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Thennati Rajamannar [a] , Namasivayam Palani [a] & Kalpattu Kuppuswamy Balasubramanian [b]

[a] Centre for Agrochemical Research SPIC Science Foundation , 110 Mount Road Guindy, Madras, 600 032, INDIA

[b] Department of Chemistry , Indian Institute of Technology , Madras, 600 036, INDIA

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ALKYLATION OF CYCLIC 1,3-DIKETONES

Thennati Rajamannar[*a], Namasivayam Palani[a]
and Kalpattu Kuppuswamy Balasubramanian[*b].

[a]Centre for Agrochemical Research
SPIC Science Foundation
110 Mount Road
Guindy Madras 600 032, INDIA.

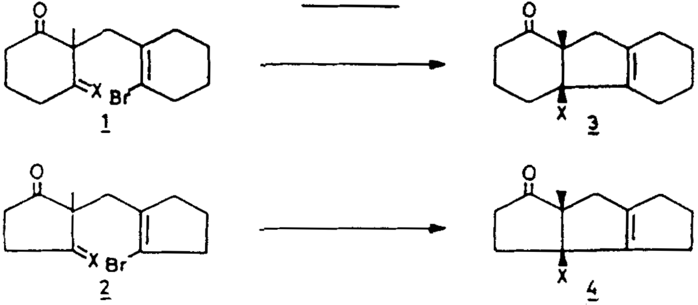
[b]Department of Chemistry
Indian Institute of Technology
Madras 600 036, INDIA.

Abstract: A simple procedure for the C-alkylation of cyclic 1,3-diketones have been reported using Triton B as base in aqueous conditions.

In connection with our ongoing research in the area of vinyl radical cyclisation[1] towards the construction of condensed carbocycles and triquinanes (Scheme 1), we needed to prepare various cyclic 1,3- diketone intermediates of the type 1 and 2.

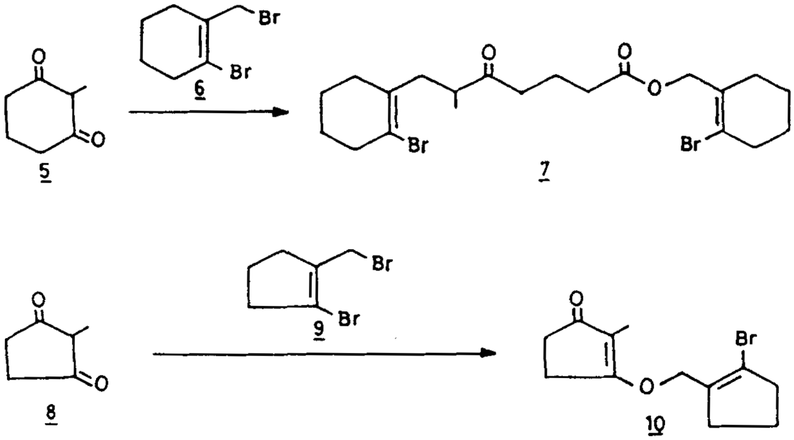
It was also of interest for us to study the behaviour of the vinyl radicals of 1 and 2 towards carbonyl addition[2], which would provide a short entry to the systems like 3 and 4.

Scheme 1



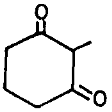
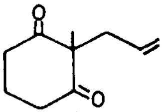
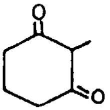
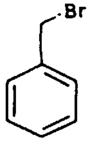
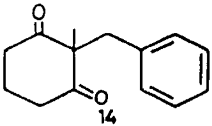
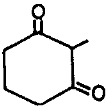
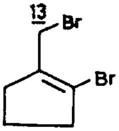
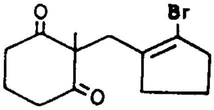
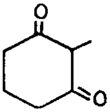
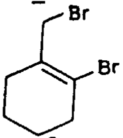
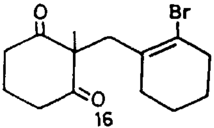
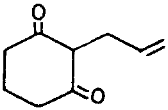
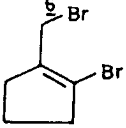
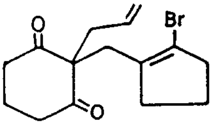
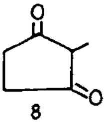
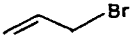
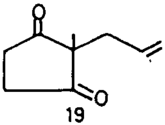
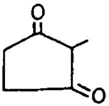
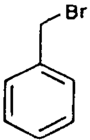
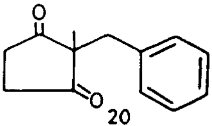
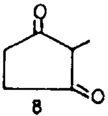
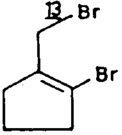
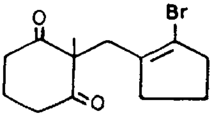
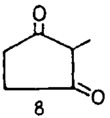
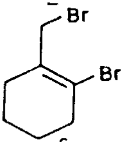
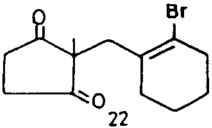
In view of this we attempted the alkylation of the dione 5 with reactive halide 6 using tetrabutylammonium hydroxide in THF afforded mainly the cleavage product 7[3]. Whereas reaction of 2-methylcyclopentane-1,3-dione 8 with halide 9 led to the exclusive formation of undesired O-alkylated product 10[4] (Scheme 2).

