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Synthesis of reactive methylene compounds of malonamic acid series: Precursors of bioactive molecules

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ABSTRACT

Organic compounds containing reactive methylene group provide excellent intermediates in synthetic organic chemistry. Such substances have been found to be useful as synthon for various antitubercular, antiviral, antidiabetic, antifertilitic, antibacterial and antifungal agents. It was with these objects in view that the work described in this paper was undertaken i.e. Synthesis of different malonamic acid series from primary aromatic amines and DEM.

Key words: Reactive methylene compounds, primary aromatic amines, DEM, refluxing.

INTRODUCTION

Reactive methylene compounds have proved to be useful precursors for the synthesis of new organic compounds which may not only have chemotherapeutic activity but can also be used as analytical reagents, dyes etc. Using such type of compounds as starting material quite a large number of antitubercular, antiviral, antibacterial, antidiabetic, anticancer, antitumor, antifungal compounds like coumarins, hydrazides, hydrazones, thiosemicarbazides, pyrazolones[1-3] etc have been prepared by condensing them with other substances. A large number of reactive methylene compounds of malonamic acid series have been prepared by earlier workers by condensation of primary aromatic amines and DEM (Diethyl malonate) [4-6]. Extensive research has been done in our lab on these compounds. Several malonamides and acids like malon anilic acid, malon toluidic acid, malon xylidic acid, malon α and β naphthilic acids, malon anisidic acid, 2,6-dibromo-4-methyl phenyl malonamic acid, malon-4-chloro-2,5-dimethoxy anilic acid[7-10] etc and their derivatives have been prepared in our lab. So, in continuation, it was thought worthwhile to synthesize a set of some reactive methylene compounds of the malonamic acid series.

EXPERIMENTAL

Material

All chemicals used in the synthesis were obtained from Sigma-Aldrich Company Melting points were determined in open capillary tubes and are uncorrected. The purities of the compounds were checked on silica-gel-coated Al plates (Merck). IR spectra were recorded in KBr on a Perkin Elmer Spectrum RX-1 FT-IR spectrophotometer at St. John's College Agra.

Synthesis of N-(R) phenyl malonamides(1-8) & N-(R) phenyl malonamic acids(9-16)

To the primary amine (0.05 moles), diethyl malonate (0.05mol) was added and refluxed for 45-60 mins. The solid separated was filtered and crystallized from ethanol. On analysis it was found to be N:N'-di-(R) phenyl malonamide[1-8]. To the filterate 20ml ethanol and a solution of Na_2CO_3 in water (5ml) was added. The reaction mixture was

hydrolysed for and then filtered. To the filterate, HCl was added. The solid thus separated was filtered, washed with water, recrystallized from ethanol and was identified as N-(R) phenyl malonamic acid[9-16].

RESULTS AND DISCUSSION

The analytical data, colour, melting points, yield %, molecular formula are recorded in Table 1. The infra-red spectra of the synthesized compounds

Table 1: Physical and analytical data of compounds

S. no	R	Mol formula	Color	m.p. (°C)	% yield	%C found (Calc.)	%H found (Calc.)	%N found (Calc.)
1.	C_4H_9	$C_{23}H_{30}O_2N_2$	White	210	29.31	75.65 (75.40)	8.20 (8.19)	7.84 (7.65)
2.	C_3H_7	$C_{21}H_{26}O_2N_2$	White	260	26.62	74.62 (74.55)	7.46 (7.69)	8.31 (8.28)
3.	3,4-di Cl	$C_{15}H_{10}O_2N_2Cl_4$	White	219	34.80	45.99 (45.92)	2.45 (2.55)	7.31 (7.14)
4.	2-Cl-5-trifluoromethyl	$C_{17}H_{10}O_2N_2Cl_2F_6$	White	140	60.00	44.66 (44.15)	2.01 (2.16)	6.21 (6.06)
5.	2,5-di OCH_3	$C_{19}H_{22}O_6N_2$	White	240	26.43	61.20 (60.96)	5.86 (5.88)	7.52 (7.49)
6.	4-NO_2	$C_{15}H_{12}O_6N_2$	Yellow	144	43.03	52.38 (52.33)	3.53 (3.49)	15.35 (15.28)
7.	3-Cl-4-F	$C_{15}H_{10}O_2N_2Cl_2F_2$	White	200	30.35	50.20 (50.14)	2.81 (2.78)	7.86 (7.79)
8.	2-F-4-Br	$C_{15}H_{10}O_2N_2Br_2F_2$	White	180	28.36	40.16 (40.06)	2.32 (2.24)	6.32 (6.28)
9.	C_4H_9	$C_{13}H_{17}O_3N$	White	132	65.79	66.52 (66.38)	7.42 (7.23)	6.15 (5.95)
10.	C_3H_7	$C_{12}H_{15}O_3N$	Greyish White	129	61.83	65.32 (65.15)	6.81 (6.78)	6.50 (6.33)
11.	3,4-di Cl	$C_9H_7O_3NCl_2$	White	135	72.67	43.86 (43.54)	2.53 (2.82)	6.15 (5.65)
12.	2-Cl-5-trifluoromethyl	$C_{10}H_7O_3NClF_3$	Light Yellow	150	45.70	43.32 (42.70)	2.33 (2.48)	5.09 (4.95)
13.	2,5-di OCH_3	$C_{11}H_{13}O_5N$	Greyish White	135	60.33	55.45 (55.23)	6.34 (6.37)	5.88 (5.86)
14.	4-NO_2	$C_9H_8O_5N_2$	Pale Yellow	137	61.03	48.67 (48.21)	3.98 (3.57)	1.41 (1.25)
15.	3-Cl-4-F	$C_9H_7O_3NClF$	White	135	71.83	46.49 (46.65)	3.67 (3.02)	6.25 (6.04)
16.	2-F-4-Br	$C_9H_7O_3NBrF$	White	151	74.28	39.82 (39.27)	2.81 (2.55)	5.49 (5.09)

