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Synthesis of substituted tricyclo[5.3.1.0^{4,9}]undecan-2,6-diones

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Abstract—The morpholine enamines of 4-acetyl-4-phenylcyclohexanone **3a**, 4-acetyl-4-isopropenylcyclohexanone **3b**, 4-acetyl-4-methylcyclohexanone **3c** react with acryloyl chloride to give 1-phenyl-4(*N*-morpholino)tricyclo[5.3.1.0^{4,9}]undecan-2,6-dione **9a**, 1-isopropenyl-4(*N*-morpholino)tricyclo[5.3.1.0^{4,9}]undecan-2,6-dione **9b**, and 1-methyl-4(*N*-morpholino)tricyclo[5.3.1.0^{4,9}]undecan-2,6-dione **9c**, respectively, along with the corresponding substituted adamantane-2,4-diones. The morpholine enamine of 4-acetyl-4-benzylcyclohexa-none **3d** and pyrrolidine enamine of 4-acetyl-4-phenylcyclohexanone **3a** yield the corresponding 1-benzyl-4(*N*-morpholino)tricyclo[5.3.1.0^{4,9}]undecan-2,6-dione 9d and 8(*R*)-methyl-1-phenyl-4(*N*-pyrrolidinyl)tricyclo[5.3.1.0^{4,9}]undecan-2,6-dione **9e**. No substituted adamantane-2,4-diones were formed in any of the latter two reactions. © 2001 Published by Elsevier Science Ltd.

We had reported[1–3] previously a substituted tricyclo [5.3.1.0^{4,9}]undecan-2,6-dione **9c** which we had isolated from the reaction of the morpholine enamine of 4-acetyl-4-methylcyclohexanone **3c** with acryloyl chloride. We now herein report the synthesis of four new substituted tricyclo [5.3.1.0^{4,9}]undecan-2,6-diones: **9a**, **9b**, **9d** and **9e**. The tricyclo[5.3.1.0^{4,9}]undecane system has not been reported previously. The synthesis is based on a general reaction of 4,4-disubstituted cyclohexanone enamines with α,β unsaturated acid chlorides. We first prepared 4,4-disubstituted cyclohexanones **3a**–**c** following literature methods[4,5] in which one of the substituents is an acetyl group (Scheme 1). 4-Acetyl-4-benzylcyclohexanone **3d** was prepared (Scheme 1) following the procedure described in Section 1. The morpholine enamines **4a**–**d** and the pyrrolidine enamine **4e** were prepared (Scheme 1) in accordance with the general procedure reported earlier[2,3] without using any catalysts.

In our earlier report[3] we had found that the reaction of morpholine enamine of 4-acetyl-4-methylcyclohexanone **3c** with acryloyl chloride yielded a mixture of **9c** and 6,7-dimethyl-6-hydroxyadamantane-2,4-dione. At that time, we could not isolate them in the pure form from the mixture. In the present work we have separated the compound **9c** (30%) completely from the adamantane product. The reactions of acryloyl chloride with morpholine enamines of **3a** and **3b** followed similar routes as that of **3c** yielding the compounds **9a** (11%) and **9b** (18%), respectively, in addition to the corresponding substituted adamantane-2,4-diones which we have reported previously.[1,2] On the contrary, the morpholine enamine of **3d** gave only the compound **9d** (33%) in its reaction with acryloyl chloride without producing any adamantane structures. The reaction of pyrrolidine enamine of **3a** with crotonoyl chloride yielded in a similar manner only the compound **9e** (22%) and none of the adamantane derivatives although the morpholine enamine of the same ketone **3a** reacted with crotonoyl chloride to give only the corresponding adamantane-2,4-dione and no substituted tricyclo[5,3,1,0^{4,9}]undecan-2,6-diones which we reported earlier[1].

The general reaction between α,β-unsaturated acid chlorides and 4,4-disubstituted cyclohexanone enamines may be shown to follow the mechanistic pathways (Scheme 2) yielding either substituted adamantane-2,4-diones or substituted tricycloundecane-2,6-diones or a mixture of both as products. The formation of adamantane-2,4-diones reported[1–3] earlier has been explained through the formation of the intermediate enolate anion (12) which cyclises onto the axially orientated acetyl group. When the acetyl group is in an equatorial conformation it may give rise to an alternative enolate anion (8) (preferably twist form) which would lead to the formation of the tricycloundecane-2,6-dione structure by cyclisation onto the iminium carbon. This mechanism has been reported[3] by us previously for the formation of **9c**. As each of the reactions of **4a**–**c** with acryloyl chloride yield both the adamantanediones and

