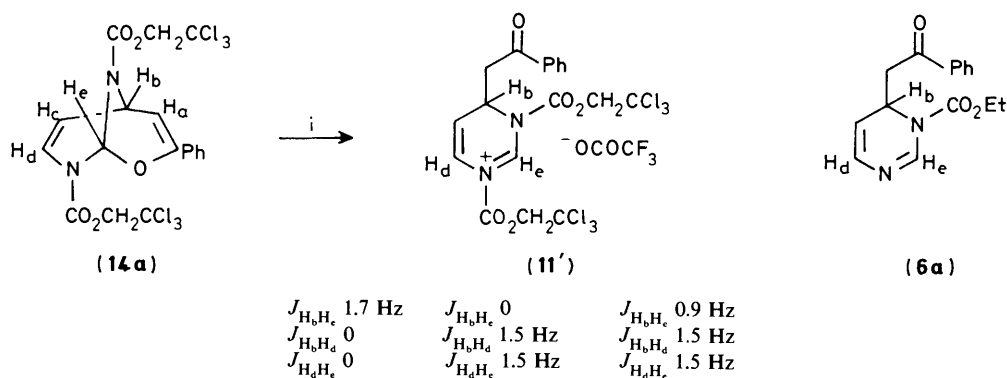
The reaction sequence is illustrated in Scheme 5. The dehydration of compounds (**9**) takes place in the first acylation to give intermediates (**6**) and the second acylation affords the dihydropyrimidinium cation (**11**). In the presence of excess of acylating reagent, the water generated is trapped not by the salt (**11**) but by the acylating reagent; therefore the intramolecular cyclization takes place to give compounds (**14**) via the enolate generated *in situ* by deprotonation (R² = H) with pyridine. Even in the case of compound (**9c**), which has no internal enolizable hydrogen, intramolecular cyclization took place to give the *exo*-methylene product (**15a**). Some examples of this type of compound obtained from pyrimidine are shown in Table 2. In the case of ethyl chloroformate, the cyclization product was not obtained, probably due to lower reactivity of the resulting dihydropyrimidinium salt.

When bicycle (**14a**) was dissolved in deuteriochloroform and



- (13) a; R¹ = EtO₂C, R² = R³ = H, R⁴ = Ph
 b; R¹ = Cl₃CCH₂O₂C, R² = R³ = H, R⁴ = Ph
 (14) a; R¹ = Cl₃CCH₂O₂C, R³ = H, R⁴ = Ph
 b; R¹ = Cl₃CCH₂O₂C, R³ = Me, R⁴ = Et
 (15) a; R¹ = Cl₃CCH₂O₂C, R² = R³ = Me

Scheme 5. Reagents: i, R¹X; ii, R¹X, pyridine; iii, water



Scheme 6. Reagent: i, TFA

from mol equiv. to an excess of trifluoroacetic acid (TFA) was added, a clear ¹H n.m.r. spectrum was obtained to show the regeneration of dihydropyrimidinium salt (11'). The long-range coupling (W coupling, *J* 1.7 Hz) between H_b and H_e is characteristic in compound (14a) but this coupling disappears on protonation and new two long-range couplings (*J* 1.5 Hz) appear between H_b and H_d and also between H_e and H_d. This pattern is closely related to that of the crude dihydropyrimidine (6a), which also has long-range coupling (*J* 1.5 Hz) between H_b and H_d and H_d and H_e, although another small coupling (0.9 Hz, between H_b and H_e) is present in compound (6a) (Scheme 6).

After quenching of the protonated mixture with 5% aqueous NaHCO₃ and purification (t.l.c.), the biscarbamate (13b) was obtained in 20% yield. This supports our presumption of the formation of intermediate (11') [(11)]. The structure of compounds (14) was thus determined, excluding alternatives (14') and (14'').

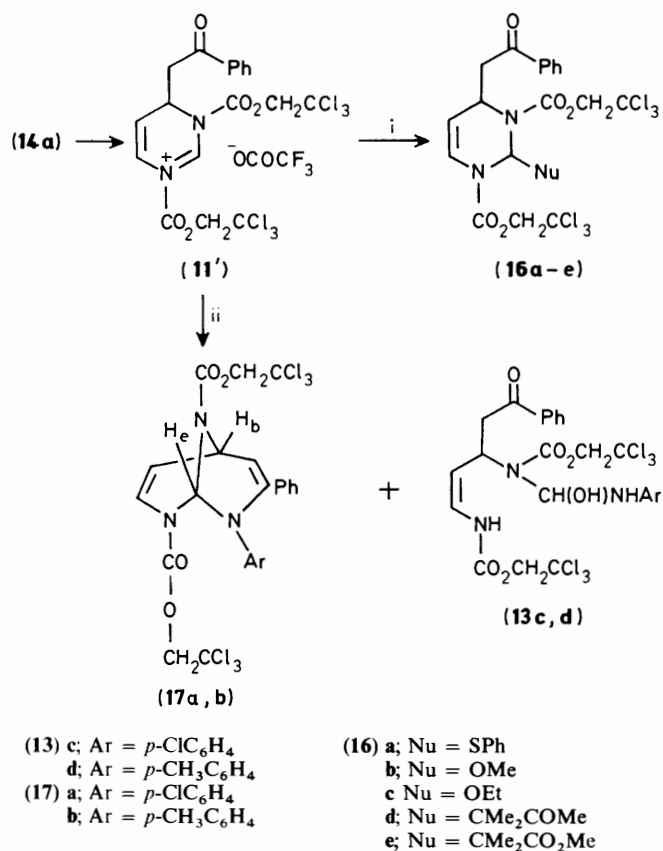
It is expected therefore that the salt (11') can be used as an intermediate for 1,2,3,4-tetrahydropyrimidine synthesis. This was realized as follows. TFA (1 mol equiv.) was added to the bicycle (14a), and then excess of ethanol was added. After being stirred for 10 min, the reaction mixture was quenched with 5%