Scheme 2



Though many methods have been reported for the alkylation of cyclic 1,3-diketones[5], we were in search of

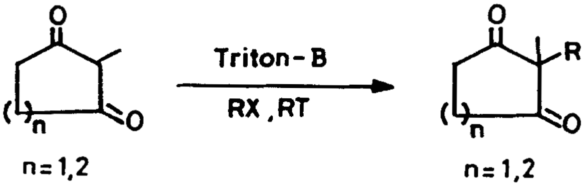
Table 1

Entry	Substrate	alkyl halide	Product	yield	m.p.
1	 5	 11	 12	70	-
2	 5	 13	 14	70	49-50°
3	 5	 9	 15	63	94-95°
4	 5	 6	 16	65	105-106°
5	 17	 9	 18	60	-
6	 8	 11	 19	65	-
7	 8	 13	 20	65	50-51°
8	 8	 9	 21	50	-
9	 8	 6	 22	53	-

an efficient and practical method which will have wider applicability and at the same time lead to minimum amounts of O-alkylation. We found that use of Triton B[6] in aqueous conditions is a convenient method for the C-alkylation of 2-methylcyclohexane and 2-methylcyclopentane 1,3-diones 5 and 8. In general these reactions are free from complications and the method is applicable to various reactive halides (Table 1). The utility of the alkylated products of cyclohexane[7] and cyclopentane[8] 1,3-diones in organic synthesis prompted us to report our results in this communication.

Treatment of an aqueous solution of 2-methylcyclohexane-1,3-dione 5 with Triton B followed by addition of akyl halide and stirring the reaction mixture at room temperature for 24-32h and work up furnished the C-alkylated products in good yields, similar reaction of 2-methylcyclopentane-1,3-dione 8 gave moderate yields of the bis alkylated products (Scheme 3).

Scheme 3

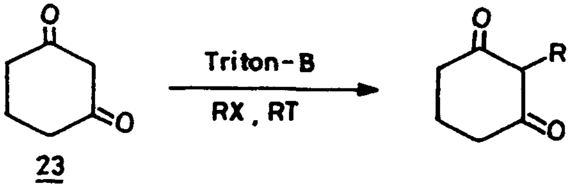


The various alkyl halides used for our study and the yields of the products obtained are given in the Table

1. In the case of 2-methylcyclopentane-1,3-dione 8 especially with alkyl halides 6 and 9 considerable amounts of the O-alkylated products were formed.

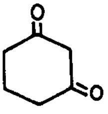
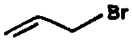
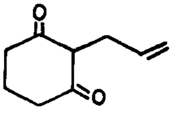
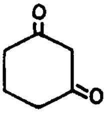
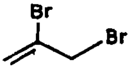
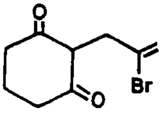
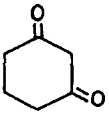
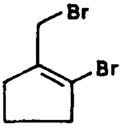
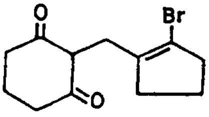
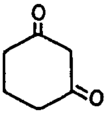
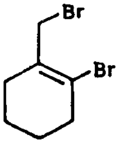
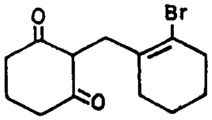
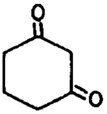
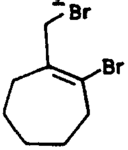
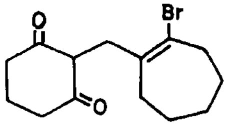
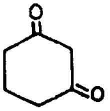
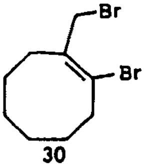
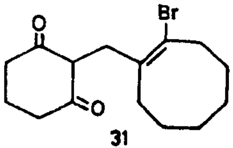
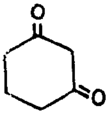
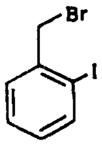
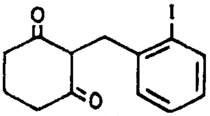
Extension of this alkylation method to cyclohexane-1,3-dione 23 afforded the mono alkylation products in good yields, which are also of interest for us in the synthesis of propellane type compounds via the vinyl radical cyclisation. Thus the procedure was found to be very facile and simple for the mono alkylation of cyclohexane-1,3-dione 23 (Scheme 4).