Keywords: morpholine; pyrrolidine; 4,4-disubstituted cyclohexanone; enamine; acryloyl chloride; substituted adamantane-2,4-dione; substituted tricyclo [5.3.1.0^{4,9}]undecan-2,6-dione.
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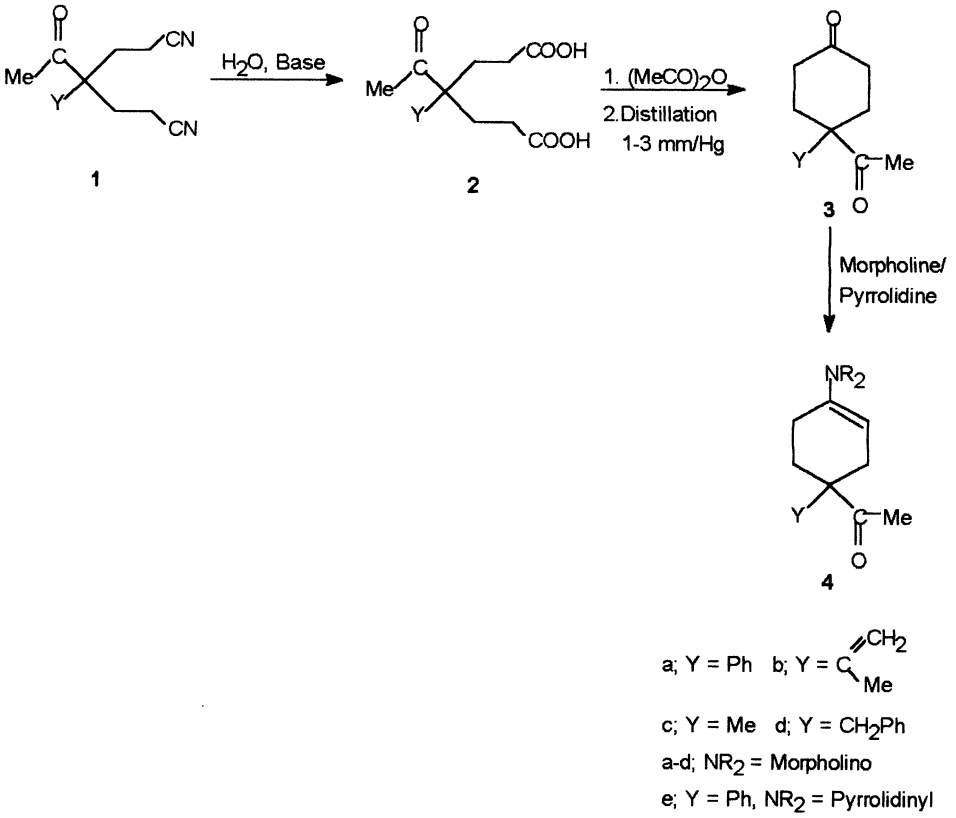


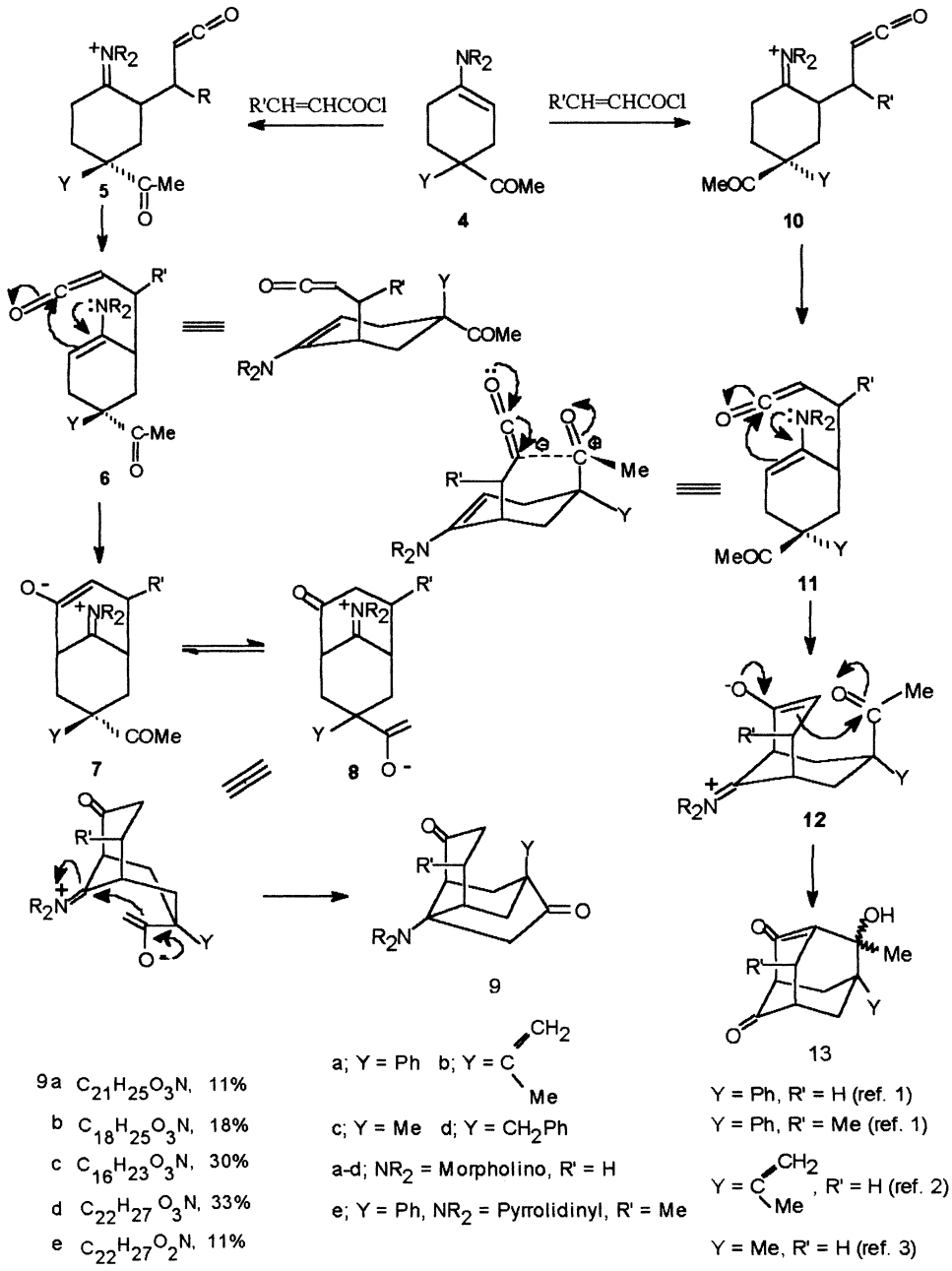
Scheme 1.

tricycloundecanes, it is evident that the substituent Y is equatorial in the enolate anion (12) and is axial in the enolate anion (8). In a similar way it may be inferred that the reactions of **4d** with acryloyl chloride and **4e** with crotonoyl chloride occur mostly through the formation of the enolate anion (8) where the substitutent Y is axial and the acetyl group is equatorial since no adamantanediones were isolated from these reactions.