aqueous NaHCO₃ and purified by t.l.c. to give compound (16c) in 90% yield. Methanol and thiophenol gave similar results as shown in Table 3. When enol silyl ether (4c) was used as a carbon nucleophile the adduct (16d) was obtained in only 9% yield, and compound (14a) was recovered (31%). The absence of compound (14a) in the protonated species was confirmed by t.l.c. and ¹H n.m.r. spectroscopy; therefore silyl ether (4c) behaved as a Lewis base,¹⁴ and enolized compound (11') to give back the starting material (14). When the more reactive ketene silyl acetal (4e) was used, similar regeneration of starting material (14a) was observed but further protonation of (14a) on the second addition of the acid followed by that of excess of (4e) gave the expected adduct (16e) in 67% yield as a mixture of diastereoisomers (Scheme 7).

When some anilines were used as nitrogen nucleophiles, simple adducts were not obtained but the bicyclo[3.3.1]nonadiene derivative (17) and hydrolysis products such as (13c) or (13d) were obtained instead. The ¹H n.m.r. spectrum of product (17) was similar to that of (14a) with respect to the large *W* coupling between H_b and H_e. Other spectral data and elemental analyses support the bicyclo[3.3.1]nonadiene structure. Water eliminated in the enamine formation caused

Table 4. Synthesis of 2,8,9-triazabicyclo[3.3.1]nona-3,6-dienes (17) from compound (14a)

Entry (17)	Ar	Drying reagent	Yield ^a (%)
1 (17b)	<i>p</i> -MeC ₆ H ₄		13
2 (17b)	<i>p</i> -MeC ₆ H ₄	MgSO ₄	38
3 (17a)	<i>p</i> -ClC ₆ H ₄	MgSO ₄	35
4 (17a)	<i>p</i> -ClC ₆ H ₄	Molecular sieves 4A	53

^a Isolated yield by t.l.c. Dichloromethane was used as solvent.Scheme 7. Reagents: i, Nucleophile; ii, ArNH₂

decomposition of intermediate (11') to give biscarbamates (13c) and (13d). Thus a drying agent such as anhydrous MgSO₄ and molecular sieves was added to the reaction mixture, whereupon the yield of bicycle (17) was raised to 53% as shown in Table 4.

Finally, the different behaviour between pyrimidine and pyridine was disclosed during quaternization and reaction with enol silyl ethers; also, the unexpected formation of bicyclo[3.3.1]nonadienes (14) and their ring-opening to dihydropyrimidinium salts such as (11') by protonation were found to be unique reactions of the pyrimidine system.

Experimental*

M.p.s were measured on a Yanagimoto micro melting point apparatus and i.r. spectra were obtained with a Hitachi 215

spectrometer. ¹H N.m.r. spectra were obtained with Varian T-60 and Hitachi R-90H spectrometers. ¹³C N.m.r. spectra were obtained with a Hitachi R-90H spectrometer. Flash column chromatography was carried out with Merck silica gel 60 (Art 9385). T.l.c. was performed on Merck silica gel GF-254 plates. R_F Values were determined on these plates.

Reaction of 1-Acetyl- (or 1-Ethoxycarbonyl)-pyrimidinium Chloride (3) with the Trimethylsilyl Ether of Enolic Acetophenone (4a). *General Procedure.*—To a solution of pyrimidine (1) (5.0 mmol) in acetonitrile (5 ml) was added acetyl chloride (or ethyl chloroformate) (5.0 mmol) at 0 °C. After the mixture was stirred for 15 min, compound (4a) (0.99 ml, 5.1 mmol) was added to the solution. The resulting reaction mixture was stirred for 5 h at room temperature, then quenched with water (ca. 20 ml). The products were extracted with ether (50 ml × 3). After drying (MgSO₄) and evaporation of the solvent, the crude mixture was separated by t.l.c. (hexane–AcOEt 2:1) to afford compound (5a) [or (5b)].

1,3-Diacetyl-2,4-diphenacyl-1,2,3,4-tetrahydropyrimidine (5a). Total yield 48% [(5a)-i:(5a)-ii (diastereoisomer ratio) = 2:3]. The less polar diastereoisomer (5a)-i had R_F 0.27 (hexane–AcOEt 2:1); m.p. 149–151 °C (Found: C, 71.0; H, 6.1; N, 6.9. C₂₄H₂₄N₂O₄ requires C, 71.27; H, 5.98; N, 6.93%); ν_{max}(KBr) 1 600br cm⁻¹; δ_H(CDCl₃) 2.1 (s, 3 H), 2.3 (s, 3 H), 2.5–4.3 (m, 4 H), 4.6–5.1 (m, 1 H), 5.6 (dd, *J* 8, 4 Hz, 1 H), 6.5 (d, *J* 8 Hz, 1 H), 6.9 (t, *J* 6 Hz, 1 H), and 7.1–8.1 (m, 10 H); δ_C(CDCl₃) 21.2 (q), 22.8 (q), 40.7 (t), 44.6 (t), 48.1 (d), 60.3 (d), 115.3 (d), 123.8 (d), 128.2 (d), 128.4 (d), 128.8 (d), 133.4 (d), 136.9 (s), 167.1 (s), 170.7 (s), 196.2 (s), and 197.6 (s); *m/z* 404 (*M*⁺, 3%), 361 (4), 241 (2), and 146 (100).

