Electronic Supplementary Material (ESI) for Green Chemistry

Supporting information

Clean synthesis of *p*-nitrotoluene from crystalline *p*-nitrobenzylbromide with zero organic discharge

Milan Dinda,[a] Manoj K. Agrawal,[a,b] Mahesh R. Gandhi,[a] Sumesh C. Upadhyay,[a] Subbarayappa Adimurthy,[a] Supratim Chakraborty,[a] and Pushpito K. Ghosh[*,a]

[a]*Central Salt and Marine Chemicals Research Institute, Council of Scientific & Industrial Research, G. B. Marg, Bhavnagar –364 002, India*

[b] *Present Address: Generic Division, Lupin Research Park, Survey No. 46/47A Nande Village, Mulshi Taluka, Pune 411042, Maharashtra, India*

[*]E-mail: pkghosh@csmcri.org; *Fax: +91-278-2567562*

Warning: p-*Nitrobenzyl bromide is a skin irritant and due care must be taken during handling and work up.*

Analytical Data

GC-MS Data

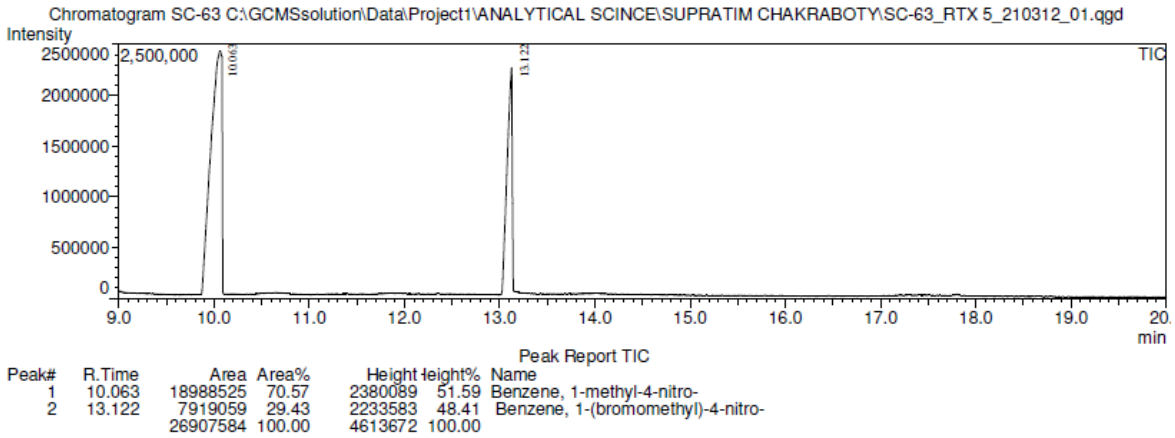
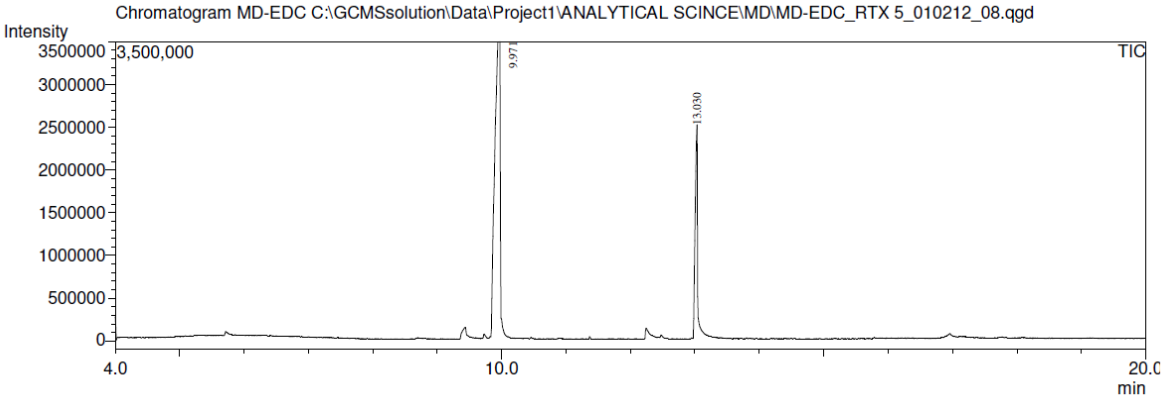


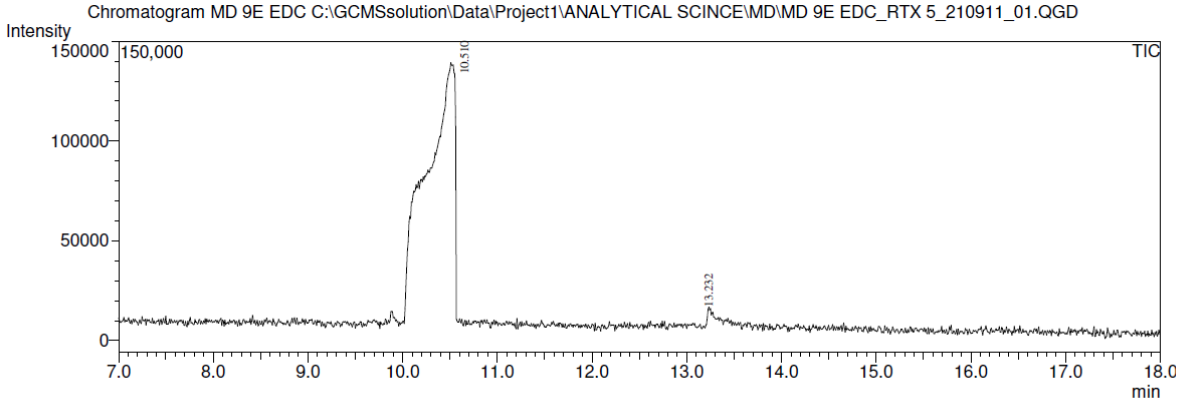
Fig S1. GC-MS of 3.0551 g (22.3 mmol) PNT and 2.4084 g (11.15 mmol) PNBBr (2:1, [PNT]:[PNBBr]) in 20 mL EDC for quantification of yields taking into account response factor



Peak Report TIC

Peak#	R.Time	Area	Area%	Height	Height%	Name	Base m/z
1	9.971	21332404	77.59	3827828	60.51	Benzene, 1-methyl-4-nitro-	91.05
2	13.030	6161056	22.41	2498151	39.49	Benzene, 1-(bromomethyl)-4-nitro-	136.05
		27493460	100.00	6325979	100.00		

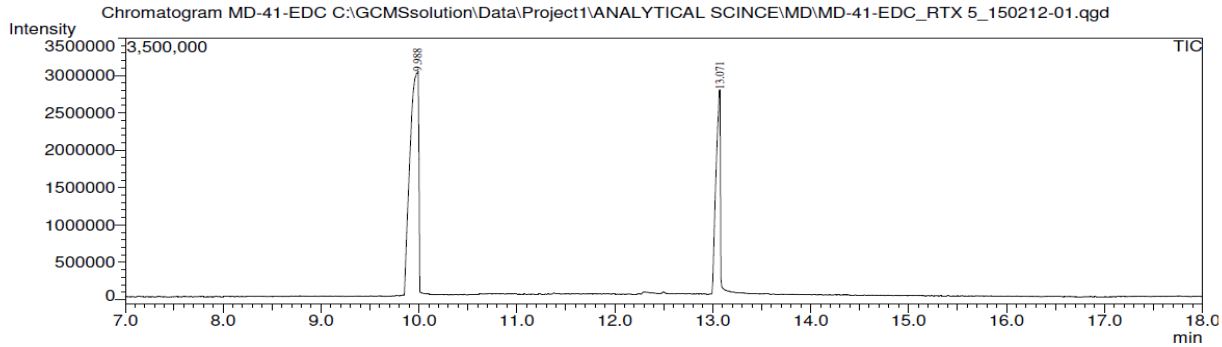
Fig S2. GC-MS of reaction mixture upon reaction with NBS (5 mmol substrate; 3:1 molar ratio of substrate to reagent) at 80°C under illumination with 100 W tungsten lamp