As shown in Scheme 3 the steric interaction due to the axially orientated substituent X or Y would be a minimum in the ketene or enolate anion where R′ is H which means acryloyl chloride. This explains why tricycloundecanediones **9a–c** are obtained along with the corresponding adamantanediones from the reactions of the enamines **4a–c** with acryloyl chloride and not with any other acid chloride. The explanation of the formation of **9d** as the predominant product in the reaction of **4d** with acryloyl chloride is provided by the $^{1}H-^{1}H$ COSY NMR spectral data of the starting 4-acetyl-4-benzylcyclohexanone **3d** which show that the substituent benzyl group is predominantly axial. The production of the tricycloundecanedione **9e** without any adamantanedione formation may be attributed to the greater reactivity of the iminium carbon bonded to nitrogen of the pyrrolidine ring onto which the enolate anion (8) cyclizes (Scheme 2). This greater reactivity probably outweighs the repulsive interaction due to the axially orientated phenyl group in the enolate anion (Scheme 3) where R′ is methyl group. The stereochemistry of 8-CH_3 group having *R* configuration in **9e** is based on the formation of the favoured ketene (Scheme 3).

In the present work we have reinvestigated the structure of the compound **9c** in more detail with the help of its ^{1}H and ^{13}C NMR, $^{1}H-^{1}H$ NMR COSY, $^{13}C-^{1}H$ NMR COSY and mass spectral data. The structures of the compounds **9a**, **9b**, **9d** and **9e** were confirmed by their elemental analysis, ^{1}H and ^{13}C NMR and mass spectroscopic methods. All the protons and carbons of these compounds were assigned by analogy with those of the compound **9c**. Preparation and characterisation of the dioxime derivatives of the compounds **9b**, **9c** and **9d** gave additional evidence for their structures (see Section 1). In addition to the spectral data the structure of **9e** was further confirmed with the help of its X-ray analysis (Fig. 1).

In the ^{1}H NMR spectra (Table 1) the equivalent CH_2-O-CH_2 methylene protons of the morpholine moiety of the compounds **9a–d** appeared as a triplet at the lowest field at δ 3.60–3.65 (3′ and 5′ protons) with coupling constant of 4.45–4.70 Hz. On the other hand 2′ and 6′ protons which are α to the nitrogen atom and also 2′ and 5′ protons (α to the nitrogen atom) of the pyrrolidine moiety in **9e** appeared as a multiplet (Table 1); the nonequivalence of these protons arising is probably due to different spatial arrangements next to the cage structure. The coupling pattern of the methylene and methine protons were ascertained clearly with different *J* values (which was not done in the previous report[3] of **9c**). The methylene protons at position 3 gave two doublets (18.7 Hz). The axial protons at positions 3 and 7 are more deshielded than the equatorial protons due to the adjacent carbonyl groups. At position 3 the axial proton also receives steric shielding from the adjacent morpholino group