The more polar diastereoisomer (5a)-ii had R_F 0.20 (hexane–AcOEt 2:1); m.p. 170–172 °C (Found: C, 71.0; H, 6.1; N, 6.9%); ν_{max}(KBr) 1 680 and 1 645 cm⁻¹; δ_H([²H₆]DMSO; 120 °C) 2.08 (s, 3 H), 2.14 (s, 3 H), 3.26 (dd, *J* 18, 5 Hz, 1 H), 3.28 (dd, *J* 18, 8 Hz, 1 H), 3.48 (dd, *J* 16, 6 Hz, 1 H), 3.60 (dd, *J* 16, 7.5 Hz, 1 H), 4.95–5.20 (m, 1 H), 5.20 (dd, *J* 8, 3.5 Hz, 1 H), 6.84 (dd, *J* 8, 2 Hz, 1 H), 6.94 (dd, *J* 7.5, 6 Hz, 1 H), and 7.29–8.10 (m, 10 H); δ_C(CDCl₃) 21.0 (q), 21.8 (q), 40.0 (t), 43.7 (t), 45.3 (d), 59.3 (d), 110.0 (d), 122.4 (d), 128.1 (d), 129.1 (d), 133.4 (d), 133.8 (d), 136.3 (s), 167.0 (s), 170.2 (s), 196.3 (s), and 197.0 (s); *m/z* 404 (*M*⁺, 1%), 361 (15), 241 (8), and 146 (100).

1,3-Bis(ethoxycarbonyl)-2,4-diphenacyl-1,2,3,4-tetrahydropyrimidine (5b). Yield 44% (diastereoisomer ratio 1:1). The less polar diastereoisomer (5b)-i had R_F 0.22 (hexane–AcOEt 8:3), and was an oil; ν_{max}(KBr) 1 700br cm⁻¹; δ_H(CDCl₃) 1.16 (t, *J* 7 Hz, 6 H), 2.74–3.50 (m, 4 H), 4.10 (q, *J* 7 Hz, 4 H), 4.64–5.00 (m, 1 H), 5.53 (dd, *J* 8, 4 Hz, 1 H), 6.43–6.86 (m, 2 H), and 7.33–8.20 (m, 10 H); *m/z* 464 (*M*⁺, 1%), 391 (2), 344 (23), 271 (16), and 105 (100).

The more polar diastereoisomer (5b)-ii had R_F 0.18 (hexane–AcOEt 8:3), and was an oil; ν_{max}(KBr) 1 690br cm⁻¹; δ_H(CDCl₃) 1.1–1.5 (m, 6 H), 3.2–3.7 (m, 4 H), 3.7–4.5 (m, 4 H), 4.8–5.4 (m, 2 H), 6.5–7.0 (m, 2 H), and 7.3–8.2 (m, 10 H); *m/z* 464 (*M*⁺, 1%), 391 (3), 344 (42), 271 (24), and 105 (100).

Reaction of 1-Acetylpyrimidinium Tetrafluoroborate (3c) with the Trimethylsilyl Ether of Enolic Acetophenone (4a).—To a solution of silver tetrafluoroborate (583 mg, 2.7 mmol) in acetonitrile (14 ml) at 0 °C were added pyrimidine (0.23 ml, 2.91 mmol) and acetyl chloride (0.21 ml, 2.88 mmol). A white precipitates were formed immediately, and the mixture was stirred for 2 h. Compound (4a) was added, the mixture was stirred for an additional 1.2 h, and the resulting mixture was quenched with 5% aqueous Na₂CO₃ and brine and extracted with dichloromethane (50 ml × 3). After drying (MgSO₄) and evaporation of the solvent, the crude mixture was subjected to flash chromatography (hexane–AcOMe 3:2; acetone; EtOH) to

* Non-systematic names are used throughout for non-ionic products.

afford compounds (**5a**)-i, (**5a**)-ii, and (**8a**) in 11, 3, and 32% yield, respectively. 3-Acetyl-2-hydroxy-4-phenacyl-1,2,3,4-tetrahydropyrimidine (**8a**) was obtained as an oil (Found: C, 64.9; H, 6.45; N, 10.5. $C_{14}H_{16}N_2O_3$ requires C, 64.60; H, 6.20; N, 10.76%; ν_{\max} (neat) 3 670—2 700, 1 690, and 1 655 cm^{-1} ; δ_H ($CDCl_3$) 2.07, 2.10 (s, 3 H), 3.23 and 3.21 (dd, J 18, 5 Hz, 1 H), 3.45 and 3.43 (dd, J 18, 5 Hz, 1 H), 4.76 (dd, J 8, 8 Hz, 1 H), 5.00—5.45 (m, 1 H), 6.77 (dd, J 11, 8 Hz, 1 H), 7.34—8.24 (m, 7 H), and 9.34 (br d, J 11 Hz, 1 H); δ_C ($CDCl_3$) 22.8, 41.8, 43.6, 111.6, 124.0, 128.8, 129.5, 134.3, 137.6, 163.1, 170.0, and 198.6; m/z 260 (M^+ , 8%), 242 (24), 199 (8), and 105 (100).

Reaction of 1-Trimethylsilylpyrimidinium Triflate (3d) with Compound (4a). General Procedure.—To a solution of pyrimidine (0.24 ml, 3.0 mmol) in acetonitrile (3 ml) at 0 °C were added trimethylsilyl triflate (0.55 ml, 3.0 mmol) and compound (**4a**) (3.0 mmol). The reaction mixture was stirred for 2—9 days at between 0 °C and room temperature. The resulting mixture was treated with 5% aqueous $NaHCO_3$ and then with brine, and was extracted with ethyl acetate (50 ml \times 3). The crude reaction mixture was used in the acylation (*vide infra*) except for (**9a**). Compound (**9a**) could be recrystallized from acetone (*ca.* 60% purity, 40% yield). 2-Hydroxy-4-phenacyl-1,2,3,4-tetrahydropyrimidine (**9a**), contaminated with sodium trifluoromethanesulphonate, had m.p. 175.5—177.5 °C; ν_{\max} (KBr) 3 330, 3 230, and 1 680 cm^{-1} ; δ_H ($[^2H_6]DMSO$) 3.10—4.07 (m, 2 H), 4.70—5.10 (m, 1 H), 5.27 (dd, J 8, 4 Hz, 1 H), 6.35 (br d, J 8 Hz, 1 H), 7.33—8.33 (m, 7 H), 10.09 (br s, 1 H), and 10.87 (br s, 1 H); δ_C ($[^2H_6]DMSO$) 45.9 (d), 46.5 (t), 109.0 (d), 121.8 (d), 128.2 (d), 129.0 (d), 133.9 (d), 136.2 (s), 150.6 (d), and 197.0 (s); m/z 120 (38%), 105 (100), and 80 (60).