Peak Report TIC

Peak#	R.Time	Area	Area%	Height	Height%	Name	Base m/z
1	10.510	2700956	98.55	130866	92.60	p-Nitrotoluene	91.05
2	13.232	39739	1.45	10460	7.40	Benzene, 1-(bromomethyl)-4-nitro-	136.05
		2740695	100.00	141326	100.00		

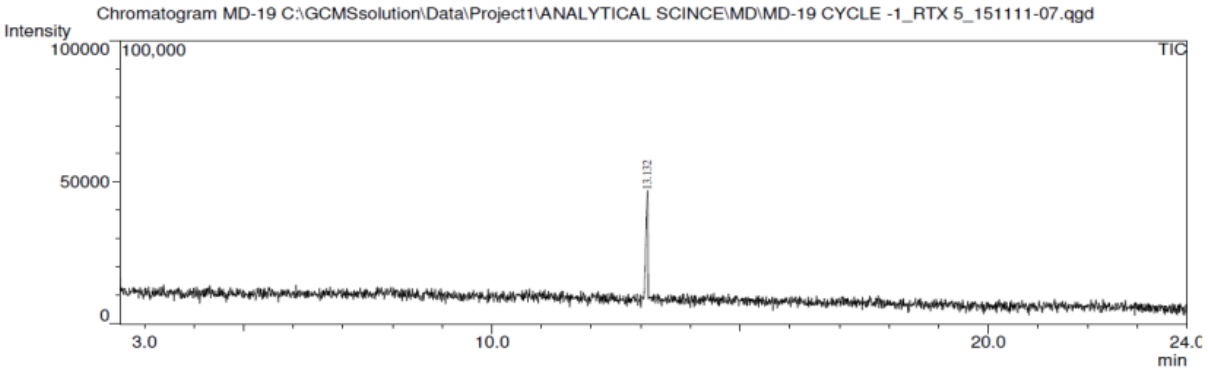
Fig. S3. GC-MS of reaction mixture upon reaction with *BR-S* (5 mmol substrate; 3:1 molar ratio of substrate to reagent) at 80°C in the absence of light



Peak Report TIC

Peak#	R.Time	Area	Area%	Height	Height%	Name	Base m/z
1	9.988	18537838	68.53	2996524	52.34	Benzene, 1-methyl-4-nitro-	91.00
2	13.071	8514560	31.47	2728775	47.66	Benzene, 1-(bromomethyl)-4-nitro-	136.05
		27052398	100.00	5725299	100.00		

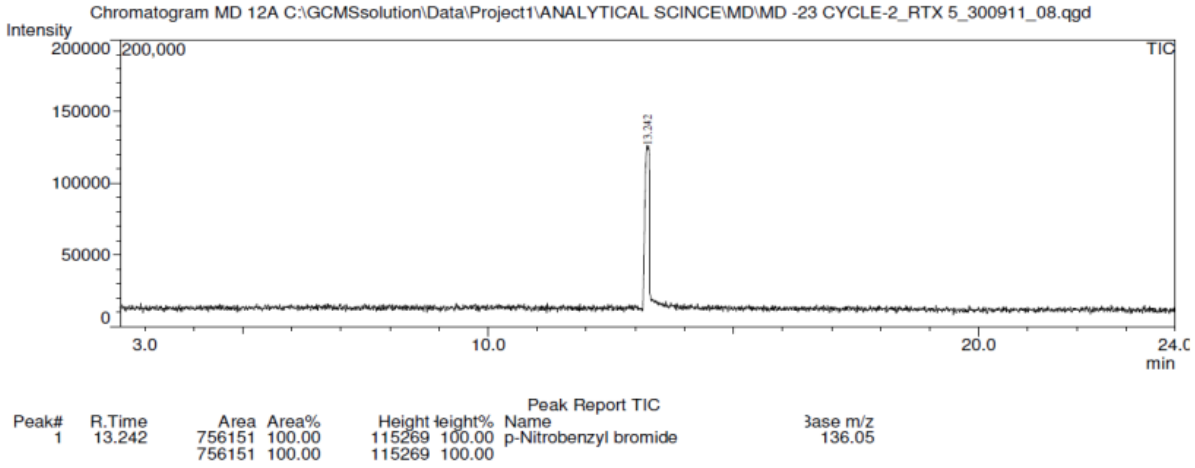
Fig. S4. The figure shows the GC-MS of the reaction mixture of Batch 1, Table 1. When corrected for response factor using the data of Figure S1, the observed peak areas of PNT and PNBBr tallied well with the values computed for a 1.9:1.1 molar ratio of PNT to PNBBr expected for quantitative formation of product in Batch 1.



Peak Report TIC

Peak#	R.Time	Area	Area%	Height	Height%	Name	Base m/z
1	13.132	102132	100.00	38465	100.00	Benzene, 1-(bromomethyl)-4-nitro-	136.05
		102132	100.00	38465	100.00		

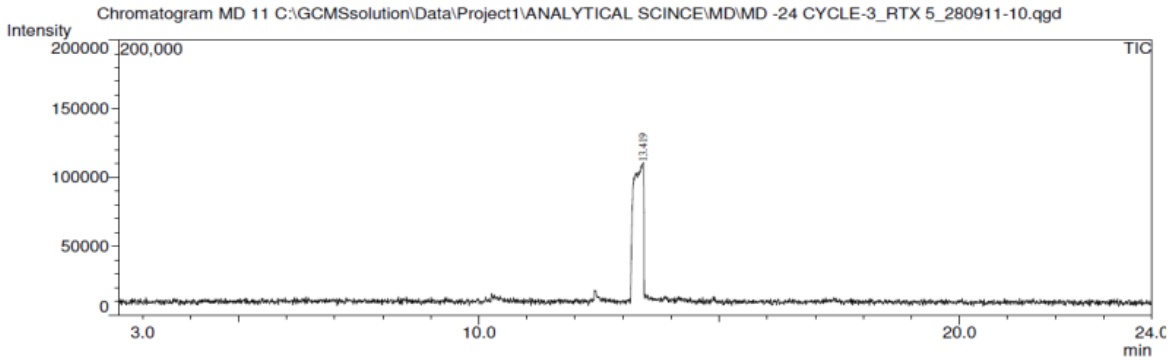
Fig. S5.1. GC-MS of crystallized product from Batch 1



Peak Report TIC

Peak#	R.Time	Area	Area%	Height	Height%	Name	Base m/z
1	13.242	756151	100.00	115269	100.00	p-Nitrobenzyl bromide	136.05
		756151	100.00	115269	100.00		