Scheme 4



The reaction proceeds to completion in 12h at room temperature and products crystallise out during the course of the reaction itself giving good yields of the mono alkylated products Table 2. All the mono alkylated cyclohexane-1,3-diones described in thid work were found to exist in the enol form in solutions, as ascertained from their nmr spectra. In the ^{13}C spectrum the carbonyl carbon signal is hardly noticed due to rapid keto enol

Table 2

Entry	Substrate	alkyl halide	Product	yield	m.p.
1	 23	 11	 17	72	125-127°
2	 23	 24	 25	70	123-124°
3	 23	 9	 26	65	170-171°
4	 23	 6	 27	70	179-180°
5	 23	 28	 29	66	166-167°
6	 23	 30	 31	65	193-194°
7	 23	 32	 33	65	154-155°

tautomerism of the 1,3- dicarbonyl moiety.The bromomethylcycloalkenyl halides used in this study were prepared from their respective cycloalkanones via the Vilsmeier-Haack bromoformylation[9] reaction. In summary Triton B/water combination provides a practical and simple method for the mono- and di- alkylation of cyclic 1,3-ketones.

EXPERIMENTAL

All the melting points are uncorrected. Infrared spectra were recorded on Perkin Elmer 1310; ^{1}H and ^{13}C nmr were recorded on Geol GSX 400 and Brucker 400 spectrometers; Mass spectra were scanned on GCMS-QP1000A.

General Experimental procedure: To the 10 mmol of the dione in 5 ml of water was added 10 mmol of 40% solution of Triton B (benzyltimethylammonium hydroxide) in methanol, followed by addition of 12 mmol of alkyl halide and stirring at room temperature for several hours, usual workup and after neccessary purification gave C-alkylated diones (Table 1 and Table 2).

2(2-Bromo-1-cyclopentenylmethyl)-2-methylcyclohexane-1,3-dione (15).

IR (KBr) cm^{-1}: 2970,2945,1710,1680,1415,1305,1210,1052, 1020.

^{1}H NMR ($CDCl_3$, 400 MHz): δ : 2.84(ddd, J=15.62,10.25,5.37 Hz, 2H); 2.72(s, 2H); 2.63(ddd, J=15.62,11.72,6.31 Hz, 2H); 2.60(m, 2H); 2.17-2.06(m, 3H); 1.91-1.81(m, 3H); 1.28(s, 3H).

^{13}C NMR ($CDCl_3$, 100 MHz): δ : 209.43(s); 135.81(s); 121.16(s); 64.98(s); 39.72(t); 37.84(t); 37.64(t); 34.79(t); 22.04(t); 18.97(q); 17.91(t).

MS: 205(100); 177(16.6); 149(25.3); 127(54.3); 121(17.1); 91(20.8); 79(68.9); 77(20.2).

m.p. 94-95°C

Analysis required C:54.75, H:6.01; found C:55.15, H:6.05.

2(2-Bromo-1-cyclohexenylmethyl)-2-methylcyclohexane-1,3-dione (16)

IR (KBr) cm^{-1}: 2985,2940,1710,1675,1435,1310,1210, 1055,1012,903.

^{1}H NMR ($CDCl_3$, 400 MHz): δ : 2.90(ddd, J=16.11,10.74,5.86 Hz, 2H); 2.82(s, 2H); 2.62(ddd, J=16.11,10.25,5.17 Hz, 2H); 2.50(m, 2H); 2.26(m, 1H); 2.16-2.09(m,1H); 1.94(m, 2H); 1.82-1.56(m, 4H); 1.28(s, 3H).

^{13}C NMR ($CDCl_3$, 100 MHz): δ : 209.64(s); 131.39(s); 124.20(s); 65.44(s); 44.73(t); 38.01(t); 37.10(t); 31.86(t); 24.55(t); 22.57(t); 18.05(t); 17.62(q).

MS: 301(3.2); 299(3.9); 220(15.7); 219(100); 173(19.7); 135(21.9); 127(58.2); 121(35.4); 93(77); 91(47.4); 79(28); 77(33).

m.p. 105-106°C

Analysis required C:56.20, H:6.40; found C:56.52, H:6.59.