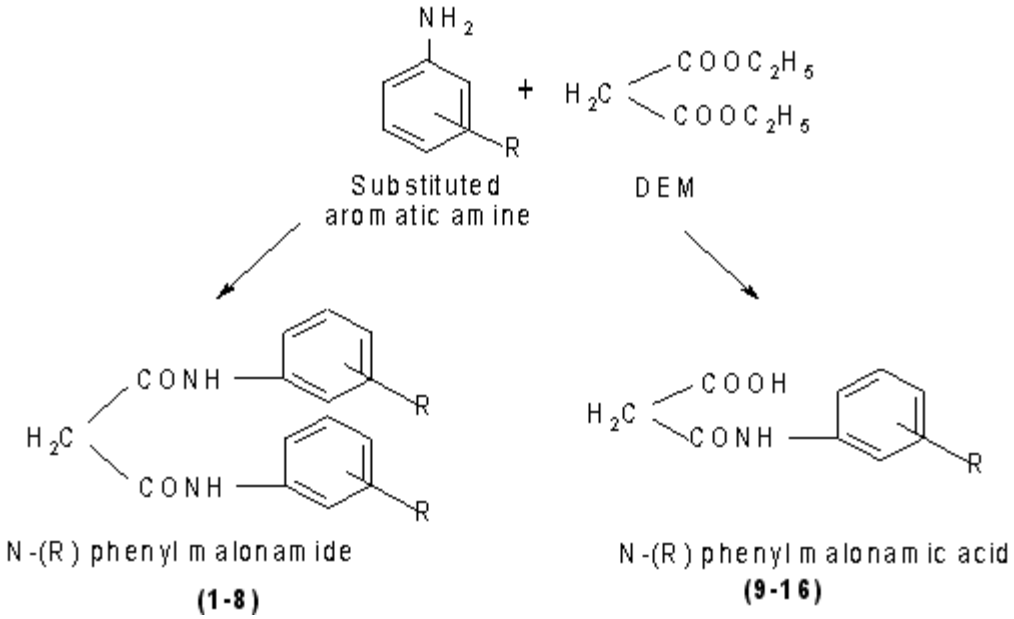

Table 2: Characterization (IR) data of compounds

Compound no	Ar C=C cm^{-1}	Ar CH cm^{-1}	CONH cm^{-1} stretching	NH cm^{-1} stretching	CH_2 cm^{-1} stretching	COOH cm^{-1} stretching
1.	1514	2696	1652	3286	1398	-
2.	1530	2963	1650	3290	1375	-
3.	1594	3125	1649	3148	1380	-
4.	1543	3198	1658	3231	1362	-
9.	1596	2929	1660	3335.8	1351	1724
10.	1537	2964	1663	3296	1375	1715
11.	1580	2900	1650	3250	1333	1705
12.	1568	3250	1660	3303	1325	1725

have been recorded in the frequency region 4000-200 cm^{-1}.

The IR (KBr) spectrum of N-(R) phenyl malonamides[1-4] and N-(R) phenyl malonamic acids[9-12] shows absorption at 1596-1514 cm^{-1} & 3286-2696 cm^{-1} indicating aromatic character. Absorption in the range 1663-1649 cm^{-1} show-CONH stretching vibrations while absorption in 3335.8-3148 cm^{-1} reveals-NH stretching.-CH_2 stretching vibrations were obtained between 1398-1325 cm^{-1} and absorption at 1725-1705 cm^{-1} confirms the presence of-COOH group. These characters lent support to the structures of compound No. 1-4, 9-12 and other compounds (5-8, 13-16).

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