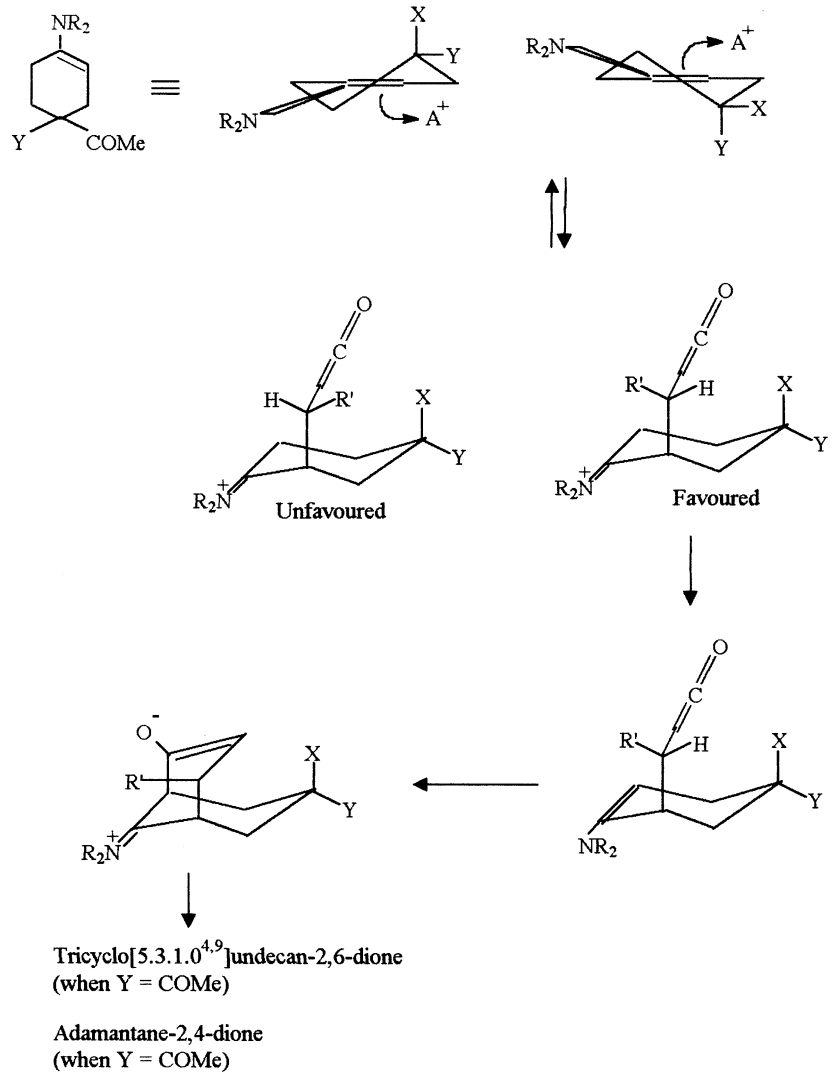


Scheme 2.

(position 4) that is equatorial. The overall effect is that 3-H^a is more upfield by 0.11–0.12 ppm than 3-H^e. Of the alicyclic part, the most downfield proton is at the bridgehead position as it is flanked by a carbonyl group and the morpholino group. 8-H^a is deshielded more than 8-H^e by 0.57–0.66 ppm due to the anisotropic effect of carbonyl group at position 6. At both the positions 10 and 11 the axial protons are more upfield than the equatorial protons, 0.30–0.53 ppm in the case of protons at 10-C and 0.20–0.41 ppm in the case of protons at 11-C, probably due to the anisotropic effect of the substituents at position 1.

The coupling constants are shown in Table 2. The geminal couplings between 10-H^a and 10-H^e and 11-H^a and 11-H^e showed the J values as 14.2–14.9 Hz and 13.2–13.9 Hz, respectively. The large J value of 9.0 Hz in **9e** and 11.9–12.1 Hz in the cases of other tricycloundecanediones were observed for vicinal coupling between 5-H and 11-H^e. The vicinal coupling between 9-H and 10-H^e also showed a large coupling constant of 11.7–11.9 Hz.

In ^{13}C NMR spectra (Table 3), the two carbonyl carbons at positions 2 and 6 resonated at the lowest field. 2-C Shifted further downfield as compared to 6-C probably due to substitution at the adjacent carbon at position 1. As expected the equivalent 2′ and 5′ carbons in **9e** and 2′ and 6′ carbons in **9a–d** α to the nitrogen atom, resonated at δ 49.45 and at 44.69–45.10 respectively, whereas 3′ and 5′ carbons α to



Scheme 3.

the oxygen atom resonated at δ 67.07–67.39 in the compounds **9a–d**.

The 1-CH_3 carbon in the case of **9c** was at the highest field (δ 19.21). Of the ring carbons the quaternary 1-C and 4-C gave less intense peaks and 4-C was deshielded significantly at δ 62.28–62.74 due to the electron withdrawing morpholino and pyrrolidinyl groups.

As expected, the 7-C was deshielded more by 5.03–5.79 ppm than 8-C due to adjacent carbonyl group at 6 position. 9-C was deshielded more than 8-C by 5.74 ppm in **9e** and by 4.37–4.60 ppm in the other compounds due to the fully substituted bridgehead carbon 4-C. Of 7-C, 8-C, 9-C, 10-C and 11-C the carbon at 10-C resonated most downfield. Besides other factors, the reason for this may be attributed to the γ-anti effect[6] which indicates that C_α (11-C), C_β (1-C) and C_γ (2-C doubly substituted by O) are compressed in the same plane.[6] 3-C gave the expected downfield shift due to the adjacent (2-C) carbonyl group and fully substituted 4-position. 5-C is more deshielded than 3-C by 6.95 ppm in **9e** and by 7.91–8.98 ppm in the other compounds.

1. Experimental

1.1. General

^1H and ^{13}C NMR spectra were recorded on a JEOL 400 instrument at the School of Pharmaceutical Sciences, Kanazawa University. A number of NMR spectra were recorded on a General Electric 300 NMR spectrometer at the department of Chemistry, Kent State University. Low-resolution mass spectra were run at the department of Chemistry, George Mason University using a Finnigan Mat Mass Spectrometer and the high-resolution mass spectra were recorded in Kanazawa University. Melting points were determined in open-ended capillary tubes and are uncorrected. All ^1H and ^{13}C NMR spectra were recorded in $CDCl_3$ if not otherwise mentioned. IR spectra were run as KBr pellets in the case of solids and solution in the case of liquids; absorptions are expressed in cm^{-1}. For column chromatography silica gel 100 (supplied by E. Merck) and light petroleum (60–80°)/chloroform=10:1 were used.