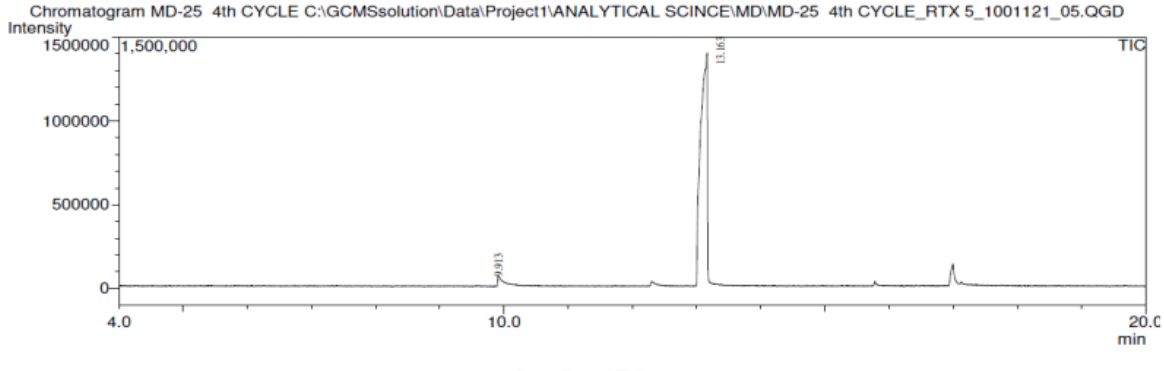
Fig. S5.2. GC-MS of crystallized product from Batch 2



Peak Report TIC

Peak#	R.Time	Area	Area%	Height	Height%	Name	Base m/z
1	13.419	1461699	100.00	102412	100.00	p-Nitrobenzyl bromide	136.05
		1461699	100.00	102412	100.00		

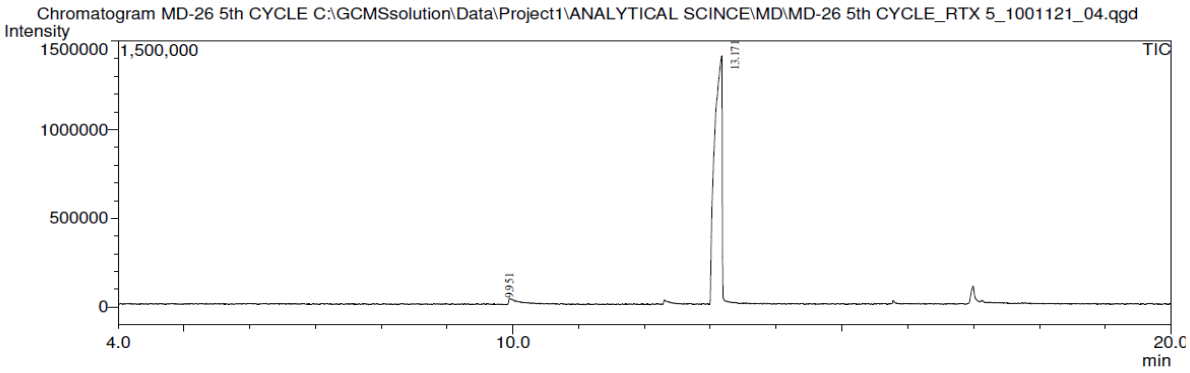
Fig. S5.3. GC-MS of crystallized product from Batch 3



Peak Report TIC

Peak#	R.Time	Area	Area%	Height	Height%	Name	Base m/z
1	9.913	274929	2.65	58788	4.06		91.05
2	13.163	10084889	97.35	1388453	95.94		136.00
		10359818	100.00	1447241	100.00		

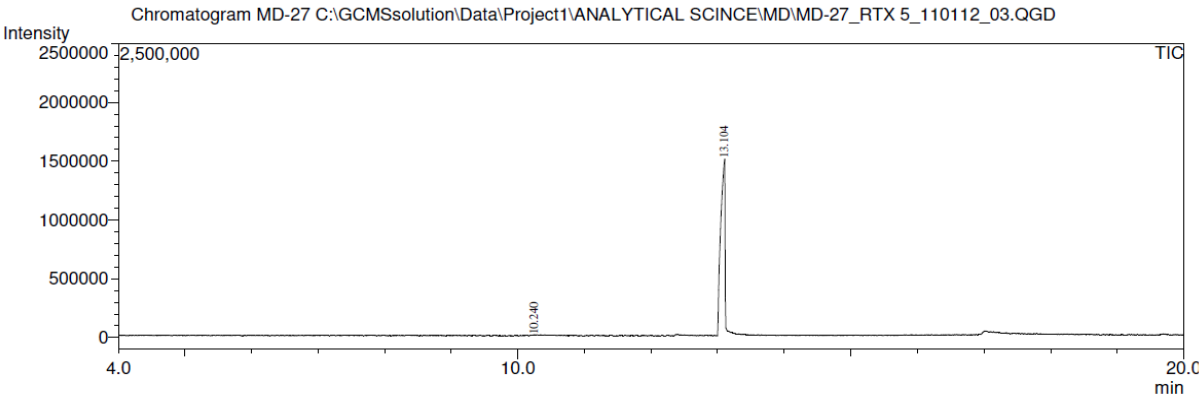
Fig. S5.4. GC-MS of crystallized product from Batch 4



Peak Report TIC

Peak#	R.Time	Area	Area%	Height	Height%	Name	Base m/z
1	9.951	288504	2.58	34121	2.38		91.05
2	13.171	10908533	97.42	1399133	97.62		136.00
		11197037	100.00	1433254	100.00		

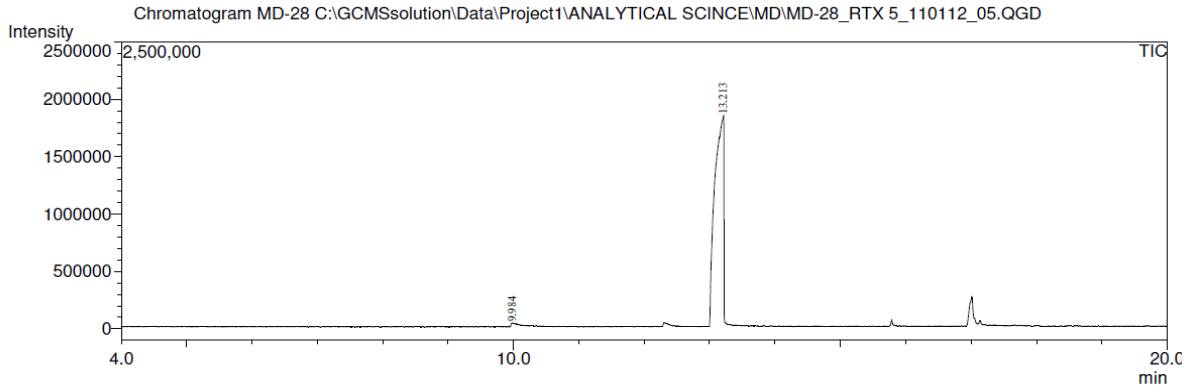
Fig. S5.5. GC-MS of crystallized product from Batch 5



Peak Report TIC

Peak#	R.Time	Area	Area%	Height	Height%	Name	Base m/z
1	10.240	101102	1.41	8509	0.56		91.10
2	13.104	7062381	98.59	1501017	99.44		136.00
		7163483	100.00	1509526	100.00		

Fig. S5.6. GC-MS of crystallized product from Batch 6



Peak Report TIC

Peak#	R.Time	Area	Area%	Height	Height%	Name	Base m/z
1	9.984	313009	1.76	31557	1.68		91.10
2	13.213	17479230	98.24	1841390	98.32		136.00
		17792239	100.00	1872947	100.00		