2-Allyl-2(2-bromo-1-cyclopentenylmethyl)cyclohexane-1,3-dione (18)

IR (neat) cm^{-1}: 2970,1720,1690,1638,1438,1210,990.

^{1}H NMR ($CDCl_3$, 400 MHz): δ : 5.45(m, 1H); 4.95(m, 2H); 2.51(m, 10H); 2.01(m, 2H); 1.60(m, 4H).

^{13}C NMR ($CDCl_3$, 100 MHz): δ : 209.50(s); 135.73(s); 132.43(d); 120.99(s); 119.38(t); 67.24(s); 40.48(t); 39.74(t); 39.37(t); 36.88(t); 35.33(t); 22.04(t); 16.72(t).

MS: 313(8.6); 309(9.5); 231(100); 189(97); 153(33.2); 91(28); 79(73.4); 77(31.3); 55(32.7).

2(2-Bromo-1-cyclopentenylmethyl)-2-methylcyclopentane-1,3-dione (21).

IR (neat) cm^{-1}: 2960,2920,2860,1760,1720,1445,1415, 1065, 915.

^{1}H NMR ($CDCl_3$, 400 MHz): δ : 2.87-2.71(m, 4H); 2.56(m, 2H); 2.52(s, 2H); 2.14(m, 2H); 1.87(m, 2H); 1.15(s, 3H).

^{13}C NMR ($CDCl_3$, 100 MHz): δ : 215.04(s); 135.23(s); 121.16(s); 55.87(s); 39.64(t); 35.70(t); 35.09(t); 34.95(t); 21.95(t); 18.85(q).

MS: 191(100); 113(94); 163(17); 79(58).

2(2-Bromo-1-cyclohexenylmethyl)-2-methylcyclopentane-1,3-dione (22).

IR (neat) cm^{-1}: 2920,2840,1755,1712,1440,1060

^{1}H NMR ($CDCl_3$, 400 MHz): δ : 2.95-2.67(m, 4H); 2.62(s, 2H); 2.50(m, 2H); 1.98(m, 2H); 1.74-1.58(m, 4H); 1.19(s, 3H).

^{13}C NMR ($CDCl_3$, 100MHz): δ : 215.38(s); 131.12(s);

124.17(s); 56.19(s); 43.12(t); 36.98(t); 35.34(t); 32.51(t); 24.59(t); 22.60(t); 18.94(q).

MS: 205(16); 113(92); 93(92); 91(83); 79(61) 77(66); 69(40); 41(100).

2(2-Bromo-1-cyclopentenylmethyl)cyclohexane-1,3-dione (26).

IR (KBr) cm^{-1}: 3500,2960,1570,1360,1275,1065.

^{1}H NMR (DMSO-d$_6$, 400 MHz): δ : 10.56(bs, 1H); 3.00(s, 2H); 2.52(m, 2H); 2.34(m, 4H); 2.06(m, 2H); 1.79(m, 4H).

^{13}C NMR (DMSO-d$_6$, 100 MHz): δ : 140.14(s); 113.25(s); 111.03(s); 39.47(t); 33.04(t); 22.18(t); 20.75(t); 20.46(t).

MS: 273(20.8); 271(21.9); 192(22); 191(100); 189(51.7); 91(27); 79(26.9); 77(23.1); 55(43.3); 41(30.5).

m.p. 170-171°C

Analysis required C:53.15, H:5.58; found C:53.04, H:5.54.

2(2-Bromo-1-cyclohexenylmethyl)cyclohexane-1,3-dione (27).

IR (KBr) cm^{-1}: 3500,3920,1570,1360,1260,1190,1000.

^{1}H NMR (DMSO-d$_6$, 400 MHz): δ : 10.50(bs, 1H); 3.08(s, 2H); 2.41-2.33(m, 6H); 1.82(m, 4H); 1.57-1.51(m, 4H).

^{13}C NMR (DMSO-d$_6$, 100 MHz): δ : 134.73(s); 117.53(s); 111.26(s); 36.41(t); 28.80(t); 28.62(t); 24.41(t); 22.02(t); 20.51(t).

MS: 287(10.6); 285(11); 206(43.6); 205(100); 203(50.7); 125(42.9); 91(33.8); 81(42.6); 79(40.6); 77(36.2); 55(62.3); 43(28.1); 41(42.9).

m.p. 179-180°C

Analysis required C:54.75, H:6.01; found C:54.66 H:6.02.

2(2-Bromo-1-cycloheptenylmethyl)cyclohexane-1,3-dione (29).