1.1.1. Preparation of 4,4-disubstituted cyclohexanones.

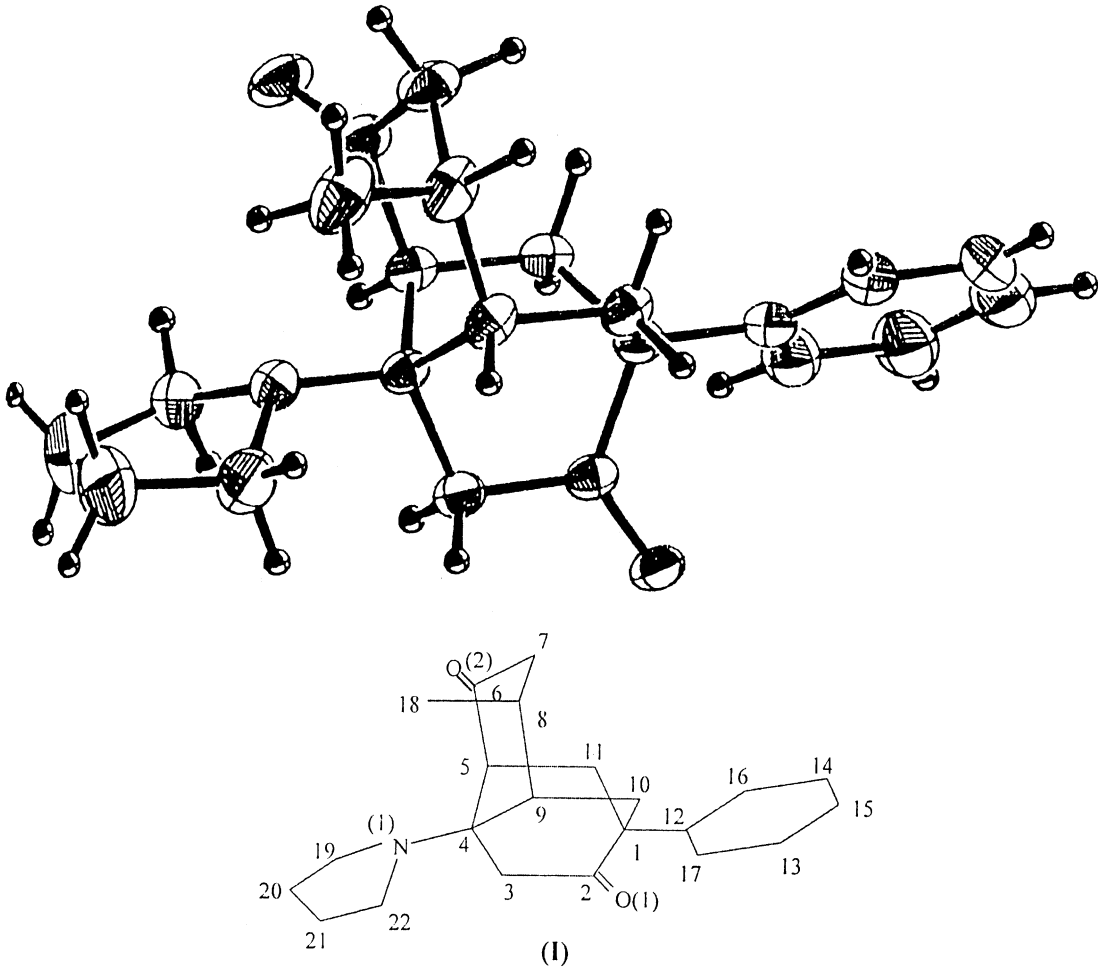


Figure 1. ORTEP stereospecific view of (**9e**).

Table 1. ^{1}H NMR spectral data of the tricycloundecanediones **9a**, **9b**, **9c**, **9d** and **9e** (chemical shifts in δ and coupling constants J in Hz)

Protons	**9a**	**9b**	**9c**	**9d**	**9e**
3-H^a	2.42	2.28	2.24	2.26	2.47
3-H^e	2.53	2.40	2.35	2.38	2.59
5-H	3.03	2.92	2.87	2.85	2.94
7-H^a	2.74	2.75	2.76	2.80	2.87
7-H^e	2.50	2.43	2.28	2.33	2.50
8-H^a	2.32	2.28	2.20	2.16	2.25
8-H^e	1.70	1.62	1.63	1.58	–
9-H	2.53	2.45	2.39	2.37	2.61
10-H^a	1.98	1.68	1.70	1.63 (m)	1.92
10-He	2.28	2.21	2.03	1.94 (m)	2.42
11-H^e	1.58	1.60	1.60	1.55	2.20
11-H^e	2.09	1.80	1.87	1.78 (m)	2.08
2′,6′-H_2	2.65–2.57	2.60–2.47	2.45–2.60	2.43–2.56	–
Morpholino	(m)	(m)	(m)	(m)	
3′,5′-H_2	3.65	3.63	3.63	3.60	–
Morpholino	(t, J=4.50)	(t, J=4.45)	(t, J=4.70)	(t, J=4.50)	
1-C_6H_5	7.39–7.16	–	–		7.41–7.15
1-C–Hc	–	4.75	–		–
1-C–Ht	–	5.02	–		–
1-C–CH_3	–	1.77 (s)	–		–
1-$CH_2C_6H_5$	–	–	–	2.81 (s)	–
1-$CH_2C_6H_5$	–	–	–	7.1–7.29 (m)	
1-CH_3	–	–	1.03		–
2′,5′-H_2	–	–	–		2.83–2.70
Pyrrolidinyl					(m)
3′,4′-H_2	–	–	–		1.68
Pyrrolidinyl					(t, J=5.50)
8-CH_3	–	–	–		1.34

Table 2. Coupling constants (J in Hz) of the tricycloundecandiones **9a**, **9b**, **9c**, **9d** and **9e**

Protons	9a	9b	9c	9d	9e
3-H^a, 3-H^e	18.7	18.7	18.7	18.7	18.7
5-H, 11-H^a	–	–	3.8	3.6	4.5
5-H, 11-H^e	11.9	12.1	12.1	12.0	9.0
7-H^a, 7-H^e	–	–	18.7	–	11.0
8-H^a, 8-H^e	12.8	12.0	15.8	–	–
9-H, 10-H^a	3.6	3.7	4.1	4.0	2.9
9-H, 10-H^e	11.7	–	11.8	11.9	–
10-H^a, 10-H^e	14.6	14.4	14.2	14.2	14.9
10-H^e, 11-H^e	3.0	–	3.4	3.4	4.5
11-H^a, 11-H^e	13.2	13.3	14.7	14.9	14.5
8-H^a, 8-CH_3	–	–	–	–	7.2