Fig. S5.7. GC-MS of crystallized product from Batch 7

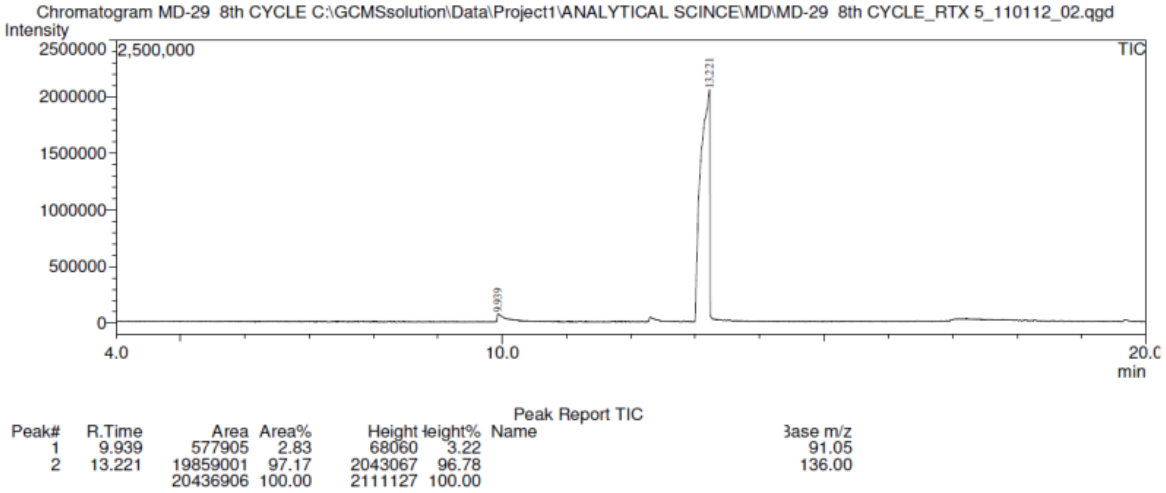


Fig. S5.8. GC-MS of crystallized product from Batch 8

$NaBH_4$ reduction of the mother liquor after 8th batch:

GC-MS Data:

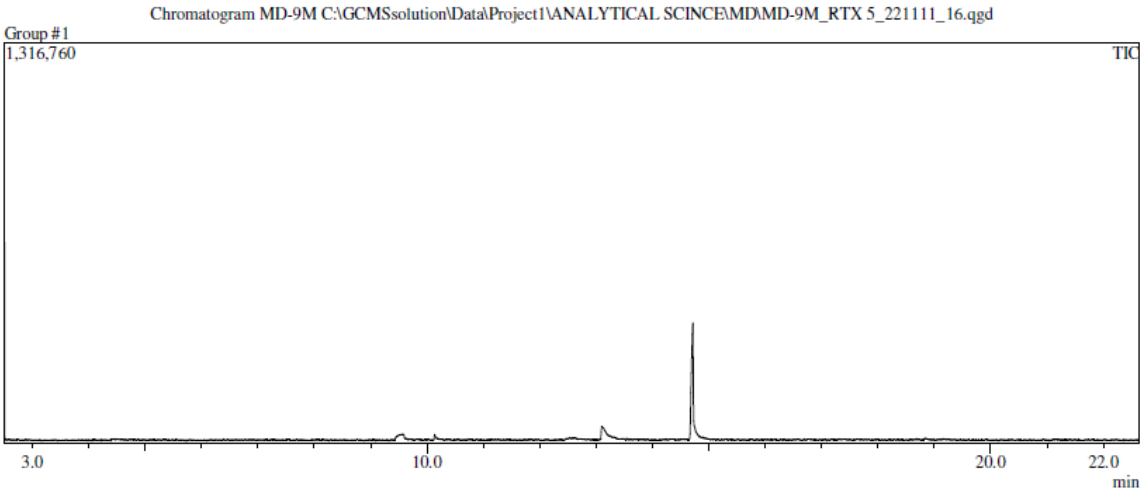
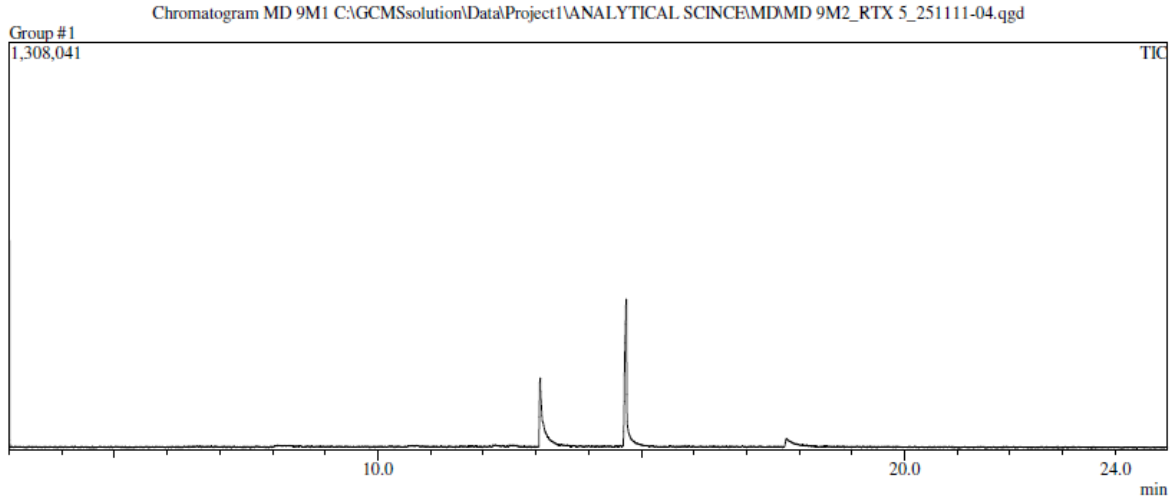


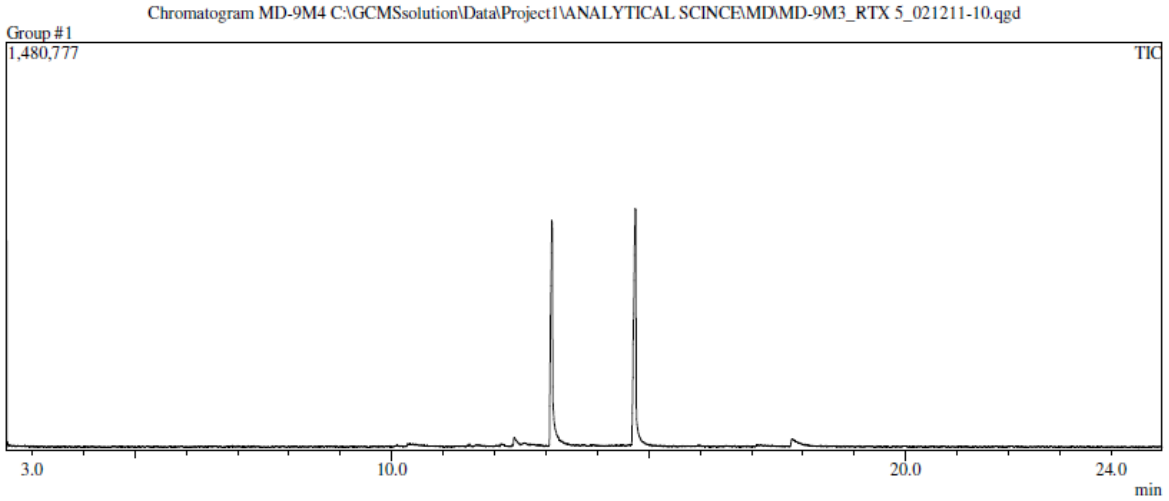
Figure S6.1 (Table S3, Entry 1)