Acylation of Compound (9). General Procedure.—The crude reaction mixture described above [from pyrimidine (1.27 mmol)] was dissolved in acetonitrile (2 ml). Triethylamine (2 ml) was added to the solution, followed by the dropwise addition of ethyl chloroformate (0.12 ml, 1.27 mmol) (at 0 °C). The mixture was stirred for 10 min and was treated successively with 5% aqueous $NaHCO_3$ (2.2 ml) and brine (40 ml), and then extracted with ethyl acetate (30 ml \times 3). The crude mixture was subjected to t.l.c. (hexane; hexane-AcOEt, 5:2) to afford compounds (**8b**—i).

3-Ethoxycarbonyl-2-hydroxy-4-phenacyl-1,2,3,4-tetrahydropyrimidine (**8b**) was an oil (43% from pyrimidine, as a mixture of diastereoisomers) (Found: C, 61.7; H, 6.3; N, 9.5. $C_{15}H_{18}N_2O_4$ requires C, 62.06; H, 6.25; N, 9.65%; ν_{\max} (neat) 3 280, 2 980, 1 720, and 1 660 cm^{-1} ; δ_H ($CDCl_3$) 1.27 (t, J 6.9 Hz, 3 H), 3.25 (dd, J 5.3, 17.6 Hz, 1 H), 3.47 (dd, J 5.1, 17.6 Hz, 1 H), 4.17 (q, J 6.9 Hz, 2 H), 4.66 (dd, J 8.8, 8.8 Hz, 1 H), 4.98—5.37 (m, 1 H), 6.53 (dd, J 10.8, 8.8 Hz, 1 H), 7.12 and 7.21 (br s, 1 H), 7.30—8.02 (m, 5 H), 8.12 (s, 1 H), and 8.35 (d, J 10.8 Hz, 1 H); m/z 290 (M^+ , 9%), 272 (17), 261 (7), 105 (95), and 84 (100).

3-Acetyl-2-hydroxy-4-(1-methyl-2-oxobutyl)-1,2,3,4-tetrahydropyrimidine (**8c**) was obtained as an oil (40% from pyrimidine, as a mixture of diastereoisomers); δ_H ($CDCl_3$) 0.81—1.32 (m, 6 H), 1.99 and 2.06 (s, 3 H), 2.37—3.10 (m, 3 H), 4.34—5.09 (m, 2 H), 6.74 (dd, J 7.5, 10.8 Hz, 1 H), 7.16 and 7.49 (d, J 8.7 Hz, 1 H), 8.10 and 8.14 (s, 1 H), and 9.06 and 9.26 (d, J 10.8 Hz, 1 H).

3-Ethoxycarbonyl-2-hydroxy-4-(1-methyl-2-oxobutyl)-1,2,3,4-tetrahydropyrimidine (**8d**) was obtained in a total yield of 30% (from pyrimidine, in a diastereoisomer ratio of 1:2). The less polar diastereoisomer, R_F 0.41 (hexane-AcOEt 2:5), was an oil (Found: C, 56.0; H, 7.8; N, 10.9. $C_{12}H_{20}N_2O_4$ requires C, 56.23; H, 7.86; N, 10.93%; ν_{\max} (neat) 3 290, 2 990, 1 718, 1 664, and 752 cm^{-1} ; δ_H ($CDCl_3$) 1.04 and 1.06 (t, J 7.2 and 7.4 Hz, 3 H), 1.19 and 1.21 (d, J 7.3 and 7.5 Hz, 3 H), 1.25 (t, J 7.0 Hz, 3 H),

2.47 and 2.50 (q, J 7.2 and 7.4 Hz, 2 H), 2.68—2.95 (m, 1 H), 4.17 (q, J 7.0 Hz, 2 H), 4.55 (dd, J 8.6, 8.6 Hz, 1 H), 4.66 and 4.87 (dd, J 8.6, 5.9 Hz and 8.6, 6.2 Hz, 1 H), 6.56 (dd, J 8.6, 10.8 Hz, 1 H), 6.73 and 6.82 (br m, 1 H), and 7.88—8.45 (m, 2 H); m/z 256 (M^+ , 4.6%), 238 (5), 227 (3), 171 (38), and 83 (100).

The more polar diastereoisomer, R_F 0.3 (hexane-AcOEt 2:5), was an oil; ν_{\max} (neat) 3 270, 2 990, 1 730, 1 662, and 750 cm^{-1} ; δ_H ($CDCl_3$) 1.04 and 1.07 (t, J 7.2 and 7.4 Hz, 3 H), 1.19 and 1.22 (d, J 7.3 and 7.5 Hz, 3 H), 1.28 (t, J 7.1 Hz, 3 H), 2.51 and 2.55 (q, J 7.2 and 7.4 Hz, 2 H), 2.80—3.15 (m, 1 H), 4.17 (q, J 7.1 Hz, 2 H), 4.42 (dd, J 8.6, 8.6 Hz, 1 H), 4.67 and 4.76 (dd, J 8.6, 3.5 and 8.6, 4.2 Hz, 1 H), 6.54 and 6.59 (dd, J 8.6, 11.4 Hz, 1 H), 7.00—7.34 (br m, 1 H), 7.96—8.20 (m, 2 H), and 8.32 (br d, J 11.4 Hz, 1 H); m/z 256 (M^+ , 5%), 238 (5), 227 (3), 171 (31), and 83 (100).