4-Acetyl-4-phenylcyclohexanone (**3a**)[4], 4-acetyl-4-isopropenylcyclohexanone (**3b**)[5], 4-cetyl-4-methylcyclohexanone (**3c**)[5] and their precursors (**1a**)[4], (**2a**)[4], (**1b**)[7], (**2b**)[8], (**1c**)[4] and (**2c**)[4] were prepared by following the literature methods (Scheme 1). 4-Acetyl-4-benzylcyclohexanone (**3d**) and its precursors (**1d**) and (**2d**) were prepared in the following way (Scheme 1).

1.1.2. 4-Acetyl-4-benzylpimelonitrile (1d). Acrylonitrile (53.0 g, 1 mol) was added dropwise to a mechanically stirred solution of benzylacetone (73.5 g, 0.50 mol), 30% potassium hydroxide solution in methanol (5 mL) and *tert*-butanol (100 mL) over 3h maintaining the temperature of the reaction mixture at 3–6°C by ice cooling. After the addition was complete, the reaction mixture was stirred for 1 h more. The crystalline solid formed was filtered off, washed with a mixture of *tert*-butanol and ethanol (8:1) and dried. Upon recrystallisation from ethanol colourless crystals of 4-acetyl-4-benzylpimelonitrile (**1d**) were obtained, yield 75.5 g, 60%, mp 74–75°C; IR ν_{max} 2248 (C≡N), 1685 (C=O), 1615, 1595 (C=C of phenyl); δ[DMSO] ^{1}H NMR: 7.30–7.07 (m, 5H, aromatic protons), 2.90 (s, 2H, $CH_2C_6H_5$), 2.56–2.49 (m, 2H, one CH_2–CN), 2.45–2.38 (m, 2H, another CH_2–CN),1.93–1.87 (m, 2H, one CH_2–CH_2–CN), 1.82–1.76 (m, 2H, another CH_2–CH_2–CN), 2.20 (s, 3H, $COCH_3$); ^{13}C NMR: 210.03 (C=O and C≡N), 136.02, 129.66, 128.21, 126.69, 120.40 (aromatic carbons), 54.12 (>C<), 39.09 ($CH_2C_6H_5$), 27.44 (CH_2–CN), 26.37 (CH_2–CH_2–CN), 11.49 ($COCH_3$); MS *m/z* 254 (M^+), 200, 131, 128, 115, 91, 77, 65, 44, 43, 28. Anal. Calcd for $C_{16}H_{18}N_2O$: C, 75.59%; H, 7.08%; N, 11.02%. Found: C, 75.47%; H, 7.14%; N, 10.92%.

1.1.3. 4-Acetyl-4-benzylpimelic acid (2d). A mixture of 4-acetyl-4-benzylpimelonitrile (**1d**) (60 g, 0.23 mol), potassium hydroxide (33.13 g, 0.59 mol) and water (350 mL) was heated to reflux for 24 h. The hot solution was treated with activated charcoal and filtered hot. The filtrate was then cooled. 4-Acetyl-4-benzylpimelic acid (**2d**) was precipitated on acidification of the filtrate with concentrated hydrochloric acid at room temperature (30°C). The precipitated acid after recrystallisation from boiling water gave colourless crystals. Yield 58.07 g, 84%, mp 114–15°C; IR ν_{max} 3500 (OH), 1715, 1700 (C=O), 1615, 1595 (C=C of phenyl); δ[DMSO] ^{1}H NMR: 12.10 (br s, 2×COOH), 7.27–7.04 (m, 5H, aromatic protons), 2.85 (s, 2H, $CH_2C_6H_5$), 2.18–2.08 (m, 4H, 2×CH_2COOH), 1.79–1.66 (m, 4H, 2×CH_2CH_2COOH), 2.14 (s, 3H, $COCH_3$); ^{13}C NMR: 211.55 ($COCH_3$), 174.07 (COOH), 137.02, 130.43, 129.72, 128.06, 127.80, 126.37 (aromatic carbons), 53.88 (>C<), 39.50 ($CH_2C_6H_5$), 28.52 (CH_2COOH), 27.60 (CH_2CH_2COOH), 26.24 ($COCH_3$); MS *m/z* 292(M^+), 232,

Table 3. ^{13}C NMR spectral data of the compounds **9a**, **9b**, **9c**, **9d** and **9e** (chemical shifts in δ)