Peak Report TIC

Peak#	R.Time	Area	Area%	Name
1	13.081	1019384	41.53	Benzene, 1-(bromomethyl)-4-nitro-
2	14.713	1434933	58.47	Benzene,(dibromomethyl)4-nitro
		2454317	100.00	

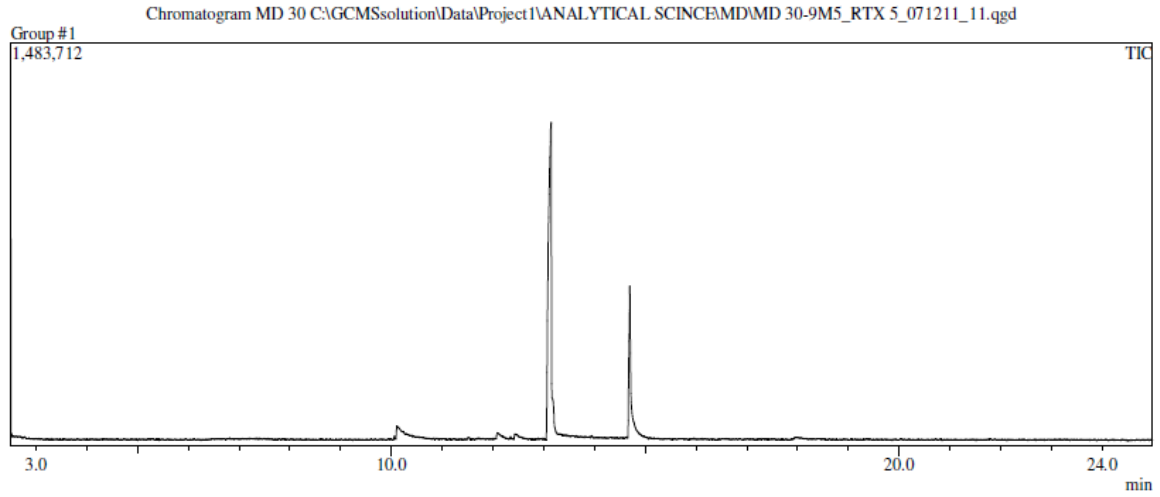
Figure S6.2 (Table S3, Entry 2)



Peak Report TIC

Peak#	R.Time	Area	Area%	Name
1	13.120	2618618	47.86	Benzene, 1-(bromomethyl)-4-nitro-
2	14.745	2853015	52.14	Benzene1,1dibromomethyl-4nitro
		5471633	100.00	

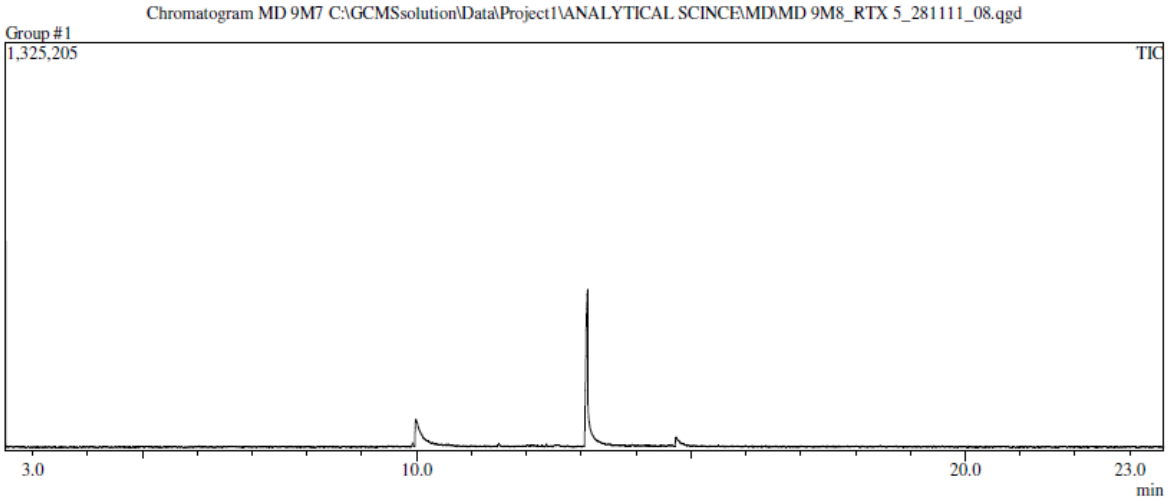
Figure S6.3 (Table S3, Entry 3)



Peak Report TIC

Peak#	R.Time	Area	Area%	Name
1	13.146	5141335	77.37	Benzene, 1-(bromomethyl)-4-nitro-
2	14.698	1503540	22.63	Benzene, 1,1 dibromomethyl)-4-nitrc
		6644875	100.00	

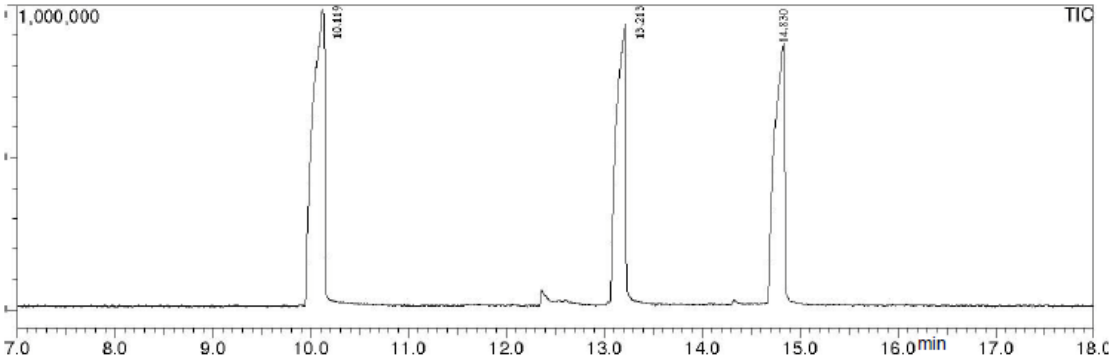
Figure S6.4 (Table S3, Entry 4)



Peak Report TIC

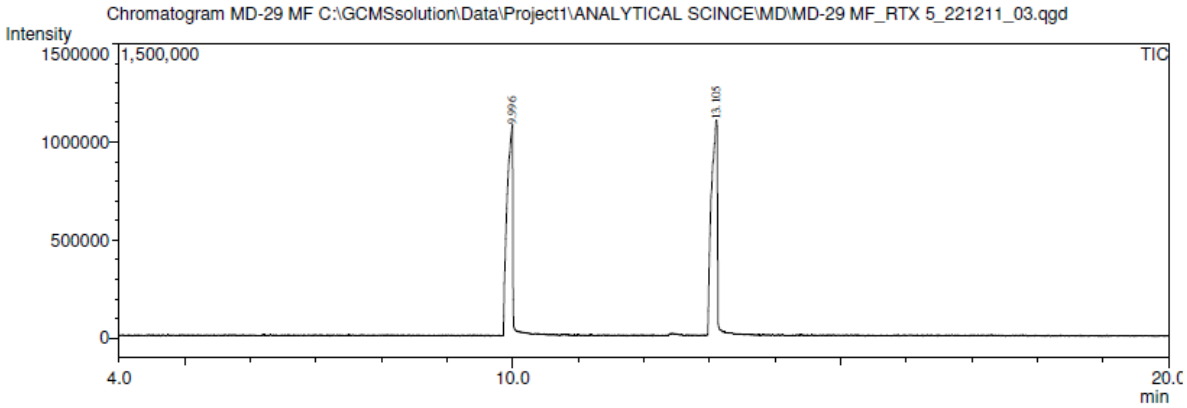
Peak#	R.Time	Area	Area%	Name
1	9.987	631678	25.70	Benzene, 1-methyl-4-nitro-
2	13.113	1704417	69.35	Benzene, 1-(bromomethyl)-4-nitro-
3	14.729	121434	4.94	Benzene1,1dibromomethyl-4nitro
		2457529	100.00	