4-(1,1-Dimethyl-2-oxopropyl)-3-ethoxycarbonyl-2-hydroxy-1,2,3,4-tetrahydropyrimidine (**8e**) was an oil (43% from pyrimidine, as a mixture of diastereoisomers) (Found: C, 56.5; H, 8.1; N, 11.0. $C_{12}H_{20}N_2O_4$ requires C, 56.24; H, 7.86; N, 10.93%; δ_H ($CDCl_3$) 1.15 (s, 3 H), 1.18 (s, 3 H), 1.21 (t, J 6.9 Hz, 3 H), 2.10 (s, 3 H), 4.80 (q, J 6.9 Hz, 2 H), 4.30—4.75 (m, 2 H), 6.48 (dd, J 7.8, 10.8 Hz, 1 H), 6.95—7.34 (m, 1 H), and 7.90—8.39 (m, 2 H).

3-Ethoxycarbonyl-2-hydroxy-4-(1-methoxycarbonyl-ethyl)-1,2,3,4-tetrahydropyrimidine (**8f**) was an oil (22% from pyrimidine, as a mixture of diastereoisomers); ν_{\max} (neat) 3 270, 3 000, and 1 730—1 648 cm^{-1} ; δ_H ($CDCl_3$) 1.21 (d, J 7.0 Hz, 3 H), 1.28 (t, J 7.0 Hz, 3 H), 2.74 (dq, J 5.3, 7.0 Hz, 1 H), 3.72 (s, 3 H), 4.17 (q, J 7.0 Hz, 2 H), 4.50 (dd, J 8.7, 8.7 Hz, 1 H), 4.57—4.96 (m, 1 H), 6.54 and 6.63 (dd, J 8.7, 10.9 Hz, 1 H), 6.90—7.18 (br m, 1 H), and 8.01—8.47 (m, 2 H); m/z 258 (M^+ , 3%), 240 (5), 171 (18), and 83 (100).

1-Ethoxycarbonyl-6-(1-methoxycarbonyl-1-methylethyl)-1,6-dihydropyrimidine (**6g**) was obtained in 32% yield (as a mixture containing *ca.* one-ninth of its mol amount (**8g**) as an impurity); δ_H ($CDCl_3$) 1.07 and 1.12 (s, 6 H), 1.25 (t, J 6.6 Hz, 3 H), 3.62 (s, 3 H), 3.85—4.68 (m, 3 H), 4.75 (dd, J 3.1, 8.6 Hz, 1 H), 6.73 (d, J 8.6 Hz, 1 H), and 7.87 (s, 1 H).

3-Acetyl-2-hydroxy-4-(α -methoxycarbonylbenzyl)-1,2,3,4-tetrahydropyrimidine (**8h**) was an oil (63% from pyrimidine, as a mixture of diastereoisomers); ν_{\max} (neat) 3 260, 3 040, 1 730, and 1 650 cm^{-1} ; δ_H ($CDCl_3$) 2.05 (s, 3 H), 3.65 and 3.71 (s, 3 H), 3.78—4.20 (m, 1 H), 4.42—4.97 (m, 1 H), 5.02—5.51 (m, 1 H), 6.51—7.00 (m, 2 H), 7.29 and 7.31 (s, 5 H), 7.68—8.26 (m, 1 H), and 8.83—9.35 (m, 1 H); m/z 290 (M^+ , 04%), 272 (0.6), 213 (0.7), and 141 (100).

3-Ethoxycarbonyl-2-hydroxy-4-(α -methoxycarbonylbenzyl)-1,2,3,4-tetrahydropyrimidine (**8i**) was an oil (68% from pyrimidine, as a mixture of diastereoisomers) (Found: C, 60.1; H, 6.4; N, 8.8. $C_{16}H_{20}N_2O_5$ requires C, 60.00; H, 6.29; N, 7.74%; ν_{\max} (neat) 3 350, 3 000, and 1 730—1 640 cm^{-1} ; δ_H ($CDCl_3$) 1.24 (t, J 7.0 Hz, 3 H), 3.63 and 3.69 (s, 3 H), 3.87 and 3.92 (d, J 9.7 and 7.0 Hz, 1 H), 4.13 (q, J 7.0 Hz, 2 H), 4.45 and 4.64 (dd, J 8.8, 8.8 Hz, 1 H), 5.15 and 5.34 (dd, J 8.8, 7.0 Hz and J 8.8, 9.7 Hz, 1 H), 6.25—6.75 (m, 1 H), 6.80—7.70 (m, 6 H), and 7.78—8.47 (m, 2 H); m/z 320 (M^+ , 3%), 302 (2), 275 (9), 171 (100), and 143 (100).

Oxidation of Dihydropyrimidines (6).—The ethyl acetate extract described above for the acylation of compounds (**9**) was dissolved in toluene (10 ml) and DDQ (295 mg, 1.3 mmol) was added to the solution. The mixture was heated to reflux for 4 h and quenched with aqueous $NaHCO_3$, then extracted with dichloromethane. The extract was subjected to t.l.c. to afford the pyrimidine (**10a**) or (**10b**).