IR (KBr) cm^{-1}: 3100,2900,1590,1470,1300,1265,1200,1000.

^{1}H NMR ($CDCl_3$, 400 MHz): δ : 5.50(bs, 1H); 3.37(s, 2H); 2.76(m, 2H); 2.46(t, J=6.35 Hz, 4H); 2.09(m, 2H); 1.96(pent, J=6.35 Hz, 2H); 1.70(m, 2H); 1.54(m, 2H); 1.35(m, 2H).

^{13}C NMR ($CDCl_3$, 100 MHz): δ : 140.24(s); 122.75(s); 111.58(s); 40.94(t); 32.62(t); 31.65(t); 31.43(t); 30.86(t); 25.70(t); 25.38(t); 20.58(t).

MS: 301(3.9); 299(3.7); 220(35.8); 219(100); 131(21.9); 125(85.8); 107(45.2); 97(25); 93(28.3); 91(78.7); 82(20.4); 81(53.6); 80(27.2); 77(73.2); 69(32.7); 67(51.6).

m.p. 166-167°C.

2(2-Bromo-1-cyclootenylmethyl)cyclohexane-1,3-dione (31).

IR (KBr) cm^{-1}: 3500,2900,1560,1400,1258,1388,1080,980.

^{1}H NMR ($CDCl_3$, 400 MHz): δ : 5.53(bs, 1H); 3.44(s, 2H); 2.73(t, J=5.86 Hz, 2H); 2.48(t, J=6.35 Hz, 4H); 2.18(t, J=5.37 Hz, 2H); 2.00(pent, J=6.35 Hz, 2H); 1.69(m, 2H); 1.51(m, 6H).

^{13}C NMR ($CDCl_3$, 100 MHz): δ : 137.40(s); 122.11(s); 112.09(s); 36.99(t); 30.58(t); 29.85(t); 28.59(t); 27.96(t); 26.39(t); 25.85(t); 20.53(t).

MS: 315(17.7); 313(18.6); 234(24.2); 233(100); 125(42.3); 109(29.8); 107(21.2); 91(32.6); 79(43.1); 77(27.7); 65(35.3); 55(68.7).

m.p. 193-194°C

<u>2(2-Iodobenzyl)cyclohexane-1,3-dione</u> (<u>33</u>).

IR (KBr) cm^{-1}: 3500,2940,1570,1565,1360,1260,1180, 1005,745.

^1H NMR ($DMSO-d_6$, 400 MHz): δ : 10.8(bs, 1H); 7.79(d, J=7.63 Hz, 1H); 7.22(t, J=7.55 Hz, 1H); 6.88(t, J=7.62 Hz, 1H); 6.86(d, J=7.58 Hz, 1H); 3.42(s, 2H); 2.42(t, J=6.19 Hz, 4H); 1.94(pent. J=6.27 Hz, 2H).

^{13}C NMR ($DMSO-d_6$, 100MHz): δ : 142.47(s); 138.35(d); 127.91(d); 127.47(d); 127.36(d); 111.96(s); 101.66(s); 33.27(t); 32.51(t); 20.51(t).

MS: 329(15.8); 217(29); 201(100); 199(20.8); 55(45.3).

m.p. 154-155°C

Analysis required C:47.58, H:3.99; found C:47.05, H:3.91.

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3. Data of the compound 7: ^{1}H NMR ($CDCl_3$, 400 MHz): δ : 4.87(s, 2H); 2.81(m, 1H); 2.56-2.22(m, 9H); 2.15(m, 2H); 2.05(m, 2H); 1.90(m, 2H); 1.65(m, 9H); 1.10(d, J=7.6 Hz, 3H).
   ^{13}C NMR ($CDCl_3$, 100 MHz): δ : 213.21(s); 173.04(s); 133.71(s); 131.03(s); 123.24(s); 121.38(s); 67.47(t); 44.49(d); 39.95(t); 36.76(t); 36.69(t); 33.17(t); 31.71(t); 28.84(t); 24.77(t); 24.45(t); 22.59(t); 22.03(t); 18.85(t); 16.06(q).
4. Data of the compound 10: ^{1}H NMR ($CDCl_3$, 400 MHz): δ : 4.73(s, 2H); 2.66-2.59(m, 4H); 2.42-2.37(m, 4H); 1.94(m, 2H); 1.56(t, J=1.46 Hz, 3H).
   ^{13}C NMR ($CDCl_3$, 100 MHz): δ : 205.38(s); 183.66(s); 130.85(s); 120.55(s); 116.77(s); 66.79(t); 40.24(t); 33.56(t); 32.28(t); 25.06(t); 21.48(t); 5.95(q).
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