Figure S6.5 (Table S3, Entry 5)



R.Time	Area	Area%	Peak Report TIC	Height	Height%	Name	Base m/z
10.119	8098925	40.32		972334	35.48	Benzene, 1-methyl-4-nitro	91.05 136.05
13.213	6087937	30.31		916233	33.44		89.00
14.830	5898309	29.37		851726	31.08	Benzene, 1-(bromomethyl)-4-nitro	
	20085171	100.00		2740293	100.00	Benzene 1,1 dibromo methyl -4nitro	

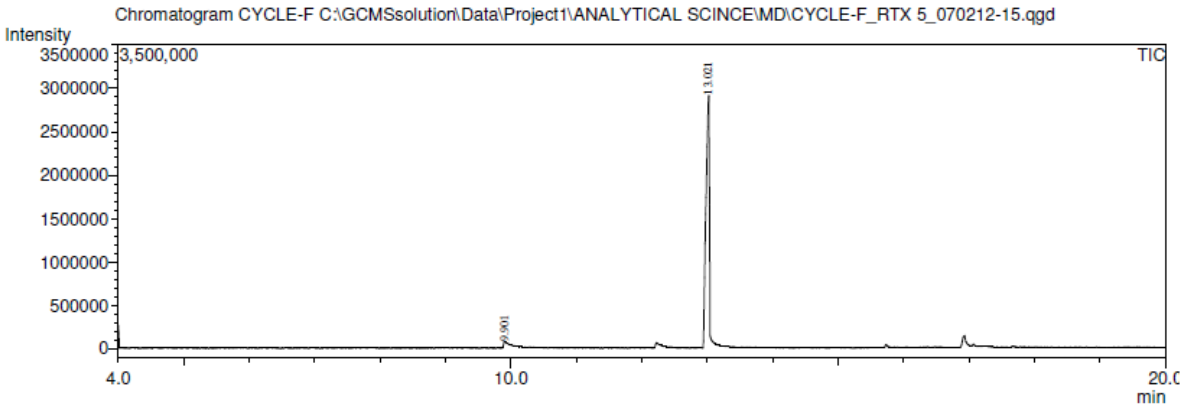
Fig. S7.1. Mother liquor of Table 1 before debromination with $NaBH_4$



Peak Report TIC

Peak#	R.Time	Area	Area%	Height	Height%	Name	Base m/z
1	9.996	6588504	48.67	1077044	49.57		91.05
2	13.105	6948678	51.33	1095937	50.43		136.00
		13537182	100.00	2172981	100.00		

Fig. S7.2. Mother liquor of Table 1 after debromination with $NaBH_4$



Peak Report TIC

Peak#	R.Time	Area	Area%	Height	Height%	Name	Base m/z
1	9.901	571270	5.12	68875	2.32	Benzene, 1-methyl-4-nitro-	65.00
2	13.021	10596303	94.88	2894478	97.68	Benzene, 1-(bromomethyl)-4-nitro-	136.05
		11167573	100.00	2963353	100.00		

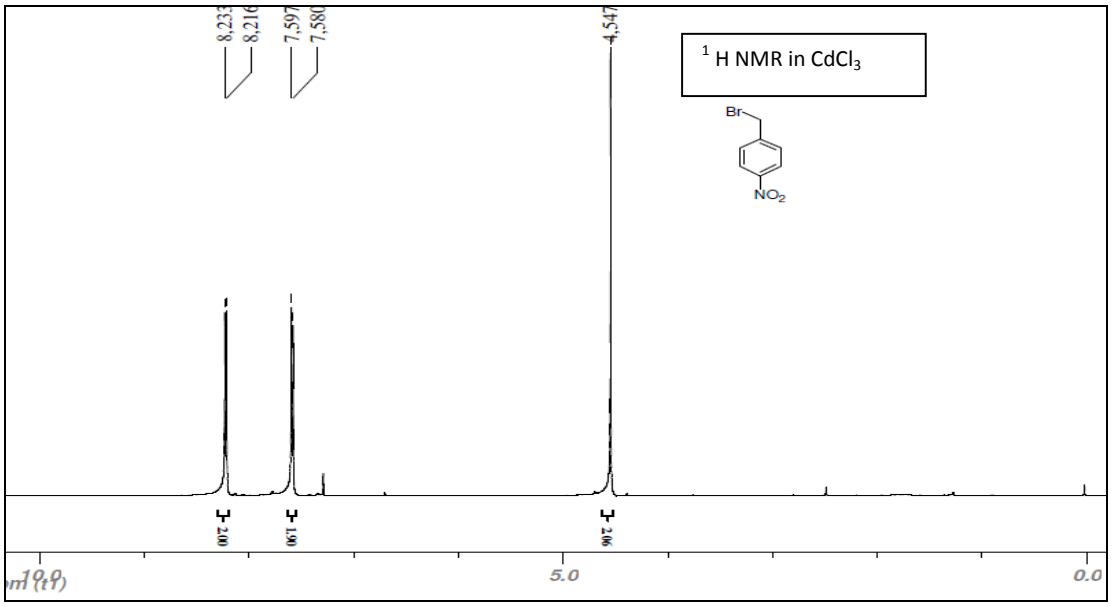
Fig. S8. GC-MS of composite of the isolated products from Batches 1- 8, Table 1.

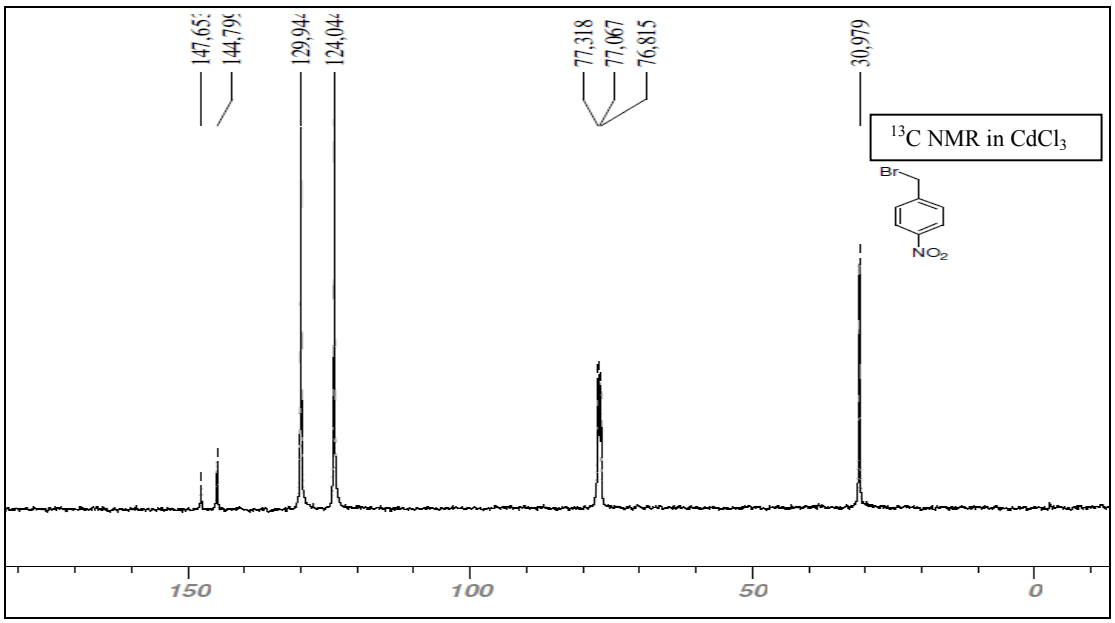
NMR (^{1}H ; ^{13}C NMR) and IR data of PNBBr