	9a	9b	9c	9d	9e
1-C	48.46	49.33	41.50	44.82	48.88
2-C	211.56	211.76	212.63	212.06	212.52
3-C	39.40	39.32	38.74	38.31	44.85
4-C	62.34	62.41	62.74	62.28	62.65
5-C	47.59	47.23	47.72	47.14	51.80
6-C	210.11	210.48	211.93	212.00	211.12
7-C	30.23	30.19	30.50	30.14	37.87
8-C	25.20	25.12	25.34	25.00	32.08
9-C	29.88	29.51	29.80	29.37	37.82
10-C	34.44	32.48	35.99	32.91	39.20
11-C	32.23	30.31	33.59	30.61	38.23
2′6′-C_2 (Morpholino)	44.89	44.82	44.99	44.69	
3′5′-C_2 (Morpholino)	67.17	67.13	67.36	67.07	
2′5′-C_2 (Pyrrolidinyl)					49.45
3′4′-C_2 (Pyrrolidinyl)					23.34
1-C–C_6H_5	138.71 (1-C				139.40 (1-C)
	128.12 (2-C)				128.07 (2-C)
	127.20 (1-C)				127.05 (1-C)
	126.97 (2-C)				126.87 (2-C)
1-C–C(CH_3)=CH_2		144.20			
1-C–C(CH_3)=CH_2		112.78			
1-C–C(CH_3)=CH_2		20.51			
1-C–CH_3			19.21		
1-C–$CH_2C_6H_5$				38.95	
1-C–$CH_2C_6H_5$				136.80 (1-C)	
				130.41 (2-C)	
				127.94 (2-C)	
				126.26 (1-C)	
8-C–CH_3					22.70

213, 185, 141, 128, 91, 65, 55. Anal. Calcd for $C_{16}H_{20}O_5$: C,65.75%, H,6.84%. Found: C,65.79%; H,6.92%.

1.1.4. 4-Acetyl-4-benzylcyclohexanone (3d). A mixture of 4-Acetyl-4-benzylpimelic acid (**2d**) (20.0 g, 68.0 mmol), freshly distilled acetic anhydride (20.92 g, 0.2 mol) and pyridine (6.2 mL) was heated to reflux for 2 h. The acetic acid formed, the excess acetic anhydride and pyridine left in the reaction mixture were removed by distillation at atmospheric pressure. The remaining viscous mass was then distilled under reduced pressure to give a colourless liquid of 4-acetyl-4-benzylcyclohexanone (**3d**), yield 9.22 g, 61%; bp 190–200°C/2 mmHg.; IR ν_{max} (liquid film) 1695 (broad, C═O), 1625, 1615, 1595 (C═C, phenyl); δ[$CDCl_3$] ^{1}H NMR: 7.29–7.03 (m, 5H, aromatic protons), 2.87 (s, 2H, $CH_2C_6H_5$), 2.39–2.32 (m, 2,6-H_2 eq), 2.32–2.25 (m, 3,5-H_2 eq) 1.77–1.69 (m, 3,5-H_2 ax and 2,6-H_2 ax), 2.23 (s, 3H, $COCH_3$); ^{13}C NMR 211.05 (C-1), 210.37 ($COCH_3$), 135.77, 129.76, 128.25, 126.95 (aromatic carbons), 52.49 (C-4), 44.55 ($CH_2C_6H_5$), 38.15 (C-2 and C-6), 32.41 (C-3 and C-5) and 25.68 ($COCH_3$), and. MS *m/z* 230(M^+), 139, 128, 115, 91, 77, 55, 43. HRMS Calcd for $C_{15}H_{18}O_2$ (M^+) 230.1306; found 230.1281.

1.2. Preparation of enamines—general method

A mixture of the 4,4-disubstituted cyclohexanone (20.83–29.0 mmol) and a slight excess of morpholine or pyrrolidine (21.83–32.20 mmol) in benzene (75–80 mL) was heated to reflux under a Dean and Stark head for 12–16 h. On cooling, the solvent and the excess of amine were removed under reduced pressure (by rotary evaporator) and the crude enamine was used without further purification since extensive decomposition occured on distillation. The following enamines were prepared:

1.2.1. 4-Acetyl-4-phenyl-1-morpholinocyclohexene (4a). Light yellow viscous mass, IR ν_{max}: 1700 (sharp, C═O of acetyl), 1638 (C═C).

1.2.2. 4-Acetyl-4-isopropenyl-1-morpholinocyclohexene (4b). Light brown viscous mass, IR ν_{max}: 1700 (sharp, C═O), 1655, 1638 (C═C).

1.2.3. 4-Acetyl-4-methyl-1-morpholinocyclohexene (4c). Light brown viscous mass, IR ν_{max}: 1700 (sharp, C═O), 1638 (C═C).

1.2.4. 4-Acetyl-4-benzyl-1-morpholinocyclohexene (4d). Light yellow viscous mass, IR $\nu_{max:}$ 1700 (sharp, C═O), 1638 (C═C).

1.2.5. 4-Acetyl-4-phenyl-1-pyrrolidinylcyclohexene (4e). Light brown viscous mass, IR ν_{max}: 1700 (sharp, C═O of acetyl), 1638 (C═C).

1.3. Synthesis of 1-phenyl-4(*N*-morpholino)tricyclo [5.3.1.$0^{4,9}$]undecan-2,6-dione (9a), 1-isopropenyl-4(*N*-morpholino)tricyclo[5.3.1.$0^{4,9}$]undecan-2,6-dione(9b), 1-methyl-4(*N*-morpholino)tricyclo [5.3.1.$0^{4,9}$]undecan-2,6-dione (9c) and 1-benzyl-4(*N*-morpholino) tricyclo [5.3.1.$0^{4,9}$]undecan-2,6-dione (9d)—general method

Acryloyl chloride (20.55–29.0 mmol) in dry benzene (40–45 mL) was added dropwise to a boiling solution of the morpholinoenamine (20.52–28.6 mmol) in dry benzene (130–170 mL) during 2 h. During the addition a solid was slowly precipitated from the reaction mixture. The mixture was then heated under reflux with stirring for 20 h, cooled and the precipitated iminium salt was filtered off and washed with dry benzene. The solid thus collected was hydrolysed by stirring with ice cold water (50 mL) for 10 h and finally extracted with ether (5×25 mL). The separated aqueous layer was further extracted with chloroform (5×25 mL). The crude tricyclic compounds were isolated from the extracts and purified by separation from adamantanediones by fractional recrystallisation in the case of (**9a**) from chloroform and light petroleum (40–60°C) and with the help of column chromatography in the case of (**9b**) and (**9c**) while the column was packed with silica gel and was eluted initially with light petroleum (60–80°C) and the gradual addition of chloroform. The compound (**9d**) was purified by recrystallisation from chloroform and light petroleum (40–60°C). The following results were obtained:

Acryloyl chloride reacting with (**4a**) gave an 11% yield of (**9a**) (0.80 g) which was purified by recrystallisation from chloroform and light petroleum (40–60°C) and obtained as colourless needles, mp 215–16°C, R_f (chloroform and ethyl acetate, 6:1) 0.52; IR ν_{max} 1725, 1698 (C═O), 1665, 1595 (C═C). MS *m/z* 339 (M^+), 338, 311, 297, 296, 253, 194, 165, 115, 56, 40. HRMS Calcd for $C_{21}H_{25}NO_3$ (M^+) 339.1834; found 339.1837.

Acryloyl chloride reacting with (**4b**) gave an 18% yield of (**9b**) (1.65 g) which was purified with the help of column chromatography and obtained as colourless plates, mp 215–16°C, R_f (chloroform and ethyl acetate, 4:1) 0.50; IR ν_{max} 1695 (broad C═O), 1635 (C═C). MS *m/z* 303 (M^+), 275, 261, 260, 217, 192, 166, 57. Anal. Calcd for $C_{18}H_{25}NO_3$: C, 71.28%, H, 8.25%, N, 4.62%. Found: C, 71.38;H, 8.35%; N, 4.62%. C, 75.81; H, 7.04%.

Acryloyl chloride reacting with (**4c**) gave a 30% yield of (**9c**) (2.41 g) which was purified with the help of column chromatography and obtained as colourless plates,mp 192–193°C, R_f (chloroform and ethyl acetate, 5:1) 0.36; IR ν_{max} 1698 (broad C═O), 1638 (C═C). MS *m/z* 277 (M^+), 275, 261, 249, 235, 234, 191, 166, 57. Anal. Calcd for $C_{16}H_{23}NO_3$: C, 69.30%, H, 8.30%; N, 5.10%. Found: C, 69.20; H, 8.70%; N, 5.10%.

Acryloyl chloride reacting with (**4d**) gave a 33% yield of (**9d**) (2.53 g) which was purified by recrystallisation from chloroform and light petroleum (40–60°C) and obtained as colourless plates, mp 221–222°C, R_f (chloroform and ethyl-acetate, 4:1) 0.64; IR ν_{max} 1715, 1700 (C═O), 1595,1586 (C═C). MS *m/z* 353(M^+), 325, 311, 310, 275, 267, 262, 261, 249, 234, 191, 57. Anal. Calcd for $C_{22}H_{27}NO_3$: C,

74.78%, H, 7.64%; N, 3.96. Found: C, 74.79; H, 7.74%; N, 3.94%.

1.4. Synthesis of 1-phenyl-8-methyl-4(*N*-pyrrolidinyl) tricyclo[5,3,1,$0^{4.9}$] undecan-2,6-dione(9e)

Under the same conditions as described in general method, the reaction of 4-acetyl-4-phenyl-1-pyrrolidinylcyclohexene (**4e**) with crotonoyl chloride produced 1-phenyl-8-methyl-4(*N*-pyrrolidinyl)tricyclo [5,3,1,$0^{4.9}$]undecan-2,6-dione (**9e**) which was isolated from the ether extract of the hydrolytic mixture of the iminium salt and purified with the help of column chromatography; yield 1.48 g, 22%, colourless plates, mp 193–94°C, R_f (chloroform and light petroleum (40–60°C), 4:1) 0.67; IR ν_{max}:1715, 1700 (broad C═O), 1650, 1600 (C═C). MS *m/z* 337(M^+), 309, 295, 294, 267, 240, 223, 211, 178, 162, 123, 103, 70, 55. Anal. Calcd for $C_{22}H_{27}NO_2$: C, 78.33%, H, 8.01%; N, 4.15%. Found: C, 78.38%; H, 8.11%; N, 4.14%.

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References

1. Ahmed, M. G.; Moeiz, S. M. I.; Ahmed, S. A.; Kiuchi, F.; Tsuda, Y.; Sampson, P. *J. Chem. Res.* **1999**, *316*, 1439–1470.
2. Huque, A. K. M. F.; Mosihuzzaman, M.; Ahmed, S. A.; Ahmed, M. G.; Andersson, R. *J. Chem. Res.* **1987**, *214*, 1701–1710.
3. Ahmed, M. G.; Huque, A. K. M. F.; Ahmed, S. A.; Mosihuzzaman, M.; Andersson, R. *J. Chem. Res.* **1988**, *362*, 2815–2835.
4. Bruson, H. A.; Riener, T. W. *J. Am. Chem. Soc.* **1942**, *64*, 2850–2858.
5. Chapman, N. B.; Sotheeswaran, S.; Toyne, K. J. *J. Org. Chem.* **1970**, *35*, 917–923.
6. Duddeck, H.; Klein, H. *Tetrahedron* **1977**, *33*, 1971–1977.
7. Bruson, H. A.; Riener, T. W. *J. Am. Chem. Soc.* **1943**, *65*, 18–23.
8. Cologne, J.; Vuillemet, R. *Bull. Soc. Chim. (Fr.)* **1961**, 2235–2238.