4-(1-Methoxycarbonyl-ethyl)pyrimidine (**10a**) was obtained as an oil (15% from pyrimidine); ν_{\max} (neat) 2 950, 1 730, and 1 550 cm^{-1} ; δ_H ($CDCl_3$) 1.57 (d, J 7.8 Hz, 3 H), 3.71 (s, 3 H), 3.90 (q, J 7.8 Hz, 1 H), 7.30 (dd, J 5.4, 1.8 Hz, 1 H), 8.60 (d, J 5.4 Hz, 1

H), and 9.13 (d, J 1.8 Hz, 1 H); m/z 166 (M^+ , 8%), 151 (7), 135 (7), and 107 (100).

4-(α -Methoxycarbonylbenzyl)pyrimidine (**10b**) was an oil (47% from pyridine) (Found: C, 68.2; H, 5.2; N, 12.1. $C_{13}H_{12}N_2O_2$ requires C, 68.41; H, 5.30; N, 12.27%); ν_{\max} (neat) 1 740, 1 582, and 1 394 cm^{-1} ; δ_H ($CDCl_3$) 3.75 (s, 3 H), 5.16 (s, 1 H), 7.27—7.43 (m, 6 H), 8.61 (d, J 4.8 Hz, 1 H), and 9.16 (d, J 1.2 Hz, 1 H); m/z 228 (M^+ , 33%) and 169 (100).

Synthesis of Acyclic Compounds (13a) and (13b).—The pyrimidine (**9a**) (0.5 mmol) was dissolved in pyridine (10 ml). Ethyl chloroformate (or 2,2,2-trichloroethyl chloroformate) (1.5 mmol) was added dropwise to the solution at room temperature. After being stirred for 15 h at room temperature, the mixture was quenched with water (40 ml) and extracted with ethyl acetate. The crude extract was subjected to t.l.c. (hexane-AcOEt 2:1) to afford the acyclic enamine (**13a**) or (**13b**).

4-Ethoxycarbonylamino-2-(N -ethoxycarbonylformamido)-but-3-enyl phenyl ketone (**13a**) was obtained in 19% yield; δ_H ($CDCl_3$) 1.30 (t, J 6.0 Hz, 3 H), 1.38 (t, J 6.0 Hz, 3 H), 3.62 (dd, J 6.6, 17.7 Hz, 1 H), 3.75 (dd, J 6.6, 17.7 Hz, 1 H), 4.20 (q, J 6.0 Hz, 2 H), 4.37 (q, J 6.0 Hz, 2 H), 4.96 (dd, J 8.7, 8.7 Hz, 1 H), 5.75 (dt, J 8.7, 6.6 Hz, 1 H), 6.75 (dd, J 8.7, 8.4 Hz, 1 H), 7.31—7.78 (m, 4 H), 7.80—8.10 (m, 2 H), and 9.12 (s, 1 H).

4-(2,2,2-Trichloroethoxycarbonylamino)-2-[N -2,2,2-trichloroethoxycarbonyl]formamido]but-3-enyl phenyl ketone (**13b**) was obtained in 36% yield; ν_{\max} (neat) 3 350, 2 960, 1 748, and 1 696 cm^{-1} ; δ_H ($CDCl_3$) 3.73 (dd, J 6.8, 19.0 Hz, 1 H), 3.75 (dd, J 6.4, 19.0 Hz, 1 H), 4.79 (s, 2 H), 4.94 (s, 2 H), 5.11 (dd, J 9.0, 9.0 Hz, 1 H), 5.75—6.05 (m, 1 H), 6.68 (dd, J 9.0, 10.8 Hz, 1 H), 7.30—8.18 (m, 6 H), and 9.28 (s, 1 H); δ_C (CD_3CN) 41.9, 44.7, 74.7, 74.8, 94.1, 95.2, 106.9, 116.6, 124.7, 127.9, 128.6, 133.6, 151.9, 152.3, 162.8, and 196.8; m/z 418 (M^+ - OCH_2CCl_3 + H, 0.7%) and 105 (100).

Synthesis of Diazabicyclononadienes (14a), (14b), and (15a). *General Procedure.*—The crude ethyl acetate extract described for the preparation of compounds (**9**) was dissolved in pyridine and 2,2,2-trichloroethyl chloroformate (*ca.* 8 mol equiv.) was added to the solution. The mixture was stirred for 19 h at room temperature, quenched with water, and extracted with ether. The product was separated on t.l.c. (hexane-AcOEt 4:1).

3-Phenyl-8,9-bis-(2,2,2-trichloroethoxycarbonyl)-2-oxa-8,9-diazabicyclo-[3.3.1]nona-3,6-diene (**14a**) was obtained in 29% from pyrimidine, m.p. 110—111 °C (Found: C, 39.4; H, 2.6; N, 4.8. $C_{18}H_{14}Cl_6N_2O_5$ requires C, 39.23; H, 2.56; N, 5.08%); ν_{\max} (KBr) 2 966, 1 740, 1 715, and 1 654 cm^{-1} ; δ_H ($[^2H_6]DMSO$; 100 °C) 4.92 (s, 2 H), 5.06 (s, 2 H), 5.16 (ddd, J 6.0, 6.0, 1.7 Hz, 1 H), 5.76 (dd, J 6.0, 8.0 Hz, 1 H), 5.89 (d, J 6.0 Hz, 1 H), 7.00 (d, J 8.0 Hz, 1 H), 7.20—7.60 (m, 5 H), and 7.63 (d, J 1.7 Hz, 1 H); δ_C (CD_3CN) 44.2 (d), 76.2 (t), 76.3 (t), 83.6 (d), 95.9 (s), 96.1 (s), 101.0 (d), 110.9 (d), 124.9 (d), 125.5 (d), 129.6 (d), 129.9 (d), 134.5 (s), 149.0 (s), 152.0 (s), and 157.0 (s); m/z 548 (M^+ , 10%), 443 (14), 373 (81), 105 (88), and 31 (100).