1) *p* - nitrobenzyl bromide (PNBBr) (Table 1, Entry 1, Fig. S5.1)

^{1}H NMR ($CDCl_3$-500 MHz): δ 8.21-8.23 (2H, d, J=8.5); 7.58-7.6 (2H, d, J=8.5); 4.55 (2H, S).

^{13}C NMR ($CDCl_3$-500 MHz): δ 147.7, 144.8, 129.9 (2C), 124.0 (2C), 31.0





IR data

V_{max} (KBr): 3051, 2840, 2378, 1604, 1534, 1344, 1224, 1099, 1011, 874, 798, 692, 592 cm^{-1}

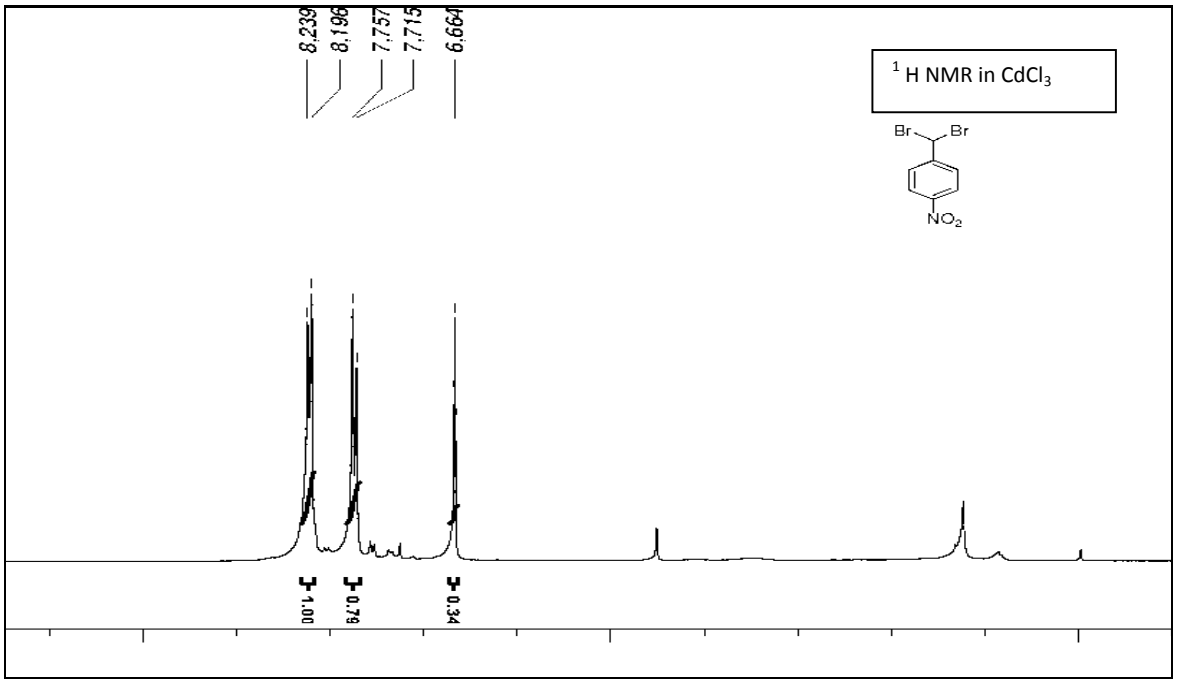
NMR (^{1}H ; ^{13}C NMR) data of $PNBBr_2$

2) 1-(dibromomethyl)-4-nitrobenzene

^{1}H NMR ($CDCl_3$-200 MHz): δ 8.24-8.2 (2H, d, J=8.6); 7.76-7.72 (2H, d, J=8.4); 6.664 (1H, S).

^{13}C NMR ($CDCl_3$-200 MHz): δ 148.3, 147.9, 127.9 (2C), 124.1 (2C), 38.6

Note: Minor peaks are ascribed to PNT and PNBBr impurities



Electronic Supplementary Material (ESI) for Green Chemistry

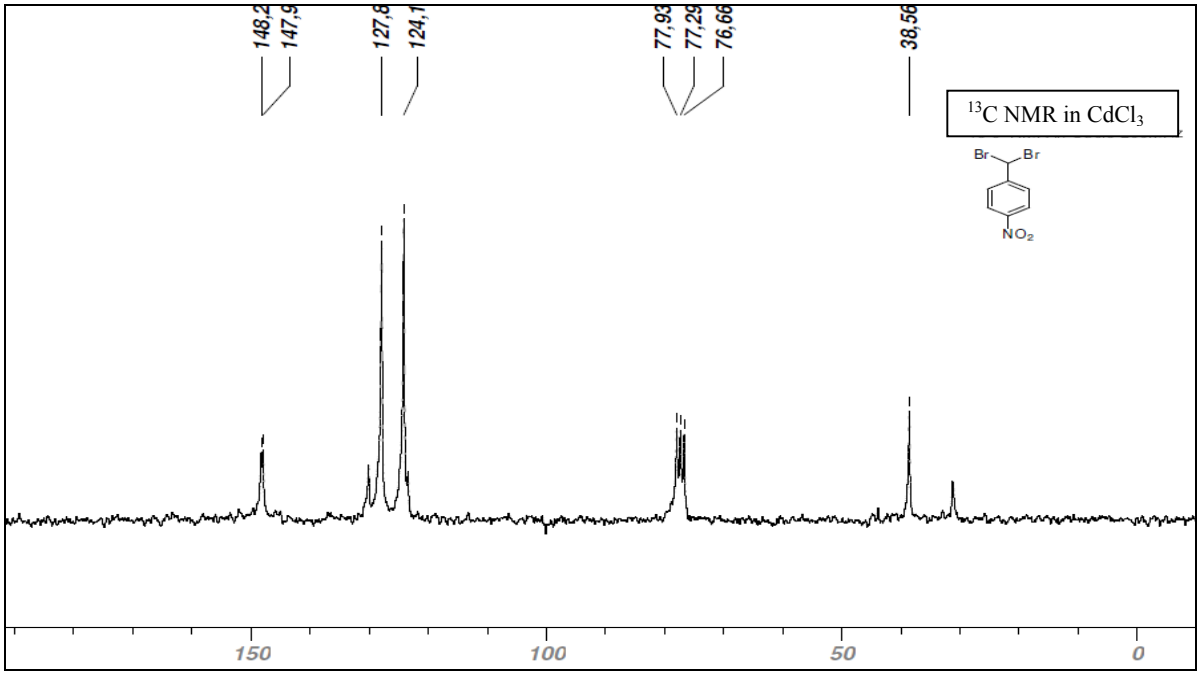


Table S1. Crystallization studies of 2:1 PNT/PNBBr in CCl_4

Entry	PNT g/mmol	PNBBr g/mmol	CCl_4/mL	Solid isolated/g	PNBBr purity (GC-Area %)
1.	1.0/7.23	0.788/3.64	1.8	1.78	33%
2.	1.0/7.23	0.788/3.64	2.7	1.78	”
3.	1.0/7.23	0.788/3.64	3.6	1.78	”
4.	1.0/7.23	0.788/3.64	4.5	0.97	”
5.	1.0/7.23	0.788/3.64	5.4	0.86	”
6.	1.0/7.23	0.788/3.64	6.3	0.82	”
7.	1.0/7.23	0.788/3.64	7.2	0.87	47.6
8.	1.0/7.23	0.788/3.64	8.1	0.73	53.8
9.	1.0/7.23	0.788/3.64	9.0	0.52	65.6
10.	20/145.9	15.76/72.9	162	15.6	64.6

Table S2: Bromination reaction-cum-cold crystallization of PNBBr in CCl_4 with recycle of mother liquor

Batch No.	PNT Kg/ (mol)	Carbon tetrachloride (L)	Br/mole	98% H_2SO_4 Kg (mol)	PNBBr Kg/(mol)	Purity (GC area %)
1	0.900 (6.56)	4.8	2.189	0.114 (1.14)	0.364 (1.68)	97.1
2	0.231(1.68)	Recycled mother liquor.	1.87	0.107 (1.07)	0.368 (1.7)	95.7
3	0.233 (1.70)	Recycled mother liquor.	1.89	0.107 (1.07)	0.369 (1.7)	99.5
4	0.234 (1.70)	Recycled mother liquor.	1.9	0.107 (1.07)	0.373 (1.72)	100
5	0.236 (1.72)	Recycled mother liquor.	1.92	0.095 (0.95)	0.371 (1.71)	98.5
6	0.235 (1.71)	Recycled mother liquor.	1.91	0.107 (1.07)	0.411 (1.9)	96.3
7	0.260 (1.90)	Recycled mother liquor.	2.11	0.107 (1.07)	0.360 (1.66)	100
8	0.228 (1.66)	Recycled mother liquor.	1.85	0.107 (1.07)	0.330 (1.52)	98.8
Total/Av	2.559 (18.63)	4.5L Carbon tetrachloride recovered	15.63	0.851 (8.51)	2.947 (13.59)	98.2

Syntheses details pertaining to Table S2

0.9 kg (6.56 mol) of PNT was dissolved in 4.8 L of CCl_4 and added into a 10 L capacity glass reactor fitted with addition funnel and reflux condenser/distillation assembly. 1.09 L of brominating agent containing 2.189 mole active Br was added. The contents were heated to

reflux temperature and illuminated externally with 3 x 100 W tungsten filament bulbs. 112 g of 98% H_2SO_4 (1.14 mol) in 0.6 L of water was taken in the addition funnel and the acid was added over a period of 2 h. *(Caution: If the reaction mass develops brown color stop the addition and allow color to disappear before continuing addition of acid.)* Reflux conditions were maintained for an additional 1 h. The reaction mass was allowed to cool to ca. 40^{o}C temperature and the contents discharged into a separating column. The organic phase was poured into a suitable wide mouth glass vessel and kept for crystallization in a deep freezer after inserting 3 broomsticks to promote crystallization. The organic phase attained a temperature of -15^{o}C and was removed after 12 hours. Crystal formation was seen. The contents were allowed to warm up to 0-4^{o}C to re-dissolve PNT which had co-crystallized with the product. The lumps of crystals were broken up and the contents centrifuged in a continuous centrifuge, which operation required barely a couple of minutes. The collected PNBBr weighed 0.364 kg (1.68 mol) and exhibited 97.1% (GC area %) purity. The mother liquor was placed back into the glass reactor. Fresh 0.231 kg (1.68 mol) of PNT, equivalent to the amount of PNBBr recovered in the first batch, was added and brominating reagent was taken at the mole ratio as shown in Table S2 below. The reaction was repeated in the same manner as above but towards the end of the reaction 0.6 L of CCl_4 was collected by changing over from reflux mode to distillation mode and kept for chilling. Cold crystallization was repeated to obtain PNBBr from the reaction mass. The crude PNBBr was washed in the centrifuge with the chilled CCl_4 and centrifuged. The mother liquor and washings were once again recycled. Eight batches were carried out in all and the data on PNBBr yield and purity for each batch and also the total yield and average purity are provided in the table S2. After the 8th batch, CCl_4 was recovered from the mother liquor and the residue was then subjected to vacuum distillation. For this purpose, the residue was first melted and purged with

nitrogen. Thereafter the temperature was raised to 140-155^{o}C and the PNT distilled over at the reduced pressure of 10-40 mm Hg. The amount of PNT recovered was 0.514 kg (3.75 mol).

Table S3.Optimization of $NaBH_4$ concentration for the reduction of mother liquor obtained in Batch 8, Table 1 of manuscript

Entry No.	$NaBH_4$ taken (with respect to the amount of $PNBBr_2$ (**1**) present in the reaction mixture)	% $PNBBr_2$ (**1**)	% PNBBr	% PNT
1.	0 equiv.	80.72	19.23	0.0
2.	2 equiv.	58.46	41.56	0.0
3.	4 equiv.	52.14	47.86	0.0
4.	6 equiv.	22.63	77.37	0.0
5.	8 equiv.	4.94	69.35	25.7

A solution was prepared by mixing $PNBBr_2$ and PNBBr for the optimization reaction of $NaBH_4$ reduction (from the GC-MS the initial mixture was found to be consisted of 80.72% $PNBBr_2$ and 19.23% PNT). Reduction reactions were carried out at room temperature with constant stirring for 2.5 h and solvent system was EDC and a few drops of methanol. Work-up was done using EDC-water mixture and with a small portion of separated organic layer GC-MS were recorded.

Electronic Supplementary Material (ESI) for Green Chemistry

Mass Balance related to the experimental results of Tables 1 and 2 in the manuscript

Table S4. Computation of Isolated yield of PNBBr with respect to PNT consumed and reagent utilized based on the data of Tables 1 and 2 and response factors computed from Figure S1.

1.	Total PNT taken	746.0 mmol
2.	PNT remaining in treated mother liquor suitable for perennial recycle	58.61 mmol
3.	PNT which could have been separated from product through more efficient washing and recycled along with treated mother liquor of Batch 8, Table 1	28.54 mmol
4.	Net PNT consumed	658.95 mmol
5.	Total Br equivalents in *BR-S* taken	659.2
5.	Gross weight of crystalline PNBBr obtained (96.9 % purity w/w)	126.3 g
6.	Actual PNBBr amount in solid product in g/mmol	122.39 g 566.62 mmol
7.	PNBBr in treated mother liquor suitable for perennial recycle	81.15 mmol
8.	Total isolated and recoverable PNBBr	647.77 mmol
9.	Yield of isolated and recoverable PNBBr with respect to PNT amount actually consumed and considering recycle of the rest of the amount taken	98.30
10.	Yield of isolated and recoverable PNBBr with respect to “Br” equivalents in *BR-S* amount taken	98.26