3-Ethyl-4-methyl-8,9-bis-(2,2,2-trichloroethoxycarbonyl)-2-oxa-8,9-diazabicyclo[3.3.1]nona-3,6-diene (**14b**) was obtained in 27% yield from pyrimidine; ν_{\max} (neat) 2 950, 1 724, and 1 638 cm^{-1} ; δ_H ($CDCl_3$) 0.98 (t, J 7.3 Hz, 3 H), 1.66 (s, 3 H), 2.12 (q, J 7.3 Hz, 2 H), 4.63 (d, J 6.0 Hz, 1 H), 4.79 (s, 2 H), 4.87 (s, 2 H), 5.43—5.84 (m, 1 H), 6.99 (d, J 7.7 Hz, 1 H), and 7.45 (s, 1 H); m/z 514 (M^+ , 7%), 499 (1), 479 (2), 367 (7), 339 (32), and 31 (100).

4,4-Dimethyl-3-methylene-8,9-bis-(2,2,2-trichloroethoxycarbonyl)-2-oxa-8,9-diazabicyclo[3.3.1]nona-3-ene (**15a**) was obtained in 37% yield from pyrimidine, m.p. 123—123.4 °C (Found: C, 35.1; H, 3.2; N, 5.3. $C_{15}H_{16}Cl_6N_2O_5$ requires C, 34.85; H, 3.12; N, 5.42%); ν_{\max} (KBr) 2 980, 1 745, and 1 712 cm^{-1} ; δ_H ($[^2H_6]DMSO$; 70 °C) 2.11 (s, 3 H), 2.27 (s, 3 H), 4.29 (d, J 5.7 Hz, 1 H), 4.40 (s, 1 H), 4.51 (s, 1 H), 4.92 (s, 2 H), 4.99 (s, 2

H), 5.43 (dd, J 8.1, 5.7 Hz, 1 H), 6.90 (d, J 8.1 Hz, 1 H), and 7.21 (s, 1 H).

Synthesis of Tetrahydropyrimidines (16a—c). *General Procedure.*—To a solution of compound (**14a**) (70.5 mg, 0.13 mmol) in dichloromethane (3 ml) was added TFA (0.012 ml, 0.15 mmol). The mixture was stirred for 10 min and thiophenol (or methanol, ethanol) (0.2 mmol) was then added. After being stirred for another 10 min the resulting mixture was quenched with 5% aqueous $NaHCO_3$ (1 ml). The product was separated on t.l.c. (hexane-AcOEt 4:1). The following products were thus prepared.

4-Phenacyl-2-phenylthio-1,3-bis-(2,2,2-trichloroethoxycarbonyl)-1,2,3,4-tetrahydropyrimidine (**16a**), as an oil (98%, as a mixture of diastereoisomers) (Found: C, 44.0; H, 3.15; N, 4.3. $C_{24}H_{20}Cl_6N_2O_5S$ requires C, 43.60; H, 3.05; N, 4.24%); ν_{\max} (KBr) 2 960, 1 720, and 1 680 cm^{-1} ; δ_H ($[^2H_6]DMSO$; 65 °C) 3.22—4.18 (m, 2 H), 4.62—5.20 (m, 5 H), 5.32 and 5.48 (dd, J 4.4, 8.4 Hz and J 3.3, 8.4 Hz, 1 H), and 7.02—8.03 (m, 11 H).

2-Methoxy-4-phenacyl-1,3-bis-(2,2,2-trichloroethoxycarbonyl)-1,2,3,4-tetrahydropyrimidine (**16b**), as a mixture of diastereoisomers; ν_{\max} (KBr) 2 960 and 1 760—1 670 cm^{-1} ; δ_H ($[^2H_6]DMSO$; 65 °C) 3.38—3.68 (m, 5 H), 4.82—5.19 (m, 5 H), 5.34 (dd, J 4.2, 8.7 Hz, 1 H), 6.78 (ddd, J 8.7, 1.1, 2.0 Hz, 1 H), 7.03 (s, 1 H), 7.37—7.73 (m, 3 H), and 7.81—8.03 (m, 2 H).

2-Ethoxy-4-phenacyl-1,3-bis-(2,2,2-trichloroethoxycarbonyl)-1,2,3,4-tetrahydropyrimidine (**16c**), as an oil (88%, as a mixture of diastereoisomers) (Found: C, 40.4; H, 3.3; N, 4.7. $C_{20}H_{20}Cl_6N_2O_6$ requires C, 40.23; H, 3.38; N, 4.69%); ν_{\max} (neat) 2 990 and 1 730—1 670 cm^{-1} ; δ_H ($CDCl_3$) 1.30 (t, J 6.6 Hz, 3 H), 3.51 (d, J 4.8 Hz, 2 H), 3.76 (q, J 6.6 Hz, 2 H), 4.50—5.51 (m, 6 H), 6.81 (d, J 7.5 Hz, 1 H), 7.21 (s, 1 H), 7.33—7.69 (m, 3 H), and 7.82—8.08 (m, 2 H).

Synthesis of Tetrahydropyrimidines (16d) and (16e). *General Procedure.*—To a solution of compound (**14a**) (89 mg, 0.16 mmol) in dichloromethane (3 ml) was added TFA (0.012 ml, 0.16 mmol). The mixture was stirred for 5 min, and compound (**4c**) or (**4e**) (0.2 mmol) was added. On monitoring on t.l.c., it was seen that some starting compound (**14a**) was regenerated. Therefore, a further aliquot of TFA (0.03 ml) was added to the mixture, followed by addition of more (**4c**) or (**4e**) (0.09 ml). The mixture was stirred for another 4 h at room temperature, quenched with 5% aqueous $NaHCO_3$ (10 ml), and extracted with ethyl acetate. The product was separated on t.l.c. Thus obtained were 2-(α,α -dimethylacetyl)-4-phenacyl-1,3-bis-(2,2,2-trichloroethoxycarbonyl)-1,2,3,4-tetrahydropyrimidine (**16d**), as an oil (9%, as a mixture of diastereoisomers); δ_H ($CDCl_3$) 1.22 and 1.25 (br s, 6 H), 2.36 (s, 3 H), 3.08 (dd, J 17.1, 9.0 Hz, 1 H), 4.08 (dd, J 17.1, 3.1 Hz, 1 H), 4.53—5.15 (m, 5 H), 5.57—5.78 (m, 1 H), 6.61 (s, 1 H), 6.79 (d, J 7.7 Hz, 1 H), 7.28—7.66 (m, 3 H), and 7.78—7.80 (m, 2 H), and 2-methoxycarbonylpropan-2-yl-4-phenacyl-1,3-bis-(2,2,2-trichloroethoxycarbonyl)-1,2,3,4-tetrahydropyrimidine (**16e**) (67%; diastereoisomer ratio 1:2). The less polar diastereoisomer, R_F 0.49 (hexane-AcOEt 3:1), was an oil; ν_{\max} (neat) 2 950 and 1 740—1 670 cm^{-1} ; δ_H ($CDCl_3$) 1.38 and 1.42 (br s, 6 H), 3.40—3.82 (m, 5 H), 4.40—5.48 (m, 6 H), 6.53—6.87 (m, 2 H), and 7.30—8.05 (m, 5 H). The more polar diastereoisomer, R_F 0.40 (hexane-AcOEt 3:1), was an oil (Found: C, 42.7; H, 4.0; N, 4.15. $C_{23}H_{24}Cl_6N_2O_7$ requires C, 42.29; H, 3.70; N, 4.29%); ν_{\max} (neat) 2 950 and 1 710—1 670 cm^{-1} ; δ_H ($CDCl_3$) 1.34 (br s, 6 H), 3.02 (dd, J 17.2, 8.7 Hz, 1 H), 3.68 (s, 3 H), 4.15 (dd, J 17.2, 3.2 Hz, 1 H), 4.42—5.12 (m, 5 H), 5.38—5.65 (m, 1 H), 6.53 (s, 1 H), 6.68 (d, J 7.9 Hz, 1 H), 7.30—7.68 (m, 3 H), and 7.78—7.98 (m, 2 H).

Synthesis of Triazabicyclononadienes (17a) and (17b). *General Procedure.*—To the mixture of compound (14a) (68 mg, 0.12 mmol) and molecular sieves 4A (or MgSO_4) (2 g) in dichloromethane (2 ml) was added TFA (0.01 ml, 0.13 mmol). The resulting mixture was stirred for 10 min, then a solution of *p*-chloroaniline (or *p*-toluidine) (0.30 mmol) in dichloromethane (4 ml) was added dropwise. The mixture was heated to reflux and stirred for 23 h, quenched with 5% aqueous NaHCO_3 , and extracted with dichloromethane. The product (17a) or (17b) was separated by t.l.c. (hexane–AcOEt 3:1) from the by-product (13c) or (13d), which was also isolated.

2-(*p*-Chlorophenyl)-3-phenyl-8,9-bis-(2,2,2-trichloroethoxycarbonyl)-2,8,9-triazabicyclo[3.3.1]nona-3,6-diene (17a) was an oil (53%) (Found: C, 44.1; H, 3.2; N, 6.1. $\text{C}_{24}\text{H}_{18}\text{Cl}_7\text{N}_3\text{O}_4$ requires C, 43.64; H, 2.75; N, 6.36%; ν_{max} (KBr) 1 730, 1 648, and 1 498 cm^{-1} ; δ_{H} (CDCl_3) 4.54–4.94 (m, 4 H), 5.21 (ddd, *J* 6.0, 4.9, 1.2 Hz, 1 H), 5.41–5.77 (m, 2 H), and 6.92–7.30 (m, 11 H).

3-Phenyl-2-(*p*-tolyl)-8,9-bis-(2,2,2-trichloroethoxycarbonyl)-2,8,9-triazabicyclo[3.3.1]nona-3,6-diene (17b) was an oil (38%) (Found: C, 47.3; H, 3.5; N, 6.2. $\text{C}_{25}\text{H}_{21}\text{Cl}_6\text{N}_3\text{O}_4$ requires C, 46.91; H, 3.31; N, 6.56%; ν_{max} (neat) 3 950, 1 720, and 1 510 cm^{-1} ; δ_{H} (CDCl_3) 2.17 (s, 3 H), 4.51–4.96 (m, 4 H), 5.19 (ddd, *J* 5.7, 5.4, 0.9 Hz, 1 H), 5.42–5.70 (m, 2 H), and 6.80–7.57 (m, 11 H).

4-(2,2,2-Trichloroethoxycarbonylamino)-2- $\{N$ -(2,2,2-trichloroethoxycarbonyl)[(*p*-chloroanilino)hydroxymethyl]-amino}but-3-enyl phenyl ketone (13c) had δ_{H} (CDCl_3) 3.25–3.67 (m, 4 H), 4.60–5.60 (m, 6 H), and 6.60–8.10 (m, 12 H).

4-(2,2,2-Trichloroethoxycarbonylamino)-2- $\{N$ -(2,2,2-trichloroethoxycarbonyl)[hydroxy(*p*-toluidino)methyl]amino}but-3-enyl phenyl ketone (13d) had δ_{H} (CDCl_3) 2.22 (s, 2 H), 3.25–3.63 (m, 4 H), 4.60–5.12 (m, 6 H), 6.38–6.68 (m, 3 H), 6.82–7.09 (m, 3 H), 7.28–7.70 (m, 3 H), 7.80–7.98 (m, 2 H), and 8.30 (br s, 1 